

PSYCHIATRY POSTGRADUATE EXAMS

Weave Study Guides

Paper I, Basic Sciences

Twenty-two guides across Papers I to IV, plus the cross-paper supplement. Study notes, model answers, mnemonics, high-yield comparisons, PYQ frequency, and quick review for every topic.

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PART I

Paper I Basic Sciences

The basic sciences. Neuro-foundations, psychology, assessment, research methods, and the genetics of psychosis.

GUIDE 01 · PART I

Neuro Foundations

Paper I · Basic Sciences. Six study modes, from notes to quick review.

Study Notes

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1. NEUROTRANSMITTERS

1.1 Definitions and Classification

NEUROTRANSMITTER VS NEUROMODULATOR

FEATURE	NEUROTRANSMITTER	NEUROMODULATOR
Action	Fast, point-to-point synaptic	Slow, diffuse, volume transmission
Receptor	Ionotropic (typically)	Metabotropic (typically)
Effect	Excitatory or inhibitory PSP	Modifies response to other NTs
Duration	Milliseconds	Seconds to minutes
Example	Glutamate, GABA	Dopamine, serotonin, neuropeptides

EXAM PEARL

Many substances act as both. Dopamine is technically a neuromodulator but is conventionally called a neurotransmitter. The distinction is functional, not absolute.

CRITERIA FOR A NEUROTRANSMITTER (DALE'S CRITERIA, MODIFIED)

1. Synthesized in the presynaptic neuron
2. Stored in synaptic vesicles
3. Released in response to depolarization (Ca^{2+} -dependent)
4. Acts on specific postsynaptic receptors
5. Has a mechanism for termination (reuptake, enzymatic degradation, diffusion)
6. Exogenous application mimics endogenous effect

CLASSIFICATION OF NEUROTRANSMITTERS

CATEGORY	EXAMPLES	KEY FEATURE
Amino acids	Glutamate, GABA, glycine, aspartate	Fast-acting, ionotropic
Monoamines	Serotonin, dopamine, nor-epinephrine, epinephrine, histamine	Modulatory, metabotropic
Acetylcholine	ACh	Both ionotropic (nicotinic) and metabotropic (muscarinic)
Peptides	Substance P, endorphins, enkephalins, orexin, NPY, CRH, oxytocin, vasopressin	Large molecules, co-released, slow

CATEGORY	EXAMPLES	KEY FEATURE
Gaseous	Nitric oxide (NO), carbon monoxide (CO)	No vesicle storage, retrograde signaling
Lipid-derived	Anandamide, 2-AG (endocannabinoids)	Retrograde signaling, on-demand synthesis
Purines	ATP, adenosine	Co-transmitter, neuromodulator

SIGNAL TRANSDUCTION: TWO MAJOR RECEPTOR CLASSES

FEATURE	IONOTROPIC	METABOTROPIC
Structure	Ligand-gated ion channel	G-protein coupled receptor (GPCR)
Speed	Fast (milliseconds)	Slow (seconds to minutes)
Mechanism	Direct ion flow	Second messenger cascade
Second messengers	None	cAMP, IP3, DAG, Ca ²⁺
Duration	Brief	Prolonged
Examples	GABA-A, NMDA, nicotinic ACh, 5-HT ₃	All dopamine, 5-HT (except 5-HT ₃), muscarinic ACh, GABA-B, mGluR

CLINICAL ANCHOR

Most psychiatric medications target metabotropic systems. Benzodiazepines are a notable exception, they act on ionotropic GABA-A receptors. Understanding this distinction explains onset differences: BZDs work in minutes, SSRIs take weeks.

1.2 Serotonin (5-Hydroxytryptamine, 5-HT)

SYNTHESIS PATHWAY

EXAM PEARL

Tryptophan is the only essential amino acid precursor for a monoamine NT. 95% of body's serotonin is in the gut (enterochromaffin cells); only 5% is in the CNS. 5-HT does NOT cross the BBB, must be synthesized centrally. Low CSF 5-HIAA = impulsivity, aggression, completed suicide.

BRAIN DISTRIBUTION

- **Cell bodies:** Raphe nuclei (dorsal and median) in the brainstem
- **Dorsal raphe** → cortex, basal ganglia, limbic system (cognition, mood, anxiety)

- **Median raphe** → hippocampus, septum (memory, theta rhythm)
- Serotonergic neurons project to virtually every brain region
- **Ascending projections:** cortex, limbic, hypothalamus
- **Descending projections:** spinal cord (pain modulation)

RECEPTOR SUBTYPES

There are **7 families** (5-HT1 through 5-HT7) with **at least 14 subtypes**. Key ones for psychiatry:

RECEPTOR	TYPE	LOCATION	FUNCTION	CLINICAL RELEVANCE
5-HT1A	Gi-coupled (inhibitory)	Raphe (autoreceptor), hippocampus, cortex	↓ Serotonin release (presynaptic); anxiolysis, mood (postsynaptic)	Buspirone (partial agonist). SSRI therapeutic delay, autoreceptor desensitization takes 2-4 weeks. Vilazodone = SSRI + 5-HT1A partial agonist
5-HT1B/1D	Gi-coupled	Nerve terminals	Autoreceptor, vasoconstriction	Triptans (migraine), 5-HT1B/1D agonists
5-HT2A	Gq-coupled (excitatory)	Cortex (layer V pyramidal), platelets	Mood, perception, psychosis, platelet aggregation	Atypical antipsychotics block 5-HT2A (key to atypicality). LSD / psilocybin = 5-HT2A agonists. Trazodone, mirtazapine = 5-HT2A antagonists
5-HT2C	Gq-coupled	Choroid plexus, cortex, limbic	Appetite, mood, DA/NE release modulation	Blockade → weight gain (olanzapine, mirtazapine). Lorcaserin (anti-obesity, withdrawn) = 5-HT2C agonist

RECEPTOR	TYPE	LOCATION	FUNCTION	CLINICAL RELEVANCE
5-HT ₃	Ionotropic (ligand-gated Na ⁺ /K ⁺)	Area postrema, vagus, hippocampus	Nausea/emesis, anxiety, cognition	Ondansetron (antiemetic). Mirtazapine blocks 5-HT ₃ (reduces nausea). Only ionotropic 5-HT receptor
5-HT ₄	Gs-coupled	GI tract, hippocampus	GI motility, cognition, memory	Prokinetics (prucalopride). Potential cognitive enhancer
5-HT ₆	Gs-coupled	Cortex, hippocampus, striatum	Cognition, memory	Research target for Alzheimer's (antagonists may enhance cognition)
5-HT ₇	Gs-coupled	Hypothalamus, thalamus, hippocampus	Circadian rhythm, mood, thermoregulation	Blocked by lurasidone and some atypical antipsychotics

TERMINATION OF SIGNAL

- **Reuptake:** SERT (serotonin transporter), target of SSRIs, SNRIs, TCAs
- **Degradation:** MAO-A (monoamine oxidase A) → 5-HIAA
- **SERT** is coded by the SLC6A4 gene. The short (s) allele of the 5-HTTLPR polymorphism → reduced SERT expression → historically linked to stress sensitivity (Caspi et al., 2003), though meta-analyses have been mixed

CLINICAL RELEVANCE SUMMARY

CONDITION · SEROTONIN ROLE

Depression Serotonin hypothesis, ↓ 5-HT. SSRIs increase synaptic 5-HT. Therapeutic effect via neuroplasticity, not just NT levels

Anxiety disorders 5-HT_{1A} in amygdala and PFC. SSRIs are first-line for GAD, panic, social anxiety, PTSD

OCD Uniquely serotonergic, responds only to serotonergic agents (SSRIs, clomipramine). Higher SSRI doses needed

Eating disorders 5-HT_{2C} regulates satiety. Bulimia responds to fluoxetine (60 mg). Tryptophan depletion worsens symptoms

Impulsivity/aggression Low CSF 5-HIAA → impulsive aggression, suicide by violent means

Psychedelics LSD, psilocybin, DMT are 5-HT_{2A} agonists, produce altered perception, ego dissolution

SEROTONIN SYNDROME

Cause: Excess serotonergic activity, usually from drug combinations (SSRI + MAOI, SSRI + tramadol, SSRI + linezolid, SSRI + St. John's wort).

Triad:

1. **Neuromuscular:** Clonus (especially lower extremity), hyperreflexia, rigidity, tremor
2. **Autonomic:** Hyperthermia, diaphoresis, tachycardia, hypertension, diarrhea
3. **Mental status:** Agitation, confusion, hypomania

Distinguishing features:

- Clonus is the hallmark (especially ocular clonus)
- Onset within 24 hours of causative agent
- Resolves within 24-72 hours after discontinuation

Differentiation from NMS:

FEATURE	SEROTONIN SYNDROME	NMS
Onset	Hours	Days to weeks
Cause	Serotonergic excess	Dopamine blockade
Muscle	Clonus, hyperreflexia	Lead-pipe rigidity
Reflexes	↑↑↑	↓ or normal
Pupils	Mydriasis	Normal
Bowel sounds	↑ (diarrhea)	↓ (ileus)
CK	Mild ↑	Markedly ↑↑↑
Treatment	Cyproheptadine (5-HT _{2A} antagonist)	Dantrolene, bromocriptine

1.3 Dopamine (DA)

SYNTHESIS PATHWAY

EXAM PEARL

Tyrosine hydroxylase is the rate-limiting enzyme for ALL catecholamines. DA is the precursor for NE and epinephrine. L-DOPA crosses BBB (used in Parkinson's); dopamine itself does not.

THE FOUR CLASSICAL DOPAMINE PATHWAYS

PATHWAY	ORIGIN → DESTINATION	FUNCTION	CLINICAL RELEVANCE
Mesolimbic	VTA → nucleus accumbens, amygdala, hippocampus	Reward, motivation, emotion, pleasure	Hyperactivity → positive symptoms of schizophrenia (hallucinations, delusions). Addiction. Antipsychotic therapeutic effect
Mesocortical	VTA → prefrontal cortex (DLPFC, vmPFC)	Executive function, cognition, motivation, working memory	Hypoactivity → negative symptoms (avolition, alogia, anhedonia) and cognitive symptoms of schizophrenia. D1 receptor deficit in PFC
Nigrostriatal	Substantia nigra pars compacta → dorsal striatum (caudate + putamen)	Motor control, procedural learning	Degeneration → Parkinson's disease (>80% DA neuron loss). Antipsychotic blockade → EPS (dystonia, akathisia, parkinsonism, tardive dyskinesia)
Tuberoinfundibular	Hypothalamus (arcuate nucleus) → anterior pituitary	Tonic inhibition of prolactin release	Blockade → hyperprolactinemia (galactorrhea, amenorrhea, sexual dysfunction, osteoporosis). All typical antipsychotics, risperidone, paliperidone

Fifth pathway (less commonly tested):

- **Mesolimbic-mesocortical overlap with thalamus:** VTA → thalamic nuclei, contributes to filtering sensory information

DOPAMINE RECEPTORS

RECEPTOR	FAMILY	MECHANISM	LOCATION	FUNCTION
D1	D1-like	Gs → ↑ cAMP	Cortex, striatum, nucleus accumbens	Motor activation, cognition, reward. Most abundant DA receptor in brain

RECEPTOR	FAMILY	MECHANISM	LOCATION	FUNCTION
D2	D2-like	Gi → ↓ cAMP	Striatum, pituitary, VTA, substantia nigra	Motor control, reward, prolactin inhibition. Primary target of all antipsychotics
D3	D2-like	Gi → ↓ cAMP	Nucleus accumbens, islands of Calleja, VTA	Reward, emotion, cognition. Cariprazine has preferential D3 partial agonism
D4	D2-like	Gi → ↓ cAMP	Frontal cortex, amygdala, hippocampus	Cognition, attention. Clozapine has high D4 affinity
D5	D1-like	Gs → ↑ cAMP	Hippocampus, hypothalamus, thalamus	Cognition, blood pressure regulation

EXAM PEARL

D2 receptor occupancy determines antipsychotic effect: 60–65% = therapeutic; >80% = EPS emerge. Therapeutic window = 65–80%. Clozapine works at ~40–60% D2 occupancy via other mechanisms (5-HT_{2A}, D₄, muscarinic).

TERMINATION OF SIGNAL

- **Reuptake:** DAT (dopamine transporter), target of cocaine (blockade), amphetamine (reversal + efflux)
- **Degradation:**
- **MAO-A and MAO-B** → DOPAC
- **COMT** (catechol-O-methyltransferase) → 3-MT, then → HVA
- **HVA** (homovanillic acid) = final metabolite measured in CSF/plasma
- COMT is especially important in PFC where DAT density is low
- **Val158Met polymorphism:** Val/Val = high COMT activity = lower PFC dopamine = potentially worse cognition; Met/Met = low COMT = higher PFC dopamine

CLINICAL RELEVANCE SUMMARY

CONDITION · DOPAMINE ROLE

Schizophrenia DA hypothesis: mesolimbic hyperactivity (positive Sx), mesocortical hypoactivity (negative/cognitive Sx)

Parkinson's disease Nigrostriatal DA neuron loss. Treatment: L-DOPA, DA agonists

Addiction Mesolimbic pathway, all drugs of abuse increase DA in nucleus accumbens (directly or indirectly)

ADHD Hypodopaminergic state in PFC. Stimulants increase DA/NE. DAT gene (SLC6A3) polymorphisms

Psychosis from substances Amphetamine, cocaine → DA surge → psychotic symptoms

Prolactinomas Treated with DA agonists (cabergoline, bromocriptine)

Tardive dyskinesia DA receptor supersensitivity from chronic D2 blockade. Treatment: VMAT2 inhibitors (valbenazine, deutetrabenazine)

1.4 Norepinephrine (NE)

SYNTHESIS

Same pathway as dopamine, one additional step:

- DβH (dopamine β-hydroxylase) is the distinguishing enzyme for NE neurons
- DβH is a copper-containing enzyme, disulfiram inhibits it

BRAIN DISTRIBUTION

- **Cell bodies:** Locus coeruleus (LC) in the dorsal pons, the SOLE source of NE for the neocortex
- LC contains ~50,000 neurons bilaterally but projects to entire cortex, hippocampus, thalamus, cerebellum, spinal cord
- **Function of LC:** Arousal, vigilance, attention, stress response, fight-or-flight
- LC fires tonically during wakefulness, less during SWS, silent during REM

RECEPTORS

RECEPTOR	TYPE	LOCATION	FUNCTION	CLINICAL RELEVANCE
α1	Gq → ↑ IP3/DAG	Postsynaptic, smooth muscle, cortex	Vasoconstriction, arousal, sympathetic activation	α1 blockade → orthostatic hypotension (prazosin, TCAs, low-potency antipsychotics). Prazosin used for PTSD nightmares (α1 antagonist)

RECEPTOR	TYPE	LOCATION	FUNCTION	CLINICAL RELEVANCE
$\alpha 2$	Gi $\rightarrow$ $\downarrow$ cAMP	Presynaptic (autoreceptor), postsynaptic in PFC	Presynaptic: $\downarrow$ NE release. Postsynaptic: $\uparrow$ PFC function	Clonidine, guanfacine = $\alpha 2$ agonists for ADHD, tics, PTSD hyperarousal. Mirtazapine = $\alpha 2$ antagonist $\rightarrow$ $\uparrow$ NE and 5-HT release
$\beta 1$	Gs $\rightarrow$ $\uparrow$ cAMP	Heart, cortex, hippocampus	Heart rate $\uparrow$, cardiac contractility, memory consolidation	Propranolol for performance anxiety, akathisia, lithium tremor
$\beta 2$	Gs $\rightarrow$ $\uparrow$ cAMP	Smooth muscle, lung, liver	Bronchodilation, vasodilation, glycogenolysis	Non-selective β -blockers (propranolol) may worsen asthma
$\beta 3$	Gs $\rightarrow$ $\uparrow$ cAMP	Adipose tissue	Lipolysis, thermogenesis	Less psychiatric relevance

TERMINATION

- **Reuptake:** NET (norepinephrine transporter), target of SNRIs, TCAs, atomoxetine, bupropion (weak)
- **Degradation:** MAO-A $\rightarrow$ MHPG (3-methoxy-4-hydroxyphenylglycol), primary CNS metabolite
- COMT also degrades NE peripherally $\rightarrow$ VMA (vanillylmandelic acid), normetanephrine

CLINICAL RELEVANCE SUMMARY

CONDITION · NE ROLE

Depression NE deficiency hypothesis (complementary to 5-HT). SNRIs, TCAs, mirtazapine target NE. NE involved in energy, motivation, concentration

ADHD NE deficit in PFC $\rightarrow$ inattention. Atomoxetine (selective NRI), guanfacine, clonidine

Anxiety/PTSD LC hyperactivity $\rightarrow$ hyperarousal, hypervigilance, exaggerated startle. Prazosin for nightmares. Propranolol for reconsolidation blockade (experimental)

Panic disorder LC is the "panic button", yohimbine ($\alpha 2$ antagonist) provokes panic attacks; clonidine ($\alpha 2$ agonist) reduces them

Mania NE excess contributes to hyperarousal, decreased sleep need

1.5 GABA (Gamma-Aminobutyric Acid)

SYNTHESIS

- **GAD** is the rate-limiting enzyme and requires pyridoxal phosphate (B6) as cofactor
- Two isoforms: GAD65 (synaptic terminals) and GAD67 (cell bodies)
- **B6 deficiency** → ↓ **GABA** → **seizures** (e.g., in isoniazid overdose, treat with IV pyridoxine)
- GAD antibodies found in: stiff-person syndrome, type 1 diabetes, autoimmune epilepsy, cerebellar ataxia

DISTRIBUTION

- **The most abundant inhibitory neurotransmitter in the CNS** (~30-40% of all synapses are GABAergic)
- Found throughout the brain, cortex, hippocampus, thalamus, basal ganglia, cerebellum, brainstem
- GABAergic interneurons regulate cortical circuits, dysfunction implicated in schizophrenia

RECEPTORS

GABA-A (IONOTROPIC)

- **Structure:** Pentameric ligand-gated chloride (Cl⁻) channel
- Most common composition: 2 α + 2 β + 1 γ subunit
- Cl⁻ influx → membrane hyperpolarization → inhibition
- **Multiple binding sites on the same receptor complex:**

BINDING SITE	AGENT	EFFECT
GABA site	GABA, muscimol	Opens Cl ⁻ channel
Benzodiazepine site (α/γ interface)	Diazepam, lorazepam, alprazolam	↑ Frequency of Cl ⁻ channel opening. Requires GABA to be present (allosteric modulator)
Barbiturate site (β subunit)	Phenobarbital, pentobarbital	↑ Duration of Cl ⁻ channel opening. At high doses, can open channel WITHOUT GABA → overdose risk
Neurosteroid site	Allopregnanolone, brexanolone	Positive allosteric modulation. Brexanolone = FDA-approved for postpartum depression
Alcohol site	Ethanol	Positive allosteric modulation at δ -containing (extrasynaptic) GABA-A receptors

BINDING SITE	AGENT	EFFECT
Picrotoxin site (channel)	Picrotoxin	Channel blocker → convulsant
Inverse agonist site	Flumazenil (partial), β -carbolines	Flumazenil = competitive antagonist at BZD site. β -carbolines = inverse agonists → anxiety, seizures

EXAM PEARL

BZDs increase FREQUENCY of Cl⁻ channel opening; barbiturates increase DURATION. Classic exam question.

Subunit specificity:

- $\alpha 1$ → sedation, amnesia, anticonvulsant (targeted by zolpidem, Z-drugs)
- $\alpha 2/\alpha 3$ → anxiolysis, muscle relaxation
- $\alpha 5$ → memory, cognition (inverse agonists may enhance cognition)
- BZDs bind at $\alpha 1/2/3/5$ containing receptors (NOT $\alpha 4$ or $\alpha 6$)

GABA-B (METABOTROPIC)

- **Structure:** GPCR (Gi-coupled)
- **Mechanism:** ↑ K⁺ conductance (postsynaptic) and ↓ Ca²⁺ entry (presynaptic) → inhibition
- **Agonist:** Baclofen (used for spasticity, alcohol withdrawal, intractable hiccups)
- **Clinical:** GABA-B involved in absence seizures (thalamocortical circuits), alcohol dependence, GHB mechanism

GABA-C (SOMETIMES CLASSIFIED AS GABA-A-RHO)

- Ionotropic, found primarily in retina
- Insensitive to BZDs and barbiturates
- Minor psychiatric relevance

TERMINATION

- **Reuptake:** GAT-1 (GABA transporter 1), target of tiagabine (anticonvulsant)
- **Degradation:** GABA-T (GABA transaminase) → succinic semialdehyde → succinic acid (enters Krebs cycle)
- Vigabatrin = irreversible GABA-T inhibitor → ↑ GABA. Used in infantile spasms. Risk: visual field defects

CLINICAL RELEVANCE SUMMARY

CONDITION · GABA ROLE

Anxiety disorders GABA deficit → hyperexcitability. BZDs enhance GABA-A. Low GABA levels found in panic disorder (MRS studies)

Epilepsy GABA-enhancing drugs are mainstay: BZDs, valproate (↑ GABA via multiple mechanisms), vigabatrin, tiagabine, gabapentin (paradoxically does NOT act on GABA receptors, acts on $\alpha_2\delta$ Ca^{2+} channels)

Alcohol Ethanol potentiates GABA-A → sedation, disinhibition. Withdrawal = GABA downregulation + glutamate upregulation → seizures, DTs

Hepatic encephalopathy ↑ Neurosteroids and "endogenous benzodiazepines" → excessive GABA tone → stupor, coma. Flumazenil sometimes helps

Schizophrenia GABAergic interneuron (specifically parvalbumin-positive) deficit in DLPFC → gamma oscillation disruption → cognitive symptoms

Insomnia GABA-A α_1 agonists (zolpidem, zaleplon, eszopiclone) promote sleep

1.6 Glutamate

SYNTHESIS

- Also derived from α -ketoglutarate (Krebs cycle) via transamination
- **Glutamate-glutamine cycle:** Glutamate released into synapse → taken up by astrocytes → converted to glutamine by glutamine synthetase → shuttled back to neuron → converted back to glutamate

DISTRIBUTION

- **The most abundant excitatory neurotransmitter in the CNS** (~50-60% of all synapses)
- Present in virtually every brain region
- Major excitatory neurotransmitter of cortical pyramidal neurons

RECEPTORS

IONOTROPIC (FAST EXCITATORY TRANSMISSION)

RECEPTOR	ION	KEY FEATURES	CLINICAL RELEVANCE
NMDA (N-methyl-D-aspartate)	Na ⁺ , K ⁺ , Ca ²⁺	Voltage-dependent Mg ²⁺ block. Requires BOTH glutamate AND glycine (co-agonist at glycine/D-serine site). Slow kinetics	Ketamine blocks NMDA → rapid anti-depressant. PCP, MK-801 block NMDA → psychosis. Memantine (Alzheimer's) = low-affinity NMDA antagonist. Long-term potentiation (LTP) = basis of learning/memory
AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid)	Na ⁺ , K ⁺	Fast transmission. Mediates most fast excitatory neurotransmission. Depolarizes membrane to relieve NMDA Mg ²⁺ block	AMPA activation is prerequisite for NMDA activation. Perampanel = AMPA antagonist (anticonvulsant)
Kainate	Na ⁺ , K ⁺	Presynaptic modulation, pain signaling	Less studied psychiatrically. Some role in epilepsy, pain

METABOTROPIC (MGLUR1-8)

GROUP	RECEPTORS	MECHANISM	FUNCTION
Group I	mGluR1, mGluR5	Gq → ↑ IP3/DAG	Postsynaptic excitation, synaptic plasticity. mGluR5 implicated in Fragile X (Mavoglurant trials)
Group II	mGluR2, mGluR3	Gi → ↓ cAMP	Presynaptic autoreceptors, ↓ glutamate release. Novel targets for schizophrenia and anxiety
Group III	mGluR4, 6, 7, 8	Gi → ↓ cAMP	Presynaptic, ↓ glutamate release

NMDA RECEPTOR IN DETAIL

EXAM PEARL

The NMDA receptor is the single most important receptor to understand for modern psychiatry exam questions.

Unique properties:

1. **Voltage-dependent Mg^{2+} block**, at resting potential, Mg^{2+} plugs the channel. Requires prior AMPA-mediated depolarization to remove Mg^{2+} → then NMDA opens
2. **Co-agonist requirement**, needs glutamate at glutamate site AND glycine/D-serine at glycine site
3. **Ca^{2+} permeability**, allows Ca^{2+} influx → activates CaMKII, CREB → gene transcription → synaptic plasticity (LTP)
4. **Multiple modulatory sites**: polyamine site, Zn^{2+} site, phencyclidine site (where ketamine/PCP bind)

EXCITOTOXICITY

- Excessive glutamate → prolonged NMDA activation → massive Ca^{2+} influx → activates destructive enzymes (calpains, endonucleases, lipases) → cell death
- Implicated in: stroke, TBI, neurodegenerative diseases (ALS, Alzheimer's, Huntington's), status epilepticus, hepatic encephalopathy

THE GLUTAMATE HYPOTHESIS OF SCHIZOPHRENIA

- **Origin**: PCP and ketamine (NMDA antagonists) produce schizophrenia-like symptoms INCLUDING negative and cognitive symptoms, something dopaminergic agents don't fully explain
- **Hypothesis**: NMDA receptor hypofunction on GABAergic interneurons → loss of inhibition on glutamatergic pyramidal neurons → downstream excess glutamate in some regions → excess dopamine in mesolimbic pathway (positive symptoms) AND deficit in mesocortical pathway (negative/cognitive symptoms)
- **Integrates** with dopamine hypothesis rather than replacing it
- **Therapeutic implications**: Glycine site agonists (D-serine, glycine, D-cycloserine) as adjuncts in schizophrenia, modest evidence

KETAMINE'S ANTIDEPRESSANT MECHANISM

1. Blocks NMDA receptors on GABAergic interneurons (preferentially)
2. → Disinhibition of glutamatergic neurons → glutamate burst
3. → Activates AMPA receptors → BDNF release → mTOR activation
4. → Rapid synaptogenesis in PFC (within hours)
5. → Antidepressant effect within hours (vs weeks for SSRIs)

CLINICAL ANCHOR

Esketamine (Spravato, intranasal S-enantiomer) = FDA-approved for treatment-resistant depression. Arketamine (R-enantiomer) may have stronger, more sustained effects with fewer dissociative side effects, in trials.

CLINICAL RELEVANCE SUMMARY

CONDITION · GLUTAMATE ROLE

Schizophrenia NMDA hypofunction hypothesis. PCP psychosis model

Depression Ketamine / esketamine, NMDA antagonist with rapid antidepressant effect

Alzheimer's Excitotoxicity contributes to neurodegeneration. Memantine (NMDA antagonist) is FDA-approved

Epilepsy Excessive glutamate → seizures. Perampanel (AMPA antagonist), felbamate (NMDA antagonist)

ALS Glutamate excitotoxicity. Riluzole (↓ glutamate release)

Alcohol Ethanol inhibits NMDA receptors. Chronic alcohol → NMDA receptor upregulation → withdrawal seizures

OCD Elevated glutamate in caudate (MRS studies). N-acetylcysteine (modulates glutamate) as adjunct

1.7 Acetylcholine (ACh)

SYNTHESIS

- **ChAT** is the synthetic enzyme and marker for cholinergic neurons
- Choline is taken up by a high-affinity choline transporter (rate-limiting)
- Degradation: **AChE (acetylcholinesterase)** rapidly hydrolyzes ACh in the synaptic cleft

BRAIN DISTRIBUTION

Two major cholinergic systems:

SYSTEM	ORIGIN	PROJECTION	FUNCTION
Basal forebrain	Nucleus basalis of Meynert (NBM), medial septum, diagonal band	Cortex, hippocampus, amygdala	Memory, attention, cortical activation. NBM degenerates in Alzheimer's
Brainstem	Pedunculopontine nucleus (PPN), laterodorsal tegmental nucleus (LDT)	Thalamus, basal ganglia	REM sleep, arousal, motor

RECEPTORS

RECEPTOR	TYPE	SUBTYPES	LOCATION	FUNCTION	CLINICAL
Nicotinic	Ionotropic (Na ⁺ /K ⁺ /Ca ²⁺ channel)	$\alpha 4\beta 2$ (CNS, high affinity), $\alpha 7$ (CNS, rapid desensitization), muscle type (NMJ)	CNS, NMJ, autonomic ganglia	Attention, arousal, reward, muscle contraction	Nicotine, varenicline ($\alpha 4\beta 2$ partial agonist for smoking cessation). $\alpha 7$ agonists under study for schizophrenia cognition
Muscarinic	Metabotropic (GPCR)	M1 (Gq), M2 (Gi), M3 (Gq), M4 (Gi), M5 (Gq)	M1: cortex, hippocampus. M2: heart, presynaptic. M3: smooth muscle, glands. M4: striatum. M5: substantia nigra	M1: cognition, memory. M2: ↓ HR. M3: secretions, GI motility. M4: motor modulation	Anticholinergic side effects (dry mouth, constipation, urinary retention, blurred vision, tachycardia, cognitive impairment). Xanomeline-trospium (KarXT / Cobenfy) = M1 / M4 agonist, FDA-approved for schizophrenia (2024)

CLINICAL RELEVANCE SUMMARY

CONDITION · ACh ROLE

Alzheimer's disease Cholinergic deficit (NBM degeneration). AChE inhibitors (donepezil, rivastigmine, galantamine) = first-line treatment

Delirium Cholinergic deficiency is a final common pathway. Anticholinergic drugs are the #1 medication cause of delirium

Parkinson's ACh-DA imbalance in striatum. Anticholinergics (trihexyphenidyl, benztropine) for tremor

Schizophrenia Xanomeline-trospium (Cobenfy) = first non-D2-blocking antipsychotic. M1 / M4 agonism

Nicotine addiction Nicotine acts on $\alpha 4\beta 2$ nAChR $\rightarrow$ DA release in nucleus accumbens.
Varenicline = partial agonist

Depression Cholinergic-adrenergic balance hypothesis (Janowsky). Scopolamine has rapid antidepressant effects (experimental)

REM sleep Cholinergic neurons in PPN/LDT generate REM. Anticholinergics suppress REM

1.8 Histamine

SYNTHESIS

- Degradation: histamine N-methyltransferase (HMT) $\rightarrow$ methylhistamine $\rightarrow$ MAO-B $\rightarrow$ methylimidazoleacetic acid

BRAIN DISTRIBUTION

- Cell bodies:** Tuberomammillary nucleus (TMN) of the posterior hypothalamus, sole source of histaminergic neurons in brain
- Projects diffusely to entire cortex, similar to NE and 5-HT

RECEPTORS

RECEPTOR	TYPE	LOCATION	FUNCTION	CLINICAL
H1	Gq	Cortex, thalamus, smooth muscle	Wakefulness, allergic response	H1 blockade $\rightarrow$ sedation + weight gain. Explains sedation from: diphenhydramine, hydroxyzine, doxepin (low dose for insomnia), olanzapine, quetiapine, mirtazapine, TCAs
H2	Gs	Gastric parietal cells, heart, brain	Gastric acid secretion, cardiac stimulation	Ranitidine, famotidine. Minor CNS role
H3	Gi	Presynaptic (autoreceptor), CNS	$\downarrow$ Histamine, ACh, DA, NE, 5-HT release	Pitolisant = H3 inverse agonist $\rightarrow$ $\uparrow$ wakefulness. FDA-approved for narcolepsy

RECEPTOR	TYPE	LOCATION	FUNCTION	CLINICAL
H4	Gi	Immune cells	Immune regulation	Not psychiatrically relevant yet

CLINICAL ANCHOR

Histamine is the "hidden neurotransmitter" in psychopharmacology. Many psychiatric drugs cause sedation and weight gain through H1 antagonism, sometimes unintended, sometimes exploited therapeutically (quetiapine low-dose, doxepin 3–6 mg for insomnia).

1.9 Glycine

- **Primary inhibitory NT in the spinal cord and brainstem** (GABA is the primary inhibitory NT in the brain)
- Acts on glycine receptors (ionotropic Cl⁻ channels), strychnine is a glycine receptor antagonist → convulsions
- **Also a co-agonist at the NMDA receptor** (glycine site), this dual role is important
- D-serine is the primary endogenous co-agonist at the NMDA glycine site in the forebrain
- D-cycloserine is a partial agonist at this site, used as adjunct in exposure therapy for anxiety disorders (enhances extinction learning)
- **Glycine transporter (GlyT1):** Reuptakes glycine near NMDA receptors. GlyT1 inhibitors (sarcosine, bitopertin) increase glycine at NMDA receptors, investigated for schizophrenia

1.10 Peptide Neurotransmitters

KEY NEUROPEPTIDES IN PSYCHIATRY

PEPTIDE	SOURCE	FUNCTION	CLINICAL RELEVANCE
Substance P	Widely distributed, especially in pain pathways and limbic regions	Pain transmission (C fibers), inflammation, mood regulation	NK1 receptor antagonists studied for depression and anxiety (aprepitant), results mixed. Substance P elevated in depression and anxiety

PEPTIDE	SOURCE	FUNCTION	CLINICAL RELEVANCE
Orexin/Hypocretin	Lateral hypothalamus	Wakefulness maintenance, appetite, reward, arousal	Deficiency → narcolepsy type 1 (with cataplexy). Autoimmune destruction of orexin neurons. DORA (dual orexin receptor antagonists): suvorexant, lemborexant = FDA-approved for insomnia
Neuropeptide Y (NPY)	Hypothalamus, amygdala, cortex	↑ Appetite, ↓ anxiety, stress resilience	Low NPY → vulnerability to PTSD, anxiety. High NPY = stress resilience (found in Special Forces soldiers). NPY the most abundant peptide in the brain
CRH/CRF	Paraventricular nucleus of hypothalamus, amygdala	Stress response, HPA axis activation, anxiety	CRH hyperactivity in depression, PTSD, anxiety. CRH antagonists studied as antidepressants, not yet successful
Oxytocin	Paraventricular and supraoptic nuclei of hypothalamus	Social bonding, trust, attachment, maternal behavior	Intranasal oxytocin studied for autism, social anxiety, PTSD. Called the "love hormone"
Vasopressin (ADH)	Supraoptic and paraventricular nuclei	Water retention, social behavior, aggression	V1b receptor implicated in anxiety and depression. AVP elevated in aggressive behavior
Endorphins/Enkephalins	Widespread	Pain modulation, reward, stress response	Opioid system. Mu receptor agonists → euphoria, analgesia. Naltrexone (antagonist) for alcohol/opioid use disorders
Cholecystokinin (CCK)	Cortex, hippocampus, GI tract	Satiety, anxiety, panic	CCK-4 injection provokes panic attacks. CCK-B receptors in brain linked to anxiety

PEPTIDE	SOURCE	FUNCTION	CLINICAL RELEVANCE
BDNF (not a classical NT but acts like one)	Hippocampus, cortex	Neuroplasticity, neuronal survival, LTP	↓ BDNF in depression. Antidepressants ↑ BDNF. Val66Met polymorphism affects activity-dependent BDNF secretion

1.11 Gaseous Neurotransmitters

NITRIC OXIDE (NO)

- **Synthesis:** L-arginine → (nitric oxide synthase, NOS) → NO + citrulline
- **nNOS** (neuronal), **eNOS** (endothelial), **iNOS** (inducible/immune)
- **Mechanism:** NOT stored in vesicles. Synthesized on demand. Freely diffuses across membranes. Acts on soluble guanylyl cyclase → ↑ cGMP
- **Functions:** Retrograde signaling (postsynaptic → presynaptic), vasodilation, LTP, penile erection
- **Clinical relevance:**
 - PDE5 inhibitors (sildenafil) work by preventing cGMP breakdown (downstream of NO)
 - NO involved in NMDA-mediated neurotoxicity
 - Role in migraine pathophysiology

CARBON MONOXIDE (CO)

- Produced by heme oxygenase (HO-1, HO-2) from heme breakdown
- Similar mechanism to NO (activates guanylyl cyclase)
- Less studied than NO in psychiatry

1.12 Endocannabinoids

THE ENDOCANNABINOID SYSTEM

COMPONENT · DETAILS

Ligands Anandamide (AEA) and 2-arachidonoylglycerol (2-AG)

Synthesis On-demand from membrane phospholipids (NOT stored in vesicles)

Receptors CB1 (CNS, cortex, hippocampus, basal ganglia, cerebellum; Gi-coupled) and CB2 (immune cells, microglia; Gi-coupled)

Termination FAAH (fatty acid amide hydrolase) degrades anandamide. MAGL (monoacylglycerol lipase) degrades 2-AG

Mechanism Retrograde signaling: Postsynaptic neuron releases endocannabinoids → act on presynaptic CB1 → ↓ NT release (both GABA and glutamate) → depolarization-induced suppression of inhibition (DSI) or excitation (DSE)

CLINICAL RELEVANCE

CONTEXT · ROLE

Cannabis/THC THC = CB1 partial agonist. CBD = does NOT directly agonize CB1/CB2 (complex pharmacology, 5-HT1A agonist, GPR55 antagonist, FAAH inhibitor)

Schizophrenia Cannabis use ↑ risk 2-6x. Elevated anandamide in CSF of first-episode psychosis (possibly compensatory). CBD (Epidiolex) approved for epilepsy; studied as antipsychotic adjunct

Pain Endocannabinoid deficiency theory for fibromyalgia, migraine, IBS

Appetite CB1 activation → ↑ appetite ("munchies"). Rimonabant (CB1 antagonist) pulled for depression/suicidality

Addiction Endocannabinoid system modulates reward circuitry

Anxiety Low-dose THC anxiolytic; high-dose anxiogenic. Anandamide may have anxiolytic properties

1.13 Master Comparison Table

WIDE COMPARISON · LANDSCAPE

NT	TYPE	SYNTHESIS ENZYME (RATE-LIMITING)	KEY RECEPTOR	PRIMARY METABOLITE	REUPTAKE TRANSPORTER	DRUG TARGET EXAMPLE
Serotonin	Monoamine (indolamine)	Tryptophan hydroxylase (TPH2)	5-HT1A, 5-HT2A	5-HIAA	SERT	SSRIs
Dopamine	Monoamine (catecholamine)	Tyrosine hydroxylase (TH)	D2	HVA	DAT	Antipsychotics
Norepinephrine	Monoamine (catecholamine)	Tyrosine hydroxylase (TH)	α 1, α 2, β 1	MHPG	NET	SNRIs, atomoxetine
GABA	Amino acid	GAD (requires B6)	GABA-A	Succinic acid	GAT-1	BZDs, valproate
Glutamate	Amino acid	Glutaminase	NMDA, AMPA	Glutamine	EAAT	Ketamine, memantine
ACh	Quaternary amine	ChAT	M1, nAChR (α 4 β 2)	Choline + acetate	CHT (choline)	AChE inhibitors
Histamine	Monoamine (imidazolamine)	Histidine decarboxylase	H1, H3	Methylimidazoleacetic acid	None (no reuptake)	H1 antagonists

2. NEUROANATOMY

2.1 Frontal Lobe

The frontal lobe constitutes ~1/3 of the cortical surface. It is the seat of executive function, personality, social behavior, and motor planning. The **prefrontal cortex (PFC)** is the most anterior portion, anterior to the motor and premotor areas.

PREFRONTAL CORTEX SUBDIVISIONS

SUBDIVISION	BRODMANN AREAS	CONNECTIONS	FUNCTIONS	LESION SYNDROME
Dorsolateral PFC (DLPFC)	BA 9, 46	Caudate (dorsal), thalamus (MD), parietal cortex, hippocampus	Executive function, working memory, planning, cognitive flexibility, set-shifting, abstract reasoning	Pseudodepression/Dysexecutive syndrome: Apathy, poor planning, reduced fluency, impaired working memory, stimulus-bound behavior, difficulty with multi-tasking. Looks like depression but isn't
Orbitofrontal cortex (OFC)	BA 11, 12, 47	Amygdala, ventral striatum, temporal pole, hypothalamus	Decision-making, impulse control, social behavior, reward evaluation, reversal learning	Pseudopsychopathic/Disinhibited syndrome: Disinhibition, impulsivity, poor social judgment, inappropriate sexual behavior, emotional lability, perseveration, utilization behavior (Phineas Gage)

SUBDIVISION	BRODMANN AREAS	CONNECTIONS	FUNCTIONS	LESION SYNDROME
Anterior cingulate cortex (ACC)	BA 24, 25, 32	DLPFC, amygdala, insula, nucleus accumbens, PAG	Motivation, error detection, conflict monitoring, emotional regulation, autonomic regulation	Akinetic mutism: Profound apathy, reduced speech, lack of spontaneous movement. Bilateral lesions → akinetic mutism. Subgenual ACC (BA 25), target for DBS in treatment-resistant depression
Ventromedial PFC (vmPFC)	BA 10, 14, 25	Amygdala, hippocampus, hypothalamus, brainstem	Emotional decision-making, fear extinction, self-referential processing, social cognition, theory of mind	Impaired somatic markers (Damasio), poor risk assessment, emotional dysregulation. Overlap with OFC syndrome

FRONTAL LOBE SYNDROMES: THE CLASSIC THREE

SYNDROME	REGION	PRESENTATION	MISDIAGNOSED AS
Pseudodepressed	DLPFC	Apathy, flat affect, ↓ verbal fluency, ↓ initiative, poor planning	Depression
Pseudopsychopathic	OFC	Disinhibition, inappropriate jokes/behavior, poor impulse control, ↓ empathy	Personality disorder, mania
Akinetic	ACC (bilateral)	Mutism, akinesia, profound apathy, incontinence	Catatonia, severe depression

KEY CLINICAL CORRELATES OF FRONTAL LOBE

CONDITION · FRONTAL INVOLVEMENT

Schizophrenia ↓ DLPFC activation (hypofrontality) during working memory tasks. ↓ gray matter volume

Depression Subgenual ACC (BA 25) hyperactivity. DBS target. DLPFC hypoactivity, left DLPFC is TMS target for depression

ADHD PFC maturation delay. DLPFC and ACC underactivation. Response to stimulants via PFC NE/DA enhancement

OCD Hyperactivity of OFC-caudate-thalamic circuit

Antisocial PD ↓ OFC volume and activity. Poor fear conditioning

Frontotemporal dementia (bvFTD) Behavioral variant → OFC and ACC atrophy → disinhibition, apathy, loss of empathy

LATERALITY OF FRONTAL FUNCTION

LEFT FRONTAL · RIGHT FRONTAL

Language production (Broca's area, BA 44-45) Prosody of speech

Verbal fluency Design fluency

Positive emotions (approach) Negative emotions (withdrawal)

Depression risk with left frontal lesion Mania/disinhibition risk with right frontal lesion

CLINICAL ANCHOR

Left DLPFC stimulation (high-frequency TMS) treats depression. Right DLPFC stimulation (low-frequency TMS or high-frequency on right) may treat mania.

2.2 Basal Ganglia

COMPONENTS

STRUCTURE	ALSO CALLED	KEY FEATURES
Caudate nucleus	Part of dorsal striatum (with putamen)	C-shaped, follows lateral ventricle. Head bulges into frontal horn. Cognitive and associative functions
Putamen	Part of dorsal striatum	Motor execution. With globus pallidus = lentiform/lenticular nucleus
Globus pallidus (GP)	External (GPe) and internal (GPi) segments	GPi = primary output nucleus. Sends inhibitory (GABA) projections to thalamus
Subthalamic nucleus (STN)	Corpus Luysii	Only EXCITATORY (glutamate) nucleus in the basal ganglia. Lesion → hemiballismus. DBS target for Parkinson's

STRUCTURE	ALSO CALLED	KEY FEATURES
Substantia nigra	Pars compacta (SNpc) and pars reticulata (SNpr)	SNpc = dopaminergic neurons (degenerates in PD). SNpr = output (like GPi)
Nucleus accumbens	Ventral striatum	Reward, motivation, addiction. Where mesolimbic DA pathway terminates

Mnemonic for dorsal striatum: Caudate + Putamen = **Striatum** (because of the striped appearance from gray and white matter bundles crossing)

BASAL GANGLIA CIRCUITS (ALEXANDER & CRUTCHER MODEL)

All circuits follow the same basic loop: **Cortex** → **Striatum** → **Pallidum/SN** → **Thalamus** → **Cortex**

CIRCUIT	CORTICAL ORIGIN	STRIATAL TARGET	OUTPUT	THALAMIC NUCLEUS	FUNCTION
Motor	SMA, premotor, motor cortex	Putamen	GPi/SNpr	VL (ventrolateral)	Voluntary movement
Oculomotor	FEF (frontal eye fields)	Caudate (body)	GPi/SNpr	VA	Saccadic eye movements
DLPFC (cognitive)	DLPFC	Caudate (dorsal head)	GPi/SNpr	VA/MD	Executive function, working memory
OFC (orbitofrontal)	Lateral OFC	Caudate (ventromedial head)	GPi/SNpr	VA/MD	Social behavior, impulse control
ACC/Limbic	ACC, medial OFC	Ventral striatum (nucleus accumbens)	Ventral pallidum	MD	Motivation, reward, emotion

DIRECT VS INDIRECT PATHWAY

FEATURE	DIRECT PATHWAY	INDIRECT PATHWAY
Effect	Facilitates movement	Inhibits movement
Striatal neurons	Express D1 receptors	Express D2 receptors
Route	Striatum → GPi (inhibitory) → Thalamus (disinhibited → excited) → Cortex	Striatum → GPe → STN → GPi (excited → more inhibition of thalamus)
DA effect	DA activates D1 → facilitates	DA inhibits D2 → disinhibits GPe → net facilitation

FEATURE	DIRECT PATHWAY	INDIRECT PATHWAY
Net result of DA	Both pathways: DA promotes movement	

CLINICAL ANCHOR

Loss of DA (Parkinson's) → underactive direct pathway + overactive indirect pathway → hypokinesia, rigidity, tremor. Excess DA → overactive direct pathway → hyperkinesia (dyskinesia, chorea).

DISORDERS OF THE BASAL GANGLIA

DISORDER	PATHOLOGY	PRESENTATION	TREATMENT
Parkinson's disease	SNpc DA neuron loss (>80%)	Resting tremor, rigidity, bradykinesia, postural instability	L-DOPA, DA agonists, MAO-B inhibitors, DBS of STN
Huntington's disease	Caudate atrophy (GABAergic medium spiny neurons), AD, chromosome 4, CAG repeat in huntingtin gene	Chorea, cognitive decline, psychiatric symptoms (depression, psychosis, irritability). Caudate atrophy → "boxcar ventricles" on imaging	VMAT2 inhibitors (tetrabenazine, deutetabenazine) for chorea. SSRIs for depression
OCD	Hyperactivity of OFC-caudate-thalamic circuit	Obsessions and compulsions	SSRIs (high dose), CBT (ERP). DBS of ventral capsule/ventral striatum or STN for refractory cases
Tourette syndrome	Dopaminergic excess in striatum	Motor and vocal tics, ADHD, OCD comorbidity	Alpha-2 agonists (clonidine, guanfacine), antipsychotics (haloperidol, aripiprazole, pimozide), CBIT
Tardive dyskinesia	D2 receptor supersensitivity (chronic blockade)	Choreiform movements of face, tongue, limbs	VMAT2 inhibitors (valbenazine, deutetabenazine). Switch to clozapine
Hemiballismus	STN lesion (usually vascular)	Wild, flinging movements of contralateral limbs	Antipsychotics (D2 blockade)

DISORDER	PATHOLOGY	PRESENTATION	TREATMENT
Wilson disease	Copper accumulation in lenticular nucleus (putamen + GP)	Dysarthria, dystonia, tremor, psychiatric symptoms (personality change, psychosis, depression), KF rings	Penicillamine, trientine, zinc

2.3 Limbic System

CORE STRUCTURES

AMYGDALA

- **Location:** Anterior medial temporal lobe, anterior to hippocampus
- **Nuclei:** Basolateral (sensory input processing), central (output to hypothalamus and brainstem), corticomedial (olfaction)
- **Functions:**
 - **Fear conditioning,** learning to associate a neutral stimulus with danger (Pavlovian fear conditioning)
 - **Emotional memory,** strengthens memory consolidation for emotionally charged events (via modulation of hippocampal function)
 - **Threat detection,** rapid, below-conscious evaluation of potential danger
 - **Social cognition,** reading facial expressions (especially fear and anger)

Connections:

- Receives input from all sensory modalities
- Outputs to: hypothalamus (autonomic responses), PAG (behavioral responses), basal forebrain (arousal), cortex (conscious awareness)
- **Two pathways for fear:** (1) Thalamus → amygdala (fast, crude, "low road," LeDoux) and (2) Thalamus → cortex → amygdala (slow, precise, "high road")

Clinical relevance:

CONDITION · AMYGDALA FINDING

PTSD Hyperactive amygdala, ↓ PFC regulation of amygdala

Social anxiety ↑ Amygdala response to faces

Depression ↑ Amygdala activity, especially to negative stimuli

Psychopathy ↓ Amygdala volume and reactivity → ↓ fear conditioning, ↓ empathy

Kluver-Bucy syndrome Bilateral amygdala lesion → hyperorality, hypersexuality, visual agnosia, placidity, hypermetamorphosis

Temporal lobe epilepsy Aura may involve fear (amygdala origin). Ictal fear is pathognomonic of temporal lobe seizures

Urbach-Wiethe disease Bilateral amygdala calcification → inability to recognize fear in faces, impaired fear conditioning (patient SM)

HIPPOCAMPUS

- **Location:** Medial temporal lobe, floor of inferior horn of lateral ventricle
- **Structure:** Archicortex with 3 layers (vs 6 in neocortex). CA1-CA4 regions, dentate gyrus, subiculum
- **Functions:**
 - **Declarative/explicit memory**, episodic (events) and semantic (facts)
 - **Spatial navigation**, place cells (O'Keefe, Nobel Prize 2014)
 - **Memory consolidation**, transfers short-term to long-term memory (to neocortex during sleep)
 - **Contextual fear conditioning**, "where" the danger was
 - **Neurogenesis**, dentate gyrus is one of two sites of adult neurogenesis (the other being the subventricular zone → olfactory bulb)

LTP (Long-Term Potentiation):

- Discovered in hippocampus (Bliss & Lomo, 1973)
- NMDA receptor-dependent (requires coincidence of presynaptic glutamate release AND postsynaptic depolarization)
- Considered the cellular basis of learning and memory
- Blocked by NMDA antagonists → amnesia

Clinical relevance:

CONDITION · HIPPOCAMPAL FINDING

Alzheimer's disease Earliest and most severe atrophy, entorhinal cortex → hippocampus. Memory loss is presenting symptom

Depression ↓ Hippocampal volume (stress-related, glucocorticoid neurotoxicity). Antidepressants ↑ hippocampal neurogenesis. BDNF hypothesis

PTSD ↓ Hippocampal volume. Impaired contextualization of fear memories (fear response generalizes)

Schizophrenia ↓ Hippocampal volume, disorganized CA1-CA3 pyramidal cells

Temporal lobe epilepsy Hippocampal sclerosis, most common substrate. Mesial temporal sclerosis on MRI

Transient global amnesia Transient hippocampal dysfunction → anterograde amnesia lasting hours

HM (Henry Molaison) Bilateral hippocampectomy → severe anterograde amnesia, intact procedural memory. Proved hippocampus essential for declarative memory

Chronic stress/Cushing's Glucocorticoid excess → hippocampal dendritic atrophy, ↓ neurogenesis

OTHER LIMBIC STRUCTURES

STRUCTURE	FUNCTION	CLINICAL RELEVANCE
Cingulate gyrus	Anterior: motivation, error detection, pain processing. Posterior: spatial memory, self-referential processing	Anterior cingulotomy for refractory OCD/pain. Default mode network includes posterior cingulate
Nucleus accumbens	Reward, motivation, pleasure, reinforcement learning	Addiction, all drugs of abuse increase DA here. DBS target for refractory depression and OCD
Septal nuclei	Reward, pleasure	Stimulation → pleasure (Olds & Milner, 1954). Projects to hippocampus via fornix. Lesion → septal rage
Insula	Interoception, disgust, empathy, craving, pain awareness	Addiction (craving), anxiety (interoceptive awareness), eating disorders. Lesion → loss of cigarette craving (Naqvi et al., 2007)
Fornix	Major output of hippocampus to mammillary bodies	Lesion → anterograde amnesia (similar to hippocampal damage)
Mammillary bodies	Relay in Papez circuit, memory	Wernicke encephalopathy (thiamine deficiency) → mammillary body necrosis → amnesia (→ Korsakoff syndrome)

2.4 Papez Circuit

COMPONENTS AND FLOW

KEY POINTS

- Proposed by James Papez (1937) as the circuit of emotion
- Now understood as primarily a **memory circuit** rather than a purely emotional circuit
- Damage at any point in the circuit → memory deficits (especially anterograde amnesia)

EXAM PEARL

The Papez circuit is a CLASSIC exam question, know the components and their connections.

CLINICAL CORRELATES BY LESION SITE

LESION SITE	CAUSE	RESULT
Hippocampus	Alzheimer's, surgery, anoxia	Anterograde amnesia
Fornix	Tumors (colloid cyst of 3rd ventricle), surgery	Anterograde amnesia
Mammillary bodies	Wernicke-Korsakoff (thiamine deficiency)	Amnesia + confabulation
Anterior thalamic nucleus	Stroke	Amnesia
Cingulate gyrus	Lesion, surgery	Akinetic mutism (bilateral), personality change

YAKOVLEV CIRCUIT (THE "OTHER" LIMBIC CIRCUIT)

Complements Papez, more related to emotion and behavior:

- Lesions → emotional dysregulation, disinhibition
- Relevant to psychopathy, OFC syndromes

2.5 Thalamus

OVERVIEW

- "**Gateway to the cortex**", nearly all sensory information relays through the thalamus (except olfaction, which goes directly to cortex)
- Reciprocal connections with cortex, thalamocortical and corticothalamic loops
- Two main nuclei types: **specific** (relay nuclei, point-to-point) and **nonspecific** (diffuse modulatory)

KEY THALAMIC NUCLEI FOR PSYCHIATRY

NUCLEUS	CONNECTIONS	FUNCTION	CLINICAL RELEVANCE
Mediodorsal (MD)	PFC (especially DLPFC and OFC), amygdala, basal ganglia	Executive function, memory, emotion, social cognition	↓ Volume in schizophrenia. Lesion → apathy, memory deficits, personality change. Most relevant thalamic nucleus for psychiatry
Anterior	Hippocampus (via mammillothalamic tract), cingulate gyrus	Memory (part of Papez circuit)	Lesion → amnesia
Ventrolateral (VL)	Cerebellum, basal ganglia → motor cortex	Motor relay	DBS target for tremor
VPL/VPM	Spinothalamic/trigeminothalamic → somatosensory cortex	Somatosensory relay	Thalamic pain syndrome (Dejerine-Roussy) → central post-stroke pain
LGN (lateral geniculate)	Retina → primary visual cortex	Visual relay	Visual hallucinations if disrupted
MGN (medial geniculate)	Inferior colliculus → auditory cortex	Auditory relay	Auditory processing deficits
Pulvinar	Association cortex, superior colliculus	Attention, visual salience	Implicated in neglect, attentional deficits
Reticular nucleus	Wraps around thalamus, receives collaterals from all thalamocortical and corticothalamic fibers	Gating, inhibits other thalamic nuclei, generates sleep spindles	Sleep spindles in N2 sleep. Absence seizures (thalamocortical oscillations involving reticular nucleus). Sensory gating deficits in schizophrenia
Intralaminar (centromedian, parafascicular)	Reticular formation, basal ganglia, diffuse cortex	Arousal, consciousness, pain	Disruption → coma. DBS target for disorders of consciousness

THALAMUS IN PSYCHIATRIC CONDITIONS

CONDITION · THALAMIC FINDING

Schizophrenia ↓ MD thalamus volume. Disrupted thalamocortical connectivity. Sensory gating deficits

Fatal familial insomnia Prion disease with selective thalamic degeneration → intractable insomnia → death

Absence epilepsy Thalamocortical oscillation (T-type Ca^{2+} channels in reticular nucleus). Ethosuximide blocks these channels

2.6 Hypothalamus

OVERVIEW

- Small (4g) but controls virtually all homeostatic functions
- Forms the floor and lateral walls of the third ventricle
- Connected to the pituitary via the infundibulum (pituitary stalk)

MAJOR NUCLEI AND FUNCTIONS

NUCLEUS/REGION	FUNCTION	CLINICAL RELEVANCE
Suprachiasmatic (SCN)	Master circadian pacemaker. Receives direct input from retina (retinohypothalamic tract, melanopsin-containing RGCs)	Circadian rhythm disorders. Jet lag. Light therapy for SAD, circadian disruption
Paraventricular (PVN)	CRH → HPA axis. Oxytocin and vasopressin production	Stress response, HPA axis dysfunction in depression. Dexamethasone suppression test
Supraoptic (SON)	Vasopressin (ADH) and oxytocin production → posterior pituitary	SIADH (from SSRIs, carbamazepine, antipsychotics). Diabetes insipidus (lithium)
Lateral hypothalamus	"Hunger center." Orexin/hypocretin neurons here	Lesion → aphagia, weight loss. Orexin loss → narcolepsy. Lateral = hunger (think Lateral = Large)
Ventromedial (VMH)	"Satiety center"	Lesion → hyperphagia, obesity, aggression. Ventromedial = satisfaction (think VM = Very Much eating when lesioned)
Arcuate	Regulates anterior pituitary hormones (releasing/inhibiting hormones). POMC/AgRP neurons for appetite. Tuberoinfundibular DA pathway origin	Tuberoinfundibular DA tonically inhibits prolactin. D2 blockade → hyperprolactinemia
Preoptic area	Thermoregulation, sexual behavior, VLPO for sleep (see Sleep section)	NMS → hypothalamic thermoregulatory failure. Fever

NUCLEUS/REGION	FUNCTION	CLINICAL RELEVANCE
Anterior hypothalamus	Parasympathetic activation, heat dissipation	Cooling. Anterior = Anti-heat
Posterior hypothalamus	Sympathetic activation, heat conservation, wakefulness	Lesion → hypothermia, somnolence. Posterior = Preservation of heat
Mammillary bodies	Part of Papez circuit, memory	Wernicke-Korsakoff syndrome

THE HPA AXIS

HPA Axis in Psychiatric Disorders:

CONDITION · HPA FINDING

Depression (melancholic) HPA hyperactivity. ↑ CRH, ↑ cortisol. Failed dexamethasone suppression (DST non-suppression). ↑ Adrenal size

PTSD Paradoxical HPA: ↓ cortisol, ↑ CRH, enhanced negative feedback (↑ glucocorticoid receptor sensitivity). Enhanced DST suppression

Cushing syndrome Chronic hypercortisolism → depression (50-80%), psychosis, cognitive deficits, hippocampal atrophy

Addison disease Chronic hypocortisolism → fatigue, depression, apathy

Early life stress Epigenetic programming of HPA axis. ↑ CRH, altered glucocorticoid receptor expression → lifelong stress vulnerability

2.7 Other Structures of Psychiatric Relevance

TEMPORAL LOBE

STRUCTURE	FUNCTION	LESION
Wernicke's area (posterior superior temporal gyrus, BA 22)	Language comprehension	Fluent aphasia (word salad, poor comprehension, unawareness of deficit)
Superior temporal gyrus	Auditory processing, language	Auditory hallucinations in schizophrenia (activation during hallucinations)
Fusiform face area (inferior temporal)	Face recognition	Prosopagnosia. Hypoactivation in autism spectrum
Temporal pole	Social cognition, semantic memory, emotional processing	bvFTD, semantic dementia

PARIETAL LOBE

STRUCTURE	FUNCTION	LESION
Somatosensory cortex (post-central gyrus)	Body sensation, body schema	Hemi-anesthesia
Right parietal	Spatial attention, visuospatial processing	Left hemispatial neglect (anosognosia for left side)
Angular gyrus (BA 39)	Reading, calculation, finger naming	Gerstmann syndrome: agraphia, acalculia, finger agnosia, left-right confusion

CEREBELLUM

- **Beyond motor:** Now recognized to contribute to cognition, emotion, and language
- **Cerebellar cognitive affective syndrome (Schmahmann):** Executive dysfunction, visuospatial deficits, language issues, personality change (blunted affect or disinhibition)
- Cerebellar abnormalities found in autism, schizophrenia, ADHD

BRAINSTEM NUCLEI SUMMARY

NUCLEUS	NT	FUNCTION	CLINICAL
Raphe nuclei	Serotonin	Mood, sleep, pain	Depression, anxiety. SSRI target
Locus coeruleus	Norepinephrine	Arousal, attention, stress	Panic, PTSD, ADHD
VTA	Dopamine	Reward, motivation	Addiction, schizophrenia
Substantia nigra	Dopamine	Motor	Parkinson's
PPN/LDT	Acetylcholine	REM sleep, arousal	REM sleep behavior disorder
TMN	Histamine	Wakefulness	Narcolepsy (pitolisant target)
Parabrachial nucleus	Multiple	Taste, pain, autonomic, arousal	Sleep-wake regulation

3. SLEEP PHYSIOLOGY

3.1 Sleep Architecture

OVERVIEW

Sleep is divided into **NREM (Non-Rapid Eye Movement)** and **REM (Rapid Eye Movement)** sleep. They alternate in cycles across the night.

NREM SLEEP STAGES

STAGE	OLD NAME	% OF SLEEP	EEG FEATURES	CHARACTERISTICS
N1	Stage 1	5%	Low-voltage mixed frequency. Theta waves (4-7 Hz). Vertex sharp waves	Lightest sleep. Transition from wake. Hypnagogic hallucinations. Hypnic jerks (myoclonic). Easy to arouse
N2	Stage 2	45-55%	Sleep spindles (12-14 Hz bursts, generated by thalamic reticular nucleus) + K-complexes (large negative sharp wave followed by positive component)	Most of the night. Memory consolidation (procedural). Arousal threshold ↑. Body temperature drops
N3	Stages 3+4 (SWS/ deep sleep)	15-25%	Delta waves (0.5-2 Hz, high amplitude >75 µV). Also called slow-wave sleep (SWS)	Deepest sleep. Most restorative. Growth hormone secretion peaks. Parasomnias of arousal (sleepwalking, sleep terrors, confusional arousals). Hardest to arouse. Predominates in first third of night

REM SLEEP

% of sleep 20-25% in adults

EEG Low-voltage, mixed frequency, resembles WAKEFULNESS ("paradoxical sleep"). **Sawtooth waves** (2-6 Hz) are characteristic. Theta activity

Eye movements Rapid, conjugate eye movements

Muscle tone **Atonia**, active inhibition of skeletal muscles via sublaterodorsal nucleus → glycinergic/ GABAergic inhibition of spinal motor neurons. Diaphragm and extraocular muscles spared

Dreaming Vivid, narrative, bizarre dreams. Most dream recall from REM

Autonomic Irregular HR, RR, BP. Penile/clitoral tumescence. Poikilothermic (body temperature regulation impaired)

Timing Predominates in last third of night. REM periods get longer across the night

REM latency Normal: 90 minutes from sleep onset. Shortened in: depression, narcolepsy. Prolonged by: alcohol, many antidepressants

KEY DIFFERENCES: NREM VS REM

FEATURE	NREM (ESPECIALLY N3)	REM
EEG	Synchronized, slow waves	Desynchronized, fast (like wake)
Muscle tone	Present (reduced)	Absent (atonia)
Dreams	Vague, thought-like	Vivid, narrative, emotional
Autonomic	Stable, ↓ HR / BP / RR	Variable, irregular
Thermoregulation	Maintained	Impaired (poikilothermic)
Parasomnias	Sleepwalking, night terrors, confusional arousal	RBD, nightmare disorder
Memory type	Declarative memory consolidation	Emotional memory, procedural memory consolidation
Predominates	First third of night	Last third of night
Growth hormone	Peak secretion	Minimal
Cortisol	Low (nadir at sleep onset)	Rising (peaks early morning)

3.2 Sleep Cycles

THE 90-MINUTE ULTRADIAN RHYTHM

- Each sleep cycle = NREM (N1 → N2 → N3 → N2) → REM
- Duration: ~90-110 minutes per cycle
- Typically 4-6 cycles per night

HOW CYCLES CHANGE ACROSS THE NIGHT

EARLY NIGHT (CYCLES 1-2) · LATE NIGHT (CYCLES 3-5)

More N3 (deep/slow-wave sleep) Less N3 (may be absent)

Shorter REM periods (5-10 min) Longer REM periods (20-40 min)

Higher arousal threshold Lower arousal threshold

Growth hormone surge Cortisol surge

CLINICAL ANCHOR

BZDs and alcohol suppress N3 (SWS) and may initially suppress REM. Missing early night sleep → lose more SWS. Missing late night sleep → lose more REM. Sleep deprivation → rebound of the suppressed stage (SWS rebound first, then REM rebound).

SLEEP ARCHITECTURE ACROSS THE LIFESPAN

AGE GROUP	TOTAL SLEEP	REM %	SWS	NOTES
Neonates	16-18 hours	50% (active sleep)	Immature	Enter REM directly (no REM latency). Polyphasic sleep
Infants (6-12 mo)	12-14 hours	30%	↑	Circadian consolidation begins
Children (5-10 yr)	10-11 hours	20-25%	Highest SWS amounts	Parasomnias peak (sleepwalking, terrors)
Adolescents	8-10 hours	20%	↓ from childhood	Circadian delay (biological night-owl shift)
Adults	7-9 hours	20-25%	15-25%	Stable
Elderly (>65)	6-7 hours	↓ slightly	↓↓ Marked reduction	More N1 / N2, fragmented sleep, advanced circadian phase, more daytime napping

3.3 Neurochemistry of Sleep

THE TWO-PROCESS MODEL (BORBELY, 1982)

PROCESS	MECHANISM	SUBSTANCE	RESULT
Process S (homeostatic sleep pressure)	Builds during wakefulness, dissipates during sleep	Adenosine accumulates in basal forebrain during wake	Longer awake = more sleep pressure. Caffeine blocks adenosine A1 and A2A receptors

PROCESS	MECHANISM	SUBSTANCE	RESULT
Process C (circadian rhythm)	24-hour oscillation independent of sleep/wake	SCN drives ~24.2-hour rhythm; entrained by light via melatonin	Alerting signal opposes Process S during daytime. Weakens at night → sleep gate opens

WAKE-PROMOTING SYSTEMS

SYSTEM	LOCATION	NT	MECHANISM	DRUGS
Ascending reticular activating system (ARAS)	Brainstem reticular formation	Multiple	Tonic cortical activation via thalamus and basal forebrain	General anesthetics suppress
Locus coeruleus	Dorsal pons	NE	Arousal, vigilance. Active in wake, ↓ in NREM, silent in REM	Modafinil partly works through NE. Stimulants
Dorsal raphe	Brainstem	5-HT	Promotes wakefulness. Active in wake, ↓ in NREM, silent in REM . BUT needed for SWS generation (complex)	SSRIs often cause initial insomnia then improve sleep
Tuberomammillary nucleus (TMN)	Posterior hypothalamus	Histamine	Wakefulness maintenance	Antihistamines (diphenhydramine, doxepin low-dose) → sedation. Pitolisant (H3 inverse agonist) → wakefulness
Lateral hypothalamus	Hypothalamus	Orexin/Hypocretin	Stabilizes wakefulness, prevents inappropriate sleep-wake transitions	Loss → narcolepsy. DORAs (suvorexant, lemborexant) block orexin → promote sleep
Basal forebrain	Below frontal cortex	ACh	Cortical activation, REM promotion	Donepezil can cause vivid dreams. Scopolamine suppresses REM

SYSTEM	LOCATION	NT	MECHANISM	DRUGS
VTA	Midbrain	DA	Arousal, motivation	Stimulants (amphetamine, methylphenidate) . Modafinil. DA promotes wakefulness
PPN/LDT	Brainstem	ACh	REM generation, arousal	Active in wake and REM, silent in NREM

SLEEP-PROMOTING SYSTEMS

SYSTEM	LOCATION	NT	MECHANISM	DRUGS
VLPO (ventrolateral preoptic area)	Anterior hypothalamus	GABA + Galanin	Inhibits ALL wake-promoting centers (LC, TMN, raphe, orexin neurons). Active during sleep	VLPO lesion → insomnia (von Economo's observation). BZDs enhance GABA = enhance sleep-promoting pathway
MnPO (median preoptic area)	Hypothalamus	GABA	Sleep promotion, responds to homeostatic sleep pressure	Works with VLPO
Parafacial zone	Brainstem	GABA	SWS promotion	Recently discovered, under investigation

THE FLIP-FLOP SWITCH MODEL (SAPER)

The sleep-wake transition is like a **flip-flop switch**, it's either in one state or the other, with rapid transitions between them:

- **Orexin stabilizes the switch in the WAKE position**, without it, the switch flips uncontrollably → narcolepsy (sudden sleep attacks, cataplexy)
- This explains why we have discrete wake and sleep states (not a gradual continuum)

NEUROCHEMISTRY OF REM SLEEP

REM-ON neurons:

- Cholinergic neurons in PPN and LDT (brainstem)
- Glutamatergic neurons in sublaterodorsal nucleus (SLD) → generate muscle atonia via glycine/GABA

REM-OFF neurons:

- Noradrenergic (LC) and serotonergic (raphe) neurons
- Silence during REM → permits REM

REM-promoting mechanism:

- During NREM, REM pressure builds (acetylcholine accumulates)
- LC and raphe gradually decrease firing → threshold reached → PPN/LDT disinhibited → REM onset
- REM lasts until NE/5-HT neurons resume firing → terminate REM

CLINICAL ANCHOR

Antidepressants that increase NE and/or 5-HT suppress REM (most SSRIs, SNRIs, TCAs, MAOIs). REM deprivation may contribute to antidepressant effect.

KEY SLEEP NEUROCHEMISTRY SUMMARY TABLE

SUBSTANCE	ROLE IN SLEEP	WAKE/SLEEP	NOTES
Adenosine	↑ Sleep pressure	Promotes sleep	Caffeine = adenosine receptor antagonist
GABA	Inhibits arousal centers	Promotes sleep	BZDs, Z-drugs, barbiturates enhance
Galanin	Co-released with GABA in VLPO	Promotes sleep	Co-transmitter in VLPO
Melatonin	Circadian signal, not a strong soporific	Promotes sleep (timing)	Exogenous use for circadian disorders. Ramelteon, tasimelteon = MT1/MT2 agonists
Orexin	Stabilizes wakefulness	Promotes wake	Loss = narcolepsy. DORAs for insomnia
Histamine	Maintains wakefulness	Promotes wake	H1 blockade = sedation. Pitolisant (H3 inverse agonist) = wakefulness
NE	Arousal, vigilance	Promotes wake	Silent in REM. ↑ NE suppresses REM
5-HT	Complex, promotes wake but needed for SWS generation via downstream mechanisms	Mixed	Silent in REM. SSRIs suppress REM. 5-HT2A blockade promotes SWS

SUBSTANCE	ROLE IN SLEEP	WAKE/SLEEP	NOTES
ACh	Cortical activation; REM generation	Wake + REM	Active in wake and REM, silent in NREM. AChE inhibitors → vivid dreams
DA	Arousal, motivation	Promotes wake	Stimulants. Modafinil
Prostaglandin D2	Promotes sleep	Promotes sleep	Acts on VLPO region. Accumulates with sleep deprivation

3.4 Circadian Rhythm

THE MASTER CLOCK: SUPRACHIASMATIC NUCLEUS (SCN)

- Located in the anterior hypothalamus, above the optic chiasm
- Contains ~20,000 neurons with endogenous ~24.2-hour rhythm
- **Entrainment (zeitgebers):** Light is the most powerful. Others: social cues, meals, exercise, temperature
- **Light pathway:** Retina (intrinsically photosensitive retinal ganglion cells, ipRGCs, containing **melanopsin**, most sensitive to blue light ~480 nm) → retinohypothalamic tract → SCN

MOLECULAR CLOCK

Transcription-translation feedback loops (TTFL):

Additional loop: REV-ERB α /ROR α regulate BMAL1 transcription

MELATONIN PATHWAY

EXAM PEARL

Melatonin onset is ~2 hours before habitual bedtime (DLMO = gold standard for circadian phase assessment). Peak: 2–4 AM. Suppressed by light (especially blue light). Exogenous melatonin = phase-shifting agent, not a strong hypnotic. Evening dose → advances phase. Morning dose → delays phase. Ramelteon (MT1/MT2) for insomnia; Tasimelteon for Non-24 sleep-wake disorder (totally blind).

CIRCADIAN DISRUPTION IN PSYCHIATRY

CONDITION · CIRCADIAN ABNORMALITY

Depression (melancholic) Phase-advanced circadian rhythm (early morning waking, shortened REM latency). "Internal desynchronization" hypothesis

Bipolar disorder Circadian instability. Social rhythm disruption triggers episodes. Clock gene polymorphisms. Lithium lengthens circadian period (GSK3 β inhibition)

SAD (Seasonal Affective Disorder) Phase delay in winter (shorter photoperiod). Light therapy (10,000 lux, 30 min morning) = first-line

Schizophrenia Fragmented circadian rhythm, delayed phase, irregular melatonin secretion

ADHD Delayed circadian phase (evening chronotype). Melatonin onset delayed. Blue-light sensitivity

Jet lag Mismatch between internal clock and external time zone

Shift work disorder Working during biological night → forced wake when SCN signals sleep

3.5 Sleep Changes in Psychiatric Disorders

DEPRESSION

SLEEP FINDING · DETAILS

↓ **REM latency** Most characteristic finding. Normal = 90 min; depression = 40-60 min. Seen in melancholic/endogenous depression

↑ **REM density** More eye movements per REM period (= more intense REM)

↑ **Total REM** Especially in first half of night (REM redistribution)

↓ **SWS (N3)** Reduced deep sleep

Early morning awakening Classic "terminal insomnia." Phase advance

↓ **Sleep efficiency** More time awake in bed

Sleep onset insomnia In atypical depression + anxiety comorbidity

Hypersomnia In atypical depression, ↑ total sleep time, daytime sleepiness

CLINICAL ANCHOR

Sleep deprivation (total or selective REM deprivation) has rapid but unsustained antidepressant effect (60% response within 24 hours). Most antidepressants suppress REM, correlates with therapeutic effect. Exceptions that don't suppress REM: bupropion, mirtazapine, trazodone, nefazodone, agomelatine.

MANIA

FINDING · DETAILS

Decreased need for sleep NOT insomnia, patients feel rested after very little sleep (3-4 hours). This is a cardinal symptom

↓ **Total sleep time** May stay awake for days

↓ **REM latency** Similar to depression

Sleep loss triggers mania Sleep deprivation can trigger manic episodes in bipolar patients. Protecting sleep is essential in management

ANXIETY DISORDERS

FINDING · DETAILS

↑ **Sleep onset latency** Difficulty falling asleep (initial insomnia). Hyperarousal at bedtime

↓ **Sleep efficiency** Fragmented sleep

↑ **N1**, ↓ **N3** Light sleep predominates

PTSD-specific Nightmares (mostly in REM), REM fragmentation, ↑ nocturnal awakenings, ↑ sympathetic tone during sleep. Prazosin reduces nightmares

SCHIZOPHRENIA

FINDING · DETAILS

Fragmented sleep Multiple awakenings, poor sleep continuity

↓ **SWS (N3)** Reduced slow-wave sleep. May correlate with negative symptoms

↓ **REM latency** Variable finding

↓ **Sleep spindles** Thalamocortical dysfunction. May relate to cognitive deficits

Reversed sleep-wake cycle Some patients sleep during day, awake at night

↓ **Total sleep time** Variable

OTHER CONDITIONS

CONDITION · SLEEP CHANGE

Alcohol use Acute: ↓ REM latency, ↑ SWS initially, then disrupted second half.

Chronic/withdrawal: severe insomnia, REM rebound (vivid nightmares, DT hallucinations)

Dementia Sundowning (agitation at dusk), fragmented sleep, ↓ SWS, ↓ REM, sleep-wake cycle disintegration

ADHD Delayed sleep onset, restless sleep, difficulty waking. Delayed circadian phase

Eating disorders Anorexia: disrupted sleep, early morning waking. Bulimia: sleep-related eating disorder possible

Borderline PD Shortened REM latency (like depression), disrupted sleep, nightmares

SUMMARY TABLE: SLEEP STAGE CHANGES BY DISORDER

DISORDER	REM LATENCY	SWS	REM	TOTAL SLEEP	KEY FEATURE
Depression (melancholic)	↓↓	↓	↑ (density)	↓	Early morning waking
Depression (atypical)	Variable	↓	Variable	↑	Hypersomnia
Mania	↓	↓	Variable	↓↓	Decreased NEED for sleep
GAD	Normal	↓	Normal	↓	↑ Sleep onset latency
PTSD	Variable	↓	Fragmented	↓	Nightmares, hyperarousal
Schizophrenia	Variable	↓↓	Variable	↓	↓ Sleep spindles
Narcolepsy	↓↓↓ (SOREMP)	Normal	↑	Normal-↑	Sleep-onset REM periods
Alcohol withdrawal	↓	↓↓	↑↑ (rebound)	↓↓	REM rebound, nightmares

3.6 Sleep Disorders Overview

INSOMNIA

Definition Difficulty initiating or maintaining sleep, or early morning awakening, despite adequate opportunity, causing daytime impairment. ≥3 nights/week for ≥3 months (chronic)

Types Sleep onset (initial), sleep maintenance (middle), early morning awakening (terminal)

Subtypes Short-sleeper phenotype (objective short sleep + hyperarousal = higher medical risk) vs normal-sleeper phenotype

Pathophysiology Spielman's 3P model: **Predisposing** (hyperarousal trait, genetics, female sex) + **Precipitating** (stress, illness, loss) + **Perpetuating** (maladaptive sleep habits, catastrophizing, time in bed)

Treatment **CBT-I** (cognitive behavioral therapy for insomnia) = FIRST-LINE. Components: sleep restriction, stimulus control, cognitive restructuring, sleep hygiene, relaxation training. Pharmacotherapy: Z-drugs (zolpidem), low-dose doxepin (H1), ramelteon (MT1/MT2), suvorexant/lemborexant (DORA), trazodone (off-label). BZDs not preferred long-term

NARCOLEPSY

FEATURE	TYPE 1 (WITH CATAPLEXY)	TYPE 2 (WITHOUT CATAPLEXY)
Cause	Autoimmune destruction of orexin/hypocretin neurons in lateral hypothalamus. CSF orexin <110 pg/mL (diagnostic). HLA-DQB1*0602 association	Unknown. Normal CSF orexin
Excessive daytime sleepiness	Irresistible sleep attacks	Same
Cataplexy	Sudden loss of muscle tone triggered by emotion (laughter, surprise). Pathognomonic	Absent
Sleep paralysis	Inability to move at sleep-wake transitions (REM atonia intruding into wakefulness)	May be present
Hypnagogic/hypnopompic hallucinations	Vivid, often frightening hallucinations at sleep onset/offset	May be present
PSG finding	SOREMP (sleep-onset REM period) = REM within 15 minutes of sleep onset	SOREMPs present
MSLT	Mean sleep latency <8 minutes + ≥2 SOREMPs	Same

FEATURE	TYPE 1 (WITH CATAPLEXY)	TYPE 2 (WITHOUT CATAPLEXY)
Treatment	EDS: modafinil/ armodafinil (first-line), solriamfetol, pitolisant, stimulants. Cataplexy: sodium oxybate (GHB, consolidates sleep + ↓ cataplexy), oxybate salts, SSRIs/SNRIs. Once-nightly agents: sodium oxybate, low-sodium oxybate	Same for EDS. No cataplexy treatment needed

PARASOMNIAS

NREM PARASOMNIAS (DISORDERS OF AROUSAL)

PARASOMNIA	STAGE	AGE	FEATURES	TREATMENT
Confusional arousals	N3	Children	Confusion on waking, disorientation, slow speech. No ambulation	Usually benign, reassurance
Sleepwalking (somnambulism)	N3	4-8 years (peak)	Eyes open, navigates, poor recall. Can do complex behaviors. Genetic. Triggers: sleep deprivation, alcohol, stress, BZDs	Safety measures. Scheduled awakenings. BZDs (clonazepam) if severe
Sleep terrors	N3	4-12 years	Sudden screaming, autonomic activation (tachycardia, diaphoresis, mydriasis), inconsolable, NO dream recall, amnesia for event	Reassurance, safety. Distinguish from nightmares (see table below). Clonazepam if severe

EXAM PEARL

NREM parasomnia features: occur in first third of night (when SWS is maximal), impaired consciousness, amnesia for the event, family history common.

REM PARASOMNIAS

PARASOMNIA	FEATURES	CLINICAL RELEVANCE
REM Sleep Behavior Disorder (RBD)	Loss of normal REM atonia → dream enactment (punching, kicking, running). Vivid, often violent dreams with full recall. PSG: REM without atonia (RSWA)	Strong predictor of α-synucleinopathies , >80% develop Parkinson's, DLB, or MSA within 10-15 years. DLB has highest conversion. Treatment: clonazepam (first-line), melatonin. Environmental safety. RBD can be caused by antidepressants (especially SSRIs, venlafaxine)
Nightmare disorder	Vivid, disturbing, well-recalled dreams from REM. Full alertness on waking. Occur in last third of night	Common in PTSD. Treatment: image rehearsal therapy (IRT), prazosin (for PTSD nightmares, evidence mixed per VA study but still used)

SLEEP TERRORS VS NIGHTMARES

FEATURE	SLEEP TERRORS (NREM)	NIGHTMARES (REM)
Stage	N3 (SWS)	REM
Timing	First third of night	Last third of night
Arousal	Partial, confused, inconsolable	Full, alert, oriented
Autonomic activation	Intense ($\uparrow\uparrow$ HR, screaming)	Mild
Dream recall	None	Vivid, detailed
Amnesia	Yes	No
Age	Children (4-12)	Any age
Treatment	Reassurance, safety	IRT, prazosin, psychotherapy

OBSTRUCTIVE SLEEP APNEA (OSA)

Definition Repetitive upper airway collapse during sleep → apneas (≥ 10 sec cessation of airflow) and hypopneas

Severity AHI (apnea-hypopnea index): Mild 5-15, Moderate 15-30, Severe >30 events/hour

Risk factors Obesity (BMI >30), male sex, age >50, neck circumference >17", retrognathia, tonsillar hypertrophy, alcohol, sedatives

Symptoms Snoring, witnessed apneas, excessive daytime sleepiness, morning headaches, nocturia, ↓ concentration

Consequences Hypertension, cardiovascular disease, stroke, metabolic syndrome, depression, cognitive impairment, ↑ accident risk

Diagnosis Polysomnography (gold standard). Home sleep apnea test (HSAT) for uncomplicated cases

Treatment CPAP (first-line for moderate-severe). Weight loss. Positional therapy. Oral appliances (mild-moderate). Surgery (UPPP) for selected cases. Hypoglossal nerve stimulation (Inspire)

Psychiatric relevance Causes or exacerbates depression, anxiety, cognitive impairment, ADHD-like symptoms. Always screen for OSA before attributing symptoms to psychiatric disorder. Antipsychotic-related weight gain → ↑ OSA risk

RESTLESS LEGS SYNDROME (RLS) / WILLIS-EKBOM DISEASE

Definition Urge to move legs, usually with uncomfortable sensation, worse at rest, worse in evening/night, relieved by movement

Pathophysiology Iron deficiency in substantia nigra → impaired DA synthesis (TH requires iron as cofactor). CNS iron deficiency even when serum ferritin is normal-ish (check ferritin, treat if <75 µg/L)

Associations Iron deficiency, pregnancy, ESRD, neuropathy, SSRI/antipsychotic use (can worsen)

Treatment Iron supplementation (if ferritin <75). α2δ ligands (gabapentin enacarbil, pregabalin, now first-line). Low-dose DA agonists (pramipexole, ropinirole, risk of augmentation with long-term use). Augmentation = worsening of RLS with chronic DA agonist use → switch to α2δ ligand

Psychiatric relevance SSRIs, SNRIs, antipsychotics, and antihistamines can worsen RLS. Bupropion is the antidepressant least likely to worsen. Mirtazapine can worsen. Must differentiate from akathisia

CIRCADIAN RHYTHM SLEEP-WAKE DISORDERS

DISORDER	FEATURE	TREATMENT
Delayed Sleep Phase (DSWPD)	Sleep onset and wake time delayed 2+ hours. Common in adolescents. "Night owls." Normal sleep quality once asleep	Morning bright light + evening melatonin (0.5-3 mg, 5-7 hours before desired sleep). Chronotherapy

DISORDER	FEATURE	TREATMENT
Advanced Sleep Phase (ASWPD)	Sleep onset and wake time advanced. Common in elderly. "Morning larks"	Evening bright light. Rare, familial forms (Per2 mutations)
Non-24-Hour Sleep-Wake	Free-running circadian rhythm (>24 hours). Common in totally blind (no light input to SCN)	Tasimelteon (MT1/MT2 agonist), FDA-approved for this indication
Irregular Sleep-Wake	No clear circadian pattern. Fragmented sleep across 24 hours	Seen in dementia, brain injury. Structured light exposure, melatonin, social zeitgebers
Shift Work Disorder	Insomnia + excessive sleepiness related to shift work schedule	Strategic napping, timed light exposure, melatonin, modafinil/armodafinil for wakefulness during shifts
Jet Lag	Temporary mismatch after rapid transmeridian travel	Timed light exposure, melatonin, short-acting hypnotics. Eastward travel harder (need to phase advance)

OTHER SLEEP DISORDERS

DISORDER · KEY FEATURES

Sleep-related eating disorder (SRED) Eating during partial arousals from NREM sleep, with limited recall. Associated with zolpidem, other sedatives

Sexsomnia Sexual behavior during NREM parasomnias. Medico-legal implications

Exploding head syndrome Loud imagined noise at sleep onset. Benign, distressing. N1 transition

Sleep-related leg cramps Painful involuntary contractions, often calves. Benign, common in elderly

Bruxism Teeth grinding during sleep. Stages N1-N2. Dental damage. Mouth guards

Periodic limb movement disorder (PLMD) Repetitive stereotyped limb movements (usually legs) during NREM. Often coexists with RLS. PLM index >15/hour on PSG

Klein-Levin syndrome Recurrent hypersomnia (sleeping 16-20 hours/day for days-weeks), with hyperphagia, hypersexuality, cognitive/behavioral changes. Rare. Young males. Self-remitting episodes

PHARMACOLOGY AND SLEEP: QUICK REFERENCE

DRUG CLASS · EFFECT ON SLEEP

SSRIs/SNRIs ↓ REM (↑ REM latency, ↓ total REM), may ↑ sleep onset latency initially, can cause insomnia, can worsen RLS, can trigger / worsen RBD

TCAs ↓ REM strongly. Sedating (H1, α 1 blockade, especially amitriptyline, doxepin). Clomipramine most REM-suppressing

MAOIs Potent REM suppression (may abolish REM entirely)

Mirtazapine ↑ SWS (5-HT2A / 2C blockade), minimal REM effect. H1 blockade → sedation. Good for insomnia

Trazodone ↑ SWS (5-HT2A blockade). Sedation (H1). Does not suppress REM. Most commonly prescribed sleep aid in US (off-label)

Bupropion ↑ REM (does not suppress). Can cause insomnia. Least likely to worsen RLS

BZDs ↓ N3 (SWS), ↑ N2 (more spindles), ↓ sleep latency. Minimal REM effect at clinical doses. Tolerance develops

Z-drugs (zolpidem) Selective α 1 GABA-A → less SWS suppression than BZDs. Complex sleep behaviors (sleepwalking, sleep-eating, sleep-driving)

Antipsychotics Sedation varies. Quetiapine: strong H1 → sedation. Olanzapine: ↑ SWS. Typical antipsychotics: variable

Lithium ↑ SWS, ↓ REM. Lengthens circadian period (GSK3 β). Can cause nephrogenic DI → nocturia

Alcohol Acute: ↓ REM latency, ↑ SWS initially, disrupted second half. Chronic: insomnia, ↓ SWS, REM rebound on withdrawal

Cannabis Acute: ↓ REM, ↑ SWS. Chronic: tolerance. Withdrawal: REM rebound, vivid dreams, insomnia

Caffeine Blocks adenosine A1 / A2A → ↓ sleep pressure, ↑ latency, ↓ total sleep, ↓ SWS. Half-life 3-7 hours

Melatonin/Ramelteon MT1 / MT2 agonism → phase-shifting, modest ↓ sleep onset latency. Does not alter sleep architecture significantly

Suvorexant/Lemborexant DORA → ↓ wakefulness, ↑ sleep onset, ↑ sleep maintenance. Preserves normal sleep architecture. May ↑ REM slightly

High-Yield Exam Pearls

NEUROTRANSMITTERS

EXAM PEARL

Rate-limiting enzymes: TH (catecholamines), TPH (serotonin), GAD (GABA), ChAT (ACh).

EXAM PEARL

BZDs increase FREQUENCY; barbiturates increase DURATION of Cl⁻ channel opening.

EXAM PEARL

5-HT₃ is the only ionotropic serotonin receptor.

EXAM PEARL

D₂ occupancy 65–80% = therapeutic window for antipsychotics.

EXAM PEARL

NMDA needs both glutamate AND glycine/D-serine plus membrane depolarization (to relieve Mg²⁺ block).

EXAM PEARL

Ketamine blocks NMDA → rapid antidepressant via AMPA → BDNF → synaptogenesis.

EXAM PEARL

Low CSF 5-HIAA = impulsive aggression, violent suicide.

EXAM PEARL

COMT Val/Val = warrior (low PFC DA). Met/Met = worrier (high PFC DA).

EXAM PEARL

Xanomeline-trospium (Cobenfy) = first non-D₂ antipsychotic (M₁/M₄ agonist).

EXAM PEARL

Orexin loss = narcolepsy type 1. DORAs (suvorexant) = insomnia treatment.

NEUROANATOMY

EXAM PEARL

Pseudodepressed = DLPFC. Pseudopsychopathic = OFC. Akinetic mutism = bilateral ACC.

EXAM PEARL

Papez circuit = hippocampus → fornix → mammillary bodies → anterior thalamus → cingulate → parahippocampal gyrus → hippocampus.

EXAM PEARL

Kluver-Bucy = bilateral amygdala lesion.

EXAM PEARL

Wernicke-Korsakoff = mammillary body damage (thiamine deficiency).

EXAM PEARL

STN is the only excitatory nucleus in basal ganglia. STN lesion → hemiballismus.

EXAM PEARL

Left DLPFC = TMS target for depression. Subgenual ACC (BA 25) = DBS target.

EXAM PEARL

MD thalamus = most psychiatrically relevant thalamic nucleus (connects to PFC).

EXAM PEARL

Huntington's = caudate atrophy, chromosome 4, CAG trinucleotide repeat.

EXAM PEARL

SCN = master clock. TMN = sole histamine source. LC = sole cortical NE source.

EXAM PEARL

HPA axis in depression: ↑ CRH, ↑ cortisol, DST non-suppression. In PTSD: ↓ cortisol, enhanced suppression.

SLEEP

EXAM PEARL

N2 is the most abundant stage (45–55%). Features: sleep spindles + K-complexes.

EXAM PEARL

SWS predominates first third of night. REM predominates last third.

EXAM PEARL

Depression: ↓ REM latency, ↑ REM density, early morning awakening.

EXAM PEARL

Mania: decreased NEED for sleep (not insomnia).

EXAM PEARL

RBD strongly predicts α -synucleinopathies (PD, DLB, MSA), >80% conversion.

EXAM PEARL

Narcolepsy type 1: CSF orexin <110 pg/mL, cataplexy, HLA-DQB1*0602.

EXAM PEARL

CBT-I is first-line for chronic insomnia (not medications).

EXAM PEARL

Flip-flop switch: VLPO (sleep) vs LC/TMN/raphe (wake), stabilized by orexin.

EXAM PEARL

RLS: iron deficiency in SN → impaired DA synthesis. Check ferritin. $\alpha 2\delta$ ligands now first-line.

EXAM PEARL

Process S = homeostatic (adenosine). Process C = circadian (SCN/melatonin).

Document prepared for NB-01: P1-Neuro-Foundations. Sources: Kaplan & Sadock's Comprehensive Textbook of Psychiatry, Stahl's Essential Psychopharmacology, Kandel's Principles of Neural Science, Sadock's Synopsis of Psychiatry. For PG exams MD Psychiatry exit examination preparation.

Model Answers

Document Type: Model Answer Bank

Sources: Kaplan & Sadock (14th ed.), Stahl's Essential Psychopharmacology (5th ed.), PG exams Master Compilation, PG exams PYQ Bank

SECTION A: NEUROTRANSMITTER PYQs (Q1–Q15)

Q1: "Define neurotransmitters. How do they differ from neuromodulators? Name excitatory neurotransmitters and describe any one in detail.": 10 marks

EXAM PEARL

Long essay candidate.

EXAM STRATEGY

Definition + comparison table first (easy marks). Pick glutamate as the excitatory NT for maximum scoring, it has the most clinical detail.

A. DEFINITION OF NEUROTRANSMITTERS [2]

A **neurotransmitter** is a chemical substance that satisfies the following criteria:

1. **Synthesized** in the presynaptic neuron
2. **Stored** in synaptic vesicles at the nerve terminal
3. **Released** in a **calcium-dependent manner** upon depolarization
4. Acts on **specific postsynaptic receptors** to produce a biological effect
5. Has a mechanism for **inactivation** (reuptake, enzymatic degradation, or diffusion)
6. Can be **mimicked by exogenous application** and **blocked by specific antagonists**

B. NEUROTRANSMITTERS VS. NEUROMODULATORS: KEY DIFFERENCES [3]

FEATURE	NEUROTRANSMITTER	NEUROMODULATOR
Action	Fast, direct synaptic transmission	Slow, modulatory, alters neuronal excitability
Site of action	Postsynaptic membrane (synaptic cleft)	Can act pre- or postsynaptically, even extrasynaptically (volume transmission)

FEATURE	NEUROTRANSMITTER	NEUROMODULATOR
Receptor type	Ionotropic (ligand-gated ion channels) predominantly	Metabotropic (G-protein coupled) predominantly
Duration	Milliseconds	Seconds to minutes
Distance	Local, confined to synapse	Diffuse, can act at distance
Effect	Excitation or inhibition (EPSP / IPSP)	Modifies the response to neurotransmitters
Examples	Glutamate, GABA, glycine	Dopamine, serotonin, norepinephrine, neuropeptides, endocannabinoids

EXAM PEARL

The distinction is not absolute. Many substances (e.g., dopamine, serotonin) can function as both neurotransmitters AND neuromodulators depending on the receptor type and circuit.

C. EXCITATORY NEUROTRANSMITTERS [2]

- **Glutamate** (principal excitatory NT in the CNS)
- **Aspartate**
- **Acetylcholine** (at nicotinic receptors)
- **Norepinephrine** (at certain receptors)
- **Substance P**
- **Histamine** (at certain receptors)

D. GLUTAMATE: DETAILED DESCRIPTION [3]

Synthesis:

- Synthesized from **glutamine** by the enzyme **glutaminase** in presynaptic terminals
- Also derived from the **Krebs cycle** (alpha-ketoglutarate via transamination)
- The **glutamate-glutamine cycle** between neurons and astrocytes is critical for recycling

Receptors (4 types):

RECEPTOR	TYPE	FUNCTION
NMDA (N-methyl-D-aspartate)	Ionotropic, Ca^{2+} , Na^{+} , K^{+}	Learning, memory, synaptic plasticity (LTP). Voltage-dependent Mg^{2+} block. Requires glycine co-agonist
AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid)	Ionotropic, Na^{+} , K^{+}	Fast excitatory transmission. Mediates most moment-to-moment glutamatergic signaling

RECEPTOR	TYPE	FUNCTION
Kainate	Ionotropic, Na ⁺ , K ⁺	Presynaptic modulation, pain signaling
mGluR (metabotropic, Groups I–III)	Metabotropic, G-protein coupled	Modulates synaptic plasticity, neuroprotection, presynaptic regulation

Inactivation:

- **Reuptake** by excitatory amino acid transporters (**EAATs**) on neurons and astrocytes
- In astrocytes: converted back to **glutamine** by **glutamine synthetase**

Clinical Relevance:

- **Excitotoxicity:** Excessive glutamate → sustained Ca²⁺ influx → neuronal death. Implicated in stroke, traumatic brain injury, neurodegenerative diseases
- **Schizophrenia:** NMDA receptor **hypofunction** hypothesis, PCP and ketamine (NMDA antagonists) produce psychotic symptoms. Explains negative and cognitive symptoms better than the dopamine hypothesis alone
- **Depression: Ketamine** (NMDA antagonist) produces rapid antidepressant effects; **esketamine** (Spravato) approved for treatment-resistant depression
- **Epilepsy:** Glutamate excess → seizure propagation
- **Alzheimer's disease: Memantine** (NMDA antagonist) used therapeutically to reduce excitotoxicity
- **Anxiety:** mGluR modulators under investigation as novel anxiolytics

Diagram description: Draw the glutamate-glutamine cycle, presynaptic neuron (glutamine → glutamate → packaged into vesicles by VGLUT → released → acts on NMDA / AMPA / Kainate / mGluR on postsynaptic neuron) → taken up by astrocyte (EAAT) → glutamine synthetase converts glutamate → glutamine → shuttled back to neuron.

(See also Q3 for amino acid neurotransmitters, Q9 for glutamate in depression)

Q2: "Neurotransmitters. Describe role of dopamine in Psychiatry.": 10 marks

EXAM STRATEGY

Brief classification of all NTs (3 marks), then focus bulk on dopamine pathways + psychiatric roles (7 marks). Overlap with Q5, Q6, Q11.

A. OVERVIEW OF NEUROTRANSMITTERS [3]

Classification:

CATEGORY · EXAMPLES

Biogenic amines (monoamines) Dopamine, norepinephrine, epinephrine (catecholamines); Serotonin (indolamine); Histamine

Amino acids Glutamate, GABA, glycine, aspartate

Neuropeptides Endorphins, enkephalins, substance P, neuropeptide Y, CRH, oxytocin, vasopressin

Acetylcholine (own class)

Purines Adenosine, ATP

Gases Nitric oxide (NO), carbon monoxide (CO)

Endocannabinoids Anandamide, 2-AG

B. DOPAMINE IN PSYCHIATRY [7]

Synthesis pathway:

Tyrosine → (tyrosine hydroxylase, **rate-limiting**) → **L-DOPA** → (DOPA decarboxylase) → **Dopamine**

Degradation: MAO-B and COMT → HVA (homovanillic acid, measured in CSF)

Dopamine Receptors:

FAMILY	SUBTYPES	MECHANISM	LOCATION
D1-like	D1, D5	Gs → ↑cAMP	Cortex, striatum
D2-like	D2, D3, D4	Gi → ↓cAMP	Striatum, limbic, VTA

The 4 Major Dopaminergic Pathways:

PATHWAY	ORIGIN → TARGET	FUNCTION	CLINICAL RELEVANCE
Mesolimbic	VTA → Nucleus accumbens, amygdala, hippocampus	Reward, motivation, emotion	Hyperactivity → positive symptoms of schizophrenia. Addiction.
Mesocortical	VTA → Prefrontal cortex (DLPFC, VMPFC)	Executive function, cognition, motivation	Hypoactivity → negative/cognitive symptoms of schizophrenia. ADHD.
Nigrostriatal	Substantia nigra (pars compacta) → Dorsal striatum (caudate/putamen)	Motor control, procedural learning	Degeneration → Parkinson's disease. Blockade → EPS (antipsychotics).

PATHWAY	ORIGIN → TARGET	FUNCTION	CLINICAL RELEVANCE
Tuberoinfundibular	Hypothalamus (arcuate nucleus) → Pituitary stalk	Inhibits prolactin release	Blockade → hyperprolactinemia (galactorrhea, amenorrhea, sexual dysfunction).

(+) **5th pathway: Thalamic pathway** (multiple origins → thalamus), involved in arousal, sleep-wake regulation.

Role in Specific Psychiatric Disorders:

- **Schizophrenia:** Dopamine hypothesis, mesolimbic hyperactivity (positive symptoms), mesocortical hypoactivity (negative / cognitive symptoms). All effective antipsychotics block D2 receptors (minimum 60–65% occupancy for efficacy, >80% → EPS).
- **Bipolar disorder:** Dopamine dysregulation contributes to both mania (↑ DA) and depression (↓ DA).
- **Depression:** Anhedonia, psychomotor retardation linked to mesocortical / mesolimbic DA deficit. Bupropion (NDRI) works via dopamine.
- **ADHD:** Mesocortical dopamine deficit in prefrontal cortex. Methylphenidate and amphetamines increase DA.
- **Substance use disorders:** All drugs of abuse converge on mesolimbic pathway → dopamine surge in nucleus accumbens.
- **OCD:** Dopamine augmentation (aripiprazole) helps treatment-resistant OCD.
- **Tourette syndrome:** Dopamine hyperactivity in basal ganglia. Responds to D2 blockers.

Diagram description: Draw the 4 dopaminergic pathways, show VTA projecting to nucleus accumbens (mesolimbic) and PFC (mesocortical); substantia nigra projecting to striatum (nigrostriatal); arcuate nucleus projecting to pituitary (tuberoinfundibular). Label each with function and disorder.

(See Q5, Q6, Q11 for expanded dopamine discussions)

Q3: "Amino Acid neurotransmitters.": 10 marks

EXAM STRATEGY

Cover all 4 amino acid NTs systematically. Table format scores well here. Glutamate and GABA deserve the most space.

A. INTRODUCTION [1]

Amino acid neurotransmitters are the most abundant neurotransmitters in the CNS. They mediate fast synaptic transmission (unlike monoamines which are slower / modulatory).

Four main amino acid NTs:

- **Excitatory:** Glutamate, Aspartate
- **Inhibitory:** GABA (gamma-aminobutyric acid), Glycine

B. GLUTAMATE [3]

- **Principal excitatory NT** in the CNS (~60% of all synapses)
- Synthesis: Glutamine → (glutaminase) → Glutamate
- Receptors: **NMDA, AMPA, Kainate** (ionotropic); **mGluR** (metabotropic)
- Removal: Reuptake via EAATs → astrocytes → converted to glutamine (glutamine synthetase)

Clinical relevance:

- NMDA hypofunction model of schizophrenia (PCP psychosis)
- Excitotoxicity → stroke, neurodegeneration (ALS, Huntington's, Alzheimer's)
- Ketamine/esketamine, rapid-acting antidepressants
- Memantine, Alzheimer's treatment
- Riluzole (glutamate release inhibitor), ALS
- Epilepsy, glutamate excess drives seizures
- Lamotrigine, mood stabilizer, reduces glutamate release

C. GABA (GAMMA-AMINOBUTYRIC ACID) [3]

- **Principal inhibitory NT** in the CNS (~40% of all synapses)
- Synthesis: Glutamate → (glutamic acid decarboxylase, **GAD**, requires vitamin B6/pyridoxine as cofactor) → GABA
- Degradation: GABA-transaminase → succinic semialdehyde → succinic acid (enters Krebs cycle)

Receptors:

RECEPTOR	TYPE	MECHANISM	CLINICAL SIGNIFICANCE
GABA-A	Ionotropic, Cl ⁻ channel	Fast inhibition (hyperpolarization)	Site of action for benzodiazepines (potentiate GABA at alpha subunit), barbiturates , alcohol , general anesthetics , neurosteroids
GABA-B	Metabotropic, Gi protein	Slow inhibition; ↓Ca ²⁺ , ↑K ⁺ ; inhibits presynaptic release	Baclofen (agonist), spasticity, alcohol withdrawal, GHB withdrawal
GABA-C	Ionotropic, Cl ⁻ (rho subunit)	Retina primarily	Limited clinical application

Clinical relevance:

- **Anxiety disorders:** GABAergic deficit model; benzodiazepines enhance GABA-A
- **Epilepsy:** Reduced GABAergic inhibition → seizures. Vigabatrin (irreversible GABA-transaminase inhibitor), valproate (↑ GABA), tiagabine (GABA reuptake inhibitor)
- **Insomnia:** Benzodiazepines, Z-drugs (zolpidem, zopiclone) act at GABA-A
- **Alcohol:** Alcohol potentiates GABA-A → cross-tolerance with benzodiazepines. Withdrawal = reduced GABAergic tone → seizures, DT
- **Hepatic encephalopathy:** Increased endogenous benzodiazepine-like substances
- **Depression:** GABAergic deficit reported; brexanolone (neurosteroid GABA-A modulator) approved for postpartum depression
- **Schizophrenia:** GABAergic interneuron dysfunction in PFC

D. GLYCINE [1.5]

- **Inhibitory NT** predominantly in the **spinal cord and brainstem**
- Acts on **glycine receptors** (Cl⁻ channels, strychnine-sensitive)
- Also functions as **obligatory co-agonist at the NMDA receptor** (glycine site/GluN1 subunit)
- Clinical relevance:
- **Strychnine** poisoning, glycine receptor blockade → spastic paralysis, convulsions
- Glycine site agonists (e.g., D-serine, D-cycloserine) investigated as adjuncts in schizophrenia (to enhance NMDA function)
- **Hyperekplexia** (startle disease), mutations in glycine receptor

E. ASPARTATE [0.5]

- Excitatory amino acid, co-localized with glutamate
- Acts on NMDA receptors
- Less well-characterized clinical role compared to glutamate

F. SUMMARY TABLE [1]

NT	TYPE	MAIN RECEPTOR	KEY CLINICAL LINK
Glutamate	Excitatory	NMDA, AMPA	Schizophrenia, depression (ketamine), excitotoxicity
GABA	Inhibitory	GABA-A, GABA-B	Anxiety, epilepsy, alcohol, insomnia
Glycine	Inhibitory	Glycine-R, NMDA (co-agonist)	Strychnine poisoning, NMDA modulation

NT	TYPE	MAIN RECEPTOR	KEY CLINICAL LINK
Aspartate	Excitatory	NMDA	Co-transmitter with glutamate

(See Q1 for detailed glutamate, Q9 for glutamate/GABA in depression)

Q4: "Relationship between neurotransmitters and various brain functions. Novel neurotransmitters.": 10 marks

EXAM STRATEGY

First half, a clear table mapping NTs to brain functions. Second half, list and discuss novel NTs (endocannabinoids, NO, neuropeptides). Examiner wants breadth here.

A. NEUROTRANSMITTERS AND BRAIN FUNCTIONS [5]

BRAIN FUNCTION	KEY NEUROTRANSMITTERS	MECHANISM
Mood regulation	Serotonin, norepinephrine, dopamine	Monoamine deficiency → depression; SSRIs, SNRIs, NDRIs restore balance
Cognition/Executive function	Dopamine (mesocortical), acetylcholine, glutamate	PFC dopamine / ACh modulate working memory, attention, planning
Memory & Learning	Glutamate (NMDA → LTP), acetylcholine (basal forebrain)	LTP at hippocampal synapses; cholinergic loss → Alzheimer's
Reward & Motivation	Dopamine (mesolimbic)	Nucleus accumbens dopamine surge; all addictive substances converge here
Anxiety	GABA (↓ = anxiety), serotonin, norepinephrine, CRH	GABAergic deficit → disinhibition of amygdala; 5-HT modulates
Motor control	Dopamine (nigrostriatal), GABA, glutamate, ACh	Basal ganglia circuitry; DA deficit → Parkinson's
Sleep-Wake cycle	Orexin/hypocretin, histamine, ACh, GABA, serotonin, norepinephrine, adenosine, melatonin	Wake-promoting (orexin, histamine, NE, ACh) vs. sleep-promoting (GABA, galanin, adenosine)
Appetite	Neuropeptide Y (↑appetite), leptin, ghrelin, serotonin, endocannabinoids	Hypothalamic regulation; 5-HT _{2C} agonism → anorexia (side effect of some SSRIs)
Pain	Endorphins, enkephalins, substance P, glutamate, GABA	Descending inhibitory pathways (periaqueductal gray); opioid system

BRAIN FUNCTION	KEY NEUROTRANSMITTERS	MECHANISM
Stress response	CRH, norepinephrine, cortisol (HPA axis)	CRH from hypothalamus activates ACTH → cortisol cascade
Aggression	Serotonin (↓ = ↑aggression), testosterone, GABA	Reduced 5-HIAA in CSF associated with impulsive violence

B. NOVEL NEUROTRANSMITTERS [5]

1. Endocannabinoids

- **Anandamide (AEA)** and **2-arachidonoylglycerol (2-AG)**
- Act on **CB1** (CNS, hippocampus, basal ganglia, cerebellum) and **CB2** (immune cells, periphery) receptors
- Unique: **retrograde signaling**, synthesized in postsynaptic neuron, travel backward to modulate presynaptic release
- Functions: pain modulation, appetite (CB1 agonism → "munchies"), mood, memory extinction (relevant to PTSD), neuroprotection
- Clinical: Cannabis (THC = CB1 partial agonist); **rimonabant** (CB1 antagonist, withdrawn, psychiatric side effects); CBD (complex pharmacology, anxiolytic, antipsychotic properties under investigation); **nabilone/dronabinol** for chemotherapy-induced nausea

2. Nitric Oxide (NO)

- Gaseous neurotransmitter, synthesized by **nitric oxide synthase (NOS)** from L-arginine
- Not stored in vesicles, produced on demand, diffuses freely across membranes
- Acts via **soluble guanylyl cyclase** → **cGMP** (not a classical receptor)
- Functions: cerebral vasodilation, synaptic plasticity (involved in LTP alongside glutamate/NMDA), penile erection
- Clinical: Sildenafil (PDE5 inhibitor) enhances NO/cGMP pathway; NOS inhibitors investigated in psychiatric disorders; NO involved in neuroinflammation

3. Neuropeptides (selected)

NEUROPEPTIDE	FUNCTION	CLINICAL RELEVANCE
Orexin/Hypocretin	Wakefulness, appetite, reward	Deficiency → narcolepsy type 1 . Suvorexant, lemborexant (dual orexin receptor antagonists, DORAs) for insomnia
Oxytocin	Social bonding, trust, maternal behavior	"Social brain", deficits in autism spectrum disorder; intranasal oxytocin trials

NEUROPEPTIDE	FUNCTION	CLINICAL RELEVANCE
CRH	Stress response, HPA axis activation	↑ in depression, PTSD, anxiety; CRH antagonists in trials
Neuropeptide Y	Anxiolytic, appetite stimulation, stress resilience	Low NPY → vulnerability to PTSD; NPY agonists investigated
Substance P	Pain transmission, neurogenic inflammation, mood	NK1 receptor antagonists trialed (but failed) as antidepressants
Galanin	Sleep promotion, feeding, cognition	Co-localized with NE in locus coeruleus; role in Alzheimer's

4. Purines

- **Adenosine:** Inhibitory NT; accumulates during wakefulness → promotes sleep. Caffeine = adenosine A1 / A2A antagonist
- **ATP:** Co-released with other NTs; acts on P2X (ionotropic) and P2Y (metabotropic) receptors; role in pain and neuroinflammation

5. D-serine

- Co-agonist at NMDA receptor glycine site
- Released by astrocytes
- Deficiency may contribute to NMDA hypofunction in schizophrenia

(See Q1 for glutamate detail, Q3 for amino acid NTs)

Q5: "Define neurotransmitters. Describe various types of neurotransmitters. Describe role of dopamine in Psychiatry.": 10 marks

EXAM PEARL

Long essay candidate.

EXAM STRATEGY

This combines Q1 (definition) + Q2 (classification + dopamine). Allocate: definition [2], classification [3], dopamine [5]. For expanded long essay version: definition [2], classification [4], dopamine [8], clinical applications [4], diagram [2].

A. DEFINITION [2]

A **neurotransmitter** is a chemical messenger synthesized in a neuron, stored in synaptic vesicles, released in a calcium-dependent manner upon depolarization, acts on specific

postsynaptic receptors to produce a biological effect, and has a defined mechanism of inactivation.

Criteria (expanded): See Q1 Section A for the 6 classical criteria.

B. CLASSIFICATION OF NEUROTRANSMITTERS [3]

By chemical structure:

CATEGORY	SUBCATEGORY	EXAMPLES
Biogenic amines	Catecholamines	Dopamine, norepinephrine, epinephrine
	Indolamine	Serotonin (5-HT)
	Imidazolamine	Histamine
Amino acids	Excitatory	Glutamate, aspartate
	Inhibitory	GABA, glycine
Acetylcholine		ACh
Neuropeptides	Opioid	Endorphins, enkephalins, dynorphins
	Non-opioid	Substance P, CRH, NPY, oxytocin, vasopressin, orexin, CCK, galanin
Purines		Adenosine, ATP
Gases		Nitric oxide, carbon monoxide
Lipids	Endocannabinoids	Anandamide, 2-AG

By function:

- **Excitatory:** Glutamate, aspartate, ACh (nicotinic), NE (some receptors)
- **Inhibitory:** GABA, glycine
- **Modulatory:** Dopamine, serotonin, NE, neuropeptides

By receptor type engaged:

- **Ionotropic** (fast): Glutamate (NMDA/AMPA/Kainate), GABA-A, glycine, nicotinic ACh
- **Metabotropic** (slow): mGluR, GABA-B, muscarinic ACh, all monoamine receptors, neuropeptide receptors

C. ROLE OF DOPAMINE IN PSYCHIATRY [5]

Synthesis: Tyrosine → L-DOPA (tyrosine hydroxylase, rate-limiting) → Dopamine (DOPA decarboxylase)

Degradation: MAO-B + COMT → HVA

Receptors: D1-like (D1, D5, Gs, ↑cAMP) and D2-like (D2, D3, D4, Gi, ↓cAMP)

4 Major Pathways + Clinical Relevance:

PATHWAY	FROM → TO	DYSFUNCTION
Mesolimbic	VTA → NAc	↑ = positive symptoms (schizophrenia), addiction
Mesocortical	VTA → PFC	↓ = negative/cognitive symptoms, ADHD
Nigrostriatal	SN → Striatum	↓ = Parkinsonism, EPS; ↑ = tardive dyskinesia, Tourette's
Tuberoinfundibular	Arcuate → Pituitary	Blockade = hyperprolactinemia

Disorder-specific roles:

- **Schizophrenia:** Revised dopamine hypothesis, mesolimbic excess + mesocortical deficit + glutamate-dopamine interaction. All antipsychotics block D2. Partial agonists (aripiprazole, cariprazine, brexpiprazole) stabilize dopamine.
- **Depression:** Dopamine deficit in reward circuits → anhedonia, avolition. Bupropion (NDRI). Pramipexole (D3 agonist) augments antidepressants.
- **Mania:** Dopamine excess. Antipsychotics (D2 blockade) are mainstay of acute mania treatment.
- **ADHD:** Mesocortical DA/NE deficit in PFC → inattention, impulsivity. Stimulants (methylphenidate, amphetamines) increase DA/NE.
- **Addiction:** All substances of abuse increase mesolimbic DA. Dopamine depleted in chronic use → anhedonia, craving.
- **Psychosis in Parkinson's:** L-DOPA increases DA globally → mesolimbic excess → hallucinations. Pimavanserin (5-HT_{2A} inverse agonist) preferred.
- **Tourette's:** Dopaminergic hyperactivity in basal ganglia. Treated with D2 blockers (haloperidol, aripiprazole).

Diagram description: Draw the 4 dopaminergic pathways as in Q2.

(Cross-references: Q1 for definitions, Q6/Q11 for expanded pathway detail)

Q6: "Describe dopaminergic pathways in the brain. What are their functions? What is their applied importance?": 10 marks

EXAM PEARL

Long essay candidate.

EXAM STRATEGY

Pathway-focused answer. Detailed anatomy + function + clinical application for each pathway.
Diagram essential.

A. INTRODUCTION [1]

Dopaminergic neurons constitute a relatively small population (~400,000–600,000 in the human brain) but have disproportionately large influence on motor control, reward, motivation, cognition, and endocrine regulation. They are organized into distinct pathways originating from midbrain and hypothalamic nuclei.

B. THE 5 DOPAMINERGIC PATHWAYS [6]

1. Mesolimbic Pathway

- **Origin:** Ventral tegmental area (VTA, A10 cell group)
- **Termination:** Nucleus accumbens (ventral striatum), amygdala, hippocampus, olfactory tubercle
- **Function:** Reward processing, motivation, pleasure, emotional salience, reinforcement learning
- **Applied importance:**
- **Schizophrenia:** Hyperactivity → positive symptoms (delusions, hallucinations, thought disorder). The "psychosis pathway."
- **Addiction:** All drugs of abuse (opioids, stimulants, alcohol, nicotine) converge on this pathway → DA surge in NAc
- **Depression:** Hypoactivity → anhedonia, reduced motivation
- Antipsychotic D2 blockade here → reduces positive symptoms

2. Mesocortical Pathway

- **Origin:** VTA (A10)
- **Termination:** Prefrontal cortex, dorsolateral PFC (DLPFC) and ventromedial PFC (VMPFC)
- **Function:**
- DLPFC: Working memory, executive function, planning
- VMPFC: Emotion regulation, social cognition, decision-making
- **Applied importance:**
- **Schizophrenia:** Hypoactivity → negative symptoms (avolition, alogia, flat affect) and cognitive symptoms (poor working memory, impaired executive function)
- **ADHD:** DA/NE deficit in PFC → inattention, poor executive function
- Antipsychotic D2 blockade here → can WORSEN negative/cognitive symptoms (clinical dilemma)

- Second-generation antipsychotics (5-HT_{2A} antagonism) may improve mesocortical DA tone

3. Nigrostriatal Pathway

- **Origin:** Substantia nigra pars compacta (SNpc, A9 cell group)
- **Termination:** Dorsal striatum (caudate nucleus and putamen)
- **Function:** Initiation and modulation of voluntary movement, procedural learning, habit formation
- **Applied importance:**
- **Parkinson's disease:** Degeneration of SNpc neurons → 70–80% DA loss → bradykinesia, rigidity, tremor
- **Antipsychotic-induced EPS:** D₂ blockade in this pathway → acute dystonia, parkinsonism, akathisia, tardive dyskinesia
- **Tardive dyskinesia:** Chronic D₂ blockade → receptor upregulation/supersensitivity → involuntary choreoathetoid movements. Treatment: **valbenazine, deutetrabenazine** (VMAT2 inhibitors)
- **Tourette syndrome:** DA hyperactivity in basal ganglia
- **Huntington's disease:** Loss of GABAergic medium spiny neurons in striatum → disinhibition of DA → chorea

4. Tuberoinfundibular Pathway

- **Origin:** Arcuate nucleus and periventricular nucleus of hypothalamus (A12)
- **Termination:** Median eminence → pituitary stalk → anterior pituitary
- **Function:** Tonic dopamine release inhibits prolactin secretion from lactotroph cells
- **Applied importance:**
- **Antipsychotic-induced hyperprolactinemia:** D₂ blockade removes tonic inhibition → ↑ prolactin → galactorrhea, amenorrhea, sexual dysfunction, osteoporosis (long-term)
- **Risperidone and amisulpride**, highest risk. **Aripiprazole** (partial D₂ agonist), lowest risk, can even reverse hyperprolactinemia
- **Prolactinoma:** DA agonists (cabergoline, bromocriptine) shrink tumor

5. Thalamic Pathway (newer)

- **Origin:** Multiple sources including periaqueductal gray, VTA, hypothalamus
- **Termination:** Thalamus
- **Function:** Arousal, wakefulness, sensory gating
- **Applied importance:** May contribute to mechanism of sleep disturbance, altered consciousness; less well-characterized clinically

C. INTEGRATED CLINICAL APPLICATION [2]

The antipsychotic dilemma:

- Effective antipsychotic action requires D2 blockade in mesolimbic pathway
- But D2 blockade simultaneously causes:
- Mesocortical: worsened negative / cognitive symptoms
- Nigrostriatal: EPS
- Tuberoinfundibular: hyperprolactinemia
- **Solution approaches:**
- Partial D2 agonists (aripiprazole, cariprazine, brexpiprazole), stabilize DA across all pathways
- 5-HT_{2A} antagonism (clozapine, quetiapine, olanzapine), increases DA release in nigrostriatal and mesocortical pathways, reducing EPS and negative symptoms
- Low D2 affinity / fast dissociation (quetiapine, clozapine), "hit and run" pharmacology

Diagram description: Draw a sagittal brain section showing: VTA (mesolimbic → NAc; mesocortical → PFC), SN (nigrostriatal → striatum), hypothalamus (tuberoinfundibular → pituitary). Color-code each pathway. Label clinical consequences of blockade at each endpoint.

D. SUMMARY TABLE [1]

PATHWAY	↑ ACTIVITY	↓ ACTIVITY / BLOCKADE
Mesolimbic	Psychosis, addiction, mania	Anhedonia, depression
Mesocortical		Negative symptoms, cognitive deficit, ADHD
Nigrostriatal	Dyskinesia, tics	Parkinsonism, EPS
Tuberoinfundibular	Normal prolactin suppression	Hyperprolactinemia

Q7: "Discuss serotonin-related pathways and its relevance to psychiatric disorders.": 10 marks

EXAM PEARL

Long essay candidate.

EXAM STRATEGY

Pathway anatomy first, then receptor subtypes (table), then disorder-by-disorder relevance. Overlap with Q8.

A. SEROTONIN (5-HYDROXYTRYPTAMINE, 5-HT): BASICS [2]

Synthesis: Tryptophan → (tryptophan hydroxylase, **TPH**, rate-limiting) → 5-hydroxytryptophan (5-HTP) → (aromatic L-amino acid decarboxylase) → **Serotonin (5-HT)**

Degradation: MAO-A → 5-HIAA (5-hydroxyindoleacetic acid; measurable in CSF, low in suicidal patients)

Storage: SERT (serotonin transporter) mediates reuptake. Stored in vesicles by VMAT2.

Location: Only ~2% of body's serotonin is in the CNS. 95% is in the gut (enterochromaffin cells). Remainder in platelets.

B. SEROTONERGIC PATHWAYS [3]

Origin: Raphe nuclei (midline brainstem), especially:

- **Dorsal raphe nucleus (DRN)**, largest; projects widely to cortex, limbic, basal ganglia
- **Median raphe nucleus (MRN)**, projects to hippocampus, septum

Projections (ascending):

PROJECTION	TARGET	FUNCTION
Raphe → Prefrontal cortex	DLPFC, OFC	Mood, impulse control, decision-making
Raphe → Limbic system (amygdala, hippocampus, cingulate)	Emotional regulation	Anxiety, fear conditioning, emotional memory
Raphe → Basal ganglia	Caudate, putamen	Motor behavior, OCD (cortico-striato-thalamo-cortical circuit)
Raphe → Hypothalamus	Feeding, sleep, temperature, sexual function	Appetite, circadian rhythm, thermoregulation
Raphe → Spinal cord (descending)	Dorsal horn	Pain modulation (descending inhibitory pathway)
Raphe → Brainstem (emetic center)	Area postrema, NTS	Nausea/vomiting (5-HT3)

C. SEROTONIN RECEPTOR SUBTYPES (14 SUBTYPES IN 7 FAMILIES) [2]

RECEPTOR	MECHANISM	LOCATION	CLINICAL SIGNIFICANCE
5-HT1A	Gi → ↓cAMP	Raphe (autoreceptor); hippocampus, cortex	Buspirone (partial agonist) → anxiolytic. SSRIs desensitize presynaptic 5-HT1A autoreceptors (explains 2-4 week lag).

RECEPTOR	MECHANISM	LOCATION	CLINICAL SIGNIFICANCE
5-HT _{1B/1D}	G _i → ↓cAMP	Cranial blood vessels; terminal autoreceptor	Triptans (agonists) → migraine treatment
5-HT _{2A}	G _q → ↑IP ₃ /DAG	Cortex, platelets	Psychedelic effects (LSD, psilocybin are agonists). Atypical antipsychotics are 5-HT _{2A} antagonists → ↓EPS, improved negative symptoms. Pimavanserin (inverse agonist) → Parkinson's psychosis.
5-HT _{2C}	G _q → ↑IP ₃ /DAG	Choroid plexus, cortex, hypothalamus	↑ → anorexia, anxiety; blockade → weight gain (olanzapine, mirtazapine). Lorcaserin (agonist, withdrawn) → weight loss.
5-HT ₃	Ionotropic, Na ⁺ , K ⁺	Area postrema, GI tract	Ondansetron (antagonist) → antiemetic. 5-HT ₃ blockade contributes to anxiolysis of mirtazapine.
5-HT ₄	G _s → ↑cAMP	GI tract, CNS	GI motility; prucalopride for constipation. Procognitive properties under study.
5-HT ₆	G _s → ↑cAMP	Cortex, hippocampus, striatum	Cognition. 5-HT ₆ antagonists investigated for Alzheimer's.
5-HT ₇	G _s → ↑cAMP	Hypothalamus, thalamus, hippocampus	Circadian rhythm, mood. Blockade by lurasidone/vortioxetine may contribute to antidepressant/procognitive effects.

D. RELEVANCE TO PSYCHIATRIC DISORDERS [3]

1. Depression

- **Monoamine hypothesis:** 5-HT deficit → depression. Evidence: reserpine (depletes 5-HT) → depression; tryptophan depletion → relapse in remitted patients
- SSRIs (fluoxetine, sertraline, etc.), block SERT → ↑ synaptic 5-HT
- SNRIs, TCAs, MAOIs also increase 5-HT

- Low CSF 5-HIAA correlates with suicidality (especially violent/impulsive attempts)

2. Anxiety Disorders

- 5-HT modulates amygdala reactivity
- SSRIs are first-line for GAD, panic disorder, social anxiety, OCD, PTSD
- Buspirone (5-HT_{1A} partial agonist), GAD

3. OCD

- Serotonin hypothesis: clomipramine (potent SRI) > desipramine (NRI) in OCD
- Higher SSRI doses needed for OCD vs. depression
- 5-HT dysregulation in cortico-striato-thalamo-cortical (CSTC) circuit

4. Schizophrenia

- 5-HT_{2A} antagonism is the hallmark of atypical antipsychotics
- Psychedelics (5-HT_{2A} agonists) produce perceptual disturbances resembling psychosis
- Pimavanserin, pure 5-HT_{2A} inverse agonist for Parkinson's psychosis

5. Eating Disorders

- 5-HT regulates satiety (5-HT_{2C} in hypothalamus)
- Bulimia: fluoxetine (60 mg) is FDA-approved
- Anorexia: serotonergic dysregulation persists after weight restoration

6. Aggression and Impulsivity

- Low serotonergic tone → impulsive aggression (low 5-HIAA in CSF)
- SSRIs reduce impulsive aggression in personality disorders

7. Sleep

- 5-HT from DRN promotes wakefulness; involved in sleep-wake regulation
- SSRIs suppress REM sleep, increase REM latency

8. Pain

- Descending serotonergic pathways from raphe → dorsal horn modulate pain
- SNRIs (duloxetine) and TCAs (amitriptyline), analgesic via 5-HT + NE

(See Q8 for neurochemistry focus, Q14/Q15 for serotonin syndrome)

Q8: "Describe neurochemistry of serotonin. Discuss the role of serotonin in psychiatric disorders.": 10 marks

EXAM STRATEGY

Heavy on neurochemistry (synthesis, metabolism, receptors, transporter) for first half. Second half overlaps with Q7, cross-reference but write concisely.

A. NEUROCHEMISTRY OF SEROTONIN [5]

Synthesis:

1. **Tryptophan** (essential amino acid from diet) → crosses BBB via large neutral amino acid transporter (competes with other amino acids, explains high-carb meals increasing brain tryptophan)
2. Tryptophan → **5-Hydroxytryptophan (5-HTP)** by enzyme **tryptophan hydroxylase (TPH)**, **rate-limiting step**
3. TPH1: peripheral (gut), TPH2: CNS-specific
4. Requires molecular oxygen, iron, and tetrahydrobiopterin (BH4) as cofactors
5. 5-HTP → **Serotonin (5-HT)** by **aromatic L-amino acid decarboxylase (AADC)**, requires pyridoxal phosphate (vitamin B6)

Storage and Release:

- Packaged into vesicles by **VMAT2** (vesicular monoamine transporter 2)
- Released by Ca^{2+} -dependent exocytosis
- Acts on 14 receptor subtypes (7 families: 5-HT1–5-HT7)

Reuptake:

- **SERT (serotonin transporter / SLC6A4)**: Primary mechanism of inactivation
- SERT is the target of SSRIs, SNRIs, TCAs, MDMA (ecstasy, reverses SERT to cause 5-HT release)
- **5-HTTLPR polymorphism**: Short allele associated with reduced SERT expression → increased amygdala reactivity → vulnerability to depression under stress (Caspi et al., 2003, though meta-analyses show complex picture)

Degradation:

- **MAO-A** (monoamine oxidase A) in mitochondria → **5-HIAA** (5-hydroxyindoleacetic acid)
- 5-HIAA excreted in urine (elevated in carcinoid syndrome)
- Low CSF 5-HIAA: biomarker for impulsive aggression and suicidality

Autoreceptor Regulation:

- **5-HT_{1A} autoreceptors** (somatodendritic, on raphe neurons): Detect rising 5-HT → negative feedback → reduce firing
- **5-HT_{1B/1D} autoreceptors** (presynaptic terminal): Reduce 5-HT release
- SSRI therapeutic lag (2–4 weeks): Initially, increased 5-HT activates autoreceptors → reduced firing. Over weeks, autoreceptors **desensitize** → increased serotonergic transmission.

EXAM PEARL

SSRI therapeutic lag = autoreceptor desensitization over 2–4 weeks. Key exam point.

Key pharmacological interactions:

DRUG CLASS · MECHANISM AT 5-HT SYNAPSE

SSRIs Block SERT → ↑ synaptic 5-HT

SNRIs Block SERT + NET

TCAs Block SERT + NET (+ antihistamine, anticholinergic)

MAOIs Block MAO-A → prevent 5-HT degradation

Buspirone 5-HT_{1A} partial agonist

Triptans 5-HT_{1B/1D} agonists

Atypical antipsychotics 5-HT_{2A} antagonists

Trazodone SERT blockade + 5-HT_{2A} antagonism (at low dose, primarily 5-HT_{2A} → sedation)

Vortioxetine SERT blockade + 5-HT_{3/7} antagonism + 5-HT_{1A} agonism + 5-HT_{1B} partial agonism → "multimodal"

MDMA Reverses SERT → massive 5-HT release

B. ROLE IN PSYCHIATRIC DISORDERS [5]

(See Q7 Section D for expanded detail; key points summarized here)

DISORDER	SEROTONIN ABNORMALITY	TREATMENT IMPLICATION
Major depression	↓ 5-HT synthesis, ↓ 5-HT _{1A} binding, ↓ SERT binding	SSRIs, SNRIs, MAOIs
Suicidality	↓ CSF 5-HIAA, ↓ 5-HT _{1A} in PFC, ↓ SERT in brainstem	State-independent biomarker of impulsive suicidality

DISORDER	SEROTONIN ABNORMALITY	TREATMENT IMPLICATION
Anxiety disorders	Amygdala hyperreactivity, 5-HT _{1A} deficit	SSRIs first-line for GAD, panic, social anxiety, PTSD
OCD	5-HT dysregulation in CSTC circuit	High-dose SSRIs, clomipramine
PTSD	5-HT modulates fear extinction	SSRIs (sertraline, paroxetine FDA-approved); MDMA-assisted therapy (5-HT release)
Bulimia	5-HT deficit in hypothalamic satiety circuits	Fluoxetine 60 mg
Impulsive aggression	↓ 5-HT in PFC → disinhibition	SSRIs reduce impulsive aggression
Schizophrenia	5-HT _{2A} hyperactivity	Atypical antipsychotics (5-HT _{2A} blockade)
Insomnia	5-HT _{2A} activation promotes wakefulness	Trazodone (5-HT _{2A} blockade → sedation)
Migraine	5-HT vasoconstriction / dilation imbalance	Triptans (5-HT _{1B} / 1D agonists)

Q9: "Role of glutamate and GABA neurotransmitters in depression.": 10 marks

EXAM STRATEGY

This tests beyond the monoamine hypothesis, examiner wants you to show knowledge of newer glutamate-based models. Cover glutamate thoroughly (6 marks), GABA (3 marks), integration (1 mark).

A. INTRODUCTION [1]

The **monoamine hypothesis** of depression (serotonin/norepinephrine deficit) has been the dominant model but explains only part of the picture. Evidence now strongly supports roles for **glutamate** (excitatory) and **GABA** (inhibitory) neurotransmitter systems in the pathophysiology and treatment of depression.

B. GLUTAMATE IN DEPRESSION [4]

Evidence for glutamatergic dysfunction:

- ↑ Glutamate levels in plasma, CSF, and brain (MRS studies) of depressed patients
- ↑ Glutamate in PFC and limbic regions correlates with severity
- Chronic stress → ↑ glucocorticoids → ↑ glutamate release → **excitotoxicity** → dendritic atrophy and synaptic loss, especially in **PFC and hippocampus**

- Reduced glial cells (astrocytes) in PFC of depressed patients → impaired glutamate clearance → further excitotoxicity
- NMDA receptor: altered subunit expression in postmortem brains of depressed / suicidal patients

NMDA receptor hypofunction model:

- **Ketamine** (NMDA antagonist) produces rapid (within hours) antidepressant effects
- Mechanism: NMDA blockade on **GABAergic interneurons** → disinhibition of glutamate release → **AMPA receptor activation** → **BDNF release** → **mTOR signaling** → rapid synaptogenesis and restoration of synaptic connections in PFC
- This is the "**synaptogenic hypothesis**" of rapid antidepressant action

Therapeutic implications, glutamate-targeting drugs:

AGENT	MECHANISM	STATUS
Ketamine (IV)	NMDA antagonist	Off-label for TRD; rapid onset (hours)
Esketamine (Spravato)	S-enantiomer of ketamine, intranasal	FDA-approved for TRD (2019) and MDD with suicidal ideation (2020)
Memantine	Low-affinity NMDA antagonist	Mixed results in depression trials
Riluzole	Glutamate release inhibitor + enhances glial uptake	Augmentation in TRD (limited evidence)
Lamotrigine	Reduces glutamate release (voltage-gated Na ⁺ channel block)	Effective in bipolar depression
D-cycloserine	NMDA glycine-site partial agonist	Enhances extinction learning in exposure therapy for anxiety / PTSD
AV-101 (L-4-chlorokynurenine)	Glycine-site antagonist	Under investigation
Dextromethorphan/bupropion (Auvelity)	NMDA antagonist + sigma-1 agonist	FDA-approved for MDD (2022)

mGluR targets:

- mGluR5 negative allosteric modulators (NAMs), antidepressant and anxiolytic properties in preclinical studies
- mGluR2/3 antagonists, enhance glutamate release → antidepressant-like effects

C. GABA IN DEPRESSION [4]

Evidence for GABAergic deficit:

- ↓ GABA levels in plasma, CSF, and occipital cortex (MRS) of depressed patients
- ↓ GAD67 (GABA synthesizing enzyme) in PFC of depressed patients (postmortem)
- ↓ GABA-A receptor binding in parahippocampal and temporal cortex
- Reduced GABAergic interneuron density in PFC (specific subtypes: **somatostatin-positive** and **parvalbumin-positive** interneurons)
- Normalize after successful antidepressant treatment (GABA levels rise with SSRIs, ECT)

Neurosteroids and GABA in depression:

- **Allopregnanolone** is an endogenous neurosteroid that is a potent **positive allosteric modulator of GABA-A receptors**
- ↓ Allopregnanolone levels found in depression, especially peripartum depression
- Stress → ↓ allopregnanolone → ↓ GABAergic inhibition → ↑ HPA axis activation → depressive symptoms

Therapeutic implications, GABA-targeting drugs:

AGENT	MECHANISM	STATUS
Brexanolone (Zulresso)	IV allopregnanolone analogue, GABA-A PAM	FDA-approved for postpartum depression (2019)
Zuranolone (Zurzuvae)	Oral neurosteroid, GABA-A PAM	FDA-approved for postpartum depression (2023); under re-view for MDD
SAGE-718	NMDA receptor PAM	Under investigation for cognitive symptoms in depression

Benzodiazepines: Not antidepressants per se, but short-term adjuncts for anxiety/insomnia in depression. GABA-A agonism does not reverse the core depressive syndrome.

D. INTEGRATION: GLUTAMATE-GABA IMBALANCE MODEL [1]

- Depression involves a **disrupted excitatory-inhibitory (E/I) balance** in key circuits (PFC, hippocampus, amygdala)
- Chronic stress → glucocorticoid excess → ↑ glutamate + ↓ GABA → excitotoxicity + loss of inhibitory control
- This leads to: dendritic atrophy (PFC), synaptic loss, reduced neuroplasticity, amygdala hyperactivity
- **Ketamine** and **neurosteroids** may work by rapidly restoring E/I balance and triggering synaptogenesis

- The field is moving from "monoamine restoration" (weeks) to "synaptic repair" (hours-days) as the paradigm for antidepressant action

Diagram description: Draw a balance scale, left side = glutamate (excitatory), right side = GABA (inhibitory). In health: balanced. In depression: glutamate side tips down (excess) and GABA side rises (deficit). Show arrows: chronic stress → glucocorticoids → glutamate excess + GABA deficit → excitotoxicity + HPA overactivation → depression. Treatment: ketamine (blocks excess glutamate signaling), neurosteroids (enhance GABA).

Q10: "Define neurotransmitters. Mono-amine neurotransmitters and its significance in psychiatric disorders.": 10 marks

EXAM STRATEGY

Definition [2], classification of monoamines [2], significance of each monoamine [6]. Focus on the clinical, link each amine to disorders and drugs.

A. DEFINITION [2]

(See Q1 Section A, use same 6-point definition)

A **neurotransmitter** is a chemical substance synthesized in a neuron, stored in vesicles, released in Ca^{2+} -dependent manner upon depolarization, acts on specific postsynaptic receptors, and has a defined inactivation mechanism. Can be mimicked by exogenous application and blocked by specific antagonists.

B. MONOAMINE NEUROTRANSMITTERS: CLASSIFICATION [2]

Monoamines contain one amino group connected to an aromatic ring by a two-carbon chain. They are subdivided into:

SUBGROUP	MEMBERS	SYNTHESIS PRECURSOR
Catecholamines	Dopamine (DA), Norepinephrine (NE), Epinephrine (E)	Tyrosine
Indolamine	Serotonin (5-HT)	Tryptophan
Imidazolamine	Histamine	Histidine

Shared features:

- Synthesized by specific enzymes with rate-limiting steps
- Stored in vesicles by **VMAT2**
- Removed from synapse by **reuptake transporters** (DAT, NET, SERT) and degraded by **MAO** and **COMT**
- All act primarily on **metabotropic (G-protein coupled) receptors**

C. SIGNIFICANCE IN PSYCHIATRIC DISORDERS [6]

1. Dopamine

(See Q2, Q5, Q6 for detailed pathways)

- **Schizophrenia:** Mesolimbic hyperactivity → positive symptoms; mesocortical hypoactivity → negative symptoms
- **Depression:** Mesocortical/mesolimbic deficit → anhedonia
- **Mania:** DA excess contributes to elevated mood, grandiosity
- **ADHD:** PFC DA/NE deficit → inattention
- **Addiction:** Mesolimbic DA surge → reinforcement
- **Parkinson's disease:** Nigrostriatal DA loss
- **Drugs acting on DA:** Antipsychotics (D2 blockers), stimulants (DA/NE releasers), bupropion (NDRI), L-DOPA

2. Serotonin (5-HT)

(See Q7, Q8 for detailed pathways)

- **Depression:** 5-HT deficit; ↓ CSF 5-HIAA correlates with suicidality
- **Anxiety disorders:** Amygdala hyperreactivity; SSRIs first-line
- **OCD:** 5-HT dysfunction in CSTC circuit; high-dose SSRIs
- **Eating disorders:** 5-HT modulates satiety
- **Impulsive aggression:** Low 5-HT → disinhibition
- **Drugs:** SSRIs, SNRIs, TCAs, MAOIs, buspirone, trazodone, vortioxetine

3. Norepinephrine (NE)

- **Origin:** Locus coeruleus (LC) → widespread cortical, limbic, spinal projections
- **Functions:** Arousal, attention, vigilance, fight-or-flight, mood, pain modulation
- **Receptors:** Alpha-1 (postsynaptic, excitatory), Alpha-2 (presynaptic autoreceptor, inhibitory), Beta-1/2/3
- **Depression:** NE deficit model; SNRIs (duloxetine, venlafaxine), NRIs (reboxetine), TCAs increase NE
- **Anxiety/PTSD:** NE hyperactivity → hyperarousal, hypervigilance. **Prazosin** (alpha-1 antagonist) → reduces PTSD nightmares. **Clonidine, guanfacine** (alpha-2 agonists) → reduce NE release
- **ADHD:** NE deficit in PFC. **Atomoxetine** (selective NRI), guanfacine, clonidine
- **Panic disorder:** LC hyperactivity → panic attacks. Yohimbine (alpha-2 antagonist) triggers panic in vulnerable individuals

4. Histamine

- **Origin:** Tuberomammillary nucleus (TMN) of posterior hypothalamus → widespread

- **Receptors:** H1 (Gq, wakefulness, allergy), H2 (Gs, gastric acid), H3 (Gi, presynaptic autoreceptor, regulates HA / other NT release), H4 (immune)
- **Functions:** Wakefulness, appetite, cognition, immune modulation
- **Clinical:**
 - H1 blockade → sedation, weight gain (major side effect of olanzapine, quetiapine, mirtazapine, TCAs, first-generation antihistamine sedatives)
 - H3 antagonists / inverse agonists (**pitolisant**) → promote wakefulness → narcolepsy treatment
 - Antihistamines (diphenhydramine, hydroxyzine) → used as anxiolytics / sedatives in psychiatry

5. Epinephrine

- Relatively minor role in CNS compared to NE
- Synthesized from NE by phenylethanolamine N-methyltransferase (PNMT)
- Primarily adrenal medulla (peripheral stress response)
- CNS: small number of epinephrine neurons in brainstem → involved in autonomic regulation, blood pressure

D. THE MONOAMINE HYPOTHESIS OF DEPRESSION [ADDITIONAL SCORING POINT]

- **Original:** Depression = deficit of monoamines (5-HT, NE, DA)
- **Evidence for:** Reserpine (depletes monoamines) → depression; all effective antidepressants increase monoamines
- **Evidence against:** Antidepressants increase monoamines within hours but therapeutic effect takes weeks; tryptophan depletion causes relapse only in previously depressed (not healthy); no consistent monoamine deficit found in unmedicated depression
- **Revised model:** Monoamine deficit → downstream effects on neuroplasticity (BDNF), HPA axis, neuroinflammation, and glutamate / GABA balance. Antidepressants work by restoring these downstream processes.

Q11: "Major dopaminergic pathways of human brain. Implications and relevance of dopamine in Psychiatry.": 10 marks

EXAM STRATEGY

Virtually identical to Q6. Same 4-pathway structure + clinical relevance. Cross-reference.

(This answer overlaps extensively with Q6. Write the same pathway table and clinical relevance. Key additions/emphasis:)

Answer: Follow Q6 structure exactly.

A. MAJOR DOPAMINERGIC PATHWAYS [5]

PATHWAY	ORIGIN	TARGET	FUNCTION
Mesolimbic	VTA	NAc, amygdala, hippocampus	Reward, motivation, emotional salience
Mesocortical	VTA	PFC (DLPFC, VMPFC)	Executive function, working memory, social cognition
Nigrostriatal	SNpc	Caudate, putamen	Voluntary motor control, procedural learning
Tuberoinfundibular	Arcuate nucleus	Anterior pituitary	Prolactin inhibition
Thalamic	Multiple	Thalamus	Arousal, sensory gating

B. IMPLICATIONS AND RELEVANCE [5]

Summary table, Dopamine in Psychiatric Disorders:

DISORDER	PATHWAY INVOLVED	DA ABNORMALITY	TREATMENT STRATEGY
Schizophrenia (positive sx)	Mesolimbic	↑ DA	D2 antagonists / partial agonists
Schizophrenia (negative/cognitive sx)	Mesocortical	↓ DA	5-HT2A antagonism (atypicals), cariprazine (D3 preferring)
ADHD	Mesocortical	↓ DA / NE	Stimulants (MPH, amphetamines), atomoxetine
Depression (anhedonia)	Mesolimbic / mesocortical	↓ DA	Bupropion, pramipexole
Mania	Mesolimbic	↑ DA	Antipsychotics, lithium
Substance use	Mesolimbic	↑ DA (acute), ↓ DA (chronic)	Naltrexone, disulfiram, contingency management
Parkinson's disease	Nigrostriatal	↓↓ DA	L-DOPA, DA agonists
EPS (antipsychotic)	Nigrostriatal	D2 blockade	Anticholinergics, switch to atypical
Tardive dyskinesia	Nigrostriatal	D2 supersensitivity	VMAT2 inhibitors (valbenazine, deutetrabenazine)

DISORDER	PATHWAY INVOLVED	DA ABNORMALITY	TREATMENT STRATEGY
Hyperprolactinemia	Tuberoinfundibular	D2 blockade	Aripiprazole add-on, switch antipsychotic
Tourette's	Nigrostriatal/ mesolimbic	↑ DA	D2 blockers, aripiprazole
Psychosis in PD	Mesolimbic	↑ DA (from L-DOPA)	Pimavanserin, quetiapine, clozapine

(See Q2, Q5, Q6 for expanded discussions of each pathway)

Q12: "What are the characteristics of a neurotransmitter? Enumerate some inhibitory neurotransmitters.": 10 marks

EXAM STRATEGY

Characteristics in detail [5], inhibitory NTs with brief description of each [5].

A. CHARACTERISTICS (CRITERIA) OF A NEUROTRANSMITTER [5]

A chemical substance must satisfy the following criteria to be classified as a neurotransmitter:

1. **Synthesis:** Must be synthesized within the presynaptic neuron. The necessary precursors and enzymes must be present in the neuron.
1. **Storage:** Must be stored in **synaptic vesicles** at the presynaptic terminal (packaged by vesicular transporters, e.g., VMAT2 for monoamines, VGLUT for glutamate, VGAT for GABA).
1. **Release:** Must be released into the synaptic cleft upon **depolarization** of the presynaptic terminal in a **calcium-dependent** manner (Ca^{2+} influx through voltage-gated Ca^{2+} channels → vesicle fusion → exocytosis).
1. **Receptor action:** Must bind to **specific receptors** on the postsynaptic membrane (or presynaptic, autoreceptors) and produce a measurable biological effect (EPSP or IPSP).
1. **Inactivation:** Must have a mechanism for **termination of action**, one or more of:
 2. **Reuptake** by specific transporters (SERT, DAT, NET, EAAT)
 3. **Enzymatic degradation** (MAO, COMT, AChE, GABA-T)
 4. **Diffusion** away from the synapse
1. **Mimicry and Antagonism:** Exogenous application should **mimic** the effect of nerve stimulation. Specific **antagonists** should block the response.
1. **Identity of action:** The substance released by nerve stimulation must be **identical** to the substance that produces the postsynaptic response when applied experimentally.

Additional modern criteria:

- Can be detected immunohistochemically in the neuron
- Knockout/knockdown of synthesis enzyme should abolish the function

B. INHIBITORY NEUROTRANSMITTERS [5]

1. GABA (Gamma-Aminobutyric Acid), the principal inhibitory NT in the CNS

- Synthesis: Glutamate → (GAD + vitamin B6) → GABA
- Receptors: GABA-A (ionotropic, Cl⁻), GABA-B (metabotropic)
- Produces **IPSPs** by increasing Cl⁻ conductance (hyperpolarization)
- ~40% of CNS synapses are GABAergic
- Clinical: Anxiety (benzodiazepines enhance GABA-A), epilepsy (valproate, vigabatrin ↑ GABA), insomnia (Z-drugs at GABA-A), alcohol action

2. Glycine, principal inhibitory NT in spinal cord and brainstem

- Receptor: Strychnine-sensitive glycine receptor (Cl⁻ channel)
- Important for spinal motor reflex inhibition
- Also co-agonist at NMDA receptor (excitatory, dual role)
- Clinical: Strychnine poisoning (glycine blockade → convulsions), hyperekplexia

3. Serotonin (5-HT), inhibitory in some circuits

- 5-HT_{1A} activation in raphe nuclei → autoinhibition
- 5-HT modulates and often inhibits downstream neurons (e.g., reduces amygdala output)
- Not a pure inhibitory NT, can be excitatory at 5-HT₂/5-HT₃ receptors

4. Dopamine, inhibitory in some circuits

- D₂ receptor activation → Gi → ↓cAMP → inhibitory
- Tuberoinfundibular: DA inhibits prolactin release
- Not purely inhibitory

5. Norepinephrine, inhibitory via alpha-2 receptors

- Alpha-2 autoreceptors → presynaptic inhibition
- Postsynaptic alpha-2 → inhibitory in some brain regions

6. Adenosine, inhibitory neuromodulator

- A₁ receptor → Gi → inhibits neurotransmitter release, reduces neuronal excitability
- Accumulates during wakefulness → promotes sleep
- Caffeine = adenosine antagonist

7. Endocannabinoids (anandamide, 2-AG), inhibitory via retrograde signaling

- CB1 receptor → Gi → reduce presynaptic NT release (both glutamate and GABA)
- Net effect often inhibitory on excitatory transmission

8. Opioid peptides (endorphins, enkephalins, dynorphins), inhibitory

- Mu, kappa, delta receptors → Gi → ↓cAMP, ↑K⁺ conductance, ↓Ca²⁺
- Pain inhibition, reward modulation

Q13: "Define receptors. Discuss various neurotransmitters relevant to affective disorders.": 10 marks

EXAM STRATEGY

Define receptors + classification [3], then discuss NTs in affective disorders (depression + bipolar) [7].

A. DEFINITION AND CLASSIFICATION OF RECEPTORS [3]

A **receptor** is a protein molecule (usually on the cell surface or intracellular) that specifically recognizes and binds a ligand (neurotransmitter, hormone, drug) and transduces this binding event into a cellular response.

Properties of receptors:

- **Specificity:** Binds only structurally complementary ligands
- **Saturability:** Finite number of receptors (can be measured, B_{max})
- **Affinity:** Measured by K_d (dissociation constant)
- **Reversibility:** Ligand binding is typically reversible
- **Signal transduction:** Binding leads to a biological effect

Classification of Neurotransmitter Receptors:

TYPE	MECHANISM	SPEED	EXAMPLES
Ionotropic (ligand-gated ion channels)	Ligand binds → ion channel opens → ion flux	Fast (msec)	GABA-A, NMDA, AMPA, Kainate, Nicotinic ACh, 5-HT ₃ , Glycine-R
Metabotropic (G-protein coupled, GPCRs)	Ligand binds → G-protein → second messenger cascade	Slow (sec-min)	All monoamine receptors (D1-5, 5-HT1-7 except 5-HT ₃ , Alpha/Beta adrenergic, H1-4), Muscarinic ACh, GABA-B, mGluR, opioid, CB1/CB2

TYPE	MECHANISM	SPEED	EXAMPLES
Receptor tyrosine kinases	Ligand binds → autophosphorylation → intracellular signaling	Slow (min-hrs)	Neurotrophin receptors (TrkA, TrkB for BDNF)
Nuclear/Intracellular	Ligand enters cell → binds intracellular receptor → gene transcription	Very slow (hrs-days)	Glucocorticoid receptors, thyroid hormone receptors

G-protein families:

G-PROTEIN	EFFECT	COUPLED RECEPTORS
Gs	↑ cAMP (stimulatory)	D1, D5, 5-HT ₄ , 5-HT ₆ , 5-HT ₇ , Beta-adrenergic, H ₂
Gi	↓ cAMP (inhibitory)	D2, D3, D4, 5-HT _{1A} /1B/1D, Alpha-2, GABA-B, Mu/Delta opioid, CB1
Gq	↑ IP ₃ /DAG (via PLC)	5-HT _{2A} /2B/2C, Alpha-1, H ₁ , M ₁ /M ₃ /M ₅

B. NEUROTRANSMITTERS RELEVANT TO AFFECTIVE DISORDERS [7]

Affective disorders = **Major Depressive Disorder (MDD)** and **Bipolar Disorder (BD)**.

1. Serotonin (5-HT), the most studied

- ↓ 5-HT → depression; ↓ 5-HIAA in CSF → suicidality
- Tryptophan depletion → relapse in remitted depressed patients
- 5-HT_{1A} receptor downregulation in depression
- SSRIs, SNRIs, MAOIs, all increase 5-HT availability
- In bipolar: SSRIs can trigger mania (switch), reflects serotonin-dopamine interaction

2. Norepinephrine (NE)

- ↓ NE → depression (psychomotor retardation, fatigue, poor concentration)
- ↑ NE → mania, mixed states
- Evidence: MHPG (NE metabolite) ↓ in depressed, ↑ in manic patients (some studies)
- Alpha-2 autoreceptor supersensitivity proposed in depression
- Drugs: SNRIs, TCAs (NRI component), mirtazapine (alpha-2 antagonist → ↑ NE)

3. Dopamine (DA)

- ↓ DA (mesocortical/mesolimbic) → anhedonia, psychomotor retardation, lack of motivation, core depression features
- ↑ DA → mania (elevated mood, increased goal-directed activity, grandiosity)

- Evidence: bupropion (NDRI) effective in depression; pramipexole (D3 agonist) augments antidepressants; all antimanic agents reduce DA (antipsychotics, lithium)
- HVA levels: ↓ in depression, ↑ in mania

4. Glutamate

- ↑ Glutamate in PFC/limbic regions in depression (MRS studies)
- Excitotoxicity → synaptic loss → depression
- **Ketamine/esketamine**, NMDA antagonist → rapid antidepressant action
- **Dextromethorphan/bupropion (Auvelity)**, approved for MDD
- Lamotrigine (↓ glutamate release), effective in bipolar depression

5. GABA

- ↓ GABA in cortex/plasma of depressed patients
- ↓ GABAergic interneuron function in PFC
- **Brexanolone** (GABA-A PAM), approved for postpartum depression
- **Zuranolone** (oral GABA-A PAM), approved for postpartum depression
- Valproate (↑ GABA), mood stabilizer in bipolar

6. Acetylcholine (ACh)

- **Cholinergic-adrenergic balance hypothesis** (Janowsky): ↑ ACh / ↓ NE = depression; ↓ ACh / ↑ NE = mania
- Evidence: Physostigmine (AChE inhibitor) → depressive symptoms; scopolamine (muscarinic antagonist) → rapid antidepressant effect (under investigation)
- Nicotinic receptor involvement in mood regulation

7. Neuropeptides and Hormones

- **CRH**: ↑ in depression → HPA axis hyperactivation → hypercortisolism
- **Substance P**: NK1 receptor antagonists showed initial antidepressant promise (not replicated)
- **Thyroid hormones**: T3 augmentation in treatment-resistant depression; hypothyroidism → depression; hyperthyroidism → mania-like symptoms
- **BDNF**: Neurotrophin, not a classical NT but downstream effector, ↓ in depression, ↑ with antidepressant treatment (neuroplasticity hypothesis)

Q14: "Define serotonin syndrome and discuss its treatment.": 10 marks

EXAM STRATEGY

Definition [2], pathophysiology [1], clinical features (Hunter criteria) [3], differential diagnosis [1], treatment [3]. Overlap with Q15.

A. DEFINITION [2]

Serotonin syndrome is a potentially life-threatening adverse drug reaction resulting from **excess serotonergic activity** in the central and peripheral nervous systems. It is caused by therapeutic drug use, intentional overdose, or drug interactions involving serotonergic agents.

It is a **clinical diagnosis**, no confirmatory laboratory test exists.

It occurs due to excessive stimulation of **5-HT_{1A} and 5-HT_{2A} receptors** (centrally and peripherally).

B. ETIOLOGY: COMMON CAUSATIVE COMBINATIONS [1]

MECHANISM · DRUG EXAMPLES

↑ **5-HT synthesis** L-tryptophan

↑ **5-HT release** MDMA (ecstasy), amphetamines, fenfluramine

↓ **5-HT reuptake** SSRIs, SNRIs, TCAs, tramadol, meperidine, dextromethorphan, St. John's Wort

↓ **5-HT metabolism** MAOIs (phenelzine, tranylcypromine, selegiline, linezolid, methylene blue)

Direct 5-HT agonism Triptans, buspirone, LSD, fentanyl

EXAM PEARL

Most dangerous combination: MAOI + SSRI/SNRI → severe/fatal serotonin syndrome. 14-day washout required when switching between MAOI and SSRI (5 weeks for fluoxetine due to long half-life of norfluoxetine).

C. CLINICAL FEATURES [3]

Triad: (1) Neuromuscular excitability, (2) Autonomic dysfunction, (3) Altered mental status

DOMAIN · FEATURES

Neuromuscular Clonus (spontaneous, inducible, ocular, key diagnostic feature), hyperreflexia, myoclonus, rigidity (lead-pipe in severe cases), tremor, hypertonicity

Autonomic Hyperthermia (can be severe, >41°C), diaphoresis, tachycardia, hypertension (or labile BP), mydriasis, diarrhea, flushing

Mental status Agitation, confusion, anxiety, restlessness, delirium, coma (severe)

Hunter Serotonin Toxicity Criteria (most widely accepted diagnostic criteria):

In the presence of a **serotonergic agent**, serotonin syndrome is diagnosed if ANY ONE of:

1. **Spontaneous clonus**
2. **Inducible clonus** + (agitation OR diaphoresis)
3. **Ocular clonus** + (agitation OR diaphoresis)
4. **Tremor** + **hyperreflexia**
5. **Hypertonia** + temperature $>38^{\circ}\text{C}$ + (ocular clonus OR inducible clonus)

Severity spectrum:

- **Mild:** Tremor, hyperreflexia, tachycardia, diaphoresis, mydriasis, diarrhea
- **Moderate:** Clonus (ocular / inducible), agitation, hyperthermia, hyperreflexia
- **Severe:** Spontaneous clonus, severe hyperthermia ($>41.1^{\circ}\text{C}$), rigidity, autonomic instability, delirium, seizures, rhabdomyolysis, DIC, metabolic acidosis, multi-organ failure, death

D. DIFFERENTIAL DIAGNOSIS [1]

CONDITION · DISTINGUISHING FEATURES

Neuroleptic Malignant Syndrome (NMS) Develops over days (vs. hours in SS); **lead-pipe rigidity** with **bradyreflexia**; caused by DA blockade (antipsychotics); elevated CK markedly; no clonus

Malignant hyperthermia Occurs with volatile anesthetics / succinylcholine; rigidity; $\uparrow$ CK

Anticholinergic toxicity Mydriasis, dry skin (vs. diaphoresis in SS), urinary retention, absent bowel sounds

Sympathomimetic toxicity Similar but no clonus / hyperreflexia

EXAM PEARL

Key distinguishing feature of serotonin syndrome: **CLONUS** (especially ocular clonus) + hyperreflexia + rapid onset (hours).

E. TREATMENT [3]

1. **Discontinue ALL serotonergic agents, MOST IMPORTANT STEP**

2. **Supportive care:**

- **Mild:** Observation, IV fluids, benzodiazepines for agitation / myoclonus, cardiac monitoring. Usually resolves within 24–72 hours.
- **Moderate-Severe:** ICU admission

3. **Specific pharmacotherapy:**

AGENT	INDICATION	MECHANISM
Cyproheptadine	First-line serotonin antagonist	Non-selective 5-HT _{1A} /5-HT _{2A} antagonist + antihistamine. 12 mg initial dose (PO/NG) , then 2 mg q2h until improvement. Maintenance: 8 mg q6h. Max 32 mg/day. Only available orally.
Chlorpromazine	Alternative if cyproheptadine unavailable	5-HT _{2A} antagonist. 50–100 mg IM. Risk: hypotension.
Benzodiazepines (diazepam, lorazepam)	Agitation, myoclonus, seizures	GABA-A agonism → reduces serotonergic excitability

4. Hyperthermia management:

- Active cooling (cooling blankets, ice packs, evaporative cooling)
- Benzodiazepines for muscle rigidity (reduces heat generation)
- **Severe (>41.1°C):** Consider **intubation + neuromuscular paralysis** (non-depolarizing agents, succinylcholine CONTRAINDICATED due to rhabdomyolysis/hyperkalemia risk) + mechanical ventilation
- **Antipyretics (paracetamol) are INEFFECTIVE**, hyperthermia is due to muscular hyperactivity, not hypothalamic set-point change

5. Avoid:

- Dantrolene (no evidence of benefit in SS, unlike NMS)
- Bromocriptine (used in NMS, not SS)
- Physical restraints (increase risk of rhabdomyolysis and lactic acidosis)

6. Monitoring:

- Core temperature, vital signs, mental status
- CK, renal function, electrolytes, coagulation (DIC screening in severe cases)

Prognosis: Most cases resolve within **24–72 hours** after stopping the offending agent (depending on drug half-life). Mortality rare with prompt treatment. Deaths typically from severe hyperthermia and multiorgan failure.

(See Q15 for expanded management + prevention focus)

Q15: "Discuss clinical presentation and management of serotonin syndrome. Also focus on preventive steps.": 10 marks

EXAM STRATEGY

Clinical features [3], management [4], prevention [3]. Heavy overlap with Q14, expand the prevention section here.

A. CLINICAL PRESENTATION [3]

(Same as Q14 Section C, use Hunter criteria)

Onset: Typically within **6–24 hours** of drug initiation, dose increase, or addition of a second serotonergic agent. 60% of cases present within 6 hours.

Hunter Criteria: Requires presence of a serotonergic agent + any one of:

1. Spontaneous clonus
2. Inducible clonus + agitation OR diaphoresis
3. Ocular clonus + agitation OR diaphoresis
4. Tremor + hyperreflexia
5. Hypertonia + temperature $>38^{\circ}\text{C}$ + ocular / inducible clonus

Examination findings:

- Lower limb > upper limb clonus
- Hyperreflexia (patellar, ankle)
- Ocular clonus (slow, continuous, lateral eye movements)
- Diaphoresis (wet skin, distinguishes from anticholinergic toxicity where skin is dry)
- Bowel sounds increased (vs. absent in anticholinergic toxicity)

B. MANAGEMENT [4]

(Same principles as Q14 Section E, formatted for quick recall)

Step 1: STOP all serotonergic agents [most critical]

Step 2: Severity-based approach:

SEVERITY	FEATURES	MANAGEMENT
Mild	Tremor, hyperreflexia, tachycardia, diaphoresis	Discontinue drug, observation 24h, supportive care, benzodiazepines PRN
Moderate	Clonus, agitation, hyperthermia ($< 40^{\circ}\text{C}$)	Above + cypheptadine (12 mg then 2 mg q2h), IV fluids, active cooling, ICU monitoring

SEVERITY	FEATURES	MANAGEMENT
Severe	Temp >41°C, rigidity, autonomic instability, delirium/coma	Above + intubation , neuromuscular paralysis (non-depolarizing, e.g., rocuronium/vecuronium), mechanical ventilation, aggressive cooling, DIC management

Key drugs:

- **Cyproheptadine**, first-line specific antidote (5-HT_{2A} antagonist). 12 mg stat PO/NG, then 2 mg q2h. Maintenance: 8 mg q6h.
- **Benzodiazepines**, agitation, myoclonus, seizures, reduces muscular hyperactivity
- **Avoid:** Antipyretics (ineffective), succinylcholine (hyperkalemia risk), physical restraints (↑ rhabdomyolysis)

C. PREVENTIVE STEPS [3]

1. Drug awareness and avoidance of dangerous combinations:

HIGH-RISK COMBINATION · RISK LEVEL

MAOI + SSRI/SNRI Potentially fatal, NEVER combine

MAOI + meperidine/tramadol/dextromethorphan Potentially fatal

SSRI + MAOI (including linezolid, methylene blue) Potentially fatal

SSRI + triptan Moderate risk (FDA warning, but clinical risk appears low)

SSRI + tramadol Moderate risk

SSRI/SNRI + lithium Low-moderate risk

Two serotonergic antidepressants Variable risk based on combination

2. Safe switching protocols:

- **SSRI to MAOI:** Washout of ≥2 weeks (5× half-life). **Fluoxetine** → **MAOI: 5 weeks** (norfluoxetine $t_{1/2}$ = 4–16 days)
- **MAOI to SSRI:** Washout of ≥2 weeks
- When adding serotonergic agents, start low and titrate slowly

3. Patient and prescriber education:

- Educate patients about symptoms of serotonin syndrome, seek emergency care if tremor, rigidity, confusion, fever occur after starting/changing medication
- Warn about OTC serotonergic agents: **dextromethorphan** (in cough syrups), **St. John's Wort**, tryptophan supplements

- **Drug interaction checking** before prescribing (electronic alerts in EMR)
- Coordinate with other prescribers (e.g., neurologist prescribing triptans while psychiatrist prescribes SSRI)

4. Special populations requiring vigilance:

- Elderly (polypharmacy, reduced metabolism)
- Patients on multiple serotonergic agents
- Perioperative patients (fentanyl, meperidine, tramadol, methylene blue, all serotonergic)
- Patients on linezolid (antibiotic, reversible MAOI)

5. Monitoring after initiation:

- When starting serotonergic agents or making combinations, monitor for early signs (tremor, restlessness, diarrhea) within first 24 hours
- Have a low threshold for recognition, mild symptoms can escalate rapidly

SECTION B: NEUROANATOMY PYQs (Q16–Q21)

Q16: "Structure and functions of Basal Ganglion.": 10 marks

EXAM STRATEGY

Name components [2], describe circuitry (direct/indirect pathways) [4], functions [2], clinical [2]. Overlap with Q17.

A. COMPONENTS OF THE BASAL GANGLIA [2]

STRUCTURE	SUBDIVISION	NOTES
Striatum	Caudate nucleus + Putamen (dorsal striatum); Nucleus accumbens (ventral striatum)	Primary input nucleus; receives cortical projections
Globus pallidus	GPe (external) + GPI (internal)	GPI = primary output nucleus (with SNpr)
Subthalamic nucleus (STN)		Excitatory (glutamatergic); key in indirect pathway
Substantia nigra	SNpc (pars compacta, dopaminergic) + SNpr (pars reticulata, GABAergic output)	SNpc provides DA modulation to striatum

Associated structures: Ventral pallidum (limbic output), pedunculopontine nucleus

B. CIRCUITRY: DIRECT AND INDIRECT PATHWAYS [4]

Input: Cortex → Striatum (glutamatergic, excitatory)

Direct Pathway (facilitates movement):

Cortex → Striatum (D1 receptors) → **inhibits** GPi/SNpr (GABAergic) → **disinhibits** thalamus → Thalamus excites cortex → **Movement facilitated**

Indirect Pathway (suppresses movement):

Cortex → Striatum (D2 receptors) → **inhibits** GPe → GPe **disinhibits** STN → STN **excites** GPi/SNpr → GPi/SNpr **inhibits** thalamus → **Movement suppressed**

Hyperdirect Pathway:

Cortex → STN (directly) → GPi → inhibits thalamus → rapid action cancellation (relevant to impulsivity/OCD)

Dopamine's modulatory role:

- **D1 receptors** on direct pathway neurons → facilitates (Go signal)
- **D2 receptors** on indirect pathway neurons → inhibits indirect pathway → net facilitation
- DA from SNpc therefore **promotes movement** via both pathways
- DA loss (Parkinson's) → ↓ direct + ↑ indirect → net inhibition → bradykinesia

Diagram description: Draw a flowchart: Cortex → Striatum (splits into direct and indirect). Direct: Striatum $\xrightarrow{\text{GABA}}$ GPi/SNpr $\xrightarrow{\text{GABA}}$ Thalamus → Cortex. Indirect: Striatum $\xrightarrow{\text{GABA}}$ GPe $\xrightarrow{\text{GABA}}$ STN $\xrightarrow{\text{Glut}}$ GPi/SNpr $\xrightarrow{\text{GABA}}$ Thalamus. Show DA from SNpc to striatum modulating both. Label D1 (direct) and D2 (indirect).

C. FUNCTIONS OF BASAL GANGLIA [2]

FUNCTION · CIRCUIT

Motor planning and execution Dorsal striatum (putamen) → motor cortex loop

Procedural/habit learning Dorsolateral striatum

Cognitive functions (working memory, planning, set-shifting) Caudate → DLPFC loop

Emotional/motivational processing Ventral striatum (NAc) → OFC/ACC loop

Reward processing NAc (mesolimbic DA)

Eye movement control Caudate → frontal eye fields loop

Action selection Direct (Go) vs. Indirect (No-Go) balance

Impulse control Hyperdirect pathway (STN)

D. CLINICAL DISORDERS [2]

DISORDER	PATHOLOGY	FEATURES
Parkinson's disease	Loss of SNpc DA neurons	Bradykinesia, rigidity, resting tremor, postural instability
Huntington's disease	Loss of GABAergic MSNs in striatum (caudate atrophy)	Chorea, cognitive decline, psychiatric symptoms
Hemiballismus	Contralateral STN lesion	Violent flinging movements of proximal limb
OCD	CSTC circuit hyperactivity (caudate)	Obsessions, compulsions, DBS of STN/ventral capsule effective
Tourette syndrome	Striatal DA hyperactivity	Motor/vocal tics
Wilson's disease	Copper deposition in lenticular nucleus (putamen + GP)	Movement disorder + psychiatric symptoms + KF rings
Tardive dyskinesia	D2 supersensitivity in striatum	Choreoathetoid movements (orofacial)
ADHD	Striatal DA/NE dysfunction	Inattention, impulsivity
Addiction	NAc DA dysregulation	Compulsive drug seeking
Depression	Ventral striatum hypoactivity	Anhedonia

(See Q17 for overlapping content with emphasis on dysfunction)

Q17: "Name the components of the basal ganglia. Describe the functions and disorders due to dysfunction of basal ganglia.": 10 marks

EXAM STRATEGY

Components [2], functions [3], disorders [5]. Nearly identical to Q16, emphasize the disorder table here.

A. COMPONENTS [2]

(Same as Q16 Section A)

Core components:

1. **Striatum**, Caudate + Putamen (dorsal); Nucleus accumbens (ventral)
2. **Globus pallidus**, GPe (external) + GPi (internal)
3. **Subthalamic nucleus (STN)**
4. **Substantia nigra**, SNpc (dopaminergic) + SNpr (GABAergic output)

Collective terms:

- **Corpus striatum** = Caudate + Putamen + Globus pallidus
- **Lentiform/Lenticular nucleus** = Putamen + Globus pallidus
- **Neostriatum** = Caudate + Putamen

B. FUNCTIONS [3]

1. **Motor control:** Initiation, scaling, and sequencing of voluntary movements via direct/indirect pathway balance
2. **Procedural learning:** Habit formation, skill learning (riding a bicycle)
3. **Cognitive processing:** Caudate-DLPFC loop → working memory, planning, cognitive flexibility
4. **Emotion/Motivation:** Ventral striatum → reward, motivation, emotional salience
5. **Action selection:** Go (direct pathway, D1) vs. No-Go (indirect pathway, D2), selecting appropriate actions while suppressing inappropriate ones
6. **Impulse control:** Hyperdirect pathway (cortex → STN) enables rapid action cancellation
7. **Eye movements:** Caudate → SNpr → superior colliculus → saccades

C. DISORDERS DUE TO BASAL GANGLIA DYSFUNCTION [5]

Hypokinetic Disorders (↓ movement):

DISORDER	PATHOLOGY	CLINICAL FEATURES	TREATMENT
Parkinson's disease	Degeneration of SNpc dopaminergic neurons (Lewy bodies, alpha-synuclein)	TRAP: Tremor (resting, pill-rolling), Rigidity (cogwheel), Akinesia/bradykinesia, Postural instability. Also: masked facies, micrographia, shuffling gait, depression, dementia	L-DOPA, DA agonists, MAO-B inhibitors, anticholinergics, DBS of STN
Drug-induced parkinsonism	D2 blockade in nigrostriatal pathway (antipsychotics)	Same as PD but bilateral, no tremor predominance	Reduce dose, switch to atypical AP, anticholinergics
Progressive supranuclear palsy	Tau pathology in basal ganglia, brainstem	Vertical gaze palsy, axial rigidity, falls, pseudobulbar palsy	Poor response to L-DOPA

Hyperkinetic Disorders (↑ movement):

DISORDER	PATHOLOGY	CLINICAL FEATURES	TREATMENT
Huntington's disease	Autosomal dominant; CAG repeat expansion in HTT gene; loss of GABAergic MSNs (caudate atrophy)	Chorea, cognitive decline (subcortical dementia), psychiatric symptoms (depression, psychosis, personality change)	Tetrabenazine / deutetrabenazine (VMAT2 inhibitors), antipsychotics
Hemiballismus	Contralateral STN lesion (usually vascular)	Violent, flinging proximal limb movements	DA blockers, tetrabenazine
Tardive dyskinesia	Chronic D2 blockade → receptor supersensitivity (striatum)	Involuntary choreiform / athetoid movements, typically orofacial (lip smacking, tongue protrusion)	Valbenazine, deutetrabenazine (VMAT2 inhibitors, FDA approved). Switch antipsychotic.
Sydenham's chorea	Autoimmune (post-streptococcal) → antibodies against basal ganglia	Chorea, emotional lability, hypotonia	Antibiotics, immunotherapy
Tourette syndrome	Dopaminergic hyperactivity in striatum	Motor + vocal tics (>1 year, onset <18 yrs)	Habit reversal therapy, aripiprazole, haloperidol, clonidine

Psychiatric Disorders with Basal Ganglia Involvement:

DISORDER · BASAL GANGLIA ABNORMALITY

OCD Caudate hyperactivity in CSTC circuit; DBS of ventral capsule/STN effective

ADHD Reduced caudate/putamen volume; DAT density changes

Depression Ventral striatum hypoactivity (anhedonia); reward circuit dysfunction

Addiction NAc DA dysregulation; sensitization and allostatic changes

Schizophrenia Increased D2 receptor density in striatum (PET studies)

Wilson's disease Copper in lenticular nucleus → dysarthria, dystonia, tremor, psychiatric sx (personality change, psychosis, depression)

Q18: "Frontal Lobe function tests.": 10 marks

EXAM STRATEGY

Organize by frontal lobe subregion, then list specific tests for each function. Table format scores well.

A. OVERVIEW OF FRONTAL LOBE FUNCTIONS [2]

FRONTAL SUBREGION · FUNCTIONS

Dorsolateral prefrontal cortex (DLPFC) Executive functions: working memory, planning, set-shifting, abstract reasoning, verbal fluency, judgment

Orbitofrontal cortex (OFC) Impulse control, decision-making, social behavior, personality, reward evaluation

Medial/Anterior cingulate cortex (ACC) Motivation, error monitoring, emotional regulation, attention

Motor cortex (precentral gyrus) Primary motor function

Premotor/Supplementary motor area Motor planning, sequencing

Broca's area (dominant hemisphere) Speech production (expressive language)

B. TESTS OF FRONTAL LOBE FUNCTION [8]

1. Executive Function / DLPFC Tests:

TEST	WHAT IT MEASURES	PROCEDURE
Wisconsin Card Sorting Test (WCST)	Set-shifting, cognitive flexibility, abstract reasoning	Patient sorts cards by color / shape / number; rule changes without warning. Frontal patients show perseverative errors (keep sorting by old rule)
Trail Making Test (Part B)	Cognitive flexibility, set-shifting, sequencing	Connect alternating numbers and letters (1-A-2-B-3-C...). Errors/slow = frontal dysfunction
Tower of London / Tower of Hanoi	Planning, problem-solving	Move disks/beads to match target configuration in minimum moves
Verbal fluency tests	Word generation, lexical/semantic retrieval	Phonemic (FAS): Name words starting with F, A, S in 1 min each. Category (semantic): Name animals in 1 min. Frontal lesions → ↓ phonemic > semantic
Stroop Test	Response inhibition, selective attention	Name the ink color of color-words printed in incongruent colors (e.g., "RED" printed in blue). Interference effect ↑ in frontal dysfunction

TEST	WHAT IT MEASURES	PROCEDURE
Digit Span Backward	Working memory	Repeat digit sequences in reverse order. Forward tests attention (parietal); backward tests frontal working memory
N-back task	Working memory	Identify whether current stimulus matches one shown N trials back
Similarities test	Abstract reasoning	"How are an apple and orange alike?" Concrete answers (both round) vs. abstract (both fruits), frontal patients give concrete answers

2. Behavioral / OFC Tests:

TEST · WHAT IT MEASURES

Iowa Gambling Task Decision-making under uncertainty, reward evaluation. Frontal (OFC) patients continue choosing high-risk/high-loss decks

Go/No-Go task Response inhibition. Press button for "go" stimuli, withhold for "no-go." Frontal patients show impulsive responses

Hayling Sentence Completion Test Response inhibition, initiation. Part 1: Complete sentence (tests initiation). Part 2: Give unrelated word (tests inhibition)

3. Motor Sequencing / Premotor Tests:

TEST · WHAT IT MEASURES

Luria hand sequence (fist-edge-palm) Motor programming, sequencing. Patient reproduces fist→edge→palm sequence. Frontal patients perseverate or cannot learn sequence

Alternating sequences (m-n-m-n) Motor programming. Draw alternating loops and peaks. Frontal patients perseverate

Rhythmic tapping Motor regulation. Tap twice when examiner taps once and vice versa

4. Bedside / Clinical Tests:

TEST · WHAT IT MEASURES

Frontal Assessment Battery (FAB) 6-item bedside screening: similarities, lexical fluency, Luria sequence, conflicting instructions, Go/No-Go, prehension (grasp reflex). Score 0-18.

Montreal Cognitive Assessment (MoCA) Includes frontal items: trail-making, phonemic fluency, abstraction

Primitive reflexes Grasp reflex (contralateral frontal), **palmomental reflex**, **glabellar tap** (Myerson sign), **snout reflex**, **rooting reflex**, all indicate frontal release / disinhibition

Utilization behavior Compulsive use of objects placed within reach (OFC lesion)

Environmental dependency Behavior dictated by environmental cues rather than internal goals

5. Comprehensive Neuropsychological Batteries:

BATTERY · NOTES

Delis-Kaplan Executive Function System (D-KEFS) Standardized battery of 9 tests for executive function

CANTAB (Cambridge Neuropsychological Test Automated Battery) Computerized; includes planning, working memory, set-shifting

Halstead-Reitan Battery Includes Category Test (abstract reasoning), Trail Making

(See Q19 for frontal lobe syndromes, the clinical correlates of these test abnormalities)

Q19: "Describe the clinical features of frontal lobe syndromes.": 10 marks

EXAM PEARL

Long essay candidate.

EXAM STRATEGY

Three classic frontal syndromes organized by region (DLPFC, OFC, medial). Include Phineas Gage reference. Add bedside features.

A. INTRODUCTION [1]

The frontal lobe constitutes ~1/3 of the cerebral cortex and is critical for executive function, personality, social behavior, motivation, and motor control. Frontal lobe syndromes are categorized based on the subregion involved. Historically, the case of **Phineas Gage** (1848), who survived a tamping iron through his OFC, first demonstrated the link between frontal damage and personality change.

B. THREE CLASSIC FRONTAL LOBE SYNDROMES [7]

1. Dorsolateral Prefrontal Syndrome (Dysexecutive Syndrome)

Lesion: DLPFC (Brodmann areas 9, 10, 46)

Impaired executive function Difficulty with planning, organizing, sequencing, problem-solving

Reduced working memory Cannot hold and manipulate information (↓ digit span backward)

Impaired set-shifting Perseveration, stuck on previous response (↑ perseverative errors on WCST)

Reduced verbal fluency ↓ words generated on FAS/category fluency

Poor abstract reasoning Concrete thinking on similarities test

Impaired judgment Poor decision-making, cannot anticipate consequences

Stimulus-bound behavior Responses driven by external stimuli rather than internal goals

Motor programming deficits Failure on Luria hand sequences

Temporal ordering deficits Cannot sequence events chronologically

2. Orbitofrontal Syndrome (Disinhibition Syndrome / Pseudopsychopathic Personality)

Lesion: OFC (Brodmann areas 11, 12, 47)

Disinhibition Impulsive, socially inappropriate behavior (e.g., inappropriate sexual comments, spending, aggression)

Personality change Previously reserved person becomes coarse, tactless, irritable, "not themselves"

Emotional lability Inappropriate jocularity (**Witzelsucht**, tendency to make puns/jokes), euphoria, or irritability

Poor social judgment Cannot read social cues, violates social norms

Impaired risk assessment Fails Iowa Gambling Task, continues risky choices despite losses

Anosmia Due to proximity to olfactory tracts (in OFC lesions from trauma or meningiomas)

Impaired response inhibition Fails Go/No-Go tasks

Environmental dependency/Utilization behavior Picks up and uses objects compulsively

Preserved intellect May perform normally on standard IQ tests but behavior is profoundly changed

Phineas Gage: Classic example, became "fitful, irreverent, impatient, profane" after OFC destruction, despite intact memory and intellect.

3. Medial Frontal / Anterior Cingulate Syndrome (Apathetic/Akinetic Syndrome / Pseudodepressive Personality)

Lesion: Medial frontal cortex, anterior cingulate cortex (ACC), supplementary motor area

Apathy Profound lack of motivation, the cardinal feature

Akinetic mutism (severe) Awake and aware but makes no voluntary movement or speech

Abulia Lack of will or initiative; reduced spontaneous behavior

Reduced emotional responsiveness Flat affect, emotional blunting (can mimic depression)

Urinary incontinence Due to loss of medial frontal control over micturition

Lower limb weakness (bilateral lesions) Medial motor cortex represents lower limbs

Alien hand syndrome (supplementary motor area lesion), hand acts with a "will of its own"

Reduced verbal output Not aphasia, simply reduced drive to communicate

Impaired error detection ACC dysfunction → cannot monitor and correct mistakes

C. OTHER FRONTAL LOBE FEATURES [1]

FEATURE · LOCALIZING VALUE

Broca's aphasia Dominant hemisphere (usually left) posterior inferior frontal gyrus, non-fluent, effortful speech with preserved comprehension

Motor deficits Contralateral hemiparesis (precentral gyrus lesion)

Gait apraxia Bilateral medial frontal, magnetic gait (feet "glued to floor")

Primitive reflexes Grasp, palmomental, snout, rooting, glabellar, indicate frontal release (loss of frontal inhibition of brainstem reflexes)

Seizures Frontal lobe epilepsy, brief, nocturnal, bizarre hypermotor seizures

Confabulation Especially with orbitofrontal damage (also basal forebrain)

D. CAUSES OF FRONTAL LOBE SYNDROMES [1]

- **Traumatic brain injury** (most common, frontal and temporal lobes are most vulnerable to contrecoup injury)
- **Cerebrovascular disease** (ACA territory infarcts → medial frontal; MCA → dorsolateral)

- **Tumors** (meningiomas, especially olfactory groove, falx; gliomas)
- **Frontotemporal dementia** (FTD), behavioral variant involves OFC and medial frontal atrophy
- **Neurosyphilis** (GPI, general paresis of the insane)
- **Multiple sclerosis** (white matter lesions disconnecting frontal circuits)
- **Normal pressure hydrocephalus** (triad: gait apraxia, incontinence, dementia, frontal features)
- **Alcoholic brain damage** (frontal atrophy)

Q20: "What is Chrono-biology? How is it relevant to Psychiatry?": 10 marks

EXAM STRATEGY

Define chronobiology [2], describe circadian system [3], psychiatric relevance [5]. Cover depression, bipolar, schizophrenia, and chronotherapeutics.

A. DEFINITION [2]

Chronobiology is the scientific study of **biological rhythms**, cyclic variations in physiological and behavioral processes. It encompasses:

RHYTHM TYPE	PERIOD	EXAMPLES
Circadian	~24 hours	Sleep-wake cycle, cortisol secretion, body temperature, melatonin
Ultradian	< 24 hours	REM-NREM cycles (~90 min), hormonal pulsatile secretion
Infradian	> 24 hours	Menstrual cycle (~28 days), seasonal rhythms
Circannual	~1 year	Seasonal affective disorder pattern

The **master clock** is the **suprachiasmatic nucleus (SCN)** of the anterior hypothalamus.

B. THE CIRCADIAN SYSTEM [3]

The SCN:

- Located above the optic chiasm in the anterior hypothalamus
- Contains ~20,000 neurons with intrinsic rhythmicity
- Receives light input via the **retinohypothalamic tract (RHT)** from **intrinsically photosensitive retinal ganglion cells (ipRGCs)** containing **melanopsin** (sensitive to blue light ~480 nm)
- Generates an endogenous rhythm of ~24.2 hours (slightly longer than 24h)

- Entrained (synchronized) to the environment primarily by **light** (the dominant **zeitgeber**)

Molecular clock mechanism:

- **Transcription-translation feedback loop:**
- CLOCK + BMAL1 proteins → activate transcription of **PER** and **CRY** genes
- PER and CRY proteins accumulate → inhibit CLOCK/BMAL1 → ↓ their own transcription
- Cycle takes ~24 hours
- Clock gene polymorphisms associated with mood disorders, chronotype, and sleep disturbances

Key circadian outputs:

- **Melatonin:** Synthesized by pineal gland; suppressed by light; ↑ at night → promotes sleep. Tryptophan → serotonin → N-acetylserotonin → melatonin (enzyme: AANAT, rate-limiting)
- **Cortisol:** Peak in early morning (6–8 AM); nadir at midnight. Circadian HPA axis regulation
- **Core body temperature:** Lowest at ~4 AM; highest at ~6 PM
- **Sleep propensity:** Two-process model, Process S (homeostatic sleep drive, adenosine accumulation) + Process C (circadian alerting signal from SCN)

C. RELEVANCE TO PSYCHIATRY [5]

1. Major Depressive Disorder (MDD)

- **Circadian abnormalities:** Phase advance of circadian rhythms (early morning awakening, shortened REM latency, early cortisol rise)
- **DST non-suppression:** HPA axis circadian disruption, dexamethasone fails to suppress cortisol
- **Sleep disturbances:** Insomnia (most common), hypersomnia, early morning awakening
- **Diurnal mood variation:** Mood typically worst in morning (melancholic subtype)
- **Seasonal Affective Disorder (SAD):** Depression recurring in winter (reduced daylight) → phase delay of circadian rhythms → treated with **bright light therapy** (10,000 lux, 30 min in morning)

2. Bipolar Disorder

- **Social Zeitgeber Theory (Ehlers):** Disruption of social rhythms (sleep, meals, activity) destabilizes circadian rhythms → triggers mood episodes
- **Mania:** markedly reduced sleep need (not insomnia, patient doesn't feel tired)
- **Depression:** hypersomnia or insomnia

- **Interpersonal and Social Rhythm Therapy (IPSRT)**, evidence-based psychotherapy stabilizing daily routines
- **Dark therapy:** Exposure to darkness/blue-light blocking glasses in evening → may reduce manic symptoms
- Clock gene polymorphisms (CLOCK, PER3, ARNTL) associated with bipolar susceptibility

3. Sleep Disorders

- **Circadian rhythm sleep-wake disorders:**
- **Delayed sleep-wake phase disorder (DSWPD):** Sleep onset and wake delayed by 2+ hours. Common in adolescents. Treatment: morning bright light + evening melatonin
- **Advanced sleep-wake phase disorder (ASWPD):** Early sleep onset and wake. Common in elderly. Treatment: evening bright light
- **Non-24-hour sleep-wake disorder:** Free-running rhythm (>24h). Common in blind individuals (no light entrainment). Treatment: tasimelteon (melatonin agonist)
- **Shift work disorder:** Misalignment between work schedule and circadian rhythm
- **Jet lag disorder**
- **Irregular sleep-wake rhythm disorder**

4. Schizophrenia

- Circadian disruption is nearly universal, sleep-wake fragmentation, reduced melatonin amplitude
- May contribute to cognitive dysfunction
- Clock gene variants associated with schizophrenia risk

5. ADHD

- Delayed circadian phase common (delayed melatonin onset)
- Sleep-onset insomnia highly prevalent
- Melatonin useful adjunct for sleep in ADHD

6. Chronotherapeutics, Therapeutic Applications:

INTERVENTION	MECHANISM	INDICATION
Bright Light Therapy (BLT)	Phase-advances circadian rhythm; suppresses melatonin; ↑ 5-HT	SAD (first-line), non-seasonal depression (augmentation), DSWPD, perinatal depression
Sleep deprivation therapy (wake therapy)	Total or partial sleep deprivation (especially late-night/early-morning)	Rapid (hours) antidepressant effect in ~60% MDD/bipolar depression. Transient, sustained with BLT + sleep phase advance

INTERVENTION	MECHANISM	INDICATION
Melatonin	MT1/MT2 agonist; chronobiotic + mild soporific	DSWPD, jet lag, insomnia in elderly / ADHD / ASD
Agomelatine	MT1/MT2 agonist + 5-HT _{2C} antagonist	MDD, resynchronizes circadian rhythms
Ramelteon	MT1/MT2 agonist	Sleep-onset insomnia
Tasimelteon	MT1/MT2 agonist	Non-24-hour disorder in blind
Suvorexant/Lemborexant	Dual orexin receptor antagonists (DORAs)	Insomnia (circadian-complementary)
IPSRT	Stabilizes social zeitgebers	Bipolar disorder
Dark therapy / Blue-light blocking	Reduces circadian-disruptive light in evening	Mania, insomnia

Q21: "Functions of Pineal Gland.": 10 marks

EXAM STRATEGY

Anatomy [1], melatonin synthesis [3], functions [4], clinical relevance [2].

A. ANATOMY [1]

- Small (~8 mm), pine cone-shaped endocrine gland
- Located at the **epithalamus**, posterior to the third ventricle, between the superior colliculi
- Outside the blood-brain barrier (highly vascularized)
- Contains **pinealocytes** (produce melatonin) and glial cells
- Receives sympathetic innervation via a multisynaptic pathway: **Retina** → **SCN** → **paraventricular nucleus (PVN)** → **intermediolateral cell column of spinal cord** → **superior cervical ganglion** → **pineal gland** (norepinephrine release on beta-1 receptors stimulates melatonin synthesis)
- Calcifies with age ("brain sand" / corpora arenacea), visible on X-ray; shift indicates space-occupying lesion

B. MELATONIN SYNTHESIS AND REGULATION [3]

Synthesis pathway:

1. **Tryptophan** → (tryptophan hydroxylase) → **5-HTP** → (AADC) → **Serotonin**
2. **Serotonin** → (arylalkylamine N-acetyltransferase, **AANAT**, rate-limiting, activated by NE via beta-1 → cAMP) → **N-acetylserotonin**

3. N-acetylserotonin → (hydroxyindole-O-methyltransferase, **HIOMT**) → **Melatonin (N-acetyl-5-methoxytryptamine)**

Regulation:

- **Light INHIBITS** melatonin production (light → retina → RHT → SCN → inhibits sympathetic output to pineal)
- **Darkness STIMULATES** melatonin (darkness → SCN disinhibits sympathetic pathway → NE release → beta-1 → cAMP → AANAT activation)
- Peak melatonin: **2–4 AM** ("hormone of darkness")
- Secretion pattern: Low during day, rises in evening (**dim light melatonin onset, DLMO**, gold standard biomarker for circadian phase), peaks at night, falls by morning
- Metabolized by liver (CYP1A2) → 6-hydroxymelatonin → excreted as 6-sulfatoxymelatonin in urine (can measure to assess melatonin production)

Melatonin receptors:

- **MT1** (Gi), promotes sleepiness, inhibits SCN firing
- **MT2** (Gi), phase-shifts circadian rhythm
- **MT3/quinone reductase**, detoxification (less studied)
- Located in SCN, pars tuberalis of pituitary, retina, immune cells, various peripheral tissues

C. FUNCTIONS OF THE PINEAL GLAND [4]

1. Circadian Rhythm Regulation (primary function)

- Melatonin is the **endocrine signal of darkness**
- Feeds back to SCN (MT1, MT2) to reinforce circadian timing
- Entrain peripheral clocks in liver, heart, immune cells
- DLMO is the most reliable marker of circadian phase

2. Sleep Regulation

- Melatonin promotes sleep onset, not a potent hypnotic but a chronobiotic (signals the brain that it is nighttime)
- Opens the "sleep gate" by reducing SCN-mediated alerting signal
- Exogenous melatonin: modestly effective for jet lag, DSWPD, elderly insomnia, pediatric sleep disorders (ADHD, ASD)

3. Seasonal/Reproductive Regulation

- In photoperiodic animals: melatonin duration signals day length → regulates seasonal breeding, coat changes
- In humans: less pronounced but melatonin influences puberty onset (pineal tumors → precocious puberty in some cases)

- Melatonin may modulate GnRH secretion

4. Antioxidant and Neuroprotection

- Melatonin is a potent **free radical scavenger** (directly neutralizes reactive oxygen and nitrogen species)
- Stimulates antioxidant enzymes (superoxide dismutase, glutathione peroxidase)
- Neuroprotective effects in neurodegeneration models (Alzheimer's, Parkinson's)
- ↓ Melatonin levels in Alzheimer's disease may contribute to sundowning and circadian disruption

5. Immune Modulation

- Melatonin enhances immune function: ↑ T-cell proliferation, ↑ NK cell activity, ↑ IL-2
- Immunosuppression seen with chronic melatonin deficiency (elderly, pinealectomy)
- Anti-inflammatory properties, reduces pro-inflammatory cytokines

6. Thermoregulation

- Melatonin promotes heat loss (peripheral vasodilation) → core body temperature drops → facilitates sleep onset
- Circadian temperature rhythm linked to melatonin secretion

7. Anti-tumor Properties

- Epidemiological: night shift workers (suppressed melatonin) have ↑ risk of breast and colorectal cancer
- Melatonin: anti-proliferative, pro-apoptotic effects in cancer cell lines
- WHO: "shift work involving circadian disruption is a probable carcinogen (Group 2A)"

D. CLINICAL RELEVANCE [2]

CLINICAL CONDITION · PINEAL/MELATONIN LINK

Seasonal Affective Disorder Abnormal melatonin duration/phase → BLT suppresses melatonin in morning

Delayed sleep phase disorder Delayed DLMO → exogenous melatonin in evening advances phase

Jet lag Melatonin timed to destination schedule resets circadian phase

Insomnia in elderly ↓ Melatonin with age → prolonged-release melatonin (Circadin)

Non-24-hour disorder (blind) No light entrainment → tasimelteon (MT1/MT2 agonist)

Depression Agomelatine (MT1/MT2 agonist + 5-HT_{2C} antagonist), antidepressant that resynchronizes circadian rhythms

Bipolar disorder Circadian disruption; melatonin administration under investigation as adjunct

ADHD/ASD Delayed melatonin onset → exogenous melatonin effective for sleep onset insomnia

Alzheimer's disease ↓ Melatonin → sundowning; melatonin supplementation may help

Pineal tumors (pinealoma) Destruction → ↓ melatonin → potential precocious puberty (controversial), sleep disruption. Compression of superior colliculi → Parinaud syndrome (upward gaze palsy)

Smith-Magenis syndrome Inverted melatonin rhythm (peak during day) → severe sleep disturbance

SECTION C: SLEEP PYQs (Q22–Q27)

Q22: "Physiology of sleep.": 10 marks

EXAM PEARL

Long essay candidate.

EXAM STRATEGY

Two-process model [2], stages [3], neurobiology [3], functions [2]. This is a very commonly asked question, must be thorough.

A. INTRODUCTION AND TWO-PROCESS MODEL [2]

Sleep is a reversible state of reduced consciousness and responsiveness, actively generated by the brain, essential for physiological restoration.

Borbely's Two-Process Model of Sleep Regulation:

PROCESS	DESCRIPTION	MEDIATORS
Process S (Homeostatic)	Sleep pressure accumulates during wakefulness; dissipates during sleep	Adenosine (accumulates in basal forebrain during wakefulness; caffeine = adenosine antagonist)
Process C (Circadian)	SCN-driven circadian alerting signal; independent of prior sleep	SCN, melatonin (DLMO signals night); varies with ~24-hour cycle

Sleep occurs when Process S is high AND Process C alerting signal is low (typically at night).

B. STAGES OF SLEEP [3]

Sleep is classified by **polysomnography (PSG)**: EEG + EOG + EMG

AASM (American Academy of Sleep Medicine) Classification:

STAGE	EEG FEATURES	CHARACTERISTICS	% OF SLEEP
Wake (W)	Alpha waves (8–13 Hz) when relaxed with eyes closed; beta waves when alert	Eyes open or closed, normal muscle tone	
N1 (NREM Stage 1)	Theta waves (4–7 Hz); vertex sharp waves	Lightest sleep, easily aroused, hypnagogic hallucinations, hypnic jerks	5%
N2 (NREM Stage 2)	Sleep spindles (12–14 Hz bursts) + K-complexes (high-amplitude biphasic waves)	Light sleep; ↓ HR, ↓ temp, ↓ muscle tone. K-complexes = cortical response to stimuli (may protect sleep)	45–55%
N3 (NREM Stage 3 / Slow-Wave Sleep, SWS)	Delta waves (0.5–2 Hz, high amplitude >75 μV), >20% of epoch	Deep / restorative sleep. Hardest to arouse. Growth hormone peak. Memory consolidation (declarative). Parasomnias (sleepwalking, night terrors)	15–20%
REM (R)	Low-voltage, mixed-frequency (resembles wake, "paradoxical sleep"); sawtooth waves	Rapid eye movements, muscle atonia (except diaphragm, extraocular muscles), vivid dreaming, penile erections / clitoral engorgement, irregular HR/RR, ↑ brain metabolism. Memory consolidation (procedural/emotional).	20–25%

Sleep architecture:

- **Sleep cycles:** 4–6 cycles per night, each ~90–110 minutes (ultradian rhythm)
- **Early night:** More SWS (N3)

- **Late night:** More REM sleep (REM periods lengthen across the night)
- **REM latency:** ~90 minutes from sleep onset (shortened in depression, narcolepsy)

C. NEUROBIOLOGY OF SLEEP-WAKE REGULATION [3]

Wake-Promoting Systems (ascending arousal system):

NUCLEUS	NEUROTRANSMITTER	NOTES
Locus coeruleus (LC)	Norepinephrine	Off in REM
Dorsal raphe nucleus (DRN)	Serotonin	Off in REM
Tuberomammillary nucleus (TMN)	Histamine	Antihistamines → sedation
Laterodorsal/pedunculopontine tegmental nuclei (LDT/PPT)	Acetylcholine	Active in wake AND REM
Basal forebrain	Acetylcholine	Cortical activation
Lateral hypothalamus	Orexin/Hypocretin	Stabilizes wakefulness; deficiency → narcolepsy
Ventral periaqueductal gray (vPAG)	Dopamine	Wake maintenance

Sleep-Promoting Systems:

NUCLEUS	NEUROTRANSMITTER	NOTES
Ventrolateral preoptic area (VLPO)	GABA + Galanin	Inhibits all wake-promoting nuclei. Lesion → insomnia
Median preoptic area (MnPO)	GABA	Sleep homeostasis
Parafacial zone	GABA	SWS generation

Flip-Flop Switch Model (Saper):

- VLPO (sleep) and arousal nuclei (wake) are **mutually inhibitory**
- System is bistable, either fully awake or fully asleep (prevents intermediate states)
- **Orexin stabilizes the switch on the wake side** → without orexin, switch is unstable → inappropriate transitions into sleep (narcolepsy with cataplexy)

REM-Sleep Regulation:

- **REM-on neurons:** LDT/PPT (cholinergic), generate REM features
- **REM-off neurons:** LC (NE) and DRN (5-HT), suppress REM. These go silent during REM.
- **Subcoeruleus/sublaterodorsal nucleus:** Generates REM atonia via inhibitory projections to spinal motor neurons (glycinergic/GABAergic)

- **REM without atonia** → REM sleep behavior disorder (RBD), acts out dreams. Preclinical marker for alpha-synucleinopathies (Parkinson's, DLB)

D. FUNCTIONS OF SLEEP [2]

FUNCTION · DETAILS

Memory consolidation SWS → declarative memory (hippocampal-cortical transfer); REM → procedural/emotional memory

Synaptic homeostasis Synaptic downscaling during SWS (Tononi & Cirelli hypothesis), resets for next day's learning

Metabolic clearance Glymphatic system most active during sleep, clears amyloid-beta, tau (Alzheimer's link)

Immune function Sleep deprivation → ↓ NK cell activity, ↑ inflammatory cytokines (IL-6, TNF-alpha)

Hormonal regulation GH peak during SWS; cortisol nadir during early sleep; TSH peak at sleep onset

Thermoregulation Core temperature drops during NREM; dysregulated during REM

Emotional processing REM sleep: emotional memory processing; REM deprivation → irritability, emotional dysregulation

Physical restoration Protein synthesis, tissue repair, growth during SWS

(See Q23 for neurobiology focus, Q24 for expanded stage detail, Q25 for clinical applications)

Q23: "Neurobiology of sleep and wakefulness": 10 marks

EXAM STRATEGY

This wants more neurobiology depth than Q22. Focus on wake systems, sleep systems, flip-flop model, REM regulation, and pharmacological correlates.

A. ASCENDING AROUSAL SYSTEM (WAKEFULNESS) [3]

Two branches of the ascending reticular activating system (ARAS):

Branch 1: Dorsal pathway (thalamic relay)

- LDT/PPT (ACh) → thalamus → cortex
- Enables thalamocortical transmission → EEG desynchronization (wakefulness)

Branch 2: Ventral pathway (extrathalamic)

- LC (NE), DRN (5-HT), TMN (histamine), lateral hypothalamus (orexin), basal forebrain (ACh), vPAG (DA) → directly to cortex and subcortical structures
- Provides diffuse cortical activation

Orexin/Hypocretin System (Key stabilizer):

- ~70,000 neurons in lateral hypothalamus
- Two peptides: Orexin A (OX-A) and Orexin B (OX-B)
- Two receptors: OX1R (binds OX-A preferentially) and OX2R (binds both equally)
- Projects widely to LC, DRN, TMN, basal forebrain, VTA
- **Function:** Stabilizes the flip-flop switch on the wake side; promotes sustained wakefulness; links wake to reward, feeding, stress
- **Loss of orexin neurons:** Narcolepsy type 1 (with cataplexy). CSF orexin < 110 pg/mL is diagnostic.

B. SLEEP-PROMOTING SYSTEM (NREM SLEEP) [2]

VLPO (Ventrolateral Preoptic Area):

- Contains GABAergic and galaninergic neurons
- Active during sleep → inhibits LC, DRN, TMN, orexin neurons
- VLPO lesion (in rats) → 70% reduction in sleep
- Activated by: adenosine (A2A receptors), cytokines (IL-1, TNF- α), prostaglandin D2, warming

Adenosine:

- By-product of ATP metabolism → accumulates during prolonged wakefulness
- Acts on A1 receptors (inhibits wake-promoting neurons) and A2A receptors (activates VLPO)
- **Caffeine** blocks A1 / A2A → promotes wakefulness
- This mediates **Process S** (homeostatic sleep drive)

Melatonin:

- MT1: inhibits SCN firing → reduces alerting signal
- MT2: shifts circadian phase
- Does not directly induce sleep but facilitates the transition (opens "sleep gate")

C. FLIP-FLOP SWITCH MODEL [2]

(See Q22 Section C for description)

- Wake side: LC, DRN, TMN, orexin (mutually reinforcing)
- Sleep side: VLPO (GABA / galanin)
- Mutual inhibition → bistable switch → sharp transitions

- Orexin stabilizes wake side → prevents unwanted sleep intrusions
- Narcolepsy = destabilized switch → state instability (sudden REM intrusions, cataplexy, sleep attacks, hypnagogic hallucinations, sleep paralysis)

Diagram description: Draw two boxes (VLPO on left, arousal nuclei on right) with mutually inhibitory arrows (GABA from VLPO, monoamines from arousal side). Orexin arrow reinforcing the arousal side. Label: orexin loss → destabilized switch → narcolepsy.

D. REM SLEEP NEUROBIOLOGY [2]

REM-on:

- **LDT/PPT (cholinergic):** Generate REM features, cortical activation, PGO waves, rapid eye movements
- **Subcoeruleus nucleus (SLD/SubC):** Generates REM atonia (glutamate → ventral medullary inhibitory neurons → glycine/GABA onto spinal motor neurons)

REM-off:

- **LC (NE) and DRN (5-HT):** Active during wake, progressively less active through NREM, **completely silent during REM**
- **vPAG (GABAergic):** Inhibits SLD during wakefulness

REM regulation:

- Reciprocal interaction model (Hobson & McCarley): Aminergic REM-off and cholinergic REM-on neurons oscillate reciprocally
- During NREM → aminergic tone gradually decreases → cholinergic neurons become disinhibited → REM begins
- REM atonia failure → **REM sleep behavior disorder (RBD)** → dream enactment → alpha-synucleinopathy risk (>80% develop PD/DLB within 15 years)

E. PHARMACOLOGICAL CORRELATES [1]

DRUG	MECHANISM	EFFECT ON SLEEP
Benzodiazepines/Z-drugs	GABA-A PAM	↓ Sleep latency, ↑ N2, ↓ SWS, ↓ REM
DORAs (suvorexant, lemborexant)	Block orexin receptors → destabilize wake	↓ Sleep latency, ↑ total sleep time, relatively preserved architecture
Antihistamines (doxepin, hydroxyzine)	H1 blockade	↑ Sleepiness, ↑ total sleep time
Melatonin agonists (ramelteon)	MT1/MT2	↓ Sleep onset latency, minimal effects on architecture

DRUG	MECHANISM	EFFECT ON SLEEP
SSRIs	↑ 5-HT	↓ REM sleep, ↑ REM latency, can cause insomnia or somnolence
TCAs (amitriptyline)	Antihistamine + anticholinergic + 5-HT/NE reuptake block	Strong REM suppression, ↑ SWS (some)
Trazodone	5-HT _{2A} antagonism + weak SERT block	↑ SWS, used as hypnotic at low dose
Prazosin	Alpha-1 antagonist	Reduces PTSD nightmares (reduces NE-driven dream intensity)
Caffeine	Adenosine antagonist	↓ Sleep, ↓ SWS

Q24: "Define sleep. Describe stages of sleep. Discuss physiology of sleep.": 10 marks

EXAM STRATEGY

Definition [1], stages [4], physiology [5]. Overlap with Q22, emphasis on stages here.

A. DEFINITION [1]

Sleep is a naturally recurring, readily reversible state of reduced consciousness, decreased motor activity, and diminished responsiveness to external stimuli, actively generated by specific brain circuits. It is distinguished from coma and anesthesia by its **reversibility** and from quiet wakefulness by its **reduced awareness**.

Characteristics: Reduced consciousness, stereotypic posture, decreased reactivity to stimuli, reversibility, cyclic recurrence (circadian), homeostatic regulation (sleep debt accumulates).

B. STAGES OF SLEEP [4]

Measured by polysomnography (PSG):

- **EEG:** Brain electrical activity
- **EOG (electrooculography):** Eye movements
- **EMG (electromyography):** Muscle tone (submental/ chin)

NREM Sleep (Non-Rapid Eye Movement), 75–80% of total sleep:

STAGE	EEG	DURATION/CYCLE	KEY FEATURES
N1	Alpha → Theta (4-7 Hz); vertex sharp waves	1–7 min; 5% of total	Transition from wake. Hypnagogic hallucinations (vivid sensory experiences). Hypnic jerks (sudden myoclonic jerks). Slow rolling eye movements. Easy to arouse.
N2	Theta background + Sleep spindles (11-16 Hz, 0.5-1.5 sec bursts) + K-complexes (large biphasic waves, >0.5 sec)	45-55% of total	Definite sleep onset. ↓ Heart rate, ↓ BP, ↓ temperature. Sleep spindles originate from thalamic reticular nucleus → thalamocortical circuits. K-complexes: cortical response to stimuli, may protect sleep continuity.
N3 (SWS)	Delta waves (0.5-2 Hz, >75 μV amplitude), ≥20% of 30-sec epoch	15-20% of total; predominant in first third of night	Deepest sleep. Very hard to arouse (high arousal threshold). GH secretion peaks. Declarative memory consolidation. Glymphatic clearance maximal. Parasomnias: sleep-walking, sleep terrors, confusional arousals. Enuresis.

REM Sleep, 20–25% of total sleep:

EEG Low-voltage, mixed-frequency, resembles wakefulness ("paradoxical sleep"). Sawtooth waves (2-6 Hz, notched). PGO waves (pontine-geniculate-occipital).

Eye movements Rapid, conjugate eye movements (phasic REM)

Muscle tone **Atonia**, complete loss of skeletal muscle tone (except diaphragm and extraocular muscles). Loss of this → RBD

Autonomic Irregular HR, BP, respiratory rate. Penile erections/clitoral engorgement (used to distinguish organic vs. psychogenic ED). Poikilothermic (lost thermoregulation)

Dreams Vivid, narrative, emotionally charged. Recalled if awakened during REM

Brain metabolism ↑ Cerebral blood flow and oxygen consumption (as high as wakefulness)

Memory Procedural and emotional memory consolidation

Cycle position Longer REM periods in second half of night; first REM period ~10 min, later REM periods ~30-60 min

Sleep cycle progression:

N1 → N2 → N3 → N2 → REM → (repeat)

- Cycle length: ~90-110 minutes
- 4-6 cycles per night
- First third of night: SWS dominant
- Last third of night: REM dominant

C. PHYSIOLOGY OF SLEEP [5]

(Combines key elements from Q22 and Q23)

1. Two-Process Model:

- Process S (homeostatic) + Process C (circadian), see Q22 Section A

2. Wake-Sleep Switch (Saper's Flip-Flop):

- VLPO (GABA / galanin) ↔ arousal nuclei (LC / DRN / TMN / orexin), mutually inhibitory
- Orexin stabilizes wakefulness

3. NREM generation:

- VLPO activation → inhibits arousal nuclei → cortical deactivation
- Thalamocortical oscillations generate sleep spindles (N2) and delta waves (N3)
- Thalamic reticular nucleus: pacemaker for spindle generation

4. REM generation:

- LDT / PPT (cholinergic) → REM-on
- LC / DRN silent during REM → REM-off neurons cease
- Subcoeruleus → spinal inhibition → atonia
- PGO waves: ponto-geniculo-occipital spikes → visual imagery in dreams

5. Hormonal changes during sleep:

HORMONE · SLEEP-RELATED PATTERN

Growth hormone Pulsatile release linked to SWS; 70% of daily GH secreted during N3

Cortisol Nadir in first half of night; rises in early morning (circadian)

Prolactin ↑ During sleep (peak 3-5 AM)

TSH Peaks at sleep onset; inhibited during sleep

Melatonin Peaks at 2-4 AM; suppressed by light

Testosterone Peaks during REM (linked to nocturnal erections)

Leptin ↑ During sleep (satiety); sleep deprivation → ↓ leptin, ↑ ghrelin → weight gain

(Cross-reference: Q22 for functions, Q23 for neurobiology detail, Q25 for clinical applications)

Q25: "Describe in detail about various types of sleep disorders in general psychiatry practice and discuss how a disturbance in sleep architecture can be used as a diagnostic tool." 10 marks

EXAM STRATEGY

Classification of sleep disorders [3], sleep architecture as diagnostic tool [4], management principles [3].

A. CLASSIFICATION OF SLEEP DISORDERS (ICSD-3) [3]

1. Insomnia Disorders

- **Chronic insomnia disorder:** Difficulty initiating/maintaining sleep or early morning awakening, ≥ 3 nights/week, ≥ 3 months, with daytime impairment. Most common sleep complaint in psychiatry.
- **Short-term insomnia:** < 3 months
- Comorbid with: depression (80%), anxiety (70%), PTSD, substance use

2. Sleep-Related Breathing Disorders

- **Obstructive Sleep Apnea (OSA):** Recurrent upper airway collapse during sleep → apneas/hypopneas → oxygen desaturation → arousals. AHI ≥ 5 with symptoms or AHI ≥ 15 . Psychiatric relevance: comorbid depression, cognitive impairment, treatment-resistant depression (screen for OSA), ADHD-like symptoms, psychosis (severe sleep deprivation).
- Treatment: CPAP, weight loss, mandibular advancement device

3. Central Disorders of Hypersomnolence

- **Narcolepsy Type 1:** Excessive daytime sleepiness + cataplexy + low CSF orexin (< 110 pg/mL). Also: sleep paralysis, hypnagogic hallucinations, disrupted nocturnal sleep
- **Narcolepsy Type 2:** EDS without cataplexy, normal CSF orexin
- **Idiopathic hypersomnia:** EDS with prolonged sleep, sleep inertia ("sleep drunkenness")

- **Kleine-Levin syndrome:** Recurrent hypersomnia (days-weeks) + cognitive/behavioral disturbance (hyperphagia, hypersexuality, derealization). Primarily adolescent males.

4. Circadian Rhythm Sleep-Wake Disorders

- Delayed sleep-wake phase, advanced phase, non-24-hour, shift work, jet lag, irregular rhythm

5. Parasomnias

NREM PARASOMNIAS (DISORDERS OF AROUSAL) · REM PARASOMNIAS

Sleepwalking (somnambulism): Complex motor behavior during N3. Eyes open, confused, amnesia. **REM Sleep Behavior Disorder (RBD):** Loss of REM atonia → dream enactment (punching, kicking). Preclinical marker for PD/DLB (>80% conversion in 15 years).

Sleep terrors: Sudden arousal from N3 with screaming, autonomic activation, confusion, amnesia. **NOT nightmares.** **Nightmare disorder:** Vivid, frightening dreams during REM; fully awake after, can recall dream. Associated with PTSD.

Confusional arousals: Confused, disoriented behavior on awakening from N3. **Recurrent isolated sleep paralysis:** Inability to move upon waking/falling asleep; conscious but paralyzed. Due to REM atonia persisting into wakefulness.

Sleep-related eating disorder: Eating during partial arousal from NREM.

6. Sleep-Related Movement Disorders

- Restless legs syndrome (RLS), periodic limb movement disorder (PLMD)
- (See Q27 for PLMD detail)

B. SLEEP ARCHITECTURE AS A DIAGNOSTIC TOOL [4]

Key principle: Specific psychiatric disorders produce characteristic polysomnographic signatures.

DISORDER	SLEEP ARCHITECTURE CHANGES	DIAGNOSTIC UTILITY
Major Depression	↓ REM latency (< 65 min, classic finding), ↑ REM density (frequency of eye movements in REM), ↑ first REM period duration, ↓ SWS, ↑ sleep latency, early morning awakening, ↓ sleep efficiency	Shortened REM latency is one of the most replicated biological markers of depression. Can help distinguish MDD from other causes of insomnia
Bipolar Disorder (Mania)	Markedly ↓ total sleep time (may sleep 0-3 hrs without feeling tired), ↓ REM latency	Reduced sleep need (not insomnia) is a cardinal diagnostic feature and early warning sign of mania

DISORDER	SLEEP ARCHITECTURE CHANGES	DIAGNOSTIC UTILITY
PTSD	↑ REM density, REM fragmentation, nightmares during REM, ↓ SWS, ↑ arousals	Dream content + autonomic activation distinguish PTSD nightmares from sleep terrors
Schizophrenia	↓ SWS (correlates with negative symptoms), ↓ REM latency (in some studies), ↓ sleep efficiency, circadian fragmentation	Not diagnostically specific but ↓ SWS correlates with cognitive deficit severity
GAD / Anxiety	↑ Sleep onset latency, ↓ sleep efficiency, ↓ SWS, ↑ N1 (light fragmented sleep)	Contrasts with depression (anxiety = difficulty falling asleep; depression = early morning awakening)
Narcolepsy	Sleep-onset REM periods (SOREMPs), REM within 15 min of sleep onset; MSLT shows mean sleep latency <8 min + ≥2 SOREMPs	MSLT (Multiple Sleep Latency Test) is the gold standard diagnostic test
OSA	Fragmented sleep, ↓ SWS, ↓ REM, frequent arousals, O2 desaturations	AHI on PSG is diagnostic
RBD	Loss of REM atonia on EMG (RSCA, REM sleep without atonia)	Video-PSG required for diagnosis
Alcohol dependence	Acute: ↓ REM, ↑ SWS. Chronic/withdrawal: REM rebound, fragmented sleep, ↓ SWS	REM rebound during withdrawal → vivid nightmares; severe → delirium tremens
Dementia (DLB)	RBD + ↓ SWS + circadian disruption	RBD as early diagnostic marker for DLB (criteria includes it as core feature)

Specific diagnostic applications:

- **MSLT (Multiple Sleep Latency Test):** For narcolepsy diagnosis, measures how quickly patient falls asleep and whether SOREMPs occur during 5 daytime nap opportunities
- **MWT (Maintenance of Wakefulness Test):** Ability to stay awake, used for fitness-to-drive assessments
- **Actigraphy:** Wrist-worn accelerometer; 1-2 week recording for circadian rhythm disorders, insomnia evaluation

C. MANAGEMENT PRINCIPLES [3]

DISORDER · FIRST-LINE TREATMENT

Chronic insomnia CBT-I (Cognitive Behavioral Therapy for Insomnia), stimulus control, sleep restriction, cognitive restructuring, sleep hygiene. Pharmacotherapy: short-term only (Z-drugs, DORAs, doxepin, melatonin agonists)

OSA CPAP; screen in all treatment-resistant depression / fatigue

Narcolepsy Modafinil / armodafinil (EDS), sodium oxybate (cataplexy + EDS + SWS enhancement), pitolisant (H3 inverse agonist)

Circadian rhythm disorders Bright light therapy + melatonin (timed appropriately)

RBD Melatonin (first-line, fewer side effects) or clonazepam; bed safety precautions; screen for neurodegeneration

NREM parasomnias Safety precautions, trigger avoidance (sleep deprivation, alcohol), benzodiazepines (clonazepam)

PTSD nightmares Prazosin (alpha-1 antagonist), Imagery Rehearsal Therapy (IRT)

RLS/PLMD (*See Q27*)

Q26: "Disorders of Sleep wake cycle.": 10 marks

EXAM STRATEGY

Focus on circadian rhythm sleep-wake disorders specifically, plus intrinsic dysregulations. Include narcolepsy and other hypersomnias.

A. CIRCADIAN RHYTHM SLEEP-WAKE DISORDERS (CRSWD) [5]

Underlying mechanism: Misalignment between the endogenous circadian clock (SCN) and the desired / required sleep-wake schedule.

1. Delayed Sleep-Wake Phase Disorder (DSWPD)

- **Description:** Habitual sleep onset and wake times delayed by ≥ 2 hours relative to conventional times
- **Prevalence:** 7-16% of adolescents / young adults
- **Features:** Cannot fall asleep until 2-6 AM; cannot wake until 10 AM-12 PM. Normal sleep quality / duration when allowed to sleep on own schedule. Chronic insomnia (sleep-onset type) and excessive morning sleepiness when forced to conventional schedule
- **Diagnosis:** Sleep diary + actigraphy for ≥ 7 days; DLMO delayed
- **Treatment:**

- **Morning bright light** (10,000 lux, 30 min upon waking) → phase advances circadian clock
- **Evening melatonin** (0.5-3 mg, 4-6 hours before desired sleep) → advances clock
- **Chronotherapy** (progressively delay sleep time by 2-3 hours/day until desired time reached, rarely used, difficult compliance)
- Avoid evening screens/blue light

2. Advanced Sleep-Wake Phase Disorder (ASWPD)

- **Description:** Sleep onset and wake times advanced by ≥ 2 hours (e.g., sleeps 6 PM, wakes 2 AM)
- **Prevalence:** Common in elderly. Familial form (CK1delta/PER2 mutations)
- **Treatment:** Evening bright light (delays clock); avoid morning bright light

3. Non-24-Hour Sleep-Wake Disorder (Free-Running)

- **Description:** Sleep-wake cycle progressively drifts later each day (~24.2 hour period) because the endogenous clock is not entrained to the 24-hour light-dark cycle
- **Prevalence:** >50% of totally blind individuals (no light entrainment via melanopsin/RHT)
- **Features:** Cyclical periods of good sleep (when rhythm aligns with desired schedule) and poor sleep (when misaligned)
- **Treatment:** **Tasimelteon** (Hetlioz, FDA-approved), MT1/MT2 agonist; melatonin

4. Shift Work Disorder

- **Description:** Insomnia and/or excessive sleepiness due to work schedule overlapping normal sleep period
- **Features:** Night/rotating shift workers. ↑ Risk of metabolic syndrome, cardiovascular disease, depression, GI problems, accidents, cancer (WHO Group 2A carcinogen)
- **Treatment:** Strategic napping, caffeine before shift, bright light during shift, dark glasses on commute home, melatonin for daytime sleep, modafinil for sleepiness during shift

5. Jet Lag Disorder

- **Description:** Temporary misalignment after rapid transmeridian travel
- **Features:** Insomnia, daytime sleepiness, GI disturbance, malaise. Eastward travel worse (requires phase advance, harder). ~1 day per time zone to adapt
- **Treatment:** Timed light exposure and melatonin; short-acting hypnotics

6. Irregular Sleep-Wake Rhythm Disorder

- **Description:** No clear circadian rhythm; multiple short sleep bouts across 24 hours
- **Features:** Common in neurodegenerative diseases (Alzheimer's, dementia, SCN degeneration), institutionalized elderly, developmental disabilities

- **Treatment:** Structured light exposure, social scheduling, melatonin

B. OTHER SLEEP-WAKE CYCLE DISORDERS [5]

1. Narcolepsy Type 1 (with cataplexy)

- Loss of orexin neurons → destabilized sleep-wake switch
- **Pentad:** Excessive daytime sleepiness, cataplexy (sudden loss of muscle tone triggered by emotion), sleep paralysis, hypnagogic/hypnopompic hallucinations, disrupted nocturnal sleep
- Diagnosis: MSLT (mean latency <8 min + ≥ 2 SOREMPs) + low CSF orexin
- **Treatment:** Modafinil/armodafinil (EDS), sodium oxybate/oxybate salts (cataplexy + sleep consolidation), solriamfetol, pitolisant

2. Narcolepsy Type 2 (without cataplexy)

- EDS with ≥ 2 SOREMPs on MSLT but no cataplexy, normal CSF orexin

3. Idiopathic Hypersomnia

- EDS with prolonged nighttime sleep (>11 hours) and/or prolonged unrefreshing naps
- Severe sleep inertia ("sleep drunkenness")
- MSLT: mean latency <8 min, <2 SOREMPs (distinguishes from narcolepsy)
- No cataplexy, normal orexin
- Treatment: Modafinil, FDA-approved: **lower-sodium oxybate** (Xywav)

4. Kleine-Levin Syndrome

- Rare; primarily adolescent males
- Recurrent episodes (days-weeks) of hypersomnia + cognitive/behavioral disturbance (hyperphagia, hypersexuality, derealization, apathy)
- Between episodes: normal sleep and behavior
- Etiology: likely autoimmune/hypothalamic
- Treatment: Lithium (prophylaxis); stimulants (during episodes)

5. Sleep-Wake Cycle Disruption in Psychiatric Disorders

DISORDER · PATTERN

Depression Insomnia (often terminal, early morning awakening) or hypersomnia (atypical);
↓ REM latency

Mania Markedly reduced sleep need (not perceived as insomnia), early morning sign

Schizophrenia Circadian disruption, fragmented sleep, delayed phase, reduced SWS

PTSD Insomnia, nightmares, hyperarousal-related sleep fragmentation

Substance use Alcohol: initial sedation, then fragmented sleep (rebound wakefulness); stimulants: insomnia; cannabis: ↓ REM; withdrawal states: severe insomnia, REM rebound

Dementia Sundowning (evening agitation/confusion), circadian fragmentation, reversed sleep-wake cycle

Delirium Severe sleep-wake cycle disruption, often complete reversal

Q27: "Periodic limb movement disorders in sleep." : 10 marks

EXAM STRATEGY

Define PLMD [2], distinguish from RLS [2], pathophysiology [2], diagnosis [2], treatment [2].

A. DEFINITION AND CLINICAL FEATURES [2]

Periodic Limb Movement Disorder (PLMD) is a sleep disorder characterized by repetitive, stereotyped **limb movements** (usually lower extremities) that occur during sleep, causing sleep fragmentation and daytime consequences.

Movement characteristics:

- **Extension of big toe** + dorsiflexion of ankle ± flexion of knee and hip (triple flexion response)
- Duration: 0.5–10 seconds per movement
- Occur in **periodic clusters** at intervals of **5–90 seconds** (typically 20–40 seconds)
- Primarily during **NREM sleep** (especially N1 and N2); less in SWS; absent in REM (due to atonia)
- Patient is usually unaware; bed partner often reports kicking

Consequences:

- Recurrent arousals → fragmented sleep → unrefreshing sleep
- Excessive daytime sleepiness
- Insomnia (difficulty maintaining sleep)

Epidemiology:

- Prevalence increases with age: 4-11% of adults; up to 45% of elderly (>65 years)
- M = F (or slight male predominance)
- >80% of patients with RLS also have PLMs, but PLMD can occur independently

B. PLMD VS. RESTLESS LEGS SYNDROME (RLS): KEY DISTINCTION [2]

FEATURE	PLMD	RLS (WILLIS-EKBOM DISEASE)
Timing	During sleep	During wakefulness (especially rest/evening)
Awareness	Patient unaware (involuntary)	Patient very aware (urge to move)
Symptoms	Repetitive limb movements during sleep → arousals	Uncomfortable sensory symptoms (crawling, burning, aching) in legs + irresistible urge to move; relieved by movement
Diagnosis	PSG required (PLMI ≥ 15 /hour + daytime consequences)	Clinical diagnosis (4 essential criteria, URGE mnemonic)
Relationship	>80% of RLS patients have PLMs	PLMD can occur without RLS
RLS Diagnostic Criteria (IRLSSG):		Urge to move legs (+ uncomfortable sensation), Rest worsens, Gets better with movement, Evening/night predominance

PLMS vs. PLMD:

- **PLMS (Periodic Limb Movements of Sleep):** The PSG finding. Common incidental finding, especially in elderly. Not a disorder unless causing clinical consequences.
- **PLMD:** PLMS + clinical consequences (insomnia, excessive daytime sleepiness) + no better explanation (no RLS, OSA, narcolepsy, medication effect).

C. PATHOPHYSIOLOGY [2]

1. Iron-Dopamine Hypothesis (shared with RLS):

- **Brain iron deficiency** (even with normal serum ferritin) → impaired dopamine synthesis (iron is cofactor for tyrosine hydroxylase)
- Reduced dopaminergic inhibition of spinal cord motor neurons → periodic leg movements
- Supportive evidence: Low CSF ferritin in PLMD/RLS; MRI shows ↓ iron in substantia nigra and thalamus; dopamine agonists are effective treatment
- Serum ferritin <50 ng/mL (some guidelines <75) → warrants iron supplementation

2. Spinal cord excitability:

- PLMs resemble the Babinski response (triple flexion withdrawal)
- Suggests disinhibition of spinal flexor reflex pathways during sleep

- May involve descending dopaminergic, serotonergic, and noradrenergic pathway dysfunction

3. Circadian component:

- PLMs and RLS symptoms both show circadian variation (worse in evening/night)
- Brain iron is lowest in evening → dopamine synthesis lowest → symptoms worst
- Melatonin may modulate dopamine release (complex interaction)

4. Associated conditions:

CONDITION · NOTES

Iron deficiency Most important modifiable risk factor

End-stage renal disease (ESRD) Very high prevalence of PLMS/RLS (20-60%)

Pregnancy 15-25% develop RLS (usually 3rd trimester; resolves postpartum)

Peripheral neuropathy Diabetic, uremic

ADHD Significant comorbidity with PLMs/RLS (may explain some sleep disturbance in ADHD)

Depression Bidirectional relationship

Medications that worsen PLMS/RLS SSRIs/SNRIs (very common cause, increase serotonin, may reduce dopaminergic tone), antipsychotics, antihistamines, antiemetics (metoclopramide)

Medications that improve Dopamine agonists, alpha-2-delta ligands, opioids

D. DIAGNOSIS [2]

Polysomnographic criteria (AASM):

- **PLM definition:** Leg movements lasting 0.5-10 seconds, occurring in series of ≥ 4 consecutive movements, with inter-movement intervals of 5-90 seconds
- **PLMI (Periodic Limb Movement Index):** Number of PLMs per hour of sleep
- Clinically significant: **PLMI ≥ 15 /hour** in adults (≥ 5 /hour in children)
- **PLMAI (PLM Arousal Index):** PLMs associated with EEG arousals; >5 /hour considered significant

Diagnostic workup:

- **PSG:** Required for PLMD diagnosis (but not for RLS, clinical)
- **Serum ferritin:** Check in all patients. Target **$>50-75$ ng/mL** (some experts: >100)
- **Iron studies:** Serum iron, TIBC, transferrin saturation

- **Renal function:** Rule out CKD/ESRD
- **Exclude other conditions:** OSA (can cause PLMs), narcolepsy, medications
- **Leg EMG (anterior tibialis):** Bilateral recording during PSG

E. TREATMENT [2]

1. Address modifiable causes:

- **Iron supplementation:** If ferritin <50-75 ng/mL → oral ferrous sulfate 325 mg + vitamin C (enhances absorption) on empty stomach. If oral fails or ferritin <30 → IV iron (ferric carboxymaltose)
- **Discontinue/substitute offending medications:** SSRIs/SNRIs → consider bupropion (does not worsen; may help); switch antipsychotic

2. Pharmacotherapy:

DRUG CLASS	AGENTS	NOTES
Alpha-2-delta ligands (first-line for RLS; used for PLMD)	Gabapentin enacarbil (FDA-approved for RLS), pregabalin, gabapentin	Reduce PLMs, improve sleep quality. Lower risk of augmentation than DA agonists.
Dopamine agonists	Pramipexole, ropinirole, rotigotine (patch)	Effective but risk of augmentation (worsening of symptoms with chronic use, symptoms occur earlier in day, spread to arms, become more intense). Use lowest effective dose.
Benzodiazepines	Clonazepam (0.25-2 mg)	Reduces arousals rather than PLMs themselves; improves sleep continuity. Risk: sedation, dependence, worsened OSA
Opioids (refractory cases)	Low-dose oxycodone/codeine	Reserved for severe, treatment-resistant cases
Levodopa	Carbidopa-levodopa	Short-acting; highest augmentation risk → not recommended for chronic use

3. Augmentation (key concept):

- Most important long-term complication of dopaminergic treatment
- Features: symptoms begin earlier in the day, intensity increases, spread to upper limbs, reduced efficacy
- Management: taper dopamine agonist, switch to alpha-2-delta ligand, check and treat iron deficiency
- Prevention: use lowest dose, prefer alpha-2-delta ligands as first-line, maintain ferritin >75 ng/mL

4. Non-pharmacological:

- Sleep hygiene
- Regular moderate exercise (not close to bedtime)
- Avoidance of caffeine, alcohol, nicotine
- Compression stockings, leg massage, warm baths (some benefit for RLS; less evidence for PLMD specifically)

QUICK REFERENCE: TOP 5 LONG ESSAY CANDIDATES

RANK	QUESTION	TOPIC	KEY SCORING STRATEGY
1	Q5	Neurotransmitters + Dopamine	Definition + full classification table + 4 DA pathways + disorder table
2	Q7	Serotonin pathways + psychiatric disorders	Pathway anatomy + receptor table (7 types) + 8 disorders
3	Q6	Dopaminergic pathways	5 pathways with anatomy + antipsychotic dilemma + diagram
4	Q22	Sleep physiology	Two-process model + stages table + neurobiology + functions
5	Q1	Neurotransmitters + excitatory NTs	Definition + comparison table (NT vs. neuromodulator) + glutamate in full detail
(alt)	Q19	Frontal lobe syndromes	Three syndromes (DLPFC/OFC/medial) + Phineas Gage + causes

CROSS-REFERENCE MAP

TOPIC	PRIMARY ANSWER	ALSO COVERED IN
NT definition/criteria	Q1, Q5, Q10, Q12	Q2, Q13
NT classification	Q2, Q5, Q10	Q3, Q4
Dopamine pathways	Q6, Q11	Q2, Q5

TOPIC	PRIMARY ANSWER	ALSO COVERED IN
Dopamine in psychiatry	Q2, Q5	Q6, Q10, Q11, Q13
Serotonin pathways/neurochemistry	Q7, Q8	Q10
Serotonin in psychiatric disorders	Q7, Q8	Q10, Q13, Q14, Q15
Serotonin syndrome	Q14, Q15	
Glutamate	Q1, Q3, Q9	Q4
GABA	Q3, Q9	Q4, Q12
Novel NTs	Q4	Q12
Affective disorder NTs	Q13	Q9, Q10
Basal ganglia	Q16, Q17	Q6 (nigrostriatal)
Frontal lobe	Q18, Q19	
Chronobiology	Q20	Q21, Q22
Pineal gland	Q21	Q20
Sleep physiology	Q22, Q23, Q24	Q20
Sleep disorders	Q25, Q26	Q27
PLMD	Q27	Q25, Q26

Mnemonics & Memory Tricks

EXAM STRATEGY

 = Indian cultural reference |  = well-known/classic mnemonic |  = novel mnemonic

1. Dopamine Pathways

 **Mnemonic: "MeMe NiTu"**

MNEMONIC

MeMe NiTu

EXAM PEARL: (sounds like "Mimi ni tu", "me too" in Swahili, or just think of it as "Me-Me, Nit-Tu")

Encodes: The four major dopamine pathways

Expansion:

LETTER	PATHWAY	ORIGIN → TARGET	FUNCTION	HYPER =	HYPO =
Me	Mesolimbic	VTA → Nucleus accumbens	Reward, motivation	Positive symptoms of schizophrenia, addiction	Anhedonia
Me	Mesocortical	VTA → Prefrontal cortex	Cognition, executive function		Negative symptoms, cognitive deficits
Ni	Nigrostriatal	Substantia nigra → Striatum (caudate + putamen)	Movement	Dyskinesia, chorea	Parkinsonism, EPS
Tu	Tuberoinfundibular	Hypothalamus → Pituitary	Inhibits prolactin		Hyperprolactinaemia

Why this works: Four syllables, two letters each, maps 1:1 to four pathways with no ambiguity.



Alternate mnemonic (clinical correlation): "Meso Rewards, Meso Thinks, Nigro Moves, Tubero Milks"

MNEMONIC

Meso Rewards, Meso Thinks, Nigro Moves, Tubero Milks

EXAM PEARL: Each pathway gets an action verb, the verb IS the function.

Expansion:

- Mesolimbic **rewards** → pleasure, motivation, positive symptoms
- Mesocortical **thinks** → working memory, planning, negative / cognitive symptoms
- Nigrostriatal **moves** → voluntary motor control, EPS when blocked
- Tuberoinfundibular **milks** → prolactin inhibition, galactorrhoea when blocked

2. Serotonin Receptor Subtypes



Mnemonic: "1A Anxious, 1B Brakes migraine, 2A Sees things, 2C Craves food, 3 Throws up, 4 Gut moves, 6 Sleeps, 7 Clocks"

MNEMONIC

1A Anxious, 1B Brakes migraine, 2A Sees things, 2C Craves food, 3 Throws up, 4 Gut moves, 6 Sleeps, 7 Clocks

EXAM PEARL: Each receptor number links to a one-word function, the number itself cues the word.

Encodes: Primary function of each major 5-HT receptor subtype

Expansion:

RECEPTOR	KEY FUNCTION	KEY DRUG LINK	MEMORY HOOK
5-HT _{1A}	Anxiolysis, mood regulation	Buspirone (agonist), vilazodone	A = Anxiety relief
5-HT _{1B}	Vasoconstriction (cranial), autoreceptor	Triptans (agonist)	B = Blood vessels / B rain pain
5-HT _{1D}	Similar to 1B, migraine	Triptans	D pairs with B
5-HT _{2A}	Hallucinations, psychedelic effects, platelet aggregation	Atypical antipsychotics (antagonist), LSD (agonist)	2A = 2 see things that Aren't there

RECEPTOR	KEY FUNCTION	KEY DRUG LINK	MEMORY HOOK
5-HT _{2C}	Appetite, weight regulation	Blocked by olanzapine → weight gain; lorcaserin (agonist)	2C = Craving/Calories
5-HT ₃	Nausea/vomiting (CTZ + vagus)	Ondansetron (antagonist)	3 = Three → Throw up
5-HT ₄	GI motility (prokinetic)	Prucalopride, tegaserod	4 = fourward movement of gut
5-HT ₆	Cognition, sleep	Experimental pro-cognitive agents	6 = six → sleep/study
5-HT ₇	Circadian rhythm, mood, cognition	Lurasidone (antagonist), vortioxetine	7 = seven → setting the clock

NEW Bonus: Atypical Antipsychotics' Serotonin Trick: "2A block = Atypical"

EXAM PEARL

All atypical antipsychotics share strong 5-HT_{2A} antagonism (relative to D₂). This is the defining feature. If an exam question asks "what distinguishes typical from atypical", it's the 5-HT_{2A}/D₂ ratio.

3. Serotonin Syndrome

Mnemonic: "HOT: Hyperactive muscles, Overactive reflexes, Tremor/Temperature"

MNEMONIC

HOT, Hyperactive muscles, Overactive reflexes, Tremor/Temperature

EXAM PEARL: Encodes the clinical triad of serotonin syndrome.

Expansion:

1. **Neuromuscular hyperactivity**, clonus (spontaneous, inducible, ocular), hyperreflexia, rigidity, tremor
2. **Autonomic dysfunction**, hyperthermia, tachycardia, diaphoresis, diarrhoea, mydriasis
3. **Mental status changes**, agitation, confusion, hypomania

Hunter Criteria (diagnostic): "CATCH IT"

MNEMONIC

CATCH IT

EXAM PEARL: Hunter Serotonin Toxicity Criteria, presence of serotonergic agent PLUS any one of:

Expansion:

- Clonus (spontaneous) → diagnostic
- Agitation + inducible clonus
- Tremor + hyperreflexia
- Clonus (inducible) + diaphoresis
- Hypertonia + temperature $>38^{\circ}\text{C}$ + ocular clonus
- Inducible clonus (ocular) + agitation/diaphoresis
- Temperature $>38^{\circ}\text{C}$ + ocular clonus

EXAM PEARL

Clonus is king. Spontaneous clonus alone is sufficient. Everything else needs combinations.



Serotonin Syndrome vs NMS Differentiator: "Serotonin is FAST, NMS is SLOW"

FEATURE	SEROTONIN SYNDROME	NMS
Onset	Hours (fast)	Days to weeks (slow)
Reflexes	Hyperreflexia	Hyporeflexia ("lead pipe")
Pupils	Mydriasis	Normal
Bowel sounds	Hyperactive	Hypoactive
Clonus	Present (hallmark)	Absent
Cause	Serotonergic agent added	Dopamine blocker started/dose increased

4. Basal Ganglia Components



Mnemonic: "CPU-SS" 🍷

MNEMONIC

CPU-SS

EXAM PEARL: (like the processor of a computer, the basal ganglia IS the brain's motor processor)

Encodes: Five major components of the basal ganglia

Expansion:

- **C** = Caudate nucleus
- **P** = Putamen
- **U** = Globus pallidus (GPe + GPi)
- **S** = Subthalamic nucleus (STN)
- **S** = Substantia nigra (SNc + SNr)

Why this works: CPU processes commands, the basal ganglia processes motor commands. Two S's at the end for the two "sub-" structures.

Key groupings to remember:

TERM	COMPONENTS	MEMORY HOOK
Striatum	Caudate + Putamen	"Striped" appearance; INPUT station
Lentiform nucleus	Putamen + Globus pallidus	"Lens-shaped"; seen together on axial cut
Neostriatum	Caudate + Putamen	Same as striatum (newer terminology)
Corpus striatum	Caudate + Putamen + Globus pallidus	All three together



Direct vs Indirect Pathway: "Direct = Do it, Indirect = Inhibit it"

- **Direct pathway** (cortex → striatum → GPi/SNr → thalamus → cortex): Net effect = **facilitates** movement. Think "D2 receptor dysfunction" in indirect, but the **D1 receptor** drives the direct path.
- **Indirect pathway** (cortex → striatum → GPe → STN → GPi/SNr → thalamus → cortex): Net effect = **suppresses** movement.
- **Dopamine from SNc** excites direct (D1) and inhibits indirect (D2) → net effect: **MORE** movement. Loss of dopamine (Parkinson's) = less movement.

5. Basal Ganglia Circuits (Cortico-Striato-Thalamo-Cortical Loops)

 **Mnemonic: "CLOCK-M"**

MNEMONIC

CLOCK-M

EXAM PEARL: (the basal ganglia runs like clockwork through five loops)

Encodes: Five parallel circuits through basal ganglia

Expansion:

LETTER	CIRCUIT	CORTICAL ORIGIN	DYSFUNCTION
C	Cognitive (dorsolateral prefrontal)	DLPFC	Executive dysfunction, cognitive symptoms of schizophrenia
L	Limbic (anterior cingulate)	ACC + amygdala + hippocampus	Mood disorders, apathy, OCD
O	Orbitofrontal	OFC	Disinhibition, personality change, OCD
C	oCulomotor	Frontal eye fields	Saccade abnormalities
K	sKeletal motor	SMA, premotor, primary motor	Movement disorders (Parkinson's, Huntington's, tardive dyskinesia)
M		(M for Motor, the most important one, same as K, reinforces it)	

Why this works: CLOCK reminds you the circuits loop, and the M at the end anchors the motor circuit (the one most tested).

6. Frontal Lobe Subdivisions

 **Mnemonic: "DOVe-A"**

MNEMONIC

DOVe-A

EXAM PEARL: (a dove = peace, but damage to frontal lobe = no peace)

Encodes: Four key prefrontal subdivisions + their syndromes

Expansion:

LETTER	REGION	SYNDROME WHEN DAMAGED	KEY FEATURES	MEMORY HOOK
D	DLPFC (dorsolateral prefrontal cortex)	Dysexecutive syndrome	Poor planning, working memory deficits, reduced verbal fluency, perseveration	D = Dysexecutive, "the Director is gone"
O	OFC (orbitofrontal cortex)	Disinhibited/sociopathic syndrome	Impulsivity, poor social judgement, witzelsucht (inappropriate jocularity), Phineas Gage	O = Obnoxious behaviour
V	VMPFC (ventromedial prefrontal cortex)	Impaired decision-making, emotional regulation	Overlaps with OFC; somatic marker hypothesis (Damasio)	V = Value judgments gone
A	ACC (anterior cingulate cortex)	Akinetic mutism / Abulia	Apathy, no spontaneous movement or speech, flat affect	A = Apathy / Abulia



Quick recall: "DLPFC plans, OFC behaves, ACC motivates, VMPFC values"

EXAM PEARL

DLPFC plans, OFC behaves, ACC motivates, VMPFC values.

7. Papez Circuit



Mnemonic: "HMAMCH": "Hippocampus Makes All Memories Come Home"

MNEMONIC

Hippocampus Makes All Memories Come Home

EXAM PEARL: Encodes the sequence of structures in the Papez circuit (the classical emotion-memory circuit).

Expansion:

Hippocampus → Mammillary bodies (via fornix) → Anterior thalamic nucleus (via mammillothalamic tract) → Cingulate gyrus → (Para)Hippocampal gyrus → back to Hippocampus

Stepwise:

1. **Hippocampus**
2. → (via **fornix**) → **Mammillary bodies**
3. → (via **mammillothalamic tract**) → **Anterior thalamic nucleus**
4. → (via anterior limb of internal capsule) → **Cingulate gyrus**
5. → **Hippocampal/parahippocampal gyrus**
6. → back to **Hippocampus**

Why this works: The sentence literally traces the circuit, Hippocampus starts and ends (memories "come home").

 **Alternate (shorter): "HiFo-MaMa-AT-Cing-HiPa"** 

MNEMONIC

HiFo-MaMa-AT-Cing-HiPa

EXAM PEARL: Think of it as a cricket commentary: "Hi Fo! MaMa AT Cing HiPa!" (Hi Forward! Mama at single, hip-pa!)

- **Hippocampus** → **Fornix** → **Mammillary bodies** → **Mammillothalamic tract** → **Anterior Thalamus** → **Cingulate gyrus** → **Hippocampal gyrus** → loop

CLINICAL ANCHOR

Korsakoff syndrome damages mammillary bodies → breaks the Papez circuit → anterograde amnesia + confabulation.

8. Limbic System Components

 **Mnemonic: "AHIMSA CHiP"** 

MNEMONIC

AHIMSA CHiP

EXAM PEARL: (Ahimsa = non-violence; the limbic system is about emotion, when damaged, ahimsa is lost)

Encodes: Major structures of the limbic system

Expansion:

- **A** = **Amygdala** (fear conditioning, emotional valence)
- **H** = **Hippocampus** (memory formation, spatial navigation)

- **I** = Insula (interoception, disgust, empathy, sometimes grouped with limbic)
- **M** = Mammillary bodies (relay in Papez circuit)
- **S** = Septal nuclei (pleasure, reward modulation)
- **A** = Anterior thalamic nucleus (relay station for Papez circuit)
- **C** = Cingulate gyrus (emotion–cognition interface, pain processing)
- **Hi** = Hippocampal gyrus / parahippocampal gyrus (contextual memory)
- **P** = Prefrontal cortex (OFC/VMPFC, limbic integration)

Why this works: "Ahimsa" is culturally intuitive and ties to the emotional core of the limbic system. CHiP is the "chip" that processes it.

Key functional associations:

STRUCTURE	PRIMARY ROLE	LESION EFFECT
Amygdala	Fear, aggression	Kluver-Bucy syndrome (bilateral)
Hippocampus	Memory consolidation	Anterograde amnesia (HM patient)
Cingulate gyrus	Motivation, error detection	Akinetic mutism (anterior), pain asymbolia
Mammillary bodies	Memory relay	Korsakoff syndrome
Septal nuclei	Pleasure/reward	Rage (septal rage in animals)

9. Sleep Stages

 **Mnemonic: "1 Theta drifts, 2 Spindles + K, 3 Delta deep, REM dreams with Beta"**

MNEMONIC

1 Theta drifts, 2 Spindles + K, 3 Delta deep, REM dreams with Beta

EXAM PEARL: Encodes EEG patterns for each sleep stage.

Expansion:

STAGE	OLD NAME	EEG PATTERN	% OF SLEEP	KEY FEATURE
N1	Stage 1	Low-amplitude theta (4-7 Hz), vertex sharp waves	5%	Light sleep, hypnic jerks, easily aroused

STAGE	OLD NAME	EEG PATTERN	% OF SLEEP	KEY FEATURE
N2	Stage 2	Sleep spindles (12-14 Hz bursts) + K-complexes	45-55%	Largest proportion of sleep; memory consolidation begins
N3	Stage 3+4	High-amplitude delta (<2 Hz, >75 uV)	15-20%	Deep/slow-wave sleep; growth hormone surge; parasomnias (sleepwalking, night terrors)
REM	REM	Low-amplitude, mixed frequency (like waking, beta/theta), saw-tooth waves	20-25%	Dreams, atonia, penile erections, REM behaviour disorder if atonia fails

NEW Mnemonic for N2 features: "Spindles K-atch memories"

EXAM PEARL

Sleep spindles and K-complexes in N2 = memory consolidation. "Spindles catch (K-atch) memories."

NEW Sleep architecture rules:

- **First third of night** = mostly N3 (deep sleep)
- **Last third of night** = mostly REM
- REM periods get **longer** as the night progresses
- Sleep cycles last ~90 minutes

MNEMONIC

Deep first, Dreams last

10. Sleep Neurotransmitters

NEW Mnemonic: "GO HAND" (wake-promoting) vs "GAM" (sleep-promoting)

MNEMONIC

MNEMONIC: "GO HAND" vs "GAM" EXAM PEARL: GO HAND = active, arousing. GAM = calm, quieting.

Encodes: Neurotransmitters that promote wakefulness vs sleep

Expansion:

Wake-promoting ("GO HAND", Go! Stay awake!):

- Glutamate
- Orexin/Hypocretin (lateral hypothalamus)
- Histamine (tuberomammillary nucleus, TMN)
- Acetylcholine (basal forebrain, LDT/PPT for REM)
- Noradrenaline/Norepinephrine (locus coeruleus)
- Dopamine (VTA, ventral periaqueductal grey)

Sleep-promoting ("GAM", like gamma, calming):

- GABA (VLPO, ventrolateral preoptic area, the "sleep switch")
- Adenosine (accumulates during wakefulness → sleep pressure; caffeine blocks adenosine receptors)
- Melatonin (pineal gland, SCN-regulated)



Key structure: VLPO (Ventrolateral Preoptic area) = "Master Sleep Switch"

EXAM PEARL

VLPO sends GABAergic inhibition to all wake-promoting centres. Flip-flop model (Saper): VLPO ↔ arousal centres mutually inhibit each other. Orexin stabilises this switch (loss of orexin → narcolepsy = unstable switching).

11. Narcolepsy Tetrad



Mnemonic: "CASH"

MNEMONIC

CASH

EXAM PEARL: Encodes the four cardinal features of narcolepsy.

Expansion:

- **C** = Cataplexy (sudden loss of muscle tone triggered by strong emotions, especially laughter)
- **A** = sleep Attacks / excessive daytime sleepiness (EDS)
- **S** = Sleep paralysis (inability to move at sleep-wake transitions)
- **H** = Hypnagogic (at sleep onset) / Hypnopompic (at waking) hallucinations

Additional high-yield facts:

- Narcolepsy Type 1 = with cataplexy, low CSF orexin/hypocretin (<110 pg/mL)
- Narcolepsy Type 2 = without cataplexy, normal orexin
- Strong HLA-DQB1*06:02 association
- MSLT: mean sleep latency <8 min + ≥2 SOREMPs (sleep-onset REM periods)
- Treatment: modafinil/armodafinil for EDS; sodium oxybate for cataplexy + EDS; solriamfetol; pitolisant (histamine H3 inverse agonist)

Why this works: CASH is universally taught and sticks immediately.

12. Neuroleptic Malignant Syndrome (NMS)

 **Mnemonic: "FALTER"**

MNEMONIC

FALTER

EXAM PEARL: Encodes the key features of NMS, the patient's body is literally "faltering", systems shutting down.

Expansion:

- **F** = Fever (hyperthermia, often >40°C)
- **A** = Autonomic instability (labile BP, tachycardia, diaphoresis)
- **L** = Leukocytosis
- **T** = Tremor / rigidity ("lead pipe" rigidity)
- **E** = Elevated CPK (creatine phosphokinase, often massively elevated, >1000 IU/L)
- **R** = Renal failure (secondary to rhabdomyolysis from sustained rigidity)



Alternate: "FEVER": Fever, Encephalopathy, Vitals unstable, Elevated CPK, Rigidity

Key management facts:

- **Stop the offending agent** (antipsychotic)
- **Dantrolene** (muscle relaxant, reduces rigidity + heat production)
- **Bromocriptine** (dopamine agonist, replaces the blocked dopamine)
- **Supportive:** IV fluids, cooling, ICU monitoring
- Mortality: 5-20% if untreated



NMS vs Serotonin Syndrome (revisited from #3):

EXAM PEARL

"NMS = Rigid and Slow, SS = Clonus and Go", NMS: lead-pipe rigidity, bradyreflexia, slow onset (days), caused by DA blockade. SS: clonus, hyperreflexia, fast onset (hours), caused by serotonin excess.

13. Excitatory vs Inhibitory Neurotransmitters



Mnemonic: "GAG inhibits, GANG excites"

MNEMONIC

GAG inhibits, GANG excites

EXAM PEARL: GAG = silence; GANG = action. Rhyming pair makes them stick together.

Encodes: The major inhibitory and excitatory neurotransmitters

Expansion:

Inhibitory ("GAG", it gags/silences neurons):

- GABA (primary inhibitory NT in the brain)
- Adenosine (inhibitory neuromodulator)
- Glycine (primary inhibitory NT in the spinal cord and brainstem)

Excitatory ("GANG", it fires neurons up):

- Glutamate (primary excitatory NT in the brain, ~90% of synapses)
- Aspartate (excitatory amino acid)
- Norepinephrine (generally excitatory, context-dependent)
- Glutamate (doubled to emphasise: it is THE excitatory neurotransmitter)



The Big Two: "GABA brakes, Glutamate gas"

EXAM PEARL

The brain runs on a balance of GABA (brakes) and glutamate (accelerator). Too much glutamate = excitotoxicity (stroke, seizures). Too much GABA = sedation, coma.

14. GABA-A vs GABA-B Receptors

 **Mnemonic: "A = fast ion Action, B = slow Biochemical (G-protein)"**

MNEMONIC

A = fast ion Action, B = slow Biochemical (G-protein)

EXAM PEARL: Encodes the fundamental difference between GABA-A and GABA-B.

Expansion:

FEATURE	GABA-A	GABA-B
Type	Ionotropic (ligand-gated Cl ⁻ channel)	Metabotropic (G-protein coupled)
Ion	Cl ⁻ influx → hyperpolarisation	K ⁺ efflux / ↓Ca ²⁺ → hyperpolarisation
Speed	Fast (milliseconds)	Slow (seconds)
Location	Postsynaptic (mainly)	Pre- and postsynaptic
Agonist drugs	Benzodiazepines, barbiturates, alcohol, propofol, zolpidem	Baclofen, GHB
Mechanism of BZDs	Increase frequency of Cl ⁻ channel opening	
Mechanism of barbiturates	Increase duration of Cl ⁻ channel opening	
Antagonist	Flumazenil (BZD site), bicuculline (GABA site)	Saclofen, phaclofen

 **Classic mnemonic: "Ben(zodiazepines) opens Frequently, Barbi(turates) stay for a longer Duration"**

MNEMONIC

Benz = Frequency, Barb = Duration



GABA-A binding sites: "The GABA-A receptor is a nightclub with 5 doors"

EXAM PEARL

The GABA-A receptor has 5 subunits (typically 2alpha + 2beta + 1gamma) with distinct binding sites: - **GABA site** (beta subunit), the main entrance - **Benzodiazepine site** (alpha-gamma interface), the VIP door (needs GABA to be present = positive allosteric modulator) - **Barbiturate site** (beta subunit), the back door (can open the channel even without GABA at high doses = direct agonist at high dose) - **Neurosteroid site**, the side door - **Alcohol site**, the emergency exit (enhances GABA at low concentrations) Visualising the receptor as a nightclub with multiple entrances helps remember that different drugs bind different sites on the SAME receptor.

15. Glutamate Receptor Subtypes



Mnemonic: "NAK"

MNEMONIC

NAK

EXAM PEARL: (sounds like "knock", glutamate knocks/excites neurons)

Encodes: Three ionotropic glutamate receptor subtypes

Expansion:

LETTER	RECEPTOR	NAMED AFTER	KEY FEATURES	CLINICAL RELEVANCE
N	NMDA	N-Methyl-D-Aspartate	Voltage-dependent Mg^{2+} block; requires glycine co-agonist; permeable to Ca^{2+} ; slow kinetics	Ketamine, PCP, memantine (antagonists); NMDA-R encephalitis (anti-NMDA antibodies); glutamate hypothesis of schizophrenia; excitotoxicity
A	AMPA	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid	Fast excitation; Na^+ influx; mediates most fast excitatory transmission	Perampanel (antagonist, for epilepsy); CX-516 and other "ampakines" for cognition

LETTER	RECEPTOR	NAMED AFTER	KEY FEATURES	CLINICAL RELEVANCE
K	Kainate	Kainic acid (from seaweed)	Pre- and postsynaptic; modulates transmitter release	Kainic acid used experimentally to create seizure models; less clinically targeted

Plus one metabotropic:

RECEPTOR	TYPE	KEY FEATURE
mGluR (Groups I, II, III)	G-protein coupled	Group I = excitatory (Gq); Groups II & III = inhibitory (Gi)

NEW **NMDA receptor: the "high-maintenance" receptor: "NMDA Needs More Demanding Attention"**

MNEMONIC

NMDA Needs More Demanding Attention

EXAM PEARL: Encodes NMDA receptor's multiple requirements for activation.

Expansion, NMDA needs ALL of these to open:

1. **Glutamate** binding (the main agonist)
2. **Glycine** (or D-serine) co-agonist binding (glycine site)
3. **Membrane depolarisation** (to relieve Mg^{2+} block, voltage-dependent)
4. This is why NMDA is a **coincidence detector**, it only fires when both presynaptic (glutamate) and postsynaptic (depolarisation) activity coincide → basis of **LTP (long-term potentiation)** → learning and memory

NEW **NMDA and Psychiatry: "KPC blocks NMDA"**

MNEMONIC

KPC blocks NMDA

EXAM PEARL: - Ketamine, NMDA antagonist → rapid antidepressant effect (esketamine nasal spray for TRD) **EXAM PEARL:** - PCP (phencyclidine), NMDA antagonist → psychosis model (better model for schizophrenia than amphetamine because it produces BOTH positive AND negative symptoms) **EXAM PEARL:** - Cycloserine (D-cycloserine), partial NMDA agonist at glycine site → augments exposure therapy for anxiety disorders

Quick-Reference Summary Table

#	TOPIC	PRIMARY MNEMONIC	TYPE
1	Dopamine pathways	MeMe NiTu	
2	5-HT receptors	1A Anxious...7 Clocks	
3	Serotonin syndrome	HOT + Hunter criteria	
4	Basal ganglia components	CPU-SS	
5	Basal ganglia circuits	CLOCK-M	
6	Frontal lobe subdivisions	DOVe-A	
7	Papez circuit	Hippocampus Makes All Memories Come Home	
8	Limbic system	AHIMSA CHiP	
9	Sleep stages	1 Theta, 2 Spindles+K, 3 Delta, REM Beta	
10	Sleep neurotransmitters	GO HAND vs GAM	
11	Narcolepsy tetrad	CASH	
12	NMS features	FALTER	
13	Excitatory vs inhibitory	GAG inhibits, GANG excites	
14	GABA-A vs GABA-B	A=fast ion, B=slow G-protein	
15	Glutamate receptors	NAK (knock)	

High-Yield Comparisons

1. Excitatory vs Inhibitory Neurotransmitters

FEATURE	EXCITATORY	INHIBITORY
Action	Depolarise postsynaptic membrane → ↑ firing	Hyperpolarise postsynaptic membrane → ↓ firing
Key examples	Glutamate, Aspartate, Acetylcholine (nicotinic)	GABA, Glycine, Serotonin (some receptors)
Main receptors	NMDA, AMPA, Kainate (glutamate); nAChR	GABA-A, GABA-B; Glycine receptors
Ion flow	Na ⁺ / Ca ²⁺ influx	Cl ⁻ influx (GABA-A) or K ⁺ efflux (GABA-B)
Clinical relevance	Excess → excitotoxicity (stroke, epilepsy, neurodegeneration); Deficit → cognitive impairment	Deficit → seizures, anxiety; Excess → sedation, coma; BZDs/barbiturates enhance GABA

EXAM PEARL

The **glutamate–GABA balance** is the fundamental excitatory–inhibitory axis of the CNS. Nearly all psychiatric drugs modulate this balance directly or indirectly.

2. Serotonin vs Dopamine vs Norepinephrine

FEATURE	SEROTONIN (5-HT)	DOPAMINE (DA)	NOREPINEPHRINE (NE)
Precursor → Synthesis	Tryptophan → 5-HTP → 5-HT (rate-limiting: tryptophan hydroxylase)	Tyrosine → L-DOPA → DA (rate-limiting: tyrosine hydroxylase)	DA → NE (enzyme: dopamine β-hydroxylase)
Key nuclei	Raphe nuclei (dorsal + median)	VTA, Substantia nigra, Arcuate nucleus	Locus coeruleus
Major pathways	Raphe → cortex, limbic, spinal cord, hypothalamus	4 classic pathways (see Table 10)	LC → cortex (diffuse), LC → limbic, descending to spinal cord
Receptor families	5-HT ₁ to 5-HT ₇ (14+ subtypes); 5-HT _{2A} → psychosis; 5-HT _{1A} → anxiety	D1-like (D1, D5): excitatory; D2-like (D2, D3, D4): inhibitory	α ₁ , α ₂ (autoreceptor), β ₁ , β ₂ , β ₃

FEATURE	SEROTONIN (5-HT)	DOPAMINE (DA)	NOREPINEPHRINE (NE)
Psychiatric role	Depression, anxiety, OCD, impulse control, sleep, appetite	Psychosis, reward, motivation, movement, prolactin regulation	Arousal, attention, mood, stress response, fight-or-flight
Key drugs	SSRIs, SNRIs, triptans, buspirone (5-HT _{1A}), ondansetron (5-HT ₃), atypical antipsychotics (5-HT _{2A} block)	Antipsychotics (D2 block), L-DOPA, amphetamines, bromocriptine	SNRIs, TCAs, atomoxetine, clonidine (α_2 agonist), prazosin (α_1 block)

EXAM PEARL

The monoamine hypothesis of depression implicates all three. SSRIs target 5-HT; SNRIs target 5-HT + NE; bupropion targets DA + NE.

3. GABA-A vs GABA-B Receptors

FEATURE	GABA-A	GABA-B
Receptor type	Ionotropic (ligand-gated Cl ⁻ channel)	Metabotropic (G-protein coupled → K ⁺ / ↓Ca ²⁺)
Mechanism	GABA binding → Cl ⁻ influx → fast IPSP → rapid inhibition	G-protein → ↑ K ⁺ efflux / ↓ Ca ²⁺ influx → slow IPSP → slow, prolonged inhibition
Location	Postsynaptic (mainly); ubiquitous in CNS	Pre- and postsynaptic; hippocampus, thalamus, cerebellum
Key drugs	BZDs (positive allosteric modulators), Barbiturates , Zolpidem, Alcohol, Neurosteroids, Flumazenil (antagonist)	Baclofen (agonist); GHB (partial agonist); Saclofen (antagonist, research)
Clinical relevance	Anxiety disorders, insomnia, seizures, alcohol withdrawal, anaesthesia; BZD dependence	Spasticity (baclofen); Alcohol dependence (baclofen off-label); Absence seizures (thalamic GABA-B)

EXAM PEARL

BZDs require GABA to be present (allosteric modulation), they increase **frequency** of Cl⁻ channel opening. Barbiturates increase **duration** of Cl⁻ channel opening and can open channels directly at high doses (hence lethal in overdose).

4. Glutamate Receptors: NMDA vs AMPA vs Kainate

FEATURE	NMDA	AMPA	KAINATE
Type	Ionotropic (Na ⁺ , Ca ²⁺ in; K ⁺ out)	Ionotropic (Na ⁺ in; K ⁺ out)	Ionotropic (Na ⁺ in; K ⁺ out)
Unique mechanism	Voltage-dependent Mg²⁺ block ; requires glycine/D-serine co-agonist ; slow kinetics	Fast kinetics; mediates majority of fast excitatory transmission	Moderate kinetics; modulatory role
Key role	LTP , synaptic plasticity, memory, neurodevelopment	Fast synaptic transmission; "workhorse" of excitatory signalling	Presynaptic modulation of neurotransmitter release; pain signalling
Drugs	Ketamine , memantine, PCP, MK-801 (antagonists); D-cycloserine (partial agonist at glycine site)	Perampanel (antagonist, epilepsy); AMPA-kines (research, cognitive enhancers)	Topiramate (partial); limited clinical drugs
Clinical significance	Ketamine → rapid antidepressant; PCP/ketamine model of schizophrenia; Memantine in Alzheimer's; Excitotoxicity in stroke	Epilepsy (perampanel); Cognitive research	Epilepsy (some role); Pain; Neurodegeneration (research)

EXAM PEARL

The **NMDA hypofunction hypothesis** of schizophrenia, PCP and ketamine block NMDA receptors and produce positive, negative, and cognitive symptoms, unlike DA agonists which mainly produce positive symptoms.

5. Frontal Lobe Subdivisions

FEATURE	DLPFC	OFC	ACC	VMPFC
Full name	Dorsolateral Prefrontal Cortex	Orbitofrontal Cortex	Anterior Cingulate Cortex	Ventromedial Prefrontal Cortex
Key functions	Executive function : working memory, planning, cognitive flexibility, abstraction	Social cognition : impulse control, reward valuation, social behaviour, decision-making	Conflict monitoring , error detection, motivation, emotional regulation, pain processing	Emotional decision-making , fear extinction, self-referential processing, moral judgement

FEATURE	DLPFC	OFC	ACC	VMPFC
Testing	WCST, Tower of London, Trail-Making B, Digit Span backward, verbal fluency	Go/No-Go, Iowa Gambling Task, reversal learning tasks	Stroop test, error-related tasks	Iowa Gambling Task, SCR during decision-making
Lesion syndrome	Pseudodepression (dorsolateral syndrome): apathy, poor planning, ↓ verbal fluency, perseveration	Pseudopsychopathic (orbitofrontal disinhibition): impulsivity, socially inappropriate, poor judgement, euphoria	Akinetic mutism (if bilateral); apathy, ↓ motivation, blunted affect	Poor risk assessment, impaired social/emotional decisions, "acquired sociopathy" (overlap with OFC)

EXAM PEARL

Phineas Gage's injury was primarily **OFC/VMPFC** → disinhibited, socially inappropriate behaviour with preserved intellect.

6. Frontal Lobe Syndromes

FEATURE	PSEUDODEPRESSED (DORSOLATERAL)	PSEUDOPSYCHOPATHIC (ORBITOFRONTAL)	AKINETIC (MEDIAL/ACC)
Lesion site	DLPFC	OFC (orbital surface)	ACC / medial frontal (bilateral)
Core features	Apathy, flat affect, ↓ motivation, psychomotor retardation, poor abstraction, perseveration	Disinhibition , impulsivity, Witzelsucht (inappropriate jocularity), hypersexuality, poor social judgement, irritability	Akinetic mutism , profound apathy, ↓ spontaneous speech/movement, incontinence (indifference)
Cognition	Impaired: working memory, planning, set-shifting	Relatively preserved IQ but impaired judgement and risk assessment	Globally reduced output; may appear preserved if stimulated
Affect	Flat, apathetic, mimics depression	Euphoric, labile, inappropriate, mimics mania/antisocial PD	Absent, mimics catatonia or severe depression
Differential	Major depression, negative symptoms of schizophrenia, hypothyroidism	Mania, ASPD, substance intoxication, FTD (behavioural variant)	Catatonia, severe depression, akinetic Parkinsonism

EXAM PEARL

"Pseudodepressed" patients do NOT have depressed mood subjectively, they lack initiative.
"Pseudopsychopathic" patients lack guilt/empathy but this is acquired, not characterological.

7. REM vs NREM Sleep

FEATURE	REM SLEEP	NREM SLEEP
EEG	Low voltage, fast, desynchronised (similar to waking, "paradoxical sleep")	N1 : theta; N2 : sleep spindles + K-complexes; N3 (SWS) : delta waves (high amplitude, slow)
EMG / Muscle tone	Atonia (active inhibition of skeletal muscles via glycine/GABA in subcoeruleus)	Reduced but present; postural tone maintained
Eye movements	Rapid, conjugate eye movements	Slow rolling (N1) → absent (N2, N3)
Dreams & mental activity	Vivid, narrative, bizarre, emotionally charged dreams; most dream recall	Thought-like, less vivid; N3 → night terrors, sleepwalking (no dream recall)
Key neurotransmitters	ACh ↑↑ (REM-on); 5-HT ↓, NE ↓, Histamine ↓ (REM-off monoamines silenced)	5-HT (raphe), NE (LC), Histamine (TMN) → promote wakefulness/NREM; GABA/galanin (VLPO) → promote NREM

EXAM PEARL

The **reciprocal interaction model** (Hobson & McCarley), REM is generated by cholinergic "REM-on" neurons (PPT/LDT) and terminated by monoaminergic "REM-off" neurons (LC, raphe). This explains why anticholinergics suppress REM and SSRIs (↑ 5-HT) suppress REM.

8. Sleep Changes in Psychiatric Disorders

DISORDER	SLEEP ARCHITECTURE CHANGES	REM CHANGES	OTHER FEATURES	CLINICAL SIGNIFICANCE
Depression	↓ SWS, ↑ awakenings, early morning awakening	↓ REM latency , ↑ REM density, ↑ first REM period duration	Sleep continuity disturbance; hypersomnia in atypical depression	↓ REM latency is a biological marker ; sleep deprivation (esp. late-night) can be acutely antidepressant

DISORDER	SLEEP ARCHITECTURE CHANGES	REM CHANGES	OTHER FEATURES	CLINICAL SIGNIFICANCE
Mania	↓↓ Total sleep time (often <3 hrs), ↓ SWS	↓ REM latency (less consistent than depression)	Decreased need for sleep (NOT insomnia, patient feels rested)	↓ Sleep need is a prodromal sign of mania; sleep deprivation can trigger mania
Schizophrenia	↓ SWS (↓ delta sleep), ↓ sleep efficiency, ↑ sleep latency	↓ REM latency (some studies); ↓ REM rebound after deprivation	Poor sleep–wake cycle regulation; correlates with negative symptoms	SWS deficit correlates with cognitive impairment and negative symptoms
Anxiety / GAD	↑ Sleep latency, ↓ sleep efficiency, ↑ Stage N1/N2	Generally preserved REM latency	Hyperarousal model, ↑ cortisol, ↑ beta activity on EEG	Insomnia in anxiety is primarily sleep-onset (vs early morning in depression)
PTSD	Fragmented sleep, ↑ awakenings, ↓ SWS	↑ REM fragmentation , nightmares (often in REM), some studies show ↑ REM density	Hyperarousal persists into sleep; exaggerated startle	Prazosin (α_1 blocker) reduces trauma-related nightmares; image rehearsal therapy
Dementia	Sundowning , disrupted circadian rhythm, ↓ SWS, ↓ total sleep	↓ REM (especially in DLB , loss of REM atonia → RBD)	DLB: RBD may precede dementia by years ; Alzheimer's: SCN degeneration	RBD is a prodromal marker for α-synucleinopathies (DLB, PD, MSA)

EXAM PEARL

The three disorders with shortened REM latency, **Depression, Narcolepsy, Schizophrenia** (mnemonic: DNS).

9. Sleep Disorders Differential

FEATURE	INSOMNIA	NARCOLEPSY	OBSTRUCTIVE SLEEP APNEA
Core complaint	Difficulty initiating/maintaining sleep or early awakening despite adequate opportunity	Excessive daytime sleepiness + cataplexy (Type 1)	Loud snoring, witnessed apneas, excessive daytime sleepiness

FEATURE	INSOMNIA	NARCOLEPSY	OBSTRUCTIVE SLEEP APNEA
Key features	Daytime fatigue, irritability, ↓ concentration; duration ≥3 months, ≥3 nights/week (chronic)	Tetrad: EDS, cataplexy, sleep paralysis, hypnagogic hallucinations; SOREMPs on MSLT	Obesity, thick neck, morning headaches, nocturia, ↑ BP; AHI ≥5 on PSG
Pathophysiology	Hyperarousal (cognitive + physiological); Spielman's 3P model (predisposing, precipitating, perpetuating)	Type 1: hypocretin/orexin deficiency (autoimmune destruction of hypothalamic neurons); HLA-DQB1*0602	Upper airway collapse during sleep → hypoxia → arousals → sleep fragmentation
Diagnosis	Clinical; sleep diary; actigraphy (PSG not routinely needed)	MSLT: mean sleep latency ≤8 min + ≥2 SOREMPs; CSF hypocretin-1 <110 pg/mL (Type 1)	Polysomnography: AHI ≥5 with symptoms or AHI ≥15
Treatment	CBT-I (first line); melatonin agonists; BzRAs (short-term); orexin receptor antagonists (suvorexant)	Modafinil/armodafinil (EDS); sodium oxybate (cataplexy + EDS); pitolisant; venlafaxine for cataplexy	CPAP (first line); weight loss; mandibular advancement; surgery (UPPP)

FEATURE	REM BEHAVIOUR DISORDER (RBD)	RESTLESS LEGS SYNDROME (RLS)	NREM PARASOMNIAS
Core complaint	Violent dream enactment during REM sleep	Urge to move legs + uncomfortable sensations, worse at rest/evening	Sleepwalking, sleep terrors, confusional arousals (arise from N3/SWS)
Key features	Loss of REM atonia → punching, kicking, shouting during dreams; bed partner often injured	Relieved by movement ; circadian pattern (worse at night); ↓ ferritin common; familial	Occur in first third of night (SWS dominant); amnesia for event; eyes open but confused
Pathophysiology	Degeneration of subcoeruleus/sublaterodorsal nucleus (brainstem REM atonia centre); α-synuclein pathology	Dopaminergic dysfunction (A11 diencephalospinal); iron deficiency in CNS; genetics	Incomplete arousal from SWS; developmental (children) or precipitated by sleep deprivation, stress, substances
Diagnosis	PSG: REM without atonia (RSCA) + clinical history of dream enactment	Clinical (IRLSSG criteria); ferritin <75 µg/L supports diagnosis; PSG with PLM index ↑	Clinical; PSG if atypical (rule out epilepsy); video-PSG shows arousal from N3

FEATURE	REM BEHAVIOUR DISORDER (RBD)	RESTLESS LEGS SYNDROME (RLS)	NREM PARASOMNIAS
Treatment	Melatonin (first line, safer); clonazepam (0.5–2 mg); bedroom safety; screen for α -synucleinopathy	Iron supplementation (if ferritin <75); dopamine agonists (pramipexole, ropinirole), watch for augmentation; gabapentinoids (first line in recent guidelines)	Reassurance (children); safety measures; address triggers; BZDs (clonazepam) if severe / dangerous

EXAM PEARL

RBD → screen for **Parkinson's disease, DLB, MSA** (>80% convert within 10–15 years). This is the strongest prodromal marker for α -synucleinopathies.

10. Dopamine Pathways

FEATURE	MESOLIMBIC	MESOCORTICAL	NIGROSTRIATAL	TUBEROINFUNDIBULAR
Origin → Target	VTA → Nucleus accumbens, amygdala, hippocampus	VTA → Prefrontal cortex (DLPFC, ACC)	Substantia nigra (pars compacta) → Dorsal striatum (caudate + putamen)	Arcuate nucleus (hypothalamus) → Pituitary stalk (median eminence)
Normal function	Reward , motivation, pleasure, emotional salience	Executive function , working memory, attention, motivation	Motor control , movement initiation, habit formation	Inhibits prolactin release from anterior pituitary
Hyperactivity	Positive symptoms of schizophrenia (hallucinations, delusions, thought disorder)	(not typically hyperactive)	Dyskinesias (tardive dyskinesia, chorea, tics)	(not typically hyperactive)
Hypoactivity	Anhedonia, amotivation, addiction vulnerability	Negative symptoms (avolition, alogia, flat affect) + cognitive symptoms of schizophrenia	Parkinsonism (tremor, rigidity, bradykinesia), EPS from antipsychotics	Hyperprolactinemia (galactorrhoea, amenorrhoea, sexual dysfunction, gynaecomastia)

FEATURE	MESOLIMBIC	MESOCORTICAL	NIGROSTRIATAL	TUBEROINFUNDIBULAR
Clinical drug effects	D2 blockade here → ↓ positive symptoms (therapeutic target of antipsychotics)	D2 blockade here → worsens negative/cognitive symptoms (limitation of typical antipsychotics)	D2 blockade here → EPS : acute dystonia, akathisia, parkinsonism, tardive dyskinesia	D2 blockade here → ↑ prolactin (worst with risperidone, amisulpride, typical antipsychotics)

EXAM PEARL

Atypical antipsychotics (clozapine, quetiapine) cause fewer EPS and less prolactin elevation because of: (1) lower D2 affinity / fast D2 dissociation ("fast-off"), (2) 5-HT_{2A} antagonism (which disinhibits DA release in nigrostriatal and tuberoinfundibular pathways), and (3) preferential mesolimbic binding.

Quick-Reference Mnemonics

MNEMONIC · WHAT IT ENCODES

"SLC for 5-HT synthesis" Serotonin ← L-tryptophan → Converted by tryptophan hydroxylase

"DNS" Disorders with ↓ REM latency: Depression, Narcolepsy, Schizophrenia

"Frequency for BZDs, Duration for Barbs" BZDs ↑ frequency of Cl⁻ channel opening; Barbiturates ↑ duration

"REM = Remember (ACh), NREM = No Monoamines off" ACh drives REM; monoamines are silent during REM

"MNTT" Four DA pathways: Mesolimbic, Nigrostriatal, Tuberoinfundibular, (meso)corTical

"First third = NREM parasomnias; Last third = REM parasomnias" Sleepwalking/terrors early; nightmares/RBD late in the night

PYQ Frequency Analysis

EXAM PEARL

Last updated: March 2026

Executive Summary

Neuro-Foundations is one of the **highest-yield topic clusters** in Paper I. Across 28 PG exams sessions, questions on neurotransmitters, neuroanatomy, and sleep appear with cumulative frequency of **~63 mentions**, nearly guaranteed to appear in some form on any exam.

EXAM STRATEGY

If you study nothing else in Paper I, study this cluster.

Topic-Level Frequency

TOPIC	EXAM MENTIONS (28 SESSIONS)	AVG PER EXAM	VERDICT
Neurotransmitters (serotonin, dopamine, GABA, glutamate, NE)	18	~0.64	Appears in 2 out of 3 exams
Sleep (physiology, stages, disorders, circadian)	28	~1.0	Appears in nearly EVERY exam
Neuroanatomy (basal ganglia, frontal lobe, limbic, Papez)	17	~0.61	Appears in 2 out of 3 exams
Combined cluster	63	~2.25	2+ questions per exam from this cluster

Sub-Topic Breakdown

Neurotransmitters (18 mentions)

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Dopamine pathways + role in psychiatry	6	"Describe dopaminergic pathways", "Role of dopamine in psychiatry"
Serotonin pathways + role	4	"Serotonin-related pathways and relevance", "Neurochemistry of serotonin"
General NT classification + definition	4	"Define neurotransmitters", "Types of neurotransmitters"
Serotonin syndrome	2	"Define serotonin syndrome and treatment", "Clinical presentation and management"
GABA + Glutamate	1	"Role of glutamate and GABA in depression"
NT receptors in affective disorders	1	"Discuss neurotransmitters relevant to affective disorders"

EXAM PEARL

Hot sub-topics: Dopamine pathways (asked 6 times!) and serotonin pathways (4 times). These are the most reliable questions.

EXAM STRATEGY

Earlier exams (2011-2016) asked broad "define neurotransmitters" questions. Recent exams (2020+) ask **specific pathway/receptor questions**, more application-level. Prepare at depth, not just breadth.

Neuroanatomy (17 mentions)

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Basal ganglia (structure, function, disorders)	4	"Components of basal ganglia", "Functions and disorders"
Frontal lobe (functions, syndromes, tests)	4	"Frontal lobe syndromes", "Frontal lobe function tests"
Limbic system / Papez circuit	3	"Papez circuit", "Limbic system and emotion"
Pineal gland / Chronobiology	2	"Functions of pineal gland", "Chronobiology relevance"

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Emotion circuits	2	"Define emotion, discuss neuronal circuit"
General neuroanatomy	2	Various

EXAM PEARL

Basal ganglia and frontal lobe syndromes are equally hot (4 each). Papez circuit appears regularly.

EXAM STRATEGY

PG exams tends to ask broader questions ("Structure and functions of basal ganglion") vs PG exams's more targeted approach. Prepare both a detailed table and a prose narrative for each topic.

Sleep (28 mentions)

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Sleep physiology / stages	8	"Physiology of sleep", "Stages of sleep", "Define sleep"
Sleep neurobiology	5	"Neurobiology of sleep and wakefulness"
Sleep disorders	8	"Disorders of sleep-wake cycle", "Types of sleep disorders"
Sleep architecture as diagnostic tool	3	"How can sleep architecture be used diagnostically"
Specific sleep disorders (PLMD, narcolepsy, etc.)	2	"Periodic limb movement disorders"
Circadian rhythm / chronobiology	2	"Chronobiology and psychiatry"

EXAM PEARL

Sleep physiology and sleep disorders are the two juggernauts, asked in nearly every alternate exam. Sleep as a diagnostic tool is an emerging pattern (appeared 2020+).

EXAM STRATEGY

PG exams asks both Paper I (physiology) and Paper II (clinical disorders) sleep questions. Know BOTH angles.

Long Essay Candidates (20-mark format)

Based on frequency and complexity, these are the most likely 20-mark long essay questions from this cluster:

RANK	TOPIC	WHY	EST. PROBABILITY
1	"Define neurotransmitters. Describe the role of dopamine/serotonin in psychiatry"	Asked 10+ times across sessions in various forms	Very High
2	"Describe the physiology of sleep. Discuss sleep changes in psychiatric disorders"	Combined physiology + clinical = perfect long essay	Very High
3	"Describe the structure and functions of the basal ganglia. Discuss disorders associated with basal ganglia dysfunction"	Structure + function + clinical = comprehensive	High
4	"Describe the frontal lobe and its functions. Discuss frontal lobe syndromes with clinical relevance"	Reliable perennial	High
5	"Describe the neurobiology of sleep and wakefulness. How is sleep architecture used as a diagnostic tool in psychiatry?"	Emerging pattern	Medium-High

Year-by-Year Appearance (Neurotransmitters only, as sample)

YEAR	QUESTION	MARKS
Dec 2011	Define neurotransmitters. Excitatory NTs. Describe one in detail.	10
Dec 2012	(No direct NT question)	
Jun 2013	Dopaminergic pathways, functions, applied importance	10
Dec 2013	(No direct NT question)	

YEAR	QUESTION	MARKS
Apr 2016	Mono-amine neurotransmitters and significance	10
Oct 2016	Major dopaminergic pathways	10
Apr 2017	Serotonin-related pathways and relevance	10
Oct 2017	Neurotransmitters and brain functions. Novel NTs.	10
Apr 2018	Define receptors. NTs relevant to affective disorders.	10
Oct 2018	Define neurotransmitters. Types. Role of dopamine.	10
Apr 2020	Glutamate and GABA in depression	10
Oct 2021	Serotonin syndrome, define and discuss treatment	10
Apr 2023	Neurochemistry of serotonin. Role in disorders.	10
Oct 2024	Characteristics of NT. Inhibitory NTs.	10
Jun 2025	Serotonin syndrome, clinical presentation + management	10

EXAM PEARL

NT questions appear in ~60% of PG exams sessions. Dopamine and serotonin alternate as the focus.

Exam Strategy Recommendations

Must-Prepare (will almost certainly be asked)

1. Dopamine, all 4 pathways with clinical relevance (can answer 6+ different PYQ variants)
2. Sleep physiology, stages, EEG, neurobiology (covers 13+ PYQ variants)
3. Serotonin, synthesis, pathways, receptors, serotonin syndrome
4. Basal ganglia, components, circuits, disorders

Should-Prepare (likely to appear)

1. Frontal lobe, subdivisions, syndromes, testing

2. Papez circuit, draw and explain
3. Sleep disorders, differential diagnosis table
4. GABA / Glutamate, emerging topic, appeared 2020+

Nice-to-Know (occasional appearance)

1. Novel neurotransmitters (endocannabinoids, neuropeptides)
2. Chronobiology and pineal gland
3. Psychoneuroimmunology

PG exams vs Exam Pattern Differences

FEATURE	PG EXAMS	PG EXAMS
Question style	Broader ("Structure and functions of...")	More targeted ("Role of dopamine in...")
Marks	10 or 20 (long essay)	Always 10
Emphasis	Clinical application heavier	Basic science + some application
Sleep questions	Split across Paper I (physiology) and Paper II (disorders)	Usually in Paper I
Frequency of NT questions	Every 2-3 years	Every 1-2 sessions

Key Takeaway

EXAM STRATEGY

"If you can write a structured 10-mark answer on dopamine pathways, serotonin pathways, sleep physiology, basal ganglia, and frontal lobe syndromes, you've covered the 5 most reliable questions in this cluster. That's 50 marks of exam-ready material from one study week."

Analysis based on PG exams Psychiatry Question Papers Dec 2011, Jun 2025 (natboard.edu.in) + PG exams MD Psychiatry Papers 2013-2022. Frequency counts are keyword-based approximations, actual question count may vary slightly due to multi-topic questions.

Quick Review

SUBJECTS: NEUROTRANSMITTERS	NEUROANATOMY	SLEEP PHYSIOLOGY

Purpose: Rapid-fire revision for MD Psychiatry exit examination

DIFFICULTY: R = RECALL (L1-2)	A = APPLICATION (L3)	AN = ANALYSIS (L4)

NEUROTRANSMITTERS (Q1-Q15)

Q1 [R]: Outline the serotonin synthesis pathway from dietary precursor to final neurotransmitter.

Answer: **Tryptophan** → (tryptophan hydroxylase, rate-limiting) → **5-hydroxytryptophan (5-HTP)** → (aromatic L-amino acid decarboxylase) → **5-hydroxytryptamine (5-HT / serotonin)**. Degraded by **MAO-A** to **5-HIAA**. Tryptophan hydroxylase requires **tetrahydrobiopterin (BH4)** as cofactor.

Q2 [R]: Outline the dopamine synthesis pathway.

Answer: **Tyrosine** → (tyrosine hydroxylase, rate-limiting, requires BH4) → **L-DOPA** → (DOPA decarboxylase / aromatic L-amino acid decarboxylase) → **Dopamine**. In noradrenergic neurons: dopamine → (dopamine beta-hydroxylase) → **norepinephrine** → (PNMT) → **epinephrine**.

Q3 [R]: Name the four dopamine pathways and the clinical condition associated with dysfunction of each.

Answer:

1. **Mesolimbic** (VTA → nucleus accumbens, amygdala), **positive symptoms** of schizophrenia (hyperactivity), reward, addiction
2. **Mesocortical** (VTA → prefrontal cortex), **negative symptoms and cognitive deficits** of schizophrenia (hypoactivity)
3. **Nigrostriatal** (substantia nigra → dorsal striatum), **extrapyramidal symptoms**, Parkinson disease
4. **Tuberoinfundibular** (hypothalamus → pituitary), **hyperprolactinemia** when blocked by antipsychotics

Q4 [R]: List the five binding sites on the GABA-A receptor complex and one agent acting at each.

Answer: The GABA-A receptor is a **ligand-gated chloride channel** (pentameric, typically 2alpha-2beta-1gamma):

1. **GABA site** (beta subunit), muscimol (agonist), bicuculline (antagonist)
2. **Benzodiazepine site** (alpha-gamma interface), diazepam (positive allosteric modulator), flumazenil (antagonist)
3. **Barbiturate site** (beta subunit, transmembrane domain), phenobarbital (increases Cl⁻ channel open **duration**)
4. **Neurosteroid site** (alpha subunit transmembrane), allopregnanolone (brexanolone), ganaxolone
5. **Ethanol site** (delta-containing extrasynaptic receptors), ethanol (potentiates tonic inhibition)

EXAM PEARL

Benzodiazepines increase **frequency** of channel opening; barbiturates increase **duration**.

Q5 [A]: A patient on fluoxetine and tramadol presents with myoclonus, diaphoresis, hyperthermia, and hyperreflexia. What is the diagnosis and how do you distinguish it from NMS?

Answer: Diagnosis: **Serotonin syndrome** (excess 5-HT from SSRI + tramadol's serotonergic action).

FEATURE	SEROTONIN SYNDROME	NMS
Onset	Hours (rapid)	Days to weeks (gradual)
Muscle tone	Clonus, hyperreflexia, myoclonus	Lead-pipe rigidity, bradyreflexia
Pupils	Mydriasis	Normal
Bowel sounds	Hyperactive	Hypoactive / absent
Causative agents	Serotonergic drugs	Dopamine blockers / DA withdrawal
Resolution	Rapid (24-72h) with drug cessation	Slow (days to weeks)
CK	Mildly elevated	Markedly elevated

Treatment: Stop offending agents, **cypiroheptadine** (5-HT_{2A} antagonist), supportive care.

Q6 [R]: What are the main serotonin receptor subtypes relevant to psychiatry and their clinical significance?

Answer:

- **5-HT1A**, anxiolytic target (buspirone is partial agonist); autoreceptor on raphe → mediates SSRI delay
 - **5-HT2A**, blocked by atypical antipsychotics; mediates hallucinations (psychedelic target), improves negative symptoms when blocked
 - **5-HT2C**, appetite/weight regulation; blockade → weight gain (olanzapine, mirtazapine)
 - **5-HT3**, nausea/emesis; blocked by ondansetron; peripherally involved in GI motility
 - **5-HT7**, circadian rhythm regulation; blocked by lurasidone
-

Q7 [An]: Explain the glutamate hypothesis of schizophrenia and how it accounts for symptoms that the dopamine hypothesis cannot.

Answer: The glutamate hypothesis proposes **NMDA receptor hypofunction** as a primary pathology. Evidence:

- **PCP and ketamine** (NMDA antagonists) produce positive, negative, AND cognitive symptoms in healthy individuals, dopamine agonists (amphetamine) produce only positive symptoms
 - NMDA hypofunction on **GABAergic interneurons** in cortex → loss of inhibition → **downstream glutamate excess** → excitotoxicity
 - Cortical glutamate dysregulation → reduced mesocortical dopamine (explaining **negative and cognitive symptoms**) and increased mesolimbic dopamine (explaining **positive symptoms**)
 - This model unifies the dopamine hypothesis as a **downstream consequence** of primary glutamatergic dysfunction
 - Therapeutic implication: glycine site agonists (D-serine, sarcosine) as adjunctive treatment
-

Q8 [A]: A patient on clozapine develops seizures. Which neurotransmitter mechanism explains this, and what is the management?

Answer: Clozapine lowers seizure threshold in a **dose-dependent** manner (risk ~5% at doses >600mg/day). Mechanism: clozapine is a potent **antihistaminic and anticholinergic** but more importantly has **weak GABA-A modulation** combined with **glutamate-enhancing properties** at cortical sites, disrupting the excitatory-inhibitory balance.

Management: **do not stop clozapine** (risk of psychotic relapse); add **sodium valproate** as preferred anticonvulsant (avoid carbamazepine, both cause agranulocytosis, additive risk). Reduce clozapine dose if possible.

CLINICAL ANCHOR

Never abruptly stop clozapine for a first seizure, the risk of rebound psychosis is high.
Valproate is the anticonvulsant of choice.

Q9 [R]: List the norepinephrine pathways and their psychiatric relevance.

Answer: Main source: **locus coeruleus** (pons) with widespread projections:

- LC → **prefrontal cortex**: attention, working memory (ADHD pathology, hypofunction)
- LC → **limbic system** (amygdala, hippocampus): emotional memory, fear conditioning, PTSD hyperarousal
- LC → **cerebellum**: motor coordination (tremor in anxiety)
- Descending pathways → **spinal cord**: pain modulation (rationale for duloxetine/SNRIs in chronic pain)

Key receptors: **alpha2 autoreceptors** (presynaptic, inhibitory, clonidine, guanfacine for ADHD/PTSD); **beta receptors** (propranolol for performance anxiety).

Q10 [An]: Why does the therapeutic effect of SSRIs take 2-4 weeks despite immediate reuptake blockade?

Answer: The delay involves **somatodendritic autoreceptor desensitization**:

1. Acute SSRI → increased 5-HT in **somatodendritic area** (raphe) → activates **5-HT1A autoreceptors** → **negative feedback reduces neuronal firing** → net 5-HT release is initially unchanged or reduced at terminals
2. Over 2-4 weeks → sustained 5-HT1A autoreceptor stimulation → **downregulation/desensitization** of autoreceptors
3. Loss of negative feedback → **restored and enhanced neuronal firing** → increased 5-HT release at synaptic terminals
4. Additionally: downstream changes in **postsynaptic receptor density, BDNF expression, and neuroplasticity** (hippocampal neurogenesis) contribute to therapeutic response

EXAM PEARL

This is why pindolol (5-HT1A antagonist) was trialed as an augmentation strategy to accelerate response.

Q11 [A]: A 45-year-old man on phenelzine eats aged cheese and develops severe occipital headache, stiff neck, and BP 220/130. Explain the mechanism.

Answer: **Tyramine-induced hypertensive crisis**. Mechanism: Phenelzine (irreversible non-selective MAOI) inhibits **MAO-A in gut wall and liver** → dietary tyramine (abundant in

aged cheese, fermented foods) is **not metabolized** and enters systemic circulation → tyramine is an **indirect sympathomimetic** that displaces norepinephrine from presynaptic vesicles → **massive NE release** → severe hypertension. Treatment: **phentolamine** (IV alpha-blocker) or sublingual **nifedipine**. This reaction is the basis for the **tyramine-restricted diet** with MAOIs.

Q12 [R]: What is the role of acetylcholine in psychiatry? Name key pathways and clinical associations.

Answer:

- **Nucleus basalis of Meynert** → **cortex**: degeneration = **Alzheimer disease** (rationale for cholinesterase inhibitors: donepezil, rivastigmine, galantamine)
 - **Septal nuclei** → **hippocampus** (via fornix): memory encoding
 - **Pedunculopontine/laterodorsal tegmental nuclei** → **thalamus**: REM sleep generation, arousal
 - **Striatal cholinergic interneurons**: balance with dopamine, anticholinergics (trihexyphenidyl) treat **EPS** by restoring DA-ACh balance
 - ACh excess → **depression** (cholinergic-aminergic balance hypothesis of mood)
 - Anticholinergic burden → **delirium**, cognitive impairment in elderly
-

Q13 [An]: How does the monoamine hypothesis of depression fail to fully explain the pathophysiology, and what complementary models exist?

Answer: Limitations of the monoamine hypothesis:

- SSRIs increase 5-HT within hours, but therapeutic effect takes weeks → **simple depletion model insufficient**
- Tryptophan depletion doesn't cause depression in healthy subjects, only in those with prior depression history
- Some effective antidepressants (tianeptine, ketamine) don't primarily increase monoamines

Complementary models:

- **Neuroplasticity hypothesis**: depression involves **reduced BDNF, hippocampal atrophy, impaired neurogenesis**; antidepressants restore these via CREB-BDNF cascade
- **Glutamate/ketamine model**: NMDA antagonism → AMPA activation → **rapid BDNF release and synaptogenesis**
- **Neuroinflammation**: elevated IL-6, TNF-alpha, CRP; inflammation → IDO activation → tryptophan shunted toward **kynurenine pathway** (neurotoxic quinolinic acid) rather than 5-HT

- **HPA axis dysregulation:** chronic cortisol → hippocampal damage, glucocorticoid receptor resistance
 - **Network model:** disrupted default mode network connectivity
-

Q14 [A]: A patient on lithium and haloperidol develops confusion, EPS, and fever. What is the concern, and how does it relate to neurotransmitter pharmacology?

Answer: Concern: **NMS** (or lithium-haloperidol encephalopathy / NMS-like syndrome). Mechanism: Haloperidol causes potent **D2 blockade** in nigrostriatal (rigidity), hypothalamic (hyperthermia, autonomic instability), and mesocortical (confusion) pathways. Lithium may potentiate this by **further reducing dopaminergic transmission** and affecting intracellular signaling. Classic NMS tetrad: **hyperthermia, rigidity, autonomic dysfunction, altered consciousness**. Labs: elevated **CK**, leukocytosis, elevated LFTs. Management: stop both drugs, **dantrolene** (muscle relaxant), **bromocriptine** (DA agonist), supportive care.

Q15 [R]: Name the key inhibitory and excitatory neurotransmitters, their receptor types, and mechanism of action.

Answer:

Inhibitory:

- **GABA:** main inhibitory NT in brain. GABA-A = **ionotropic** (Cl⁻ channel); GABA-B = **metabotropic** (G-protein, increases K⁺ / decreases Ca²⁺; target of baclofen)
- **Glycine:** main inhibitory NT in **spinal cord and brainstem**; also co-agonist at NMDA receptor glycine site

Excitatory:

- **Glutamate:** main excitatory NT. **NMDA** (ligand-gated Na⁺ / Ca²⁺, requires glycine co-agonist, Mg²⁺ block at rest); **AMPA** (fast Na⁺ influx, mediates fast excitatory transmission); **Kainate; metabotropic (mGluR1-8)**, G-protein coupled
 - NMDA receptor uniquely requires **simultaneous** glutamate binding + glycine binding + membrane depolarization (to relieve Mg²⁺ block) → coincidence detector for **LTP and memory**
-

NEUROANATOMY (Q16-Q27)

Q16 [R]: List the components of the Papez circuit in order.

Answer: Hippocampus → (via fornix) → **mammillary bodies** → (via **mammillothalamic tract**) → **anterior thalamic nucleus** → (via **thalamocortical fibers**) → **cingulate gyrus** → (via **cingulum**) → **parahippocampal gyrus / entorhinal cortex** → **hippocampus**

Function: **emotional processing and memory consolidation**. Damage to any component → amnesia (e.g., mammillary body damage in **Korsakoff syndrome**, hippocampal damage in **Alzheimer disease**).

Q17 [R]: Name the frontal lobe neuropsychological tests and what each assesses.

Answer:

- **Wisconsin Card Sorting Test (WCST): set-shifting, cognitive flexibility, abstract reasoning** (dorsolateral PFC); perseverative errors = frontal dysfunction
 - **Stroop Test: response inhibition, selective attention** (anterior cingulate/DLPFC); naming ink color of incongruent color words
 - **Trail Making Test (TMT):** Part A = processing speed, visual scanning; **Part B = cognitive flexibility, set-shifting** (alternating numbers-letters); B-A difference indexes executive function
 - **Verbal fluency: phonemic** (FAS, dorsolateral PFC) and **semantic** (animals, temporal lobe); reduced output = frontal/temporal pathology
 - **Go/No-Go: response inhibition** (orbitofrontal cortex)
 - **Tower of London/Hanoi: planning and problem-solving** (dorsolateral PFC)
-

Q18 [An]: Explain the basal ganglia circuits relevant to psychiatry, including the direct and indirect pathways.

Answer: The basal ganglia form parallel cortico-striato-thalamo-cortical loops:

Motor circuit (relevant to EPS):

- **Direct pathway** (facilitates movement): Cortex → Striatum (D1 receptors) → inhibits **GPe/SNr** → disinhibits **thalamus** → cortex activated → **movement initiated**
- **Indirect pathway** (inhibits movement): Cortex → Striatum (D2 receptors) → inhibits **GPe** → disinhibits **STN** → excites **GPe/SNr** → inhibits thalamus → **movement suppressed**
- Dopamine from SNc **facilitates direct** (D1) and **inhibits indirect** (D2) → net effect = movement facilitation
- Loss of DA (Parkinson) → overactive indirect pathway → **bradykinesia, rigidity**
- D2 blockade (antipsychotics) mimics DA loss → **EPS**

Psychiatric circuits:

- **Dorsolateral prefrontal loop:** executive function, working memory
- **Orbitofrontal loop:** impulse control, social behavior (damage → disinhibition, personality change)
- **Anterior cingulate loop:** motivation (damage → abulia, akinetic mutism)

- **OCD model:** hyperactivity of **orbitofrontal-caudate circuit** → compulsive behavior; SSRIs and DBS target this circuit
-

Q19 [A]: A 55-year-old man presents with profound amnesia for recent events, confabulation, and peripheral neuropathy after years of alcohol dependence. Identify the lesion and circuit involved.

Answer: Korsakoff syndrome due to **thiamine (B1) deficiency**. Lesion: bilateral **mammillary bodies** and **medial dorsal thalamic nuclei**. Circuit: disruption of the **Papez circuit** at the mammillary body-anterior thalamic node → severe **anterograde amnesia** with relative preservation of remote memory. Confabulation reflects frontal dysfunction (orbitofrontal involvement). Usually preceded by **Wernicke encephalopathy** (acute triad: confusion, ophthalmoplegia, ataxia, lesions in periaqueductal gray, medial thalamus, mammillary bodies). Prevention: parenteral **thiamine before glucose** in any malnourished/alcoholic patient.

CLINICAL ANCHOR

Always give IV thiamine BEFORE glucose in any malnourished or alcohol-dependent patient presenting with confusion, glucose without thiamine can precipitate Wernicke encephalopathy.

Q20 [R]: Describe the functional localization of the temporal lobe relevant to psychiatry.

Answer:

- **Superior temporal gyrus:** primary auditory cortex (Heschl's gyrus); **Wernicke's area** (dominant hemisphere, posterior part), damage → receptive aphasia
 - **Middle/inferior temporal gyri:** visual object recognition, semantic memory
 - **Medial temporal lobe:** **hippocampus** (declarative memory encoding), **amygdala** (fear conditioning, emotional valence), **entorhinal cortex** (gateway to hippocampus)
 - **Temporal pole:** social cognition, theory of mind
 - Psychiatric associations: **temporal lobe epilepsy** → interictal personality (Geschwind syndrome: hypergraphia, hyperreligiosity, altered sexuality); **auditory hallucinations** (superior temporal gyrus activation); Kluver-Bucy syndrome (bilateral amygdala damage → hyperorality, hypersexuality, visual agnosia, placidity)
-

Q21 [A]: A patient with a right parietal lobe stroke neglects the left side of space, fails to dress the left side, and denies any deficit. Explain the syndromes involved.

Answer: Three overlapping syndromes:

1. **Hemispatial neglect (contralateral neglect syndrome):** failure to attend to left hemispace, due to damage to **right inferior parietal lobule and temporoparietal junction**; right hemisphere dominant for spatial attention

2. **Dressing apraxia:** inability to orient garments to the body, parietal association cortex damage disrupting body schema
3. **Anosognosia:** denial of illness, associated with **right parietal and insular** damage; disruption of self-monitoring networks

The right hemisphere dominance for spatial attention explains why **left neglect (from right lesions) is far more common and severe** than right neglect from left lesions. Tested by **line bisection, cancellation tasks, clock drawing**.

Q22 [R]: What are the key limbic system structures and their functions?

Answer:

- **Amygdala:** fear conditioning, emotional memory, threat detection (hyperactive in anxiety/PTSD; Kluver-Bucy if bilateral damage)
 - **Hippocampus:** declarative memory encoding and consolidation (atrophied in Alzheimer, chronic depression, PTSD, Cushing)
 - **Cingulate gyrus:** anterior = motivation, error detection, emotional regulation; posterior = autobiographical memory, default mode network
 - **Hypothalamus:** autonomic regulation, HPA axis, circadian rhythm, feeding, temperature
 - **Septal nuclei:** pleasure, reward (interconnected with nucleus accumbens)
 - **Mammillary bodies:** memory relay in Papez circuit (Korsakoff)
 - **Fornix:** major hippocampal output tract to mammillary bodies
 - **Nucleus accumbens:** reward, motivation, addiction (mesolimbic DA terminal)
-

Q23 [An]: Why is the prefrontal cortex particularly vulnerable in adolescence and how does this relate to psychiatric illness onset?

Answer: The PFC is the **last brain region to fully myelinate** (not complete until mid-20s), undergoing extensive **synaptic pruning** during adolescence. This creates vulnerability because:

- **Immature DLPFC** → poor impulse control, decision-making, risk assessment, while limbic system (amygdala) is already mature → **emotional dominance over cognitive control**
- Synaptic pruning is **experience-dependent and activity-regulated**, aberrant pruning (excessive in schizophrenia, complement C4 gene overexpression) → loss of cortical gray matter → onset of **psychosis in late adolescence**
- Cannabis exposure during this window disrupts **endocannabinoid-mediated pruning** → increased risk of psychosis
- Peak onset of **schizophrenia, bipolar disorder, eating disorders, and substance use** coincides with this maturational window

- Explains why **conduct disorder** → **antisocial PD** trajectory involves prefrontal maturation failure

Q24 [R]: What are the major white matter tracts relevant to psychiatry?

Answer:

- **Arcuate fasciculus:** connects Wernicke's → Broca's; damage → **conduction aphasia** (impaired repetition, fluent speech, intact comprehension)
- **Uncinate fasciculus:** temporal pole ↔ orbitofrontal cortex; abnormal in **psychopathy, PTSD, anxiety**
- **Cingulum bundle:** runs within cingulate gyrus; connects medial frontal to medial temporal; disrupted in **depression, OCD**
- **Fornix:** hippocampus → mammillary bodies; damage → **amnesia**
- **Corpus callosum:** interhemispheric transfer; damage → disconnection syndromes (alien hand, split-brain phenomena)
- **Superior longitudinal fasciculus:** frontoparietal connection; abnormal in **ADHD, schizophrenia**
- **Internal capsule (anterior limb):** target for **capsulotomy** in refractory OCD

Q25 [A]: A patient has fluent speech with paraphasic errors, intact comprehension, but cannot repeat phrases. Localize the lesion.

Answer: Conduction aphasia. Lesion: **arcuate fasciculus** (white matter tract connecting Wernicke's area in posterior superior temporal gyrus to Broca's area in inferior frontal gyrus) or **left supramarginal gyrus / inferior parietal lobule**. Speech is fluent (Broca's intact), comprehension preserved (Wernicke's intact), but the disconnection between the two areas impairs **repetition**. Characteristic feature: **conduite d'approche**, repeated self-corrective attempts to produce the target word, getting progressively closer.

Q26 [An]: Compare and contrast dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC) syndromes with clinical examples.

Answer:

FEATURE	DLPFC SYNDROME	OFC SYNDROME
Other name	Dysexecutive syndrome	Pseudopsychopathic syndrome
Personality	Apathetic, flat, lacking initiative	Disinhibited , impulsive, socially inappropriate
Cognition	Impaired planning, set-shifting, working memory	Intact cognition on standard testing

FEATURE	DLPFC SYNDROME	OFC SYNDROME
Behavior	Stimulus-bound, perseverative, reduced verbal fluency	Puerile jocularity (Witzelsucht), poor judgment, risk-taking
Tests affected	WCST (perseveration), TMT-B, verbal fluency	Go/No-Go, Iowa Gambling Task
Clinical examples	Frontal lobe tumors, vascular dementia, depression	Frontotemporal dementia (behavioral variant), TBI (orbitofrontal contusion)
Psychiatric mimic	Depression, negative symptoms of schizophrenia	Mania, antisocial personality

A third syndrome: **anterior cingulate/medial frontal** → abulia, akinetic mutism (extreme apathy with intact awareness).

Q27 [A]: A patient with chronic alcohol use develops horizontal nystagmus, gait ataxia, and confusion. Which structures are damaged and what is the acute treatment?

Answer: Wernicke encephalopathy, a medical emergency. Damaged structures:

- **Periaqueductal/periventricular gray matter** → ophthalmoplegia, nystagmus (CN III, VI nuclei)
- **Medial thalamus** (dorsomedial nucleus) → confusion, memory impairment
- **Mammillary bodies** → if chronic, progresses to Korsakoff
- **Superior cerebellar vermis** → gait ataxia (wide-based, truncal)

Treatment: **IV thiamine 500mg TDS for 3-5 days BEFORE any glucose administration** (glucose metabolism consumes thiamine and can precipitate or worsen Wernicke). Classic triad present in only ~16% of cases, maintain high clinical suspicion in any malnourished, alcoholic, or hyperemesis patient. Low threshold to treat empirically.

EXAM PEARL

Classic Wernicke triad (confusion + ophthalmoplegia + ataxia) is present in only ~16% of cases. Treat empirically in any at-risk patient.

SLEEP PHYSIOLOGY (Q28-Q40)

Q28 [R]: Describe the EEG characteristics of each sleep stage.

Answer:

- **Wake (eyes open): beta waves** (>13 Hz, low amplitude, desynchronized)

- **Wake (eyes closed): alpha waves** (8-13 Hz, posterior dominant, attenuates with eye opening)
- **N1 (Stage 1): theta waves** (4-7 Hz); **vertex sharp waves**; alpha dropout; hypnic jerks may occur
- **N2 (Stage 2):** theta background with **sleep spindles** (12-14 Hz, 0.5-1.5s bursts, generated by **thalamic reticular nucleus**) and **K-complexes** (high-amplitude biphasic waves, largest EEG waves)
- **N3 (Stage 3, SWS): delta waves** (0.5-4 Hz, >75 uV); >20% of epoch = N3; dominated by synchronized cortical slow oscillations
- **REM: low-voltage, mixed-frequency** (resembles wake, "paradoxical sleep"); **sawtooth waves** (2-6 Hz, triangular); **rapid eye movements** on EOG; **atonia** on EMG

Q29 [R]: What is the mechanism of REM atonia and its clinical significance?

Answer: During REM sleep, the **sublaterodorsal nucleus (SLD)** / **subcoeruleus** in the pons activates **glycinergic and GABAergic interneurons** in the **ventral horn of the spinal cord**, producing **active motor inhibition** (atonia) of all skeletal muscles except the **diaphragm and extraocular muscles**.

Pathway: Pontine SLD → **ventromedial medulla (magnocellularis)** → glycine/GABA release → spinal motor neuron hyperpolarization → **atonia**

Clinical significance:

- **REM Sleep Behavior Disorder (RBD):** loss of atonia → dream enactment (punching, kicking); associated with **alpha-synucleinopathies**, ~80% convert to **Parkinson disease, DLB, or MSA** within 10-15 years (prodromal marker)
- **Narcolepsy:** intrusion of REM atonia into wakefulness → **cataplexy**

CLINICAL ANCHOR

RBD is the strongest prodromal biomarker for alpha-synucleinopathies. All RBD patients should be counselled about this risk and screened regularly.

Q30 [R]: What is the role of orexin (hypocretin) and what happens in its deficiency?

Answer: **Orexin/hypocretin** is produced by neurons in the **lateral hypothalamus**. Two subtypes: orexin-A and orexin-B, acting on OX1 and OX2 receptors.

Functions: **stabilizes wakefulness**, promotes arousal, regulates sleep-wake transitions, modulates reward and feeding

Orexin deficiency = Narcolepsy Type 1:

- **Selective autoimmune destruction** of orexin-producing neurons (associated with HLA-DQB1*0602)

- CSF orexin-1 levels **<110 pg/mL** (diagnostic)
- Clinical tetrad: **excessive daytime sleepiness, cataplexy, sleep paralysis, hypnagogic hallucinations**
- **Sleep-onset REM periods (SOREMPs)** on MSLT (≥ 2 SOREMPs + mean sleep latency ≤ 8 min)

Pharmacological application: **suvorexant, lemborexant** (dual orexin receptor antagonists, DORAs), used as hypnotics by blocking orexin-mediated arousal.

Q31 [R]: Explain the SCN-melatonin circadian regulation system.

Answer: The **suprachiasmatic nucleus (SCN)** in the **anterior hypothalamus** is the master circadian pacemaker:

- **Retinohypothalamic tract:** specialized retinal ganglion cells (containing **melanopsin**, blue-light sensitive) project directly to SCN → entrains clock to light-dark cycle (**zeitgeber**)
- SCN → **superior cervical ganglion** (multisynaptic sympathetic pathway) → **pineal gland**
- In darkness: sympathetic activation releases NE → beta-adrenergic receptors on pinealocytes → activates **AANAT** (arylalkylamine N-acetyltransferase) → converts serotonin → **N-acetylserotonin** → **melatonin**
- In light: pathway suppressed → melatonin secretion inhibited
- Melatonin peaks at **2-4 AM**, promotes sleep via **MT1** (inhibits SCN firing) and **MT2** (phase-shifts the clock) receptors

Clinical relevance: **Delayed sleep-wake phase disorder** (circadian misalignment; treated with morning light + evening melatonin), **jet lag**, shift work disorder, **non-24-hour sleep-wake disorder** (common in blind individuals lacking light entrainment).

Q32 [An]: Explain why shortened REM latency occurs in depression and its significance.

Answer: Normal REM latency is **70-90 minutes** (first REM period). In depression, REM latency shortens to **<65 minutes** (sometimes <45 min). Mechanism:

The **cholinergic-aminergic balance model** (McCarley-Hobson, modified):

- REM sleep is **promoted by cholinergic neurons** (LDT / PPT in pons) and **suppressed by aminergic neurons** (serotonin from raphe, NE from locus coeruleus)
- In depression: **monoaminergic deficiency** (reduced 5-HT and NE) → relative **cholinergic dominance** → earlier and more intense REM onset
- This aligns with the **cholinergic supersensitivity hypothesis** of depression (Janowsky)

- Physostigmine (cholinesterase inhibitor) can precipitate depressive symptoms and shorten REM latency

Significance:

- Shortened REM latency is a **biological marker** of depression (sensitivity ~60-70%)
- Predicts **response to antidepressants** (most antidepressants suppress REM)
- More pronounced in **endogenous/melancholic depression**
- All effective antidepressants (except bupropion, nefazodone, agomelatine) **suppress REM** and lengthen REM latency

Q33 [R]: What are the complete sleep changes seen in major depression?

Answer: Sleep architecture disturbances in depression:

1. **Shortened REM latency** (<65 min), most characteristic
2. **Increased REM density** (more REMs per REM period), especially first REM period
3. **Increased total REM sleep** (shift of REM to first half of night)
4. **Reduced slow-wave sleep (SWS/N3)**, particularly in older depressed patients
5. **Early morning awakening** (terminal insomnia), classic for melancholic depression
6. **Sleep continuity disturbance:** increased sleep latency, frequent awakenings, reduced sleep efficiency
7. **Reduced total sleep time**

This pattern contrasts with **atypical depression** (hypersomnia, increased sleep time).

EXAM PEARL

Therapeutic implication: **sleep deprivation (wake therapy)** for one night produces rapid antidepressant response in ~60% of patients (particularly total or late-night/REM deprivation), though effects are typically reversed by recovery sleep.

Q34 [A]: A 25-year-old medical student complains of irresistible daytime sleep attacks, sudden collapse when laughing, and terrifying images while falling asleep. What investigations do you order and what results do you expect?

Answer: Suspected **Narcolepsy Type 1**. Investigations and expected findings:

1. **Polysomnography (overnight):** rule out OSA and other sleep disorders; may show **shortened REM latency** (SOREMP within 15 min of sleep onset)
2. **Multiple Sleep Latency Test (MSLT)** (next day, 5 nap opportunities at 2-hour intervals): expect **mean sleep latency ≤8 minutes** and **≥2 SOREMPs** (sleep-onset REM periods within 15 min)

3. **CSF orexin-1 (hypocretin-1):** <110 pg/mL (or <1 / 3 of normal mean), highly specific for Type 1
4. **HLA typing: DQB1*0602** positive (~98% of Type 1, but also in 25% of general population, low specificity, not diagnostic alone)
5. **Epworth Sleepiness Scale:** subjective measure of daytime somnolence (score >10)

Symptom correlation: sleep attacks = EDS; collapse with laughter = **cataplexy** (pathognomonic for Type 1); terrifying images = **hypnagogic hallucinations** (REM intrusion into wake).

Q35 [An]: How does the two-process model of sleep regulation explain the mechanism of sleep deprivation therapy in depression?

Answer: Borbely's Two-Process Model:

- **Process S (homeostatic):** sleep pressure that accumulates during wakefulness (mediated by **adenosine** accumulation); dissipated during SWS
- **Process C (circadian):** SCN-driven alerting signal that varies across 24 hours; opposes Process S during the day

In depression, there is a proposed **deficiency in Process S buildup** or a **phase advance in the circadian component** → sleep is initiated before adequate homeostatic pressure → premature REM onset, poor SWS, early awakening.

Sleep deprivation therapy works by:

1. **Extending wakefulness** → **massively increased Process S (adenosine)** → recalibrates the homeostatic set point
 2. Increased SWS pressure in recovery → **normalizes sleep architecture**
 3. Adenosine accumulation modulates **glutamatergic signaling** → may potentiate synaptic plasticity (similar to ketamine's mechanism)
 4. Phase-resetting: combines with **sleep phase advance** (sleeping 5PM-midnight, gradually shifting later) to sustain the effect
-

Q36 [A]: An elderly patient on multiple medications develops visual hallucinations, fluctuating cognition, and appears to act out dreams at night. What is the unifying diagnosis, and what sleep disorder is associated?

Answer: Dementia with Lewy Bodies (DLB). The associated sleep disorder is **REM Sleep Behavior Disorder (RBD)**.

Connection: DLB involves **alpha-synuclein deposition** in brainstem nuclei including the **sublaterodorsal nucleus/subcoeruleus** (REM atonia center) → loss of REM atonia → dream enactment. RBD often **precedes** cognitive symptoms by years/decades.

DLB diagnostic criteria (revised McKeith 2017):

- Core features: **fluctuating cognition, visual hallucinations, RBD, parkinsonism** (2 core = probable DLB)
- Suggestive biomarkers: reduced dopamine transporter uptake (DaT scan), low uptake on cardiac MIBG, PSG-confirmed REM without atonia

Management: **avoid antipsychotics** (severe neuroleptic sensitivity in DLB); if absolutely needed, quetiapine or clozapine (lowest D2 affinity). Treat RBD with **melatonin** (first-line) or low-dose clonazepam. Cholinesterase inhibitors (rivastigmine) for cognitive symptoms.

CLINICAL ANCHOR

Antipsychotics can cause severe, potentially fatal neuroleptic sensitivity reactions in DLB. This is a prescribing emergency, flag on every chart.

Q37 [R]: List the neurotransmitters involved in sleep-wake regulation and their roles.

Answer:

Wake-promoting:

- **Orexin/hypocretin** (lateral hypothalamus), stabilizes wakefulness
- **Norepinephrine** (locus coeruleus), cortical arousal, suppresses REM
- **Serotonin** (dorsal raphe), maintains wakefulness, suppresses REM
- **Histamine** (tuberomammillary nucleus, TMN), arousal (antihistamines → sedation)
- **Acetylcholine** (basal forebrain, LDT/PPT), cortical activation in both wake AND REM
- **Dopamine** (VTA, ventral periaqueductal gray), arousal, motivation (modafinil increases DA)
- **Glutamate** (reticular formation, cortex), general excitation

Sleep-promoting:

- **GABA** (ventrolateral preoptic area, VLPO), inhibits all wake-promoting centers ("flip-flop switch")
- **Adenosine** (basal forebrain), homeostatic sleep drive (blocked by caffeine at A1/A2A receptors)
- **Melatonin** (pineal), circadian sleep signal
- **Galanin** (VLPO), co-released with GABA

REM-specific:

- ACh (LDT/PPT) **promotes** REM; NE and 5-HT **suppress** REM → REM occurs when aminergic neurons are silent ("REM-off") and cholinergic neurons fire ("REM-on")

Q38 [A]: A 50-year-old obese man presents with excessive daytime sleepiness, morning headaches, and his wife reports loud snoring with apneic episodes. What is the pathophysiology and what PSG findings do you expect?

Answer: Obstructive Sleep Apnea (OSA). Pathophysiology: pharyngeal muscle relaxation during sleep → **upper airway collapse** → apnea (cessation of airflow ≥ 10 seconds despite continued respiratory effort) → hypoxemia, hypercapnia → **cortical micro-arousals** to restore airway patency → fragmented sleep architecture.

Expected PSG findings:

- **Apnea-Hypopnea Index (AHI) ≥ 5 /hour** (mild 5-15, moderate 15-30, severe >30)
- **Oxygen desaturation** events ($<90\%$) correlating with apneas
- **Increased N1, decreased N3 (SWS) and REM**, fragmentation with arousals prevents deepening
- **EEG arousals** (3-15 second alpha/beta bursts) following apneic events
- **Paradoxical thoracoabdominal movement** during obstructive events
- Morning headaches from **nocturnal CO₂ retention**

Treatment: **CPAP** (first-line), weight loss, positional therapy, mandibular advancement devices. Psychiatric relevance: untreated OSA mimics/exacerbates **depression, cognitive impairment, ADHD symptoms, treatment-resistant mood disorders**.

Q39 [An]: Why do benzodiazepines reduce SWS and how does this differ from the sleep effects of trazodone and gabapentin?

Answer:

Benzodiazepines:

- Enhance GABA-A at the **alpha1 subunit** → promote N2 (increase spindle activity) but **suppress SWS (N3 delta activity)** by reducing the synchronized cortical slow oscillations that generate delta waves
- Also suppress REM
- Result: increased total sleep time but **reduced restorative sleep quality** → next-day cognitive impairment, tolerance develops, rebound insomnia on withdrawal

Trazodone:

- **5-HT_{2A} antagonism** (primary at low doses) → disinhibits SWS, serotonin normally suppresses SWS via 5-HT_{2A} receptors on cortical pyramidal neurons
- **H1 antagonism** → sedation without significant GABA effects
- Result: **increases SWS, improves sleep architecture quality**, hence popular for insomnia in depression

Gabapentin/pregabalin:

- Bind **alpha2-delta subunit of voltage-gated calcium channels** → reduce excitatory neurotransmitter release
- **Increase SWS/delta sleep** via enhancement of cortical slow oscillations
- Do not suppress REM significantly
- Result: improved sleep quality with **enhanced restorative SWS**, useful in anxiety, fibromyalgia, alcohol withdrawal insomnia

EXAM PEARL

For patients needing restorative sleep, **trazodone or gabapentin preferred** over benzodiazepines.

Q40 [An]: Explain the flip-flop switch model of sleep-wake regulation and why it is clinically relevant.

Answer: Saper's Flip-Flop Switch Model:

The model proposes that sleep-wake transitions are governed by **mutually inhibitory circuits** that function like an electrical flip-flop switch, producing rapid, complete transitions rather than gradual ones:

Wake side: Ascending arousal system, **TMN** (histamine), **LC** (NE), **raphe** (5-HT), **VTA** (DA), **basal forebrain** (ACh), **lateral hypothalamus** (orexin)

Sleep side: **VLPO** (ventrolateral preoptic area), releases **GABA and galanin** to inhibit ALL wake-promoting centers

Stabilizer: **Orexin** from lateral hypothalamus provides a **finger on the wake side of the switch**, reinforces wakefulness and prevents unwanted transitions

Mutual inhibition: When one side is active, it suppresses the other → **self-reinforcing bistable state** (fully awake OR fully asleep, minimal intermediate states).

Clinical relevance:

1. **Narcolepsy (orexin loss):** the switch lacks its stabilizer → unstable, frequent unwanted transitions → intrusion of REM into wakefulness (cataplexy, sleep paralysis, hypnagogic hallucinations) and intrusion of wakefulness into sleep (fragmented nighttime sleep)
2. **General anesthetics:** activate VLPO → flip the switch to sleep side (dexmedetomidine, propofol)
3. **Antihistamines, sedatives:** weaken the wake side → state instability → drowsiness
4. **Delirium:** represents a **failure of the flip-flop switch** → unstable oscillation between states → hallucinations, fluctuating consciousness, sleep-wake cycle disruption
5. **DORAs (suvorexant):** pharmacologically weaken orexin's stabilizing input → allow natural sleep onset without distorting sleep architecture (preserve SWS and REM,

advantage over benzodiazepines)

Exam-critical facts covered: serotonin synthesis, dopamine synthesis, 4 DA pathways, GABA-A binding sites, glutamate hypothesis, Papez circuit, all sleep stages with EEG features, orexin/narcolepsy, REM atonia, frontal lobe tests, SCN-melatonin axis, serotonin syndrome vs NMS, basal ganglia circuits, sleep changes in depression.

GUIDE 02 · PART I

Psychology Core

Paper I · Basic Sciences. Six study modes, from notes to quick review.

Study Notes

EXAM PEARL

Document type: Comprehensive study notes Last updated: March 2026

PART ONE: DEFENSE MECHANISMS

1.1 Definition and Historical Context

Defense mechanisms are unconscious psychological strategies used by the ego to manage conflict between the id, superego, and external reality. They reduce anxiety arising from unacceptable thoughts, feelings, or impulses.

- **Anna Freud** (1936, *The Ego and the Mechanisms of Defence*): First systematic classification. Identified 10 principal defense mechanisms. Emphasized that defenses are normal, universal, and only pathological when rigid, inflexible, or developmentally inappropriate.
- **George Vaillant** (1977, *Adaptation to Life*): Organized defenses into a **hierarchical model** based on maturity level. Drew from the Grant Study, a 35-year longitudinal study of Harvard men. Key finding: mature defenses predict better physical health, career success, and relationships.

Core principle: All people use defense mechanisms. The clinical question is not *whether* defenses are present, but *which level* predominates and *how rigidly* they are deployed.

1.2 Vaillant's Hierarchy of Defense Mechanisms

LEVEL	MATURITY	CHARACTERISTIC	CLINICAL IMPLICATION
Level IV	Mature	Conscious-adjacent, adaptive	Associated with health and resilience
Level III	Neurotic	Common in adults under stress	Associated with anxiety, somatoform presentations
Level II	Immature	Common in personality disorders, adolescents	Associated with interpersonal dysfunction

LEVEL	MATURITY	CHARACTERISTIC	CLINICAL IMPLICATION
Level I	Psychotic/Narcissistic	Reality-distorting	Associated with psychosis, severe PD

1.3 Mature Defense Mechanisms (Level IV)

These defenses integrate reality, interpersonal needs, and private feelings. They maximize gratification while allowing awareness of feelings, ideas, and consequences.

SUBLIMATION

- **Definition:** Channeling unacceptable impulses (aggression, sexual drives) into socially valued activities.
- **Example:** A person with aggressive impulses becomes a competitive surgeon. A person with voyeuristic tendencies becomes a research journalist.
- **Disorder context:** Healthy adaptation; its *absence* is notable in impulse control disorders.
- **Key point:** Unlike other defenses, sublimation allows the instinct to be expressed, just redirected. The drive finds a constructive outlet.

HUMOR

- **Definition:** Using comedy to express feelings or thoughts without personal discomfort or immobilization, without unpleasant effect on others.
- **Example:** A terminally ill patient jokes about their condition to lighten the mood during rounds. "I finally have an excuse to skip my mother-in-law's birthday."
- **Disorder context:** Absence of humor correlates with depression, alexithymia. Gallows humor in healthcare workers = adaptive (until it isn't).
- **Key point:** Differs from sarcasm or hostile wit, which are aggressive. True humor as a defense does not target or wound others.

ALTRUISM

- **Definition:** Vicarious but constructive and gratifying service to others. Differs from altruistic surrender (neurotic self-sacrifice).
- **Example:** A recovering alcoholic volunteers at a rehabilitation center. A bereaved parent starts a support group.
- **Disorder context:** Pathological altruism (compulsive caregiving) is seen in dependent personality disorder, that is *not* mature altruism.
- **Key point:** The person genuinely benefits emotionally. It is not martyrdom.

SUPPRESSION

- **Definition:** **Conscious** or semi-conscious decision to postpone attention to a conflict or impulse. "I'll deal with this later."

- **Example:** A doctor sets aside personal grief to manage an emergency, then processes it after the shift.
- **Disorder context:** The only mature defense with a conscious component. Absence = being overwhelmed by affect (panic disorder, PTSD).
- **Key point:** Suppression ≠ repression. Suppression is **conscious** postponement. Repression is **unconscious** exclusion.

ANTICIPATION

- **Definition:** Realistic planning for future discomfort. Experiencing emotional reactions in advance and preparing.
- **Example:** A patient facing surgery discusses fears and makes a will beforehand. A student prepares coping strategies before exams.
- **Disorder context:** Its absence → anxiety disorders (catastrophizing without preparation). Present in high-functioning anxious individuals.

1.4 Neurotic Defense Mechanisms (Level III)

These defenses alter internal feelings or instinctual expression. They are common in everyday life but can become pathological when rigid.

INTELLECTUALIZATION

- **Definition:** Using abstract thinking, generalizations, or philosophical reasoning to distance from the emotional content of a situation.
- **Example:** A patient diagnosed with cancer discusses the epidemiology and molecular biology of the tumor rather than expressing fear. A bereaved person gives a detailed factual account of the death without any affect.
- **Disorder context:** OCPD (primary defense), obsessional states, some presentations of ASD.
- **Key point:** The person *knows* the facts but does not *feel* them. Affect is divorced from content.

ISOLATION OF AFFECT

- **Definition:** Separating an idea from its associated feeling. The thought remains conscious; the emotion is stripped away.
- **Example:** A surgeon describes a botched procedure in a flat, detached tone. A trauma survivor narrates their assault with no visible distress.
- **Disorder context:** OCD (classic defense, the obsession persists but the emotion is walled off), PTSD (emotional numbing).
- **Key point:** Closely related to intellectualization, but here the specific feeling is removed from a specific idea, not replaced with abstract thinking.

REACTION FORMATION

- **Definition:** Transforming an unacceptable impulse into its opposite. The person adopts attitudes and behaviors diametrically opposed to the underlying wish.
- **Example:** A parent with unconscious hostility toward their child becomes excessively overprotective. A person with homosexual desires becomes vocally homophobic.
- **Disorder context:** **OCD** (cleanliness rituals against anal-sadistic wishes), phobias, some personality styles.
- **Key point:** The behavior is typically excessive and inflexible, a clue to the underlying reversed impulse.

DISPLACEMENT

- **Definition:** Redirecting an emotion from its original object to a safer, less threatening substitute.
- **Example:** A man yelled at by his boss kicks the dog when he gets home. A child angry at a parent destroys a toy.
- **Disorder context:** **Phobias** (classic mechanism, anxiety displaced from unconscious conflict onto a neutral object, e.g., Little Hans displacing castration anxiety onto horses).
- **Key point:** The emotion is preserved; only the target changes.

REPRESSION

- **Definition:** **Unconscious** exclusion of distressing thoughts, wishes, or experiences from conscious awareness. The cornerstone defense in psychoanalytic theory.
- **Example:** A child who was sexually abused has no memory of the event. A person "forgets" a distressing appointment.
- **Disorder context:** **Hysteria/Conversion disorder** (Freud's original model, repressed conflict converts to somatic symptoms), dissociative amnesia.
- **Key point:** Repression is the foundation upon which many other defenses are built. It is **unconscious**, the person does not know they are doing it.

DISSOCIATION

- **Definition:** Disruption of normally integrated functions of consciousness, memory, identity, or perception. A temporary but drastic modification of identity to avoid distress.
 - **Example:** A person in a car accident feels they are watching the event from outside their body. A trauma victim "spaces out" and loses time.
 - **Disorder context:** **Dissociative disorders** (DID, dissociative amnesia, depersonalization/derealization), **conversion disorder**, PTSD, BPD.
 - **Key point:** Ranges from mild (highway hypnosis, daydreaming) to severe (dissociative identity disorder). Can be adaptive in acute trauma, pathological when chronic.
-

1.5 Immature Defense Mechanisms (Level II)

Common in personality disorders, depression, and adolescence. Reduce distress but at significant interpersonal cost.

PROJECTION

- **Definition:** Attributing one's own unacceptable feelings, impulses, or thoughts to another person.
- **Example:** A hostile person perceives others as hostile. "I don't hate him, he hates me." A jealous spouse accuses the partner of infidelity.
- **Disorder context:** **Paranoid personality disorder**, paranoid schizophrenia, delusional disorder (persecutory type). Also seen in BPD.
- **Key point:** The projected content is disowned. The person genuinely believes it originates in the other.

PROJECTIVE IDENTIFICATION

- **Definition:** A two-part process: (1) the person projects unacceptable parts of the self onto another, (2) the recipient *actually begins to feel and act out* the projected material. It is an interpersonal defense.
- **Example:** A BPD patient in therapy projects rageful helplessness onto the therapist. The therapist begins to feel incompetent and frustrated, *actually experiencing* the patient's disowned feelings.
- **Disorder context:** **Borderline personality disorder** (hallmark defense), narcissistic PD. Central concept in Kleinian object relations.
- **Key point:** This is the defense mechanism most important for therapists to recognize. It creates powerful countertransference. Understanding it protects the therapeutic alliance.

PASSIVE AGGRESSION

- **Definition:** Indirect expression of aggression toward others through passivity, masochism, or turning against the self.
- **Example:** A resentful employee "forgets" deadlines. A patient who is angry at the therapist misses sessions. Procrastination as covert defiance.
- **Disorder context:** Formerly passive-aggressive PD (DSM-III-R), now seen across many personality presentations, depression.

ACTING OUT

- **Definition:** Direct expression of an unconscious wish or impulse through action, avoiding awareness of the accompanying affect.
- **Example:** A teenager angry at parents runs away from home. A patient in therapy who feels rejected by the analyst has an affair. Self-harm as expression of inner turmoil.

- **Disorder context:** **Antisocial PD**, BPD (impulsive subtype), adolescent behavioral disorders, substance use disorders.
- **Key point:** The action substitutes for conscious reflection. The person does rather than feels.

FANTASY (SCHIZOID FANTASY/AUTISTIC FANTASY)

- **Definition:** Excessive daydreaming as a substitute for human relationships, more effective action, or problem-solving.
- **Example:** A socially isolated person creates elaborate inner worlds of success and connection. An avoidant patient imagines confronting their abuser but never does.
- **Disorder context:** **Schizoid personality disorder**, schizotypal PD, avoidant PD.

IDEALIZATION

- **Definition:** Attributing exaggerated positive qualities to another person. The object is seen as all-good, perfect, without flaws.
- **Example:** A BPD patient tells the new therapist, "You're the best doctor I've ever had, unlike all the others." A new romantic partner is viewed as flawless.
- **Disorder context:** **BPD** (part of the splitting cycle), narcissistic PD, dependent PD.

DEVALUATION

- **Definition:** Attributing exaggerated negative qualities to another. The object is seen as worthless, contemptible.
- **Example:** The same BPD patient, after a perceived slight, says, "You're the worst doctor. You don't care about anyone." A narcissistic individual dismisses anyone who threatens their self-esteem.
- **Disorder context:** **BPD**, narcissistic PD. Often alternates with idealization.

SPLITTING

- **Definition:** Inability to integrate positive and negative qualities of self or others into a cohesive whole. Objects are perceived as either all-good or all-bad, with rapid oscillation.
 - **Example:** A BPD patient sees the nurse as wonderful and the doctor as terrible, then reverses next week. "You're either with me or against me."
 - **Disorder context:** **Borderline personality disorder** (cardinal defense), narcissistic PD. Theorized to arise from failure of integration in Mahler's rapprochement subphase.
 - **Key point:** Splitting is the foundational defense in BPD. It gives rise to idealization/devaluation, projective identification, and interpersonal chaos.
-

1.6 Psychotic/Narcissistic Defense Mechanisms (Level I)

These defenses significantly distort external reality. Associated with psychotic states and severe personality pathology.

DENIAL

- **Definition:** Refusal to acknowledge some painful aspect of external reality or subjective experience that is apparent to others.
- **Example:** A patient told they have terminal cancer says, "The tests must be wrong." An alcoholic insists they can stop anytime. A mother refuses to believe her child has died.
- **Disorder context:** Psychosis, substance use disorders, mania (denial of illness, anosognosia), grief (first stage per Kubler-Ross).
- **Key point:** Denial operates on **external reality** (vs. repression, which operates on internal wishes). When denial is total and reality-testing is lost, it becomes psychotic.

DISTORTION

- **Definition:** Grossly reshaping external reality to suit inner needs. Includes unrealistic megalomaniacal beliefs, hallucinations, wish-fulfilling delusions.
- **Example:** A patient with psychosis believes they are a deity. A narcissistic individual genuinely perceives universal admiration. A patient in mania believes they have supernatural powers.
- **Disorder context:** Psychosis, mania, severe narcissistic PD.

PSYCHOTIC PROJECTION (DELUSIONAL PROJECTION)

- **Definition:** Projection taken to the point of frank delusion. Perceived persecution without basis in reality.
 - **Example:** A patient believes the government is poisoning their food. A person with delusional jealousy is certain their partner is unfaithful despite no evidence.
 - **Disorder context:** Paranoid schizophrenia, delusional disorder, psychotic episodes.
-

1.7 Additional Defense Mechanisms (Exam-Relevant)

UNDOING

- **Definition:** Performing an act designed to symbolically negate or "undo" a previous thought, impulse, or action deemed unacceptable.
- **Example:** An OCD patient touches a "contaminated" doorknob and then washes hands 50 times. A person who has aggressive thoughts prays compulsively afterward. Lady Macbeth's hand-washing.
- **Disorder context:** **OCD** (classic, obsessional undoing is a core feature).

CONVERSION

- **Definition:** Symbolic representation of intrapsychic conflict through physical symptoms (paralysis, blindness, seizures) without organic pathology.
- **Example:** A soldier develops paralysis of his shooting arm before deployment. A woman in an abusive marriage develops psychogenic blindness.
- **Disorder context:** **Conversion disorder/Functional neurological symptom disorder.**
- **Key point:** The symptom has *symbolic meaning* related to the conflict. Often accompanied by *la belle indifférence* (lack of concern about the deficit).

REGRESSION

- **Definition:** Return to an earlier stage of development in the face of unacceptable thoughts or impulses.
- **Example:** A hospitalized adult begins thumb-sucking. A child who was toilet-trained starts bedwetting after a sibling's birth. An adult under stress becomes clingy and dependent.
- **Disorder context:** Dissociative disorders, schizophrenia (severe regression), medical illness.

RATIONALIZATION

- **Definition:** Offering rational, logical explanations for behaviors actually driven by unconscious motives.
- **Example:** "I didn't get the job because they were biased" (vs. acknowledging poor preparation). An alcoholic says, "I only drink to be social."
- **Disorder context:** Substance use disorders, personality disorders, everyday life.

SOMATIZATION

- **Definition:** Converting psychological distress into physical symptoms as a way of communicating or managing affect.
- **Example:** A patient with unresolved grief presents with chronic headaches and fatigue. A depressed patient reports only somatic complaints (masked depression).
- **Disorder context:** Somatic symptom disorder, illness anxiety disorder, depression (especially in Indian/South Asian cultural contexts).

TURNING AGAINST THE SELF

- **Definition:** Redirecting aggression or negative impulses from an external object toward oneself.
- **Example:** A person angry at a loved one develops self-harming behavior. Depression as anger turned inward (Freudian model).
- **Disorder context:** Depression (classic psychoanalytic formulation), self-harm, masochism.

1.8 Defense Mechanisms in Specific Disorders

OCD

DEFENSE · HOW IT MANIFESTS

Isolation of affect Obsessional thoughts without corresponding emotion

Undoing Compulsive rituals to "cancel out" the obsession

Reaction formation Excessive cleanliness against anal-sadistic impulses

Intellectualization Detailed, affect-free rumination

Displacement Anxiety displaced to specific objects/situations

PHOBIA

DEFENSE · HOW IT MANIFESTS

Displacement Anxiety transferred from unconscious conflict to phobic object

Projection Internal danger perceived as external threat

Avoidance Behavioral extension of displacement, staying away from phobic stimulus

Classic exam example (Little Hans): Oedipal conflict → castration anxiety → displaced onto horses → phobia of horses.

HYSTERIA / CONVERSION DISORDER

DEFENSE · HOW IT MANIFESTS

Repression Conflict is pushed out of consciousness entirely

Conversion Conflict expressed as somatic symptom

Dissociation Fragmentation of consciousness, identity, or memory

Denial La belle indifference, denial of disability's significance

PERSONALITY DISORDERS

PERSONALITY DISORDER · PRIMARY DEFENSES

Borderline PD Splitting, projective identification, idealization/devaluation, acting out, dissociation

Narcissistic PD Idealization (of self), devaluation (of others), projection, denial, distortion

OCPD Intellectualization, isolation of affect, reaction formation, undoing

Paranoid PD Projection, denial

Schizoid PD Fantasy (autistic/schizoid), intellectualization, withdrawal

Antisocial PD Acting out, projection, denial, omnipotent control

Dependent PD Regression, idealization

Histrionic PD Repression, regression, dissociation, somatization

1.9 Therapeutic Relevance

In psychodynamic psychotherapy:

- Defenses are not "broken." They are adaptive strategies that became rigid.
- Therapy aims to help the patient move from lower-level to higher-level defenses, not eliminate defenses.
- **Interpretation of defenses** is a core technique: naming the defense, linking it to the underlying conflict, exploring its origin.

Sequence of working with defenses:

1. **Recognition:** Therapist identifies the defense pattern
2. **Confrontation:** Gently bringing the defense to the patient's attention
3. **Clarification:** Exploring what the defense protects against
4. **Interpretation:** Linking the defense to unconscious conflict and developmental origins
5. **Working through:** Repeated examination until the patient can use higher-level defenses

Countertransference clue: If the therapist feels confused, angry, or incompetent, consider projective identification. If the therapist feels bored, consider intellectualization or isolation of affect. If the therapist feels heroic, consider idealization.

1.10 George Vaillant's Longitudinal Study

Study: Grant Study of Adult Development (1938–ongoing).

- Followed 268 Harvard sophomores for 35+ years.
- Vaillant joined in the 1960s and introduced defense mechanism rating scales.

Key findings:

- Men who predominantly used **mature defenses** had better physical health, more satisfying marriages, higher career achievement, and greater life satisfaction.
- Men using **immature defenses** had higher rates of mental illness, unemployment, divorce, and substance abuse.

- Defense style at age 20 predicted health outcomes at age 65.
- Defenses are **not static**, people can mature in their defensive repertoire over the lifespan (a hopeful finding for psychotherapy).
- **Alcohol abuse** was the single most powerful destroyer of defense maturation.

Exam relevance: Vaillant demonstrated that defense mechanisms are not just theoretical constructs, they are measurable, longitudinally predictive, and clinically meaningful.

PART TWO: DEVELOPMENTAL PSYCHOLOGY

2.1 Erikson's Eight Psychosocial Stages

Erik Erikson (1902–1994) proposed that development continues across the entire lifespan (unlike Freud, who focused on childhood). Each stage presents a **psychosocial crisis**, a turning point where the individual can develop a basic **virtue** (strength) or suffer a maladaptive outcome.

Key principles:

- Development is **epigenetic**, each stage builds on the resolution of previous stages.
- A "crisis" is not a catastrophe but a necessary turning point.
- Complete resolution is not required, a *favorable ratio* of positive to negative is sufficient.

STAGE-BY-STAGE SUMMARY

STAGE	AGE	PSYCHOSOCIAL CRISIS	BASIC VIRTUE	KEY RELATIONSHIP	PSYCHOPATHOLOGICAL OUTCOME
1	0–1 yr	Trust vs Mistrust	Hope	Mother / primary caregiver	Depression, psychosis, substance dependence, paranoid traits
2	1–3 yr	Autonomy vs Shame & Doubt	Will	Parents	OCD, OCPD, excessive self-doubt, passive aggression
3	3–6 yr	Initiative vs Guilt	Purpose	Family	Conversion disorder, phobias, psychosomatic illness, inhibition

STAGE	AGE	PSYCHOSOCIAL CRISIS	BASIC VIRTUE	KEY RELATIONSHIP	PSYCHOPATHOLOGICAL OUTCOME
4	6–12 yr	Industry vs Inferiority	Competence	School, peers	Learning difficulties, low self-esteem, avoidant behavior, identity foreclosure
5	12–20 yr	Identity vs Role Confusion	Fidelity	Peer groups, role models	Identity diffusion, BPD, delinquency, cult susceptibility
6	20–40 yr	Intimacy vs Isolation	Love	Partners, friends	Avoidant PD, schizoid withdrawal, chronic loneliness, relationship dysfunction
7	40–65 yr	Generativity vs Stagnation	Care	Family, community, work	Midlife crisis, narcissistic preoccupation, depression
8	65+ yr	Integrity vs Despair	Wisdom	Mankind / life itself	Late-life depression, existential despair, fear of death

DETAILED STAGE NOTES

Stage 1, Trust vs Mistrust (0–1 year)

- **Core task:** Developing a basic sense that the world is reliable and safe.
- **Positive resolution:** The infant experiences consistent, responsive caregiving → develops **hope**, the enduring belief that wishes can be fulfilled.
- **Negative resolution:** Inconsistent or neglectful care → **basic mistrust**, the world is unpredictable, unreliable.
- **Clinical link:** Forms the foundation for attachment security. Severe mistrust → paranoid features, inability to form therapeutic alliance, substance dependence (seeking external sources of comfort).
- **Corresponds to:** Freud's oral stage, Bowlby's attachment formation.

Stage 2, Autonomy vs Shame & Doubt (1–3 years)

- **Core task:** Gaining a sense of self-control and independence (toilet training is the classic arena).
- **Positive resolution:** "I can do things myself" → **will**, determination to exercise choice.
- **Negative resolution:** Excessive control or shaming → doubt, rigidity, need for external structure.
- **Clinical link:** OCD (need for control, shame, doubt as core affect), OCPD, passive-aggressive patterns. The "anal character" in Freudian terms.
- **Corresponds to:** Freud's anal stage, Mahler's practicing subphase.

Stage 3, Initiative vs Guilt (3–6 years)

- **Core task:** Taking initiative, exploring, asking "why?" Developing a sense of purpose and direction.
- **Positive resolution:** "I can make things happen" → **purpose**.
- **Negative resolution:** Guilt over assertiveness → inhibition, psychosomatic complaints.
- **Clinical link:** Conversion disorder, phobias (displacement of Oedipal guilt), excessive guilt in depression.
- **Corresponds to:** Freud's phallic/Oedipal stage.

Stage 4, Industry vs Inferiority (6–12 years)

- **Core task:** Mastering skills, gaining competence in school and social domains.
- **Positive resolution:** "I can learn and succeed" → **competence**.
- **Negative resolution:** Repeated failure or discouragement → feelings of inadequacy, giving up.
- **Clinical link:** ADHD (chronic inferiority from school failures), specific learning disorders, avoidant traits, social anxiety beginning in childhood.

Stage 5, Identity vs Role Confusion (12–20 years)

- **Core task:** Developing a coherent sense of self, values, and direction.
- **Positive resolution:** **Fidelity**, ability to sustain loyalties and commitments.
- **Negative resolution:** Identity diffusion, "Who am I?" remains unanswered.
- **Clinical link:** BPD (identity disturbance is a DSM criterion), adolescent crises, vulnerability to cults or extremist groups, delinquency.
- **Erikson's concept of "moratorium":** A socially sanctioned period of role experimentation. College, gap years, travel = healthy moratorium. Indefinite moratorium = pathological.
- **Marcia's Identity Statuses** (extension of Erikson):

STATUS	CRISIS EXPERIENCED?	COMMITMENT MADE?	DESCRIPTION
Identity Achievement	Yes	Yes	Explored options, made choices
Moratorium	In process	No	Actively exploring
Foreclosure	No	Yes	Adopted identity without exploration (e.g., family pressure)
Identity Diffusion	No	No	No exploration, no commitment

Stage 6, Intimacy vs Isolation (20–40 years)

- **Core task:** Forming deep, committed relationships without losing one's identity.
- **Positive resolution:** **Love**, the capacity for mutual devotion.
- **Negative resolution:** Isolation, superficial relationships, fear of commitment.
- **Clinical link:** Avoidant PD, schizoid PD, chronic relationship difficulties, loneliness as a risk factor for depression.

Stage 7, Generativity vs Stagnation (40–65 years)

- **Core task:** Contributing to the next generation through parenting, mentoring, creative work.
- **Positive resolution:** **Care**, a widening concern beyond the self.
- **Negative resolution:** Self-absorption, stagnation, "midlife crisis."
- **Clinical link:** Narcissistic preoccupation, depression in middle age, professional burnout.

Stage 8, Integrity vs Despair (65+ years)

- **Core task:** Reviewing one's life with a sense of meaning and acceptance.
- **Positive resolution:** **Wisdom**, accepting one's life as it was, including failures.
- **Negative resolution:** Regret, bitterness, fear of death.
- **Clinical link:** Late-life depression, existential anxiety, end-of-life care considerations.

2.2 Piaget's Cognitive Development

Jean Piaget (1896–1980) described four stages of cognitive development. Children are not "little adults", they think qualitatively differently at each stage.

Key concepts across all stages:

- **Schema:** A cognitive framework for organizing information.
- **Assimilation:** Fitting new information into existing schemas.
- **Accommodation:** Modifying schemas to fit new information.

- **Equilibration:** The drive to balance assimilation and accommodation.

STAGE SUMMARY

STAGE	AGE	KEY ACHIEVEMENTS	KEY LIMITATIONS
Sensorimotor	0–2 yr	Object permanence, goal-directed behavior	No symbolic thought
Preoperational	2–7 yr	Symbolic play, language explosion	Egocentrism, centration, no conservation
Concrete Operational	7–11 yr	Conservation, reversibility, seriation, classification	Cannot think abstractly
Formal Operational	11+ yr	Abstract reasoning, hypothetical-deductive thinking	Not universally achieved

SENSORIMOTOR STAGE (0–2 YEARS)

The infant learns through sensory experiences and motor actions. No internal representation of objects initially.

Six substages:

SUBSTAGE	AGE	KEY FEATURE
1. Reflex activity	0–1 mo	Innate reflexes (sucking, grasping)
2. Primary circular reactions	1–4 mo	Repeating actions centered on own body (thumb-sucking)
3. Secondary circular reactions	4–8 mo	Repeating actions that affect environment (shaking a rattle)
4. Coordination of secondary schemes	8–12 mo	Goal-directed behavior, early object permanence (A-not-B error)
5. Tertiary circular reactions	12–18 mo	Active experimentation, trial-and-error ("little scientist")
6. Mental representation	18–24 mo	Full object permanence , deferred imitation, symbolic thought begins

Object permanence: The understanding that objects continue to exist when out of sight. Develops gradually across substages 4–6. Tested by hiding an object under a cloth.

A-not-B error (substage 4): Infant searches for object at location A (where it was previously found) even after seeing it hidden at location B. Disappears by substage 6.

Clinical relevance: Failure to develop object permanence → separation anxiety disorder may persist. Piaget's stages are used in developmental assessments (Bayley Scales draw on Piagetian tasks).

PREOPERATIONAL STAGE (2–7 YEARS)

The child can use symbols (language, pretend play) but cannot yet perform logical operations.

Key features:

- **Symbolic function:** Language, drawing, pretend play. A stick becomes a sword.
- **Egocentrism:** Inability to take another's perspective. The "three mountains task", child assumes others see what they see.
- **Animism:** Attributing life to inanimate objects ("The sun is angry today").
- **Centration:** Focusing on one aspect of a situation and ignoring others.
- **Lack of conservation:** Cannot understand that quantity is preserved when appearance changes. Classic example: pouring water from a short wide glass to a tall thin glass, child says there is "more" water in the tall glass.
- **Irreversibility:** Cannot mentally reverse an action.

Clinical relevance: Preoperational thinking can re-emerge under stress or cognitive decline (dementia). Children at this stage are egocentric witnesses, important in forensic child psychiatry.

CONCRETE OPERATIONAL STAGE (7–11 YEARS)

Logical thinking emerges, but only for concrete (not abstract) problems.

Key achievements:

- **Conservation:** Understanding that quantity remains the same despite changes in shape/arrangement. Develops for number first, then mass, then volume (horizontal decalage).
- **Reversibility:** Understanding that actions can be mentally reversed.
- **Seriation:** Arranging objects along a dimension (e.g., shortest to tallest).
- **Classification:** Grouping objects by shared features. Understanding class inclusion (roses are a subset of flowers).
- **Decentration:** Considering multiple aspects simultaneously.
- **Loss of egocentrism:** Can take others' perspectives.

Clinical relevance: This is the stage at which children can meaningfully participate in CBT (logical reasoning about thoughts). Before age 7, therapy must be more play-based.

FORMAL OPERATIONAL STAGE (11+ YEARS)

Abstract, hypothetical, and systematic thinking becomes possible.

Key achievements:

- **Abstract reasoning:** Can think about concepts not physically present (justice, love, infinity).
- **Hypothetical-deductive reasoning:** Can form hypotheses and test them systematically. "If X, then Y. Let me test X."
- **Propositional thought:** Can evaluate the logic of statements without reference to real-world content.
- **Metacognition:** Thinking about thinking.

Clinical relevance:

- Adolescent onset of existential anxiety, identity questioning, and philosophical preoccupation corresponds to formal operational thought.
- Not all adults fully achieve formal operations, some remain at concrete operational (relevant in forensic psychiatry, intellectual disability).
- Psychotherapy modalities like CBT and psychodynamic therapy require formal operational capacity.

2.3 Attachment Theory

BOWLBY'S ATTACHMENT THEORY

John Bowlby (1907–1990) proposed that attachment is an innate biological system designed to maintain proximity to a caregiver for survival. It is not a byproduct of feeding (contra behaviorism).

Core principles:

- Attachment is a **primary drive** (not secondary to hunger).
- The attachment figure serves as a **secure base** for exploration and a **safe haven** in distress.
- **Internal working models** (IWMs): Mental representations of self, others, and relationships formed from early attachment experiences. These persist into adulthood and shape relationship patterns.
- **Monotropy:** Bowlby proposed a hierarchy of attachment figures with one primary figure (controversial, later revised to acknowledge multiple attachments).

Bowlby's Four Phases of Attachment Development:

PHASE	AGE	BEHAVIOR
1. Pre-attachment (Indiscriminate social responsiveness)	0–6 weeks	Responds to any caregiver. Crying, grasping, smiling are non-specific signals.

PHASE	AGE	BEHAVIOR
2. Attachment-in-the-making (Discriminating social responsiveness)	6 weeks – 6-8 months	Differential responding to familiar vs. strangers. Not yet full attachment.
3. Clear-cut attachment	6-8 months – 18-24 months	Separation anxiety, stranger anxiety, use of caregiver as secure base. Active proximity-seeking.
4. Reciprocal relationships (Goal-corrected partnership)	24 months +	Understands caregiver's goals and feelings. Can tolerate separation with explanation. Negotiates.

Separation anxiety peaks at 8–12 months. **Stranger anxiety** peaks at 8–10 months. These are normal developmental milestones, not pathology.

AINSWORTH'S STRANGE SITUATION PROCEDURE

Mary Ainsworth (1913–1999) created the **Strange Situation**, a structured laboratory observation to classify infant attachment at 12–18 months. Eight episodes of separation and reunion with mother and a stranger.

ATTACHMENT STYLE	% IN NORMATIVE SAMPLES	CHILD BEHAVIOR	CAREGIVER STYLE
Secure (B)	60–65%	Distressed on separation, quickly soothed on reunion, uses mother as secure base	Sensitive, responsive, consistent
Anxious-Ambivalent/Resistant (C)	10–15%	Extremely distressed on separation, not easily consoled on reunion (clings but also resists contact), preoccupied with mother	Inconsistent availability, sometimes responsive, sometimes not
Anxious-Avoidant (A)	20–25%	Little distress on separation, avoids/ignores mother on reunion, treats stranger similarly	Consistently rejecting, dismissive of emotional needs
Disorganized/Disoriented (D)	5–10% (added by Main & Solomon, 1986)	Contradictory behaviors, approaching while averting gaze, freezing, stereotypies	Frightening or frightened caregiver (often history of abuse, unresolved trauma, or mental illness)

ADULT ATTACHMENT (AAI AND BEYOND)

Adult Attachment Interview (AAI), developed by Mary Main. A semi-structured interview about childhood attachment experiences. Classified by *how* the person narrates (coherence), not *what* they report.

AAI CLASSIFICATION	CORRESPONDS TO INFANT PATTERN	NARRATIVE STYLE
Autonomous/Secure	Secure (B)	Coherent, balanced, values attachment
Dismissing	Avoidant (A)	Brief, idealizing or derogating, claims not to remember
Preoccupied	Ambivalent (C)	Long, angry, confused, still enmeshed with past
Unresolved/Disorganized	Disorganized (D)	Lapses in reasoning when discussing loss or trauma

CLINICAL IMPLICATIONS OF ATTACHMENT THEORY

Insecure attachment is a risk factor for:

- **Depression:** Anxious attachment → interpersonal dependence, fear of abandonment → vulnerability to loss events.
- **Anxiety disorders:** Ambivalent attachment → separation anxiety disorder, generalized anxiety.
- **Personality disorders:** Disorganized attachment → strongest predictor of BPD. Avoidant attachment → schizoid, avoidant PD.
- **Relationship difficulties:** Internal working models shape adult romantic relationships. "Earned security" is possible through corrective experiences (therapy, healthy relationships).
- **Parenting:** Attachment style is transmitted intergenerationally. AAI classification during pregnancy predicts infant attachment at 12 months with ~75% accuracy.

Therapeutic alliance as an attachment relationship:

- The therapist functions as a secure base.
- Patients with insecure attachment will re-enact their attachment patterns in therapy.
- Recognizing this is essential for managing ruptures and building trust.

2.4 Other Developmental Theorists

MARGARET MAHLER: SEPARATION-INDIVIDUATION

Mahler (1897–1985) described the psychological birth of the infant through three main phases:

PHASE	AGE	DESCRIPTION
Normal Autism	0–1 month	Sleepy, self-absorbed, minimal responsiveness (concept now controversial)
Symbiosis	1–5 months	Infant and mother experienced as a fused unit. No self-other differentiation.
Separation-Individuation	5–36 months	Gradual psychological separation from mother

Separation-Individuation subphases:

SUBPHASE	AGE	DESCRIPTION
Differentiation	5–10 mo	"Hatching", beginning to distinguish self from mother. Checking back.
Practicing	10–16 mo	Walking! Exuberant exploration. "Love affair with the world." Brief returns to mother for "emotional refueling."
Rapprochement	16–24 mo	Realization of separateness brings anxiety. Ambivalence, wants independence but needs reassurance. Rapprochement crisis = clinging alternating with pushing away.
Object Constancy	24–36 mo	Internal representation of mother maintained even when she is absent. Can tolerate ambivalence.

Clinical relevance: BPD is theorized (by Mahler/Masterson) to result from failure at the rapprochement subphase, the child cannot integrate good and bad object representations → splitting. Object constancy failure → abandonment intolerance.

DONALD WINNICOTT

Key concepts:

- **Good-enough mother:** A caregiver who meets the infant's needs adequately (not perfectly). Gradually introduces tolerable frustrations that promote development. "Perfect" mothering is actually harmful, it prevents the child from developing coping capacity.
- **Transitional object:** An object (blanket, teddy bear) that represents the transition between subjective omnipotence and objective reality. It is the child's first "not-me"

possession.

- **Transitional space:** The intermediate area of experience between inner and outer reality. Art, play, religion, and psychotherapy all occur in transitional space.
- **True self vs False self:** True self = spontaneous, authentic. False self = compliant, developed to protect the true self when caregiving is inadequate. Severe false-self pathology → feeling empty, "going through the motions."
- **Holding environment:** The therapist provides a safe psychological "holding" that mirrors the mother's early containment of the infant.

LEV VYGOTSKY

Key concept, Zone of Proximal Development (ZPD):

- The gap between what a learner can do independently and what they can do with guidance from a more skilled person.
- Learning occurs in the ZPD, not below it (too easy, no growth) or above it (too hard, frustration).
- **Scaffolding** (term from Bruner, building on Vygotsky): Structured support that is gradually removed as competence increases.

Clinical relevance:

- Psychotherapy as scaffolding, the therapist operates within the patient's ZPD.
- Relevant to psychoeducation: pitching information at the right level.
- In child psychiatry, informs educational interventions.

PART THREE: THEORIES OF EMOTION + GRIEF + AGGRESSION

3.1 Classical Theories of Emotion

JAMES-LANGE THEORY (1884)

- **Model:** Event → physiological arousal → conscious emotion. "I am afraid because I am running."
- **Sequence:** Stimulus → peripheral bodily changes (trembling, sweating, heart racing) → brain interprets these changes → experience of emotion.
- **Key claim:** Emotions ARE the perception of bodily changes. Without the body's response, there is no emotion.
- **Evidence for:** People with spinal cord injuries report diminished emotional intensity. Facial feedback hypothesis (forcing a smile can improve mood).
- **Criticism:** Cannon's objections, visceral responses are too slow and too undifferentiated to account for the rapidity and variety of emotions. People with severed spinal cords still

experience emotions (though diminished).

CANNON-BARD THEORY (1927)

- **Model:** Event → simultaneous physiological arousal AND conscious emotion (both originate centrally via the thalamus).
- **Sequence:** Stimulus → thalamus → simultaneously sends signals to (1) cortex (conscious emotion) and (2) body (physiological response).
- **Key claim:** Emotional experience and bodily response are **independent, simultaneous** events.
- **Evidence for:** Physiological arousal patterns are similar across different emotions (challenge to James-Lange). Emotions can occur faster than visceral changes.
- **Criticism:** Oversimplifies the role of the thalamus. Bodily feedback does influence emotional experience.

SCHACHTER-SINGER TWO-FACTOR THEORY (1962)

- **Model:** Event → undifferentiated physiological arousal → cognitive appraisal / label → specific emotion.
- **Two factors:** (1) Physiological arousal + (2) cognitive interpretation of that arousal.
- **Key study:** Adrenaline injection study, participants injected with epinephrine attributed their arousal to the emotional context (happy or angry confederate) when they had no explanation for their physical symptoms.
- **Key claim:** Arousal tells you *something is happening*. Cognition tells you *what* is happening. The same arousal can become anger, fear, or excitement depending on context.
- **Clinical relevance:** Panic disorder, misattribution of normal arousal as catastrophic. Excitation transfer in aggression. Cognitive therapy for anxiety (reappraisal of bodily sensations).

SUMMARY COMPARISON TABLE

THEORY	SEQUENCE	WHERE EMOTION "HAPPENS"
James-Lange	Stimulus → body → brain → emotion	Periphery (body first)
Cannon-Bard	Stimulus → brain → body + emotion simultaneously	Thalamus (central, parallel)
Schachter-Singer	Stimulus → body + cognition → labeled emotion	Cognition (appraisal is key)

PAPEZ CIRCUIT THEORY (1937)

James Papez proposed a circuit for emotional processing:

Circuit: Hippocampus → Fornix → Mammillary bodies → Mammillothalamic tract → Anterior thalamic nucleus → Cingulate cortex → back to Hippocampus.

- Originally proposed as the "stream of feeling."
- Now understood as more related to **memory** than pure emotion, but historically important.
- Clinical relevance: Lesions in the Papez circuit → amnesia (Korsakoff syndrome, mammillary body damage), emotional dysregulation.

MACLEAN'S TRIUNE BRAIN (1960S)

Paul MacLean proposed three evolutionary layers of the brain:

LAYER	STRUCTURE	FUNCTION
Reptilian brain	Brainstem, basal ganglia	Basic survival, reflexes, stereotyped behavior
Paleomammalian brain (Limbic system)	Amygdala, hippocampus, hypothalamus, cingulate	Emotion, motivation, memory, social behavior
Neomammalian brain	Neocortex	Abstract thought, language, planning, reasoning

- MacLean coined the term "**limbic system**."
- **Criticism:** Oversimplified. The three layers do not function independently, they are deeply interconnected. Evolution did not simply "add layers." However, the concept remains useful as a teaching heuristic.

3.2 Basic Emotions

EKMAN'S SIX BASIC EMOTIONS (1972)

Paul Ekman studied facial expressions cross-culturally (including isolated tribes in Papua New Guinea) and identified six universal emotions recognized across all cultures:

1. **Happiness**, zygomatic smile (Duchenne smile includes orbicularis oculi)
2. **Sadness**, inner brow raise, lip corner depression
3. **Anger**, brow lowering, lip pressing, nostril flaring
4. **Fear**, brow raise, eye widening, lip stretching
5. **Disgust**, nose wrinkling, upper lip raising
6. **Surprise**, brow raise, jaw drop

Clinical relevance:

- Alexithymia (inability to identify emotions), common in psychosomatic conditions, ASD, PTSD.
- Flat affect in schizophrenia, reduced facial expression of emotion.

- Ekman's Facial Action Coding System (FACS) used in research and lie detection.

PLUTCHIK'S WHEEL OF EMOTIONS (1980)

Robert Plutchik proposed **eight primary emotions** arranged in four pairs of opposites:

PAIR · EMOTIONS

1 Joy ↔ Sadness

2 Trust ↔ Disgust

3 Fear ↔ Anger

4 Surprise ↔ Anticipation

- Emotions vary in **intensity** (e.g., annoyance → anger → rage).
 - **Dyads:** Combining adjacent emotions creates secondary emotions (joy + trust = love; fear + surprise = alarm).
 - **Clinical use:** Useful framework for psychoeducation about emotions in therapy (especially with alexithymic patients or those with limited emotional vocabulary).
-

3.3 Neural Circuits of Emotion

AMYGDALA

- **Location:** Medial temporal lobe, anterior to hippocampus.
- **Function:** Fear conditioning, threat detection, emotional memory consolidation.
- **Fear conditioning paradigm:** Neutral stimulus (tone) paired with aversive stimulus (shock) → amygdala learns to associate tone with threat → conditioned fear response.
- **Two pathways (LeDoux):**
- **Low road:** Thalamus → amygdala (fast, crude, "shoot first, ask questions later")
- **High road:** Thalamus → cortex → amygdala (slow, accurate, contextual processing)
- **Clinical relevance:** Amygdala hyperactivation in PTSD, social anxiety disorder, specific phobias. Amygdala lesions (Kluver-Bucy syndrome) → loss of fear, hypersexuality, visual agnosia, hyperorality.

PREFRONTAL-LIMBIC CONNECTIONS

- **Ventromedial PFC (vmPFC):** Emotional decision-making, extinction of conditioned fear (dampens amygdala). Damage → poor social judgment (Phineas Gage).
- **Dorsolateral PFC (dlPFC):** Working memory, cognitive control over emotion. Hypoactive in depression.
- **Orbitofrontal cortex (OFC):** Reward processing, impulse control. Damage → disinhibition, personality change, aggression.

- **Key principle:** Top-down regulation. The PFC inhibits/modulates limbic activity. When PFC control is weakened (alcohol, brain injury, PTSD), limbic responses dominate → impulsivity, emotional dysregulation.

ANTERIOR CINGULATE CORTEX (ACC)

- **Function:** Conflict monitoring, emotional regulation, error detection, pain processing.
- **Dorsal ACC:** Cognitive conflict monitoring.
- **Subgenual ACC (Brodmann area 25):** Overactive in depression (target of deep brain stimulation trials).
- **Clinical relevance:** ACC dysfunction in OCD (error detection gone haywire), depression, chronic pain syndromes.

INSULA

- **Function: Interoception,** awareness of internal bodily states (heartbeat, gut feelings, temperature). Bridges body and emotion.
- **Anterior insula:** Subjective emotional experience, empathy, disgust.
- **Clinical relevance:** Insula dysfunction in alexithymia (poor interoception → cannot identify emotions), anxiety disorders (heightened interoceptive awareness → panic), addiction (craving representation).

3.4 Emotional Intelligence

GOLEMAN'S MODEL (1995)

Daniel Goleman popularized emotional intelligence (EI), building on Salovey and Mayer's original model.

Five domains:

DOMAIN	DEFINITION	CLINICAL/EXAM RELEVANCE
Self-awareness	Recognizing one's own emotions, strengths, weaknesses	Alexithymia = failure of self-awareness. Core target in therapy.
Self-regulation	Managing emotions, controlling impulses, adapting	Impulsivity in BPD, ADHD. DBT skills training targets this.
Motivation	Internal drive, optimism, commitment to goals	Depression = motivational deficit. Anhedonia undermines this domain.
Empathy	Understanding others' emotions, perspective-taking	Deficient in ASPD, narcissistic PD. Central to therapeutic relationship.

DOMAIN	DEFINITION	CLINICAL/EXAM RELEVANCE
Social skills	Managing relationships, conflict resolution, leadership	Social skills deficits in ASD, schizophrenia, social anxiety disorder.

Clinical relevance:

- EI is a stronger predictor of life success than IQ in many domains.
- Low EI is associated with substance abuse, interpersonal violence, poor therapeutic alliance.
- EI can be developed through psychotherapy (especially DBT, mentalizing-based therapy).
- **Alexithymia** can be conceptualized as a severe deficit in emotional intelligence, particularly self-awareness and self-regulation.

3.5 Grief, Bereavement, and Mourning

DEFINITIONS

TERM · DEFINITION

Bereavement The state of having experienced a loss (the objective fact of loss)

Grief The emotional, cognitive, behavioral, and physiological reaction to loss

Mourning The social and cultural process of adapting to loss (rituals, wearing black, shiva)

KUBLER-ROSS FIVE STAGES (1969)

From *On Death and Dying*, originally described for patients facing their own death, later applied broadly to grief.

STAGE	DESCRIPTION	CLINICAL NOTE
1. Denial	"This can't be happening"	Protective buffer. Allow, do not force reality.
2. Anger	"Why me?" Displaced onto doctors, family, God	Normalize. Do not take personally.
3. Bargaining	"If only..." Deals with God or fate	May include guilt over past actions
4. Depression	Deep sadness as reality sinks in. Withdrawal.	Preparatory grief. Distinguish from clinical depression.
5. Acceptance	"It will be okay." Not happiness, quiet acknowledgment.	Not all individuals reach this stage.

Important caveats:

- Stages are **not linear or universal**. People may skip stages, revisit them, or experience several simultaneously.
- Kubler-Ross herself later acknowledged this model was never meant to be a rigid framework.
- Despite criticism, it remains the most commonly asked model in exams.

WORDEN'S FOUR TASKS OF MOURNING (1991)

A more active, task-based model than Kubler-Ross. The bereaved person must **work through** these tasks:

TASK · DESCRIPTION

1. Accept the reality of the loss Overcome denial. The person is gone and will not return.

2. Process the pain of grief Allow and work through the emotional pain. Suppression → complicated grief.

3. Adjust to the world without the deceased External adjustments (daily tasks), internal adjustments (identity, sense of self), spiritual adjustments (meaning-making).

4. Find an enduring connection while embarking on a new life Maintain a bond with the deceased while reinvesting in living. Not "moving on" but "moving forward."

Clinical relevance: Worden's model is useful therapeutically. It identifies *where* a person is stuck (which task is incomplete) and guides intervention.

BOWLBY'S FOUR PHASES OF GRIEF (1980)

PHASE	DURATION	DESCRIPTION
1. Numbing	Hours to days	Shock, disbelief, emotional blunting
2. Yearning and Searching	Weeks to months	Pining for the deceased, restlessness, scanning crowds, auditory / visual misperceptions of the deceased
3. Disorganization and Despair	Months	Aimlessness, withdrawal, difficulty with daily functioning
4. Reorganization	Variable	New identity, new routines, return to functioning

Key point: Bowlby's model connects grief to attachment theory, grief is essentially an attachment response to loss of the attachment figure.

NORMAL GRIEF VS MAJOR DEPRESSION

FEATURE	NORMAL GRIEF	MAJOR DEPRESSION
Predominant affect	Emptiness and loss, comes in waves ("pangs of grief")	Persistent depressed mood, pervasive
Self-esteem	Generally preserved	Worthlessness, self-loathing
Thoughts of death	Wishing to be with the deceased	Suicidal ideation due to worthlessness
Guilt	Related to the deceased ("I should have been there")	Global, pervasive ("I am bad")
Functioning	Fluctuating, can have "good days"	Persistently impaired
Duration	Improving over weeks to months	Persistent beyond 2 weeks (MDD)
Response to comfort	Temporarily improved	Minimal improvement
Psychomotor change	Mild	Can be severe retardation or agitation

PROLONGED GRIEF DISORDER (PGD)

New in DSM-5-TR (2022) and ICD-11.

DSM-5-TR criteria (simplified):

- Death of a person close to the bereaved at least **12 months** ago (6 months in ICD-11).
- Since the death, **persistent and pervasive** grief response characterized by intense longing/yearning AND preoccupation with the deceased.
- At least 3 of 8 symptoms: identity disruption, disbelief, avoidance of reminders, intense emotional pain, difficulty reintegrating, emotional numbness, meaninglessness, intense loneliness.
- Causes clinically significant distress or impairment.
- Duration and severity exceed expected social, cultural, or religious norms.
- Not better explained by another mental disorder.

Risk factors for PGD:

- Insecure attachment (anxious/preoccupied)
- Sudden, violent, or unexpected death
- Loss of a child or partner
- History of mood/anxiety disorders
- Limited social support
- Dependent relationship with the deceased

Management:

- **First-line:** Grief-focused CBT (e.g., Shear's Complicated Grief Treatment, exposure-based, integrates CBT and attachment theory).
- Pharmacotherapy: SSRIs may help comorbid depression but limited evidence for grief per se. Some evidence for escitalopram + grief therapy.
- Supportive counseling, group therapy.
- Avoid benzodiazepines (interfere with emotional processing of grief).

3.6 Aggression

DEFINITION AND TYPES

Aggression: Behavior intended to cause harm to another person (physical or psychological) who is motivated to avoid that harm.

TYPE	ALSO CALLED	CHARACTERISTICS	NEURAL SUBSTRATE
Predatory (Instrumental)	Proactive, cold	Planned, goal-directed, low arousal, no anger required	Ventral striatum, PFC (intact, calculating)
Affective (Reactive/Hostile)	Impulsive, hot	Unplanned, provocation-driven, high arousal, anger	Amygdala hyperactivation, PFC hypoactivation

BIOLOGICAL BASIS OF AGGRESSION

Neurotransmitters:

SYSTEM · ROLE

Serotonin (5-HT) Low serotonin → increased aggression (most robust finding). Low CSF 5-HIAA correlates with impulsive violence and completed suicide.

Norepinephrine Increased NE → heightened arousal, fight-or-flight activation

Dopamine Increased DA in mesolimbic pathway → reward from aggressive acts (especially predatory aggression)

GABA Inhibitory. Low GABA tone → disinhibition → aggression. Alcohol reduces GABA inhibition.

Testosterone Higher levels associated with aggression. Correlation, not simple causation. Organizational (prenatal) vs activational (adult) effects.

Cortisol Low cortisol → reduced fear of consequences → antisocial behavior (conduct disorder, ASPD)

Neuroanatomy:

STRUCTURE · ROLE IN AGGRESSION

Amygdala Threat detection, fear-based aggression. Stimulation → rage in animals.

Hyperactive in reactive aggression.

Prefrontal cortex Inhibition of aggressive impulses. Damage → disinhibited aggression (Phineas Gage). **Hypoactive** in violent offenders.

Hypothalamus Ventromedial → predatory aggression. Dorsolateral → affective aggression (animal studies).

Orbitofrontal cortex Impulse control, reward processing. Damage → personality change, aggression, poor judgment.

Genetics:

- **MAOA gene** ("warrior gene"): Low-activity variant + childhood maltreatment → significantly increased risk of violent behavior (Caspi et al., 2002). Gene alone does not determine aggression, gene-environment interaction.
- Twin studies: ~50% heritability for aggression.

PSYCHOLOGICAL THEORIES OF AGGRESSION

1. Frustration-Aggression Hypothesis (Dollard et al., 1939)

- **Original:** Frustration always leads to aggression; aggression is always caused by frustration.
- **Revised (Berkowitz, 1989):** Frustration leads to *negative affect*, which *increases the probability* of aggression (but does not guarantee it). Aggression can have other causes. Negative affect is the mediator.
- **Clinical relevance:** Explains irritability in depression, anger outbursts in ADHD, road rage.

2. Social Learning Theory (Bandura, 1973)

- Aggression is **learned through observation and reinforcement**, not instinct alone.
- **Bobo Doll Experiment (1961):** Children who observed an adult model behaving aggressively toward an inflatable doll imitated that behavior, punching, kicking, using a mallet. Children who observed a non-aggressive model were significantly less aggressive.
- Key concepts:
- **Observational learning (modeling):** Aggression is learned by watching others.
- **Vicarious reinforcement:** Seeing aggression rewarded increases imitation.
- **Self-efficacy for aggression:** "I can be aggressive and get what I want."

- **Clinical relevance:** Media violence exposure, domestic violence modeling (children who witness IPV are more likely to perpetrate it), gang culture. Forms the basis for social skills training and anger management interventions.

3. General Aggression Model (GAM, Anderson & Bushman, 2002)

- Integrates biological, cognitive, and social factors into one framework.
- Inputs (person factors + situation factors) → internal states (affect, cognition, arousal) → appraisal → aggressive or non-aggressive behavior.
- Most comprehensive current model.

PREDICTORS OF VIOLENCE

Best validated predictors of violent behavior (for exam purposes):

FACTOR · DETAILS

Past history of violence Single strongest predictor

Substance use Alcohol is the substance most associated with violence

Young age and male sex Peak violence in males aged 15–25

Active psychotic symptoms Command hallucinations, persecutory delusions (modest risk increase)

Non-adherence to treatment In psychiatric patients

Access to weapons Increases lethality

Personality factors Low empathy, impulsivity, callous-unemotional traits

Psychopathy (PCL-R) Strong predictor of instrumental violence

Structured risk assessment tools:

- **HCR-20** (Historical-Clinical-Risk Management): Most widely used. 20 items across historical, clinical, and risk management domains.
- **PCL-R** (Psychopathy Checklist, Revised): Hare's instrument. Score $\geq 30/40$ = psychopathy.
- **VRAG** (Violence Risk Appraisal Guide): Actuarial tool.

MANAGEMENT OF AGGRESSION

Acute management (psychiatric emergency):

STEP · INTERVENTION

1. De-escalation Calm voice, non-threatening posture, offer choices, reduce stimulation, validate feelings

2. Oral medication Lorazepam 1–2 mg OR haloperidol 5 mg + promethazine 25 mg OR olanzapine 10 mg (IM if needed)

3. Intramuscular medication If oral refused, haloperidol 5 mg + lorazepam 2 mg IM (combination is gold standard)

4. Physical restraint Last resort. Time-limited. Regular monitoring. Document indication and review.

Long-term management:

- Treat underlying disorder (psychosis, mania, substance use, personality disorder).
- **Pharmacotherapy for chronic aggression:** SSRIs (serotonin enhancement), mood stabilizers (lithium, best evidence for anti-aggressive effect; valproate; carbamazepine), beta-blockers (propranolol), atypical antipsychotics (clozapine, best for aggression in schizophrenia).
- **Psychotherapy:** Anger management (CBT-based), DBT (for BPD-related aggression), social skills training, substance abuse treatment.

HIGH-YIELD COMPARISON TABLES FOR QUICK REVISION

Quick Revision: Defense Mechanisms by Level

LEVEL	DEFENSES	MEMORY HOOK
Mature	Sublimation, Humor, Altruism, Suppression, Anticipation	S-H-A-S-A, "Shasa is mature"
Neurotic	Intellectualization, Isolation, Reaction formation, Displacement, Repression, Dissociation	I-I-R-D-R-D
Immature	Projection, Passive aggression, Acting out, Fantasy, Idealization, Devaluation, Splitting	P-P-A-F-I-D-S
Psychotic	Denial, Distortion, Psychotic projection	D-D-P

Quick Revision: Piaget vs Erikson (Parallel Ages)

AGE	PIAGET STAGE	ERIKSON CRISIS
0–2 yr	Sensorimotor	Trust vs Mistrust

AGE	PIAGET STAGE	ERIKSON CRISIS
2–6 yr	Preoperational	Autonomy vs Shame (1–3) → Initiative vs Guilt (3–6)
7–11 yr	Concrete Operational	Industry vs Inferiority
12+ yr	Formal Operational	Identity vs Role Confusion

Quick Revision: Attachment Types and Adult Outcomes

INFANT PATTERN	ADULT AAI	RELATIONSHIP STYLE	PSYCHOPATHOLOGY RISK
Secure	Autonomous	Comfortable with intimacy and independence	Low
Avoidant	Dismissing	Emotionally distant, self-reliant	Schizoid, avoidant PD
Ambivalent	Preoccupied	Clingy, anxious, jealous	Depression, anxiety, dependent PD
Disorganized	Unresolved	Chaotic, approach-avoidance	BPD, dissociative disorders, PTSD

Quick Revision: Theories of Emotion: One-Liner Each

THEORY · ONE-LINER

James-Lange "I tremble, therefore I fear", body first

Cannon-Bard "I tremble AND fear simultaneously", parallel processing

Schachter-Singer "I tremble + I'm in a dark alley = fear", arousal + cognitive label

Papez Hippocampal circuit for emotion + memory

MacLean Three-layered brain: reptilian → limbic → neocortex

Quick Revision: Grief Models at a Glance

MODEL	FRAMEWORK	NUMBER OF COMPONENTS
Kubler-Ross	5 stages (Denial → Anger → Bargaining → Depression → Acceptance)	5
Worden	4 tasks (Accept → Process → Adjust → Connect)	4

MODEL	FRAMEWORK	NUMBER OF COMPONENTS
Bowlby	4 phases (Numbing → Yearning → Disorganization → Reorganization)	4

EXAM PEARL

Document: D1-Defense-Development-Emotion.md **Status:** Complete **Word count target:** ~6000 words (20+ page equivalent with formatting)

Model Answers

EXAM PEARL

Document: D2, Model Answers PYQ **Source:** PG exams Dec 2011, Jun 2025 + PG exams 2013-2022 **Generated:** March 2026

SECTION A: DEFENSE MECHANISMS (Q1-Q7)

Q1: "Enumerate various psychodynamic theories with relevance to personality disorders. Mention commonly encountered defense mechanisms with explanation.": 10 marks

Exam Strategy: Two-part answer. Spend 4 marks on psychodynamic theories (brief, tabular), 6 marks on defense mechanisms with personality disorder links.

A. Psychodynamic Theories Relevant to Personality Disorders [4]

1. **Freud's Structural Model**, Personality disorders arise from fixation at early psychosexual stages. Ego functions are compromised, leading to reliance on **primitive defense mechanisms**. Borderline features reflect failure of ego integration.
1. **Object Relations Theory (Kernberg)**, Personality disorders result from failure of object relations development. **Borderline personality organization** is characterized by identity diffusion, primitive defenses (splitting, projective identification), and intact reality testing. Kernberg's three-tier model:
 2. **Neurotic organization**, integrated identity, mature defenses (obsessive-compulsive, depressive PDs)
 3. **Borderline organization**, identity diffusion, splitting, projective identification (borderline, narcissistic, antisocial PDs)
 4. **Psychotic organization**, loss of reality testing
1. **Self Psychology (Kohut)**, Narcissistic personality disorder arises from failure of **mirroring** and **idealizing** self-object needs in childhood. The grandiose self remains unmodified. Empathic failures lead to narcissistic rage and fragmentation.
1. **Attachment Theory (Bowlby)**, Insecure attachment patterns (anxious-preoccupied, dismissive-avoidant, fearful-avoidant) map onto personality disorder clusters:
 2. **Cluster B**, anxious-preoccupied or disorganized attachment
 3. **Cluster C**, anxious-preoccupied (dependent PD), dismissive-avoidant (avoidant PD)

1. **Interpersonal Theory (Sullivan)**, Personality is the "enduring pattern of interpersonal situations." Personality disorders reflect maladaptive interpersonal schemas developed in early relationships.

B. Commonly Encountered Defense Mechanisms [6]

DEFENSE MECHANISM	LEVEL	EXPLANATION	PERSONALITY DISORDER ASSOCIATION
Splitting	Immature	Viewing self/ others as all-good or all-bad; inability to integrate ambivalence	Borderline PD
Projective identification	Immature	Projecting intolerable feelings onto another AND inducing those feelings in them	Borderline PD
Idealization/Devaluation	Immature	Oscillating between seeing others as perfect vs. worthless	Narcissistic PD, Borderline PD
Denial	Immature	Refusing to acknowledge external reality	Antisocial PD, Narcissistic PD
Projection	Immature	Attributing own unacceptable feelings to others	Paranoid PD
Dissociation	Neurotic	Disconnection from awareness of self, body, or surroundings	Borderline PD
Reaction formation	Neurotic	Adopting behavior opposite to the unconscious impulse	Obsessive-compulsive PD
Intellectualization	Neurotic	Excessive abstract thinking to avoid affective distress	Obsessive-compulsive PD, Schizoid PD
Acting out	Immature	Enacting unconscious wishes or conflicts through action rather than reflection	Antisocial PD, Borderline PD

EXAM PEARL

Cross-reference: Q2 (classification), Q6 (mature defenses), Q7 (defenses in treatment)

Q2: "Define defense mechanisms. Classify them and name the defense mechanisms used in phobia.": 10 marks [1+5+4]

Exam Strategy: Quick definition, detailed classification table (Vaillant's hierarchy is the standard), then phobia-specific defenses with examples.

A. Definition [1]

Defense mechanisms are **unconscious psychological strategies** employed by the ego to manage conflict between the **id** (instinctual drives), the **superego** (moral conscience), and **external reality**. They protect the individual from **anxiety** arising from these conflicts. First described by **Sigmund Freud** and systematically classified by **Anna Freud** (1936, *The Ego and the Mechanisms of Defense*).

B. Classification (Vaillant's Hierarchy, 1977) [5]

LEVEL	DEFENSE MECHANISMS	CHARACTERISTICS
I. Mature (Healthy)	Sublimation, Altruism, Suppression, Humor, Anticipation	Adaptive; integrate conflicting feelings; associated with good mental health
II. Neurotic	Repression, Displacement, Reaction formation, Intellectualization, Isolation of affect, Rationalization, Dissociation	Partially adaptive; keep threatening ideas out of awareness but cause interpersonal difficulties
III. Immature	Projection, Passive aggression, Acting out, Splitting, Projective identification, Idealization/Devaluation, Somatization, Fantasy	Maladaptive in adults; seen in personality disorders and severe psychopathology
IV. Pathological (Psychotic)	Denial (psychotic), Distortion, Delusional projection	Grossly distort external reality; seen in psychotic states

C. Defense Mechanisms Used in Phobia [4]

Phobias are classically understood through the psychoanalytic model as anxiety displaced from an **internal conflict** onto an **external object or situation**.

1. **Displacement**, The **primary defense** in phobia. Anxiety associated with an unconscious conflict is shifted onto a substitute external object. *Example:* A child's fear of his father's anger is displaced onto dogs (dog phobia).
1. **Projection**, Internal danger is perceived as external threat. The individual's own aggressive or sexual impulses are projected outward. *Example:* Unconscious hostility toward a parent is experienced as the external world being dangerous (agoraphobia).
1. **Avoidance** (behavioral, but psychoanalytically reinforces repression), The phobic object is avoided, which prevents the return of the repressed material. This maintains the

symptom.

1. **Symbolization**, The phobic object **symbolically represents** the original source of anxiety. *Example:* In Little Hans (Freud, 1909), the horse symbolized the father; fear of the horse = fear of castration by the father.
1. **Regression**, Return to an earlier developmental stage under anxiety. May accompany phobic symptoms, particularly in children.

EXAM PEARL

Freud's model of phobia formation: Repression of unacceptable impulse --> anxiety not fully contained --> displacement onto external object --> avoidance of object = symptom formation

EXAM PEARL

Cross-reference: Q4-Q5 (defense mechanisms in OCD, different profile)

Q3: "What are defense mechanisms? Discuss briefly four mature defense mechanisms with examples.": 10 marks

Exam Strategy: Brief definition (2 marks), then 2 marks per mature defense = 8 marks for four defenses. Give clear clinical/everyday examples.

A. Definition [2]

Defense mechanisms are **unconscious psychological operations** that function to protect the ego from anxiety arising from conflict between instinctual drives (id), internalized moral standards (superego), and external reality. They were first described by Sigmund Freud and systematically classified by Anna Freud. **George Vaillant** (1977) organized them into a hierarchy from pathological to mature, demonstrating that mature defenses correlate with better psychosocial adjustment, career success, and physical health in longitudinal studies (Grant Study, Harvard).

B. Four Mature Defense Mechanisms [8]

1. Sublimation [2]

- **Definition:** Channeling socially unacceptable impulses (aggression, sexuality) into **socially valued** activities.
- **Mechanism:** The impulse is not blocked but redirected, the drive finds expression in a modified, constructive form.
- **Example:** A person with aggressive impulses becomes a **surgeon** or takes up **competitive sports**. An individual with strong sexual drives channels this energy into **artistic creation**.

- **Clinical significance:** Considered the most adaptive defense. The impulse achieves some satisfaction, so there is minimal intrapsychic conflict. Psychoanalytic therapy aims to help patients move from lower-level defenses toward sublimation.

2. Humor [2]

- **Definition:** Expressing uncomfortable or threatening feelings through **comedy or wit** without producing discomfort in self or others.
- **Mechanism:** The individual acknowledges the painful reality but finds a way to frame it that reduces its emotional impact, without denying or distorting it.
- **Example:** A patient diagnosed with cancer says, "Well, at least I'll finally lose weight." A psychiatry resident jokes about the chaos of night duty with colleagues.
- **Clinical significance:** Humor allows the ego to face a threatening situation while maintaining a sense of mastery. It is distinct from **sarcasm** (which is hostile and often immature) and **denial through laughter** (which avoids the feeling entirely).

3. Altruism [2]

- **Definition:** Vicarious but constructive service to others that produces **gratification** without self-sacrifice or martyrdom.
- **Mechanism:** The individual meets their own needs by helping others. Unlike reaction formation, the altruistic act is genuinely satisfying and not performed out of guilt.
- **Example:** A person who was abused as a child volunteers at a **child welfare organization**. A recovering alcoholic becomes an **AA sponsor**.
- **Clinical significance:** Altruism is adaptive because it transforms personal pain into prosocial action. It is distinguished from **self-sacrificing behavior** (which is masochistic and neurotic) by the presence of genuine pleasure in helping.

4. Suppression [2]

- **Definition:** **Conscious or semiconscious** decision to postpone dealing with an uncomfortable thought, feeling, or impulse.
- **Mechanism:** Unlike repression (which is unconscious), suppression involves **intentional setting aside** of distressing material with the expectation of returning to it later.
- **Example:** A surgeon suppresses worry about a family problem during a complex operation, planning to deal with it after work. A student postpones grief about a breakup until after exams.
- **Clinical significance:** Suppression is the **most conscious** of the mature defenses. It preserves the individual's ability to function in the present without permanent avoidance. Vaillant's longitudinal data showed suppression was one of the strongest predictors of life satisfaction.

Other mature defenses (for completeness): **Anticipation** (realistically planning for future discomfort) and **Asceticism** (deriving pleasure from renunciation, sometimes classified as

mature, sometimes neurotic).

EXAM PEARL

Cross-reference: Q6 (ego + ego functions + mature defenses), Q1 (defenses in personality disorders)

Q4: "Psychological defense mechanisms attributed as causation of OCD.

Psychological treatments for OCD.": 10 marks [4+6]

Exam Strategy: First part is purely psychoanalytic theory. Second part should cover ERP (most evidence), CBT, and mention psychodynamic therapy. Weight the second part more heavily.

A. Defense Mechanisms in OCD [4]

Psychoanalytic theory posits that OCD arises from **fixation at the anal-sadistic stage** of psychosexual development (18 months to 3 years). The child experiences conflict between the desire for aggressive, messy self-expression and parental demands for cleanliness and control. The ego employs specific defenses:

1. **Isolation of affect**, The **primary defense** in OCD. The thought is allowed into consciousness but is **separated from its associated affect**. The person can describe violent obsessional thoughts without displaying emotional distress. *Example:* A patient describes intrusive thoughts of stabbing his child in a calm, detached manner.
1. **Undoing**, A compulsive act is performed to **symbolically reverse** an unacceptable thought or impulse. *Example:* A patient who has an aggressive thought toward his mother must immediately perform a counting ritual to "undo" the thought and prevent harm.
1. **Reaction formation**, The person adopts attitudes and behaviors that are the **diametrically opposite** of the unconscious impulse. *Example:* A person with unconscious aggressive impulses toward others becomes excessively kind, polite, and scrupulously concerned about others' welfare.
1. **Displacement**, Anxiety from the core conflict is shifted to a less threatening substitute. *Example:* Anxiety about loss of control in one's life is displaced onto a need to keep one's desk perfectly organized.
1. **Regression**, Return to anal-stage concerns (orderliness, control, cleanliness, parsimony) as a defense against genital-stage conflicts.
1. **Ambivalence**, Inability to resolve opposing feelings (love/hate) leads to doubt and indecision, the core phenomenology of obsessional neurosis as described by Freud.

B. Psychological Treatments for OCD [6]

1. Exposure and Response Prevention (ERP) [2], First-line psychological treatment (APA, NICE guidelines)

- **Mechanism:** Based on **behavioral learning theory**, obsessions produce anxiety; compulsions reduce anxiety (negative reinforcement). ERP breaks this cycle.
- **Exposure:** Graded or flooding exposure to feared stimuli (e.g., touching a "contaminated" surface)
- **Response prevention:** Patient refrains from performing the compulsive ritual
- **Process:** Habituation occurs, anxiety peaks and then naturally declines without the compulsion
- **Evidence:** ~60-70% response rate; comparable to SSRIs; combined ERP + SSRI is superior to either alone

2. Cognitive Behavioral Therapy (CBT) [2]

- **Cognitive model (Salkovskis, 1985):** Intrusive thoughts are normal; OCD develops when the individual appraises intrusions as indicating **personal responsibility for harm**
- **Key cognitive distortions in OCD:**
 - Inflated responsibility
 - Overestimation of threat
 - Thought-action fusion ("thinking it = doing it")
 - Need for certainty
 - Perfectionism
 - Overimportance of thoughts
- **Techniques:** Cognitive restructuring, behavioral experiments, Socratic questioning, pie chart technique for responsibility reattribution
- CBT is often combined with ERP in practice

3. Acceptance and Commitment Therapy (ACT) [1]

- Third-wave CBT approach
- Emphasizes **psychological flexibility** rather than symptom reduction
- Teaches **defusion** (seeing thoughts as thoughts, not facts), acceptance of intrusions, values-based action
- Growing evidence base, particularly for treatment-resistant OCD

4. Psychodynamic therapy [1]

- Not first-line for OCD
- May be useful as **adjunctive** therapy for patients with significant personality pathology, interpersonal difficulties, or insight deficits
- Explores the unconscious meaning of obsessions and compulsions

- Modern short-term psychodynamic therapy (ISTDP) has preliminary evidence

EXAM PEARL

Cross-reference: Q5 (similar question, different mark split), Q2 (defense mechanisms in phobia, compare displacement-dominant vs. isolation-dominant)

Q5: "Define defense mechanism and its purposes. Defense mechanisms used in obsessive compulsive disorder.": 10 marks [3+7]

Exam Strategy: More marks on OCD defenses here than Q4. Expand clinical examples and add Freud's specific formulation. Overlap with Q4 is expected, add depth, not repetition.

A. Definition and Purposes of Defense Mechanisms [3]

Definition: Defense mechanisms are **unconscious psychological processes** that mediate the individual's reaction to emotional conflict and internal/external stressors. They operate outside awareness to protect the ego from anxiety.

Purposes:

1. **Anxiety reduction**, Primary function; manage the signal anxiety that arises when unconscious impulses threaten to enter awareness
2. **Conflict resolution**, Mediate between the competing demands of id (instincts), superego (moral standards), and external reality
3. **Maintenance of self-esteem**, Protect against narcissistic injury and feelings of inadequacy
4. **Adaptation**, Enable psychological functioning under stress; mature defenses promote healthy adaptation (Vaillant's longitudinal data)
5. **Regulation of affect**, Modulate emotional intensity to keep it within tolerable limits
6. **Social functioning**, Enable interpersonal relationships by managing disruptive impulses (e.g., sublimating aggression)

B. Defense Mechanisms in OCD [7]

Freud conceptualized obsessional neurosis as arising from **regression to the anal-sadistic stage** with specific defenses mobilized against unacceptable aggressive and sexual impulses.

1. Isolation of Affect [1.5]

- The **hallmark defense** of OCD
- The obsessional thought enters consciousness but is **divorced from its emotional significance**
- The patient can describe horrifying obsessions (harming children, blasphemous thoughts) with little apparent distress

- Distinguished from alexithymia: in isolation, the affect existed and was detached; in alexithymia, the affect was never adequately processed
- *Example:* A religious person has intrusive blasphemous images but discusses them intellectually, as if they belong to someone else

2. Undoing [1.5]

- A compulsive act performed to **magically negate** a preceding unacceptable thought or action
- The act is typically repetitive and ritualistic
- Represents a regression to **magical thinking** (preoperational thought)
- *Example:* A man who thinks "I hope my wife dies" must immediately tap the table three times and say a prayer. Handwashing after "contamination" symbolically undoes the contaminating (aggressive/sexual) thought

3. Reaction Formation [1.5]

- Conscious attitudes and behaviors are the **polar opposite** of the unconscious impulse
- In OCD: unconscious aggression --> conscious overconcern for others' safety; unconscious messiness --> compulsive cleanliness; unconscious sadism --> excessive kindness
- *Example:* A mother with unconscious hostility toward her child becomes pathologically overprotective, checking on the child hundreds of times per day
- Distinguished from genuine concern by its **excessive, rigid, and compulsive** quality

4. Displacement [1]

- Anxiety is transferred from the **true source** (unconscious conflict) to a **substitute** (the obsessional content)
- Explains why obsessional themes often seem unrelated to the patient's core conflicts
- *Example:* Anxiety about job performance is displaced onto a need to check door locks repeatedly

5. Intellectualization [0.5]

- A variant of isolation; excessive use of abstract thinking and intellectual analysis to distance from emotional content
- Common in obsessional personalities; gives the impression of insight without emotional engagement
- *Example:* An OCD patient gives elaborate theoretical explanations for their symptoms without emotional connection

6. Regression [0.5]

- Return to anal-stage preoccupations: **orderliness, control, parsimony, obstinacy** (Freud's "anal triad")
- Regression occurs from the **oedipal/phallic stage** back to the anal-sadistic stage due to castration anxiety
- The anal concerns become the template for the obsessional character

7. Ambivalence [0.5]

- Not strictly a defense but a core feature of the obsessional position
- Simultaneous opposing emotions (love-hate, obedience-defiance) toward the same object
- Because neither impulse is resolved, the patient is trapped in **doubt** and **indecision**
- Freud called this the "diphasic" nature of obsessional symptoms

EXAM PEARL

Cross-reference: Q4 (includes psychological treatment), Q2 (phobia defenses, compare: phobia = displacement + projection dominant; OCD = isolation + undoing + reaction formation dominant)

Q6: "What is ego? Functions of ego? Enumerate mature defense mechanisms and describe any three with examples.": 10 marks

Exam Strategy: Three-part answer. Ego definition (1), ego functions (3), mature defenses enumeration + three described (6). The Bellak ego functions list scores well here.

A. Definition of Ego [1]

In Freud's **structural model** of the mind (1923, *The Ego and the Id*), the **ego** is the component of personality that operates on the **reality principle**. It mediates between the instinctual demands of the **id**, the moral constraints of the **superego**, and the requirements of **external reality**. The ego develops from the id during infancy as the child begins to differentiate self from environment. It is partly conscious, partly preconscious, and partly unconscious.

B. Functions of the Ego (Bellak's Ego Functions, 1973) [3]

Bellak and colleagues described **12 major ego functions**, which are used in clinical assessment of ego strength:

#	EGO FUNCTION	DESCRIPTION
1	Reality testing	Ability to distinguish between internal and external stimuli; accurate perception of reality
2	Judgment	Anticipating consequences of actions; social appropriateness

#	EGO FUNCTION	DESCRIPTION
3	Sense of reality	Feeling of reality about self and the world; depersonalization/ derealization indicate impairment
4	Regulation of drives and affects	Ability to modulate impulses and tolerate frustration
5	Object relations	Capacity for stable, meaningful interpersonal relationships
6	Thought processes	Adequacy of memory, concentration, attention, language, abstraction
7	Adaptive regression in service of ego (ARISE)	Ability to relax ego controls for creativity, humor, play
8	Defensive functioning	Effectiveness and adaptiveness of defense mechanisms used
9	Stimulus barrier	Threshold for and management of sensory stimulation
10	Autonomous functioning	Basic ego apparatuses (perception, motor, memory) free from conflict
11	Synthetic-integrative function	Ability to organize and unify diverse experiences into coherent wholes
12	Mastery-competence	Sense of competence in interacting with the environment

C. Mature Defense Mechanisms [6]

Enumeration: Sublimation, Humor, Altruism, Suppression, Anticipation, Asceticism (Vaillant's hierarchy)

1. Sublimation [2]

- Channeling socially unacceptable impulses into **constructive and socially valued** outlets
- The drive finds partial expression, the form changes but the energy is preserved
- *Example:* A person with strong aggressive urges becomes a successful trial lawyer or competitive athlete. An individual with voyeuristic impulses becomes a documentary filmmaker.
- **Clinical significance:** The gold standard of defenses. Therapy aims to facilitate sublimation of previously repressed or acted-out impulses.

2. Anticipation [2]

- **Realistically** planning for future events that may cause distress
- Distinguished from **worry** (which is anxious and unproductive), anticipation involves concrete, goal-directed preparation
- *Example:* A patient with bipolar disorder, recognizing early warning signs of mania, proactively contacts their psychiatrist, adjusts sleep schedule, and informs a trusted family member. A student facing exams creates a study schedule weeks in advance.
- **Clinical significance:** Widely promoted in relapse prevention programs (substance use, mood disorders). Requires intact reality testing and capacity for future-oriented thinking.

3. Suppression [2]

- **Conscious or semiconscious** postponement of attention to a distressing thought, impulse, or situation
- The individual is aware of the distressing material but deliberately decides: "I'll deal with this later"
- Distinguished from **repression** (unconscious) and **denial** (refuses to acknowledge the reality)
- *Example:* A surgeon puts aside personal worries during a critical operation. A grieving person manages to function at work by setting aside thoughts of their loss until the evening.
- **Clinical significance:** Vaillant's 45-year Grant Study showed that men who used suppression had better psychosocial adjustment, marital satisfaction, and physical health than those using lower-level defenses.

EXAM PEARL

Cross-reference: Q3 (four mature defenses in detail, use humor and altruism there to avoid overlap), Q1 (defenses in personality disorders)

Q7: "How do you classify the defense mechanisms? Describe their classical use in treatment of psychiatric disorders.": 10 marks [3+7] -- LONG ESSAY CANDIDATE

Exam Strategy: This is the comprehensive defense mechanisms question. Classification first, then disorder-by-disorder mapping. For 20-mark version: expand classification with examples, add more disorders, include treatment implications.

10-MARK VERSION

A. Classification of Defense Mechanisms [3]

The most widely used classification is **Vaillant's hierarchical model (1977)**, derived from longitudinal research:

Level I, Mature Defenses

- Sublimation, Humor, Altruism, Suppression, Anticipation
- Associated with healthy adjustment, good relationships, successful careers
- Goal of psychotherapy: shift patients toward mature defenses

Level II, Neurotic Defenses

- Repression, Displacement, Reaction formation, Intellectualization, Isolation of affect, Rationalization, Dissociation, Externalization
- Common in neurotic disorders (anxiety, phobias, OCD)
- Partially adaptive; keep distressing material from awareness

Level III, Immature Defenses

- Projection, Passive aggression, Acting out, Splitting, Projective identification, Idealization/Devaluation, Somatization, Schizoid fantasy
- Common in personality disorders and severe psychopathology
- Maladaptive in adults; distort interpersonal relationships

Level IV, Pathological (Psychotic) Defenses

- Psychotic denial, Distortion, Delusional projection
- Grossly distort external reality
- Seen in psychotic disorders

DSM-5 Defensive Functioning Scale (in Section III) also classifies defenses along a similar hierarchy.

B. Defense Mechanisms in Psychiatric Disorders, Use in Treatment [7]

DISORDER	CHARACTERISTIC DEFENSES	TREATMENT IMPLICATIONS
Phobia	Displacement, projection, avoidance, symbolization	Identify displaced conflict; behavioral therapy (exposure) bypasses the defense; psychodynamic therapy addresses the symbolic meaning
OCD	Isolation of affect, undoing, reaction formation, regression	ERP directly challenges undoing; psychodynamic therapy addresses the underlying aggression; cognitive therapy targets inflated responsibility
Conversion disorder	Repression, conversion (somatic symbolization), dissociation, "la belle indifference"	Insight-oriented therapy to make repressed conflict conscious; hypnosis; physiotherapy without reinforcing sick role

DISORDER	CHARACTERISTIC DEFENSES	TREATMENT IMPLICATIONS
Depression	Introjection, turning against the self, regression	Freud: depression = anger turned inward (aggression against the introjected lost object). Therapy: externalize the anger, mourn the loss
Mania	Denial, omnipotence, projection, acting out	Defense against underlying depression; treatment addresses the depressive core once mood stabilized
Paranoia	Projection, denial	Unacceptable homosexual or aggressive impulses projected outward ("I don't hate him, he hates me"). Treatment: supportive therapy, gradual reality testing; confrontation is contraindicated
Borderline PD	Splitting, projective identification, idealization / devaluation, acting out	TFP (Transference-Focused Psychotherapy, Kernberg) specifically targets primitive defenses. Therapist interprets splitting in the transference. DBT addresses behavioral manifestations
Narcissistic PD	Idealization / devaluation, omnipotence, denial, projection	Self-psychological approach (Kohut): empathic immersion, repair of self-object failures. Kernberg: confront grandiosity and underlying emptiness
Antisocial PD	Projection, acting out, omnipotence, denial	Defense structure is ego-syntonic and resistant to treatment. MBT may improve mentalization. Limit-setting essential
PTSD	Dissociation, denial, regression, repression	Dissociation is both defense and symptom; phase-based treatment: stabilization first, then processing of traumatic material

Therapeutic principles across disorders:

1. **Identify the predominant defense level**, this guides treatment selection and prognosis
2. **Do not prematurely dismantle adaptive defenses**, even neurotic defenses serve a protective function
3. **Interpret defenses in the transference**, the therapy relationship recreates the patient's defensive style in real time

4. **Goal is defense maturation, not elimination**, move the patient up the hierarchy (Vaillant)
-

20-MARK EXPANDED VERSION

A. Classification of Defense Mechanisms [6]

Historical evolution:

- **Sigmund Freud** (1894), first described repression as a defense against intolerable ideas
- **Anna Freud** (1936), *The Ego and the Mechanisms of Defense*, first systematic classification of 10 defenses
- **Melanie Klein** (1946), described primitive defenses (splitting, projective identification) in the paranoid-schizoid position
- **George Vaillant** (1977), hierarchical model based on the Grant Study (268 Harvard men followed for 30+ years); demonstrated that defense maturity predicts psychosocial adjustment

Vaillant's Hierarchy (with examples):

Level I, Mature Defenses

DEFENSE	DEFINITION	EXAMPLE
Sublimation	Channeling unacceptable impulses into valued activities	Aggression --> surgery, competitive sport
Humor	Expressing distress through wit without discomfort	Cancer patient jokes about finally losing weight
Altruism	Constructive service to others providing vicarious gratification	Abuse survivor volunteers at a shelter
Suppression	Conscious postponement of distressing material	Surgeon sets aside personal worry during operation
Anticipation	Realistic planning for future distress	Bipolar patient creates a mania action plan

Level II, Neurotic Defenses

DEFENSE	DEFINITION	EXAMPLE
Repression	Unconscious exclusion of distressing material from awareness	Abuse survivor has no memory of childhood trauma
Displacement	Shifting affect from original object to a substitute	Anger at boss --> kicking the dog at home

DEFENSE	DEFINITION	EXAMPLE
Reaction formation	Adopting behavior opposite to the unconscious impulse	Unconscious hostility --> excessive kindness
Intellectualization	Excessive abstract thinking to avoid affect	Patient discusses diagnosis in purely academic terms
Isolation of affect	Thought enters awareness stripped of emotion	Surgeon describes a traumatic case without feeling
Rationalization	Providing logical explanations for irrational behavior	"I didn't want that promotion anyway" (sour grapes)
Dissociation	Disruption of consciousness, memory, identity, or perception	Abuse survivor "spaces out" during arguments

Level III, Immature Defenses

DEFENSE	DEFINITION	EXAMPLE
Splitting	All-good or all-bad perception of self/others	"My therapist is the best" --> "My therapist is useless"
Projection	Attributing own unacceptable feelings to others	"I'm not angry, you're the one who's hostile"
Projective identification	Projecting feelings AND inducing them in the other	Borderline patient projects rage; therapist feels angry
Acting out	Enacting impulses through behavior	Angry at therapist --> misses next session
Passive aggression	Indirect expression of hostility	"I forgot to do what you asked"
Somatization	Expressing psychological distress through bodily symptoms	Marital conflict --> chronic headaches
Schizoid fantasy	Retreat into autistic fantasy to avoid conflict	Isolated person creates elaborate inner world
Idealization/Devaluation	Others are seen as perfect or worthless	Narcissistic patient idealizes then devalues therapist

Level IV, Pathological Defenses

DEFENSE	DEFINITION	EXAMPLE
Psychotic denial	Denying external reality entirely	Patient denies having a terminal illness despite evidence
Distortion	Grossly reshaping external reality to meet inner needs	Grandiose delusions
Delusional projection	Projection of persecutory delusions onto external world	Paranoid delusions

B. Defense Mechanisms in Treatment of Psychiatric Disorders [14]

1. Anxiety Disorders, Phobias [2]

Characteristic defenses: Displacement, projection, symbolization, avoidance

Freud's model (Little Hans, 1909):

- Castration anxiety (oedipal conflict) --> repression fails --> anxiety displaced onto external object (horse) --> avoidance of horse = phobic symptom
- The phobic object symbolically represents the feared figure

Treatment implications:

- **Psychodynamic therapy:** Interpret the symbolic meaning of the phobic object; trace the displacement back to the original conflict; work through the underlying anxiety
- **Behavioral therapy (exposure):** Directly bypasses the displacement by confronting the feared stimulus; habituation reduces conditioned anxiety
- **CBT:** Addresses catastrophic misappraisals ("the spider will attack me"), targets the cognitive distortion that maintains the displacement
- **Clinical pearl:** In psychodynamic treatment, resolving the phobia without addressing the underlying conflict may lead to symptom substitution

2. Obsessive-Compulsive Disorder [2]

Characteristic defenses: Isolation of affect, undoing, reaction formation, intellectualization, regression

Psychoanalytic model:

- Regression from oedipal stage to anal-sadistic stage
- Core conflict: control vs. loss of control, obedience vs. defiance
- Obsessions = the forbidden thought breaking through (isolation strips the affect)
- Compulsions = undoing (magical reversal of the thought)

Treatment implications:

- **ERP (first-line):** Directly prevents the undoing behavior; the patient must tolerate the anxiety without the compulsive ritual. The defense is dismantled behaviorally.
- **Cognitive therapy (Salkovskis):** Targets inflated sense of responsibility, challenges reaction formation and intellectualization by examining the actual evidence for harm
- **Psychodynamic therapy (adjunctive):** Useful for character pathology; addresses the underlying aggression and need for control; interprets isolation of affect in therapy ("You describe these thoughts as if they belong to someone else")

3. Conversion Disorder / Functional Neurological Symptom Disorder [2]

Characteristic defenses: Repression, conversion (somatization of affect), dissociation

Psychoanalytic model:

- Intolerable conflict is repressed but finds somatic expression, the body speaks what the mind cannot
- **Primary gain:** Anxiety is kept out of awareness
- **Secondary gain:** The symptom elicits caregiving or avoids responsibility
- **La belle indifference:** Lack of concern about the symptom (due to successful repression)

Treatment implications:

- **Insight-oriented therapy:** Help the patient become aware of the repressed conflict; as the conflict is verbalized, the somatic symptom loses its function
- **Hypnosis:** Bypasses repression to access dissociated material
- **Physical rehabilitation:** Presented as "retraining" rather than implying the symptom is fake
- **Avoid confrontation:** "Your symptoms are not real" reinforces the defense rather than resolving it

4. Depression [2]

Characteristic defenses: Introjection, turning against the self, regression, denial

Freud's model (Mourning and Melancholia, 1917):

- After loss of a loved object, the ego identifies with (introjects) the lost object
- Ambivalent feelings toward the object (love + hate) are now directed at the self
- Self-criticism in depression = aggression turned against the introjected object ("I am worthless" = "the person who left me is worthless")

Treatment implications:

- **Psychodynamic therapy:** Help the patient recognize and externalize the anger directed at the introjected object; mourn the loss; separate self-representation from object-representation
- **CBT (Beck):** Addresses the cognitive triad (negative view of self, world, future), which are the cognitive manifestations of introjection and turning against the self
- **IPT:** Directly addresses the interpersonal losses and role transitions that trigger the introjective process

5. Mania and Bipolar Disorder [1.5]

Characteristic defenses: Denial, omnipotence, projection, acting out, manic defense (Klein)

Psychoanalytic model (Klein):

- Mania is a defense against underlying depression

- The "manic defense" involves **denial of depressive reality, omnipotent control, and contempt** for the lost object
- The manic patient denies dependency, loss, and vulnerability

Treatment implications:

- During mania: pharmacological stabilization first; psychotherapy is not effective during acute mania
- After stabilization: psychodynamic therapy addresses the underlying depressive core, dependency needs, and fear of loss
- Psychoeducation about the defensive function of mania improves insight and medication adherence

6. Paranoid Conditions and Paranoid Personality [1.5]

Characteristic defenses: Projection, denial, reaction formation

Freud's model (Schreber case, 1911):

- Core conflict: unacceptable homosexual or aggressive impulse
- Sequence: "I love him" --> "I don't love him, I hate him" (reaction formation) --> "I don't hate him, he hates me" (projection) --> paranoid delusion

Treatment implications:

- **Do not confront or interpret projection prematurely**, this destroys the therapeutic alliance
- **Supportive therapy:** Build trust gradually; be reliable and transparent
- **CBT for persecutory delusions:** Gentler approach, examine evidence, develop alternative explanations
- **Clinical pearl:** The therapist must tolerate being mistrusted without becoming defensive

7. Borderline Personality Disorder [2]

Characteristic defenses: Splitting, projective identification, idealization/devaluation, acting out, omnipotent control

Kernberg's model:

- Identity diffusion: failure to integrate positive and negative representations of self and others
- Splitting keeps contradictory ego states apart to prevent the anxiety of ambivalence
- Projective identification: the patient induces in the therapist the feelings they cannot tolerate

Treatment implications:

- **TFP (Transference-Focused Psychotherapy, Kernberg):** Systematically interprets splitting and projective identification as they emerge in the transference. "You see me as entirely helpful today, but last session I was entirely useless, can we think about how both might be true?"
- **DBT (Linehan):** Addresses the behavioral consequences of immature defenses (self-harm as acting out, interpersonal chaos from splitting) through skills training and validation
- **MBT (Bateman & Fonagy):** Improves mentalizing capacity, when the patient can reflect on their own and others' mental states, the need for projective identification decreases
- **Schema Therapy (Young):** Addresses the early maladaptive schemas and mode cycling that underlie splitting and projective identification; limited reparenting addresses the unmet needs

8. Somatoform / Somatic Symptom Disorders [1]

Characteristic defenses: Somatization, denial, regression, repression

Treatment:

- Regular scheduled appointments (not symptom-driven)
- Validate the suffering without reinforcing the defense
- Gradually introduce psychological formulations alongside medical care

Summary, Defense Level as Treatment Guide:

DEFENSE LEVEL	TREATMENT APPROACH	GOAL
Mature	Enhance and reinforce	Maintain adaptive functioning
Neurotic	Insight-oriented therapy, CBT	Conscious recognition of defense; develop alternatives
Immature	Structured therapies (DBT, TFP, MBT, Schema Therapy)	Improve mentalizing; develop integrative capacity
Pathological	Pharmacotherapy first, then supportive therapy	Restore reality testing; stabilize before insight work

EXAM PEARL

Cross-reference: Q1 (psychodynamic theories + personality disorders), Q2 (phobia defenses), Q4-Q5 (OCD defenses)

SECTION B: DEVELOPMENTAL PSYCHOLOGY (Q8-Q13)

Q8: "Define personality. Describe briefly the eight stages of life cycle and personality development as given by Erik Erikson.": 10 marks

Exam Strategy: Brief definition (2 marks), then a concise table of all 8 stages with crisis, virtue, and brief description (8 marks). Table format scores fastest.

A. Definition of Personality [2]

Personality is defined as the **enduring pattern of inner experience and behavior** that deviates from the expectations of the individual's culture, is pervasive and inflexible, has onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment (DSM-5 conceptualization).

More broadly: personality is the characteristic set of **cognitions, emotions, motivations, and behaviors** that define an individual's unique adjustment to life. It is shaped by biological temperament, developmental experiences, and sociocultural factors.

B. Erikson's Eight Stages of Psychosocial Development [8]

Erik Erikson (1902-1994) proposed that personality development occurs across the **entire lifespan** (not just childhood, as Freud suggested). Each stage presents a **psychosocial crisis**, a turning point where the individual can develop a **virtue** (positive outcome) or maladaptation (negative outcome).

STAGE	AGE	PSYCHOSOCIAL CRISIS	VIRTUE	KEY RELATIONSHIPS	BRIEF DESCRIPTION
1. Trust vs. Mistrust	0-1 year	Can I trust the world?	Hope	Mother/primary caregiver	Consistent, responsive caregiving --> basic trust; neglect/inconsistency --> mistrust, insecurity
2. Autonomy vs. Shame & Doubt	1-3 years	Can I do things myself?	Will	Parents	Encouragement of exploration --> sense of autonomy; excessive control/criticism --> shame and self-doubt

STAGE	AGE	PSYCHOSOCIAL CRISIS	VIRTUE	KEY RELATIONSHIPS	BRIEF DESCRIPTION
3. Initiative vs. Guilt	3-6 years	Is it okay for me to act?	Purpose	Family	Child initiates activities, makes plans; if punished for initiative -> guilt and inhibition
4. Industry vs. Inferiority	6-12 years	Can I succeed in the world?	Competence	School, peers	Mastery of academic and social skills; failure or lack of encouragement --> inferiority
5. Identity vs. Role Confusion	12-20 years	Who am I?	Fidelity	Peers, role models	Consolidation of personal identity (occupation, values, sexuality); failure --> identity diffusion
6. Intimacy vs. Isolation	20-40 years	Can I love and be loved?	Love	Partners, friends	Capacity for committed, intimate relationships; failure --> emotional isolation
7. Generativity vs. Stagnation	40-65 years	Can I contribute to the next generation?	Care	Family, community	Productivity, mentoring, creativity; failure --> self-absorption, stagnation
8. Ego Integrity vs. Despair	65+ years	Was my life meaningful?	Wisdom	All of humanity	Acceptance of one's life as lived; failure -> despair, fear of death, regret

Key principles of Erikson's theory:

1. **Epigenetic principle**, Each stage builds on resolution of previous stages; unresolved crises leave vulnerability
2. **Lifelong development**, Unlike Freud, Erikson extended developmental tasks across the entire lifespan
3. **Psychosocial** (not just psychosexual), Social relationships and cultural context are central
4. **Each crisis is never fully resolved**, The ratio of positive to negative determines the outcome
5. **Clinical relevance**, Identity diffusion is central to borderline PD (Kernberg); Erikson's model directly informs developmental counseling and life review therapy in elderly

EXAM PEARL

Cross-reference: Q11 (psychopathological outcomes, expand this for the 20-mark version), Q10 (Piaget, cognitive counterpart)

Q9: "Piaget's stages of cognitive development. Sensory-motor stages of cognitive development.": 10 marks [4+6]

Exam Strategy: First part covers all 4 stages briefly. Second part requires detailed breakdown of the 6 sensorimotor substages, this is where the marks are.

A. Piaget's Four Stages of Cognitive Development [4]

Jean Piaget (1896-1980) proposed that cognitive development proceeds through **four invariant, universal stages**. Each stage represents a qualitatively different way of thinking. Children actively construct knowledge through interaction with the environment (**constructivism**).

STAGE	AGE	KEY FEATURES	MILESTONE
1. Sensorimotor	0-2 years	Knowledge through senses and motor actions; no symbolic thought	Object permanence (understanding objects exist when not visible)
2. Preoperational	2-7 years	Symbolic thought (language, pretend play); egocentric; intuitive reasoning	Symbolic function (words/images represent objects); lacks conservation
3. Concrete Operational	7-11 years	Logical thought about concrete objects; reversibility; classification; seriation	Conservation (quantity doesn't change with appearance); decentration

STAGE	AGE	KEY FEATURES	MILESTONE
4. Formal Operational	11+ years	Abstract and hypothetical reasoning; systematic problem-solving	Hypothetico-deductive reasoning ; propositional thought

Key Piagetian concepts:

- **Schema**, Mental framework for organizing information
- **Assimilation**, Fitting new information into existing schemas
- **Accommodation**, Modifying schemas to fit new information
- **Equilibration**, Drive to balance assimilation and accommodation

B. Sensorimotor Stage, Six Substages [6]

SUBSTAGE	AGE	NAME	DESCRIPTION	EXAMPLE
1	0-1 month	Reflexive activity	Innate reflexes (sucking, grasping, rooting); no differentiation between self and environment	Neonate sucks on anything placed near mouth (breast, finger, blanket)
2	1-4 months	Primary circular reactions	Infant repeats pleasurable actions centered on own body ; first habits	Baby accidentally sucks thumb --> finds it pleasurable --> repeats
3	4-8 months	Secondary circular reactions	Infant repeats actions directed at external objects to produce interesting effects; more intentional	Shakes a rattle, hears sound, shakes again; kicks mobile to make it move
4	8-12 months	Coordination of secondary schemes	Intentional goal-directed behavior ; combines schemas to achieve goals; early object permanence	Removes blanket covering a toy (means-end behavior); A-not-B error still present

SUBSTAGE	AGE	NAME	DESCRIPTION	EXAMPLE
5	12-18 months	Tertiary circular reactions	Active experimentation; trial and error ; "little scientist"; varies actions deliberately	Drops food from highchair at different angles to see what happens; explores objects by banging, throwing, mouthing
6	18-24 months	Mental representation / Internalization of schemes	Symbolic thought begins; mental images; deferred imitation; language emergence; complete object permanence	Finds hidden object even after invisible displacement; pretend play; uses words to represent objects

Object permanence development across substages:

- Substages 1-3: No search for hidden objects ("out of sight, out of mind")
- Substage 4: Searches for hidden objects but makes **A-not-B error** (searches in location A even when object was moved to B while watching)
- Substage 5: Follows visible displacements correctly
- Substage 6: Follows **invisible** displacements; complete object permanence achieved

Clinical relevance:

- Developmental assessment of infants uses sensorimotor milestones (e.g., Bayley Scales)
- Autism spectrum disorder: delays in imitation (substage 6), pretend play, joint attention
- Intellectual disability: delayed or incomplete progression through substages
- Piaget's tasks (conservation, classification) are used in cognitive assessment

EXAM PEARL

Cross-reference: Q10, Q13 (general Piaget questions), Q8 (Erikson, psychosocial counterpart to cognitive development)

Q10: "What is Piaget's theory of cognitive development? Stages of intellectual development according to Piaget's theory." 10 marks

Exam Strategy: The question asks for theory first, then stages. Describe core Piagetian concepts (schemas, assimilation, accommodation, equilibration) before the stage table. Overlap with Q9, emphasize theory here, not sensorimotor substages.

A. Piaget's Theory of Cognitive Development [4]

Jean Piaget proposed a **constructivist** theory of cognitive development: children are not passive recipients of knowledge but **active builders** who construct understanding through interaction with the environment.

Core principles:

1. **Schemas**, Organized patterns of thought and action that represent knowledge. Schemas change with development (from sensorimotor action patterns to abstract mental operations).
1. **Assimilation**, Interpreting new experiences in terms of **existing schemas**. *Example*: A child who knows "dog" sees a cat and calls it "dog" (fitting new information into existing schema).
1. **Accommodation, Modifying existing schemas** or creating new ones when new experiences cannot be assimilated. *Example*: The child learns that the cat is different and creates a new schema for "cat."
1. **Equilibration**, The driving force of development. When assimilation and accommodation are balanced, the child is in a state of **cognitive equilibrium**. Disequilibrium (encountering something that doesn't fit) motivates accommodation and growth.
1. **Invariant sequence**, All children pass through the same stages in the same order, though the rate may vary. Stages cannot be skipped.
1. **Qualitative changes**, Each stage represents a fundamentally different way of thinking, not just "more" knowledge.

B. Stages of Intellectual Development [6]

Stage 1: Sensorimotor (0-2 years) [1.5]

- Intelligence expressed through **motor actions** and sensory exploration
- No symbolic representation, the infant "thinks" by doing
- Six substages from reflexive activity to mental representation
- **Landmark achievement: Object permanence**, understanding that objects continue to exist when not perceived (develops gradually, complete by 18-24 months)
- **A-not-B error**, Classic Piagetian demonstration of incomplete object permanence (substage 4)

Stage 2: Preoperational (2-7 years) [1.5]

- **Symbolic function**, ability to use symbols (words, images, pretend play) to represent objects
- Subdivided into: **preconceptual** (2-4 years) and **intuitive** (4-7 years)
- **Key limitations**:

- **Egocentrism**, Cannot take another's perspective (Three Mountains Task)
- **Centration**, Focuses on one dimension at a time
- **Lack of conservation**, Fails to understand that quantity is unchanged by changes in appearance (pours water from short wide glass to tall narrow glass and says "more water")
- **Irreversibility**, Cannot mentally reverse operations
- **Animism**, Attributes life to inanimate objects ("the sun is angry")
- **Transductive reasoning**, Reasoning from particular to particular (not inductive or deductive)

Stage 3: Concrete Operational (7-11 years) [1.5]

- **Logical thought** applied to **concrete** (tangible, physically present) objects and events
- **Key acquisitions:**
- **Conservation**, Understands number, mass, volume remain the same despite perceptual changes
- **Reversibility**, Can mentally reverse operations
- **Decentration**, Considers multiple dimensions simultaneously
- **Seriation**, Orders objects along a quantitative dimension
- **Classification**, Groups objects by shared attributes; understands class inclusion
- **Transitivity**, If $A > B$ and $B > C$, then $A > C$
- **Limitation:** Cannot reason about abstract or hypothetical situations

Stage 4: Formal Operational (11+ years) [1.5]

- **Abstract, hypothetical, and systematic** reasoning
- **Key acquisitions:**
- **Hypothetico-deductive reasoning**, Generates hypotheses and tests them systematically
- **Propositional thought**, Evaluates the logic of propositions without reference to concrete examples
- **Combinatorial thinking**, Considers all possible combinations systematically
- **Metacognition**, Thinking about thinking
- **Limitation:** Not all individuals reach full formal operations (research suggests many adults remain primarily concrete operational in certain domains)
- **Adolescent egocentrism (Elkind):**
- **Imaginary audience**, belief that others are constantly watching and evaluating
- **Personal fable**, belief in one's own uniqueness and invulnerability

Clinical relevance:

- **Intellectual disability:** Arrested development at earlier stages (mild ID = concrete operational; severe ID = preoperational or sensorimotor)
- **Child psychotherapy:** Interventions must match the child's cognitive stage (e.g., concrete metaphors for preoperational children; abstract formulations only for formal operational adolescents)
- **Consent and capacity:** Understanding of consent requires formal operational thought
- **Psychoeducation:** Must be pitched at the patient's cognitive level

EXAM PEARL

Cross-reference: Q9 (sensorimotor substages in detail), Q13 (neurocognitive development, same content), Q8 (Erikson, parallel psychosocial development)

Q11: "According to Erik Erikson, write the eight stages of the life cycle. What are the psychopathological outcomes if each stage is not mastered successfully?": 10 marks -- LONG ESSAY CANDIDATE

Exam Strategy: This question specifically asks for psychopathology, that's where the marks are. The stage listing is necessary but the examiner wants disorder linkages. For 20-mark: expand psychopathology and add treatment implications.

10-MARK VERSION

STAGE	AGE	CRISIS	VIRTUE	PSYCHOPATHOLOGICAL OUTCOMES IF NOT MASTERED
1. Trust vs. Mistrust	0-1 yr	Can I trust?	Hope	Psychosis (loss of basic trust in reality); paranoid personality ; reactive attachment disorder; insecure attachment; substance dependence (seeking comfort from substances); schizophrenia (Erikson linked fundamental mistrust to psychotic withdrawal)

STAGE	AGE	CRISIS	VIRTUE	PSYCHOPATHOLOGICAL OUTCOMES IF NOT MASTERED
2. Autonomy vs. Shame & Doubt	1-3 yr	Can I act independently?	Will	OCD (doubt and need for control); obsessive-compulsive personality; paranoia (shame projected outward); dependent personality disorder; conduct problems in children
3. Initiative vs. Guilt	3-6 yr	Is it okay to act?	Purpose	Conversion disorder (guilt over initiative leads to somatic inhibition); phobias (oedipal anxiety); psychosomatic disorders; inhibited personality; sexual dysfunction (guilt about desire)
4. Industry vs. Inferiority	6-12 yr	Can I succeed?	Competence	Depression (sense of inferiority and worthlessness); work inhibition; ADHD complications (failure to achieve Industry); avoidant personality; school refusal; underachievement

STAGE	AGE	CRISIS	VIRTUE	PSYCHOPATHOLOGICAL OUTCOMES IF NOT MASTERED
5. Identity vs. Role Confusion	12-20 yr	Who am I?	Fidelity	Borderline personality disorder (identity diffusion, Kernberg); identity crisis; substance use (experimenting to find self); gender dysphoria (when identity exploration is blocked); joining cults or extremist groups; delinquency
6. Intimacy vs. Isolation	20-40 yr	Can I love?	Love	Schizoid personality (avoidance of intimacy); depression; social anxiety disorder; avoidant personality disorder; domestic violence (distorted intimacy); sexual disorders; relationship dysfunction
7. Generativity vs. Stagnation	40-65 yr	Can I contribute?	Care	Midlife crisis ; depression; narcissistic personality traits; substance use; marital breakdown; burnout; excessive self-absorption; failure to mentor or contribute

STAGE	AGE	CRISIS	VIRTUE	PSYCHOPATHOLOGICAL OUTCOMES IF NOT MASTERED
8. Integrity vs. Despair	65+ yr	Was it worth it?	Wisdom	Late-life depression ; anxiety about death; chronic bitterness and regret; hypochondriasis; alcohol dependence; elder suicide; demoralization

Key clinical applications:

1. **Developmental assessment**, When taking a psychiatric history, Erikson's framework identifies which developmental tasks were compromised
2. **Therapy planning**, Treatment can focus on the unresolved crisis (e.g., trust-building in therapy for a patient with Stage 1 failure)
3. **Life review therapy**, Uses Erikson's framework for elderly patients (Stage 8)
4. **Identity diffusion in BPD**, Kernberg directly borrowed Erikson's concept for his structural model

20-MARK EXPANDED VERSION

A. Erikson's Eight Stages, Overview [5]

Erik Erikson (1902-1994), a psychoanalyst trained by Anna Freud, extended Freud's psychosexual theory into a **psychosocial model** spanning the entire lifespan. Key innovations:

- Development does not end in childhood, it continues into old age
- **Social and cultural context** shapes development as much as biological drives
- Each stage presents a **psychosocial crisis**, a dialectical tension between opposing tendencies
- Successful resolution produces a **virtue** (ego strength); unsuccessful resolution produces vulnerability
- The **epigenetic principle**: each stage builds on previous ones; later stages can remediate earlier failures to some degree

B. Detailed Stage Analysis with Psychopathology [12]

Stage 1: Trust vs. Mistrust (0-1 year) [1.5]

- **Corresponding Freudian stage**: Oral

- **Task:** Develop a sense that the world is a safe, predictable, nurturing place
- **Critical factor:** Consistency and responsiveness of primary caregiver
- **Psychopathological outcomes:**
- **Psychosis / Schizophrenia**, Erikson proposed that the most profound failure of trust results in withdrawal from shared reality. Sullivan similarly linked early maternal deprivation to schizophrenic detachment.
- **Paranoid personality disorder**, Pervasive distrust and suspiciousness
- **Reactive attachment disorder / Disinhibited social engagement disorder**, Direct sequelae of disrupted early caregiving
- **Substance dependence**, Substances substitute for the absent nurturing object (oral fixation + trust failure)
- **Depression** (anaclitic), Spitz's description of hospitalism in infants deprived of maternal care
- **Borderline PD**, Contributes to the abandonment schema; trust failure makes all later relationships unstable

Stage 2: Autonomy vs. Shame and Doubt (1-3 years) [1.5]

- **Corresponding Freudian stage:** Anal
- **Task:** Develop a sense of personal control and independence
- **Critical factor:** Balance between parental encouragement and appropriate limit-setting
- **Psychopathological outcomes:**
- **Obsessive-compulsive disorder**, Excessive doubt and need for control; Freud linked OCD to anal fixation, Erikson reframed this as unresolved autonomy crisis
- **Obsessive-compulsive personality disorder**, Rigidity, perfectionism, stubbornness (anal triad: orderliness, parsimony, obstinacy)
- **Paranoia**, Shame is an annihilation emotion; when intolerable, it is projected outward as suspiciousness
- **Dependent personality disorder**, Failed autonomy --> excessive reliance on others for decisions and reassurance
- **Oppositional defiant disorder**, Exaggerated assertion of autonomy through defiance

Stage 3: Initiative vs. Guilt (3-6 years) [1.5]

- **Corresponding Freudian stage:** Phallic/Oedipal
- **Task:** Develop purpose, direction, and the ability to plan and initiate action
- **Critical factor:** Family's response to the child's emerging assertiveness and curiosity (including sexual curiosity)
- **Psychopathological outcomes:**

- **Conversion disorder**, Guilt over sexual / aggressive initiative is converted into somatic symptoms; "la belle indifference" reflects successful repression
- **Phobias**, Anxiety from oedipal conflict is displaced (Little Hans); guilt about initiative becomes fear of external objects
- **Sexual dysfunction**, Excessive guilt about sexual initiative; performance anxiety
- **Inhibited personality**, Generalized passivity, inability to assert or initiate
- **Psychosomatic disorders**, Bodily expression of guilt and inhibited aggression

Stage 4: Industry vs. Inferiority (6-12 years) [1.5]

- **Corresponding Freudian stage**: Latency
- **Task**: Master skills, achieve competence, develop a work ethic
- **Critical factor**: School experience, peer relationships, learning success
- **Psychopathological outcomes**:
- **Depression**, Sense of inferiority, inadequacy, and worthlessness becomes a cognitive template ("I am incompetent")
- **Avoidant personality disorder**, Fear of failure leads to avoidance of challenges
- **School refusal**, Anxiety about performance and social evaluation
- **Work inhibition / Procrastination**, Extends into adult occupational dysfunction
- **ADHD impact**, Children with ADHD frequently fail to achieve industry due to executive dysfunction, leading to secondary inferiority and depression

Stage 5: Identity vs. Role Confusion (12-20 years) [1.5]

- **Corresponding Freudian stage**: Genital (onset)
- **Task**: Integrate childhood identifications into a coherent sense of self
- **Critical factor**: Exploration of roles, values, relationships, and vocation
- **Erikson's concept of identity formation**:
- **Identity achievement**, Crisis explored, commitment made (optimal)
- **Moratorium**, Actively exploring, no commitment yet (healthy transitional state)
- **Foreclosure**, Commitment without exploration (adopts parents' identity wholesale)
- **Identity diffusion**, No exploration, no commitment (pathological)
- **Psychopathological outcomes**:
- **Borderline personality disorder**, Kernberg's "identity diffusion" is directly borrowed from Erikson; inability to integrate contradictory self-representations
- **Substance use disorders**, Substances used to experiment with altered identity or escape confusion
- **Eating disorders**, Distorted body image as a component of identity confusion

- **Cult involvement / Radicalization**, Seeking premature identity resolution through group identity
- **Gender dysphoria**, When identity exploration is blocked or not supported
- **Conduct disorder / Delinquency**, Negative identity formation ("if I can't be good, I'll be the best at being bad")

Stage 6: Intimacy vs. Isolation (20-40 years) [1.5]

- **Task**: Form deep, committed, reciprocal relationships
- **Prerequisite**: Stable identity (Stage 5 resolution)
- **Psychopathological outcomes**:
 - **Schizoid personality disorder**, Active avoidance of intimate relationships
 - **Avoidant personality disorder**, Desires intimacy but is paralyzed by fear of rejection
 - **Social anxiety disorder**, Anxiety about social evaluation prevents connection
 - **Depressive disorders**, Loneliness and isolation as triggers
 - **Domestic violence**, Distorted expressions of intimacy; control substituted for connection
 - **Sexual disorders**, Intimacy avoidance expressed through sexual dysfunction or paraphilic substitution

Stage 7: Generativity vs. Stagnation (40-65 years) [1.5]

- **Task**: Contribute to the next generation through parenting, mentoring, creativity, or productivity
- **Psychopathological outcomes**:
 - **Midlife crisis**, Awareness of mortality and unfulfilled generativity
 - **Narcissistic personality traits**, Self-absorption instead of generativity
 - **Depression**, Existential depression related to perceived meaninglessness
 - **Substance use**, Self-medication for stagnation
 - **Burnout**, When generativity becomes compulsive rather than meaningful
 - **Marital breakdown**, Partners who have grown apart after child-rearing

Stage 8: Ego Integrity vs. Despair (65+ years) [1.5]

- **Task**: Accept one's life as lived; face death without overwhelming fear
- **Psychopathological outcomes**:
 - **Late-life depression**, Most common psychiatric presentation; loss, isolation, disability, and despair converge
 - **Suicide in the elderly**, Highest completion rates of any age group; despair + access to means + physical illness
 - **Anxiety disorders**, Fear of death, health anxiety, generalized worry
 - **Hypochondriasis**, Preoccupation with bodily decline

- **Alcohol dependence**, Often underrecognized in the elderly ("hidden alcoholism")
- **Demoralization syndrome**, Distinct from depression; characterized by meaninglessness, hopelessness, and helplessness without full depressive syndrome

C. Clinical Applications [3]

1. **Psychiatric history-taking**, Erikson's framework guides systematic developmental inquiry
2. **Psychodynamic formulation**, Identifying the unresolved stage directs therapeutic focus
3. **Life review therapy (Butler)**, Structured reminiscence using Erikson's stages helps elderly patients achieve integrity
4. **Developmental counseling**, Anticipatory guidance for patients facing stage-specific challenges
5. **Understanding personality disorders**, Kernberg's structural model maps directly onto Eriksonian stages
6. **Schema Therapy**, Early maladaptive schemas (Young) correspond to unmet developmental needs at specific Eriksonian stages

EXAM PEARL

Cross-reference: Q8 (basic stage listing), Q12 (attachment theory, Stage 1 elaboration)

Q12: "Discuss briefly attachment theory and its implications for psychiatry." 10 marks [5+5]

Exam Strategy: Equal split. Cover Bowlby's theory + Ainsworth's classification in Part A. Part B should cover clinical implications across the lifespan.

A. Attachment Theory [5]

John Bowlby (1907-1990) proposed that the infant has an innate, biologically driven need to form a **close emotional bond** with a primary caregiver (attachment figure). This bond serves a **survival function**, proximity to the caregiver provides protection from predators and environmental threats.

Key concepts:

1. **Internal working model**, The infant develops mental representations of self and others based on early caregiving experiences. These models are **templates for all future relationships**.
2. Responsive caregiver --> "I am worthy of love; others are reliable"
3. Unresponsive caregiver --> "I am unworthy; others cannot be trusted"
1. **Secure base**, The attachment figure provides a safe base from which the child explores the environment. Exploration and attachment are complementary systems.

1. **Separation anxiety**, Normal developmental phenomenon (6-8 months onset); distress when separated from the attachment figure.

1. **Phases of attachment (Bowlby):**

2. Pre-attachment (0-6 weeks): Indiscriminate social responsiveness

3. Attachment-in-the-making (6 weeks-6 months): Differential responsiveness to caregiver

4. Clear-cut attachment (6-24 months): Separation anxiety, stranger anxiety, active proximity-seeking

5. Goal-corrected partnership (24+ months): Child understands caregiver has separate goals; negotiation begins

Mary Ainsworth's Strange Situation (1978):

A laboratory paradigm to classify infant attachment patterns (12-18 months):

ATTACHMENT PATTERN	BEHAVIOR	CAREGIVER STYLE	PREVALENCE
Secure (B)	Distressed by separation; comforted by re-union; explores from secure base	Responsive, sensitive, consistent	60-65%
Insecure-Avoidant (A)	Little distress at separation; ignores caregiver on return; suppresses attachment needs	Rejecting, emotionally unavailable	20-25%
Insecure-Ambivalent/Resistant (C)	Highly distressed; not easily comforted; clingy yet angry at reunion	Inconsistent, unpredictable	10-15%
Disorganized (D) (Main & Hesse, 1990)	Contradictory behaviors (approach + freeze); caregiver is both source of comfort and source of fear	Frightening, maltreating, or frightened caregiver	10-15% (higher in clinical populations)

Adult Attachment (George, Kaplan, Main, Adult Attachment Interview):

ADULT PATTERN	CORRESPONDING INFANT PATTERN	DESCRIPTION
Autonomous/Secure	Secure	Coherent narrative of childhood; values attachment
Dismissing	Avoidant	Minimizes attachment importance; idealized or derogatory parents

ADULT PATTERN	CORRESPONDING INFANT PATTERN	DESCRIPTION
Preoccupied	Ambivalent	Enmeshed in childhood relationships; angry, passive, or confused
Unresolved	Disorganized	Lapses in reasoning when discussing loss or trauma

B. Implications for Psychiatry [5]

1. Personality Disorders [1]

- **Borderline PD**, Strongly associated with **disorganized attachment** and **preoccupied attachment**; fear of abandonment is the central feature; unstable relationships reflect disrupted internal working models
- **Avoidant PD**, Dismissive attachment; deactivation of attachment needs
- **Dependent PD**, Anxious-preoccupied attachment; hyperactivation of attachment system
- **Antisocial PD**, Early disruption of attachment (institutional rearing, multiple placements); callous-unemotional traits linked to attachment failure

2. Depression [0.5]

- Bowlby proposed that **early loss** (separation from or death of an attachment figure) predisposes to depression
- Insecure attachment is a robust risk factor for depression across the lifespan
- Beck's cognitive triad (negative view of self, world, future) maps onto insecure internal working models

3. Anxiety Disorders [0.5]

- Separation anxiety disorder directly reflects attachment system activation
- Agoraphobia, loss of secure base
- Social anxiety, anxious-preoccupied attachment style

4. Childhood Disorders [0.5]

- **Reactive attachment disorder (RAD)**, Failure to form attachment due to institutional rearing or severe neglect
- **Disinhibited social engagement disorder (DSED)**, Indiscriminate sociability without selective attachment

5. Psychotherapy [1]

- **The therapeutic relationship is an attachment relationship**, the therapist provides a secure base
- **Transference**, reactivation of early attachment patterns in therapy

- **Mentalization-Based Treatment (Bateman & Fonagy)**, Developed from attachment theory; disorganized attachment impairs mentalizing capacity
- **Schema Therapy**, Limited reparenting directly addresses unmet attachment needs
- **EFT for couples (Johnson)**, Explicitly attachment-based; restructures insecure bonds

6. Neurobiology [0.5]

- Insecure attachment alters **HPA axis regulation** (cortisol reactivity)
- Disorganized attachment associated with **reduced hippocampal volume** and altered stress response
- Oxytocin system is modulated by early attachment experiences

7. Intergenerational Transmission [0.5]

- Attachment patterns are transmitted across generations with ~75% concordance
- Parent's unresolved trauma (AAI "unresolved" classification) predicts disorganized attachment in their child
- Clinical implication: treating maternal mental health protects the infant's attachment

8. Forensic Psychiatry [0.5]

- Disrupted attachment is a risk factor for violence and offending
- Assessment of attachment patterns informs risk formulation

EXAM PEARL

Cross-reference: Q8, Q11 (Erikson Stage 1, trust/mistrust), Q19-Q23 (grief, Bowlby's phases of grief were derived from attachment theory)

Q13: "Briefly write about stages of neuro-cognitive development according to Jean Piaget.": 10 marks

Exam Strategy: Straightforward. This is the same as Q10 with "neurocognitive" emphasis. Add brain maturation correlates to stand out.

A. Overview of Piaget's Theory [2]

Piaget proposed that cognitive (neurocognitive) development proceeds through **four sequential, invariant stages**. Each stage represents a qualitative shift in how the child processes information. Development is driven by the interplay of **maturation, experience, social transmission**, and **equilibration** (the drive to resolve cognitive disequilibrium).

B. Four Stages of Neurocognitive Development [8]

Stage 1: Sensorimotor (Birth to 2 years) [2]

- **Cognitive characteristics:** Intelligence is expressed through sensory perception and motor action. No symbolic representation. The infant learns by doing, grasping, sucking,

looking, shaking.

- **Six substages:** Reflexive activity --> Primary circular reactions (body-centered) --> Secondary circular reactions (object-centered) --> Coordination of schemes (goal-directed) --> Tertiary circular reactions (experimentation) --> Mental representation
- **Key achievement: Object permanence,** Understanding that objects continue to exist when not perceived. Develops gradually; complete by 18-24 months.
- **Neurocognitive correlate:** Maturation of **prefrontal cortex** (working memory needed for object permanence); development of **dorsolateral PFC** enables inhibition of prepotent response in A-not-B task. Rapid synaptogenesis and myelination.

Stage 2: Preoperational (2-7 years) [2]

- **Cognitive characteristics:** Emergence of **symbolic function**, language, pretend play, drawing. Thought is dominated by perception rather than logic.
- **Key features:**
- **Egocentrism,** Cannot take another person's perspective (Three Mountains Experiment)
- **Animism,** Attributes life to inanimate objects
- **Centration,** Focuses on one aspect of a situation, ignoring others
- **Lack of conservation,** Cannot understand that quantity remains the same despite perceptual transformation
- **Transductive reasoning,** Reasoning from particular to particular
- **Neurocognitive correlate:** Rapid development of **Broca's and Wernicke's areas** (language); **right hemisphere** dominant for spatial/holistic processing; **Theory of Mind** begins to develop (medial PFC, temporoparietal junction), false belief task typically passed at age 4-5.

Stage 3: Concrete Operational (7-11 years) [2]

- **Cognitive characteristics: Logical operations** applied to concrete objects and events. The child can think systematically but only about tangible reality.
- **Key achievements:**
- **Conservation,** Number, mass, weight, volume (acquired in this order)
- **Reversibility,** Mental operations can be reversed
- **Seriation,** Ordering objects by size, weight, etc.
- **Classification,** Grouping by shared attributes; class inclusion understood
- **Decentration,** Considering multiple dimensions simultaneously
- **Neurocognitive correlate: Prefrontal cortex** maturation enables working memory, inhibitory control, and cognitive flexibility. Corpus callosum myelination improves interhemispheric integration. Gray matter peaks in frontal and parietal lobes.

Stage 4: Formal Operational (11+ years) [2]

- **Cognitive characteristics: Abstract, hypothetical, and systematic** reasoning. The adolescent can think about thinking (metacognition).
- **Key achievements:**
- **Hypothetico-deductive reasoning**, Formulates hypotheses and tests them systematically (pendulum task)
- **Propositional thought**, Evaluates truth of verbal statements independent of concrete referents
- **Combinatorial thinking**, Considers all possible combinations
- **Metacognition**, Awareness of one's own cognitive processes
- **Adolescent egocentrism** (Elkind): imaginary audience + personal fable
- **Limitation:** Not universally achieved, some adults remain primarily concrete operational, especially in unfamiliar domains
- **Neurocognitive correlate:** Continued **prefrontal cortex development** through mid-20s (explains risk-taking in adolescents despite abstract reasoning ability); **synaptic pruning** refines neural circuits; **white matter** tracts (especially frontal-parietal connections) continue myelinating.

Clinical relevance of Piaget's stages:

- **Assessment of cognitive disability:** Placing the patient's cognitive level guides intervention planning
- **Child psychotherapy:** Therapeutic techniques must match the child's cognitive stage
- **Informed consent:** Formal operations required for meaningful consent
- **Psychoeducation:** Pitch explanations at the patient's cognitive level
- **Autism spectrum disorder:** Impaired Theory of Mind (ToM) development; delays in symbolic play

EXAM PEARL

Cross-reference: Q9 (sensorimotor substages in detail), Q10 (theory + stages), Q8 (Erikson, psychosocial parallel)

SECTION C: EMOTION, GRIEF, AND AGGRESSION (Q14-Q25)

Q14: "Define emotion. Discuss neuronal circuit of emotion with the help of a diagram.": 10 marks [2+5+3]

Exam Strategy: Definition (2), Papez circuit + amygdala pathways (5), diagram (3). Draw a clear labeled diagram, marks are allocated for it.

A. Definition of Emotion [2]

Emotion is a complex psychological state involving three components:

1. **Subjective experience**, The conscious feeling (e.g., "I feel afraid")
2. **Physiological response**, Autonomic and neuroendocrine changes (e.g., tachycardia, sweating, cortisol release)
3. **Behavioral expression**, Observable actions and expressions (e.g., facial expression, fight/flight, approach/avoidance)

Emotions are **adaptive responses** that prepare the organism for action in response to environmental stimuli. They involve rapid, often automatic appraisal of the significance of a stimulus for the individual's well-being.

B. Neuronal Circuits of Emotion [5]

1. The Papez Circuit (1937) [2]

James Papez proposed the first detailed neural circuit for emotion, involving a loop of limbic structures:

Circuit path:

Hippocampus --> Fornix --> **Mammillary bodies** --> Mammillothalamic tract --> **Anterior thalamic nucleus** --> Internal capsule --> **Cingulate gyrus** --> Cingulum --> **Parahippocampal gyrus** --> Hippocampus

Function: The Papez circuit integrates **cortical** (cognitive) and **subcortical** (visceral) components of emotion. The cingulate gyrus was proposed as the "seat of emotional experience" (cortical representation), while the hypothalamus mediates the expression of emotion.

2. The Limbic System (MacLean, 1952) [1]

Paul MacLean expanded Papez's model into the **limbic system** concept, adding:

- **Amygdala**, now recognized as the central structure for fear processing
- **Septal nuclei**, pleasure and reward
- **Orbitofrontal cortex**, emotional regulation, decision-making
- **Insula**, interoception, disgust

3. The Amygdala, Central Hub of Emotional Processing [2]

Joseph LeDoux's research established two parallel pathways for emotional processing:

a. Low road (Thalamo-amygdala pathway), "Quick and dirty"

- Sensory input --> Thalamus --> **Amygdala** (direct)
- **Fast** (12 ms), imprecise
- Enables rapid threat detection before conscious awareness
- Underlies fear conditioning and startle responses

b. High road (Thalamo-cortico-amygdala pathway), "Slow and accurate"

- Sensory input --> Thalamus --> **Sensory cortex** --> **Amygdala**
- **Slower** but more detailed processing
- Allows cortical evaluation and contextual modulation of emotional response

Amygdala outputs:

- --> **Hypothalamus** --> autonomic responses (sympathetic activation, HPA axis)
- --> **Periaqueductal gray (PAG)** --> behavioral responses (freezing, fight/flight)
- --> **Basal forebrain** --> arousal and attention
- --> **Prefrontal cortex** --> conscious emotional experience, regulation

4. Prefrontal Cortex, Emotional Regulation

- **Medial PFC**, extinction of conditioned fear; regulates amygdala via inhibitory projections
- **Orbitofrontal cortex**, stimulus-reward associations; decision-making (Damasio's somatic marker hypothesis)
- **Ventrolateral PFC**, explicit emotion regulation (cognitive reappraisal)

C. Diagram [3]

EXAM PEARL

Cross-reference: Q15 (similar question, neural pathways), Q16 (theories of emotion), Q25 (aggression, biological basis involves overlapping circuits)

Q15: "Define emotion. Neural pathways of emotion with a diagram.": 10 marks [2+8]

Exam Strategy: Same content as Q14 but with 8 marks on neural pathways. Expand Papez circuit, LeDoux's two pathways, and add the ventral and dorsal streams. Use the diagram from Q14 and add more detail.

A. Definition [2]

(Same as Q14)

Emotion is a complex psychophysiological state comprising: (1) **subjective experience** (conscious feeling), (2) **physiological arousal** (autonomic and neuroendocrine changes), and (3) **behavioral expression** (facial expression, approach/avoidance). Emotions serve an **adaptive function**, they prioritize cognitive processing and prepare the organism for action.

B. Neural Pathways of Emotion [6]

1. Papez Circuit (1937) [1.5]

The first model of a dedicated emotional circuit in the brain:

Pathway: Hippocampal formation --> Fornix --> **Mammillary bodies** (hypothalamus) --> Mammillothalamic tract (of Vicq d'Azyr) --> **Anterior thalamic nuclei** --> **Cingulate gyrus** --> Cingulum bundle --> **Parahippocampal gyrus** (entorhinal cortex) --> Hippocampus

Functions:

- Cingulate gyrus: Subjective emotional experience
- Hippocampus: Emotional memory, context
- Hypothalamus (mammillary bodies): Emotional expression (autonomic, endocrine)
- Anterior thalamus: Relay between limbic and cortical processing

Clinical: Damage to the mammillary bodies (Wernicke-Korsakoff syndrome) disrupts both memory and emotional processing. Cingulate lesions produce akinetic mutism (loss of emotional drive).

2. LeDoux's Dual Pathway Model (1996) [2]

Low road (Subcortical / Thalamo-amygdala):

- Sensory stimulus --> Lateral geniculate / Medial geniculate (thalamus) --> **Lateral nucleus of amygdala** (direct)
- Rapid (~12 ms), coarse processing
- Evolutionarily old; enables survival responses before conscious recognition
- *Example:* Freezing at a stick on a forest path (looks like a snake) before conscious identification

High road (Cortical / Thalamo-cortico-amygdala):

- Sensory stimulus --> Thalamus --> **Primary sensory cortex** --> **Association cortex** --> **Lateral/basolateral amygdala**
- Slower (~200-300 ms), detailed, contextual processing
- Allows cortical override: "It's a stick, not a snake" --> amygdala response dampened
- Mediated by prefrontal cortex projections to amygdala

3. Amygdala Nuclei and Their Connections [1.5]

AMYGDALA NUCLEUS	INPUT	OUTPUT	FUNCTION
Lateral nucleus	Sensory thalamus, sensory cortex	Basolateral nucleus	Sensory gateway; fear conditioning
Basolateral nucleus	Lateral nucleus, hippocampus, PFC	Central nucleus	Integration of sensory and contextual information
Central nucleus	Basolateral nucleus	Hypothalamus, PAG, brainstem	Output station, generates autonomic, endocrine, and behavioral responses

Central nucleus outputs:

- --> **Lateral hypothalamus** --> Sympathetic activation (tachycardia, blood pressure rise)
- --> **Paraventricular nucleus (PVN)** --> HPA axis activation (cortisol)
- --> **Periaqueductal gray (PAG)** --> Freezing, analgesia, vocalization
- --> **Dorsal motor nucleus of vagus** --> Parasympathetic (bradycardia in extreme fear, vasovagal)
- --> **Locus coeruleus** --> Noradrenergic arousal
- --> **Ventral tegmental area** --> Dopaminergic reward / salience

4. Prefrontal Cortex, Top-Down Regulation [1]

- **Ventromedial PFC (vmPFC)** --> Amygdala: Fear extinction; integrates visceral signals with decision-making (Damasio's somatic marker hypothesis)
- **Dorsolateral PFC (dlPFC)** --> vmPFC --> Amygdala: Cognitive reappraisal; volitional regulation of emotion
- **Orbitofrontal cortex (OFC)**: Stimulus-reward reversal; social emotions (regret, embarrassment)
- **Anterior cingulate cortex (ACC)**: Conflict monitoring; error detection; emotional salience

Clinical correlations:

- **PTSD**: Amygdala hyperactivation + vmPFC hypoactivation = impaired fear extinction
- **Depression**: ACC and PFC hypoactivity; amygdala hyperreactivity
- **Anxiety disorders**: Enhanced amygdala sensitivity; impaired prefrontal regulation
- **Psychopathy**: Reduced amygdala reactivity to distress cues
- **Kluver-Bucy syndrome**: Bilateral amygdala damage --> emotional flattening, hypersexuality, hyperorality

C. Diagram [2]

(Same diagram as Q14, adapted with amygdala nuclei detail)

EXAM PEARL

Cross-reference: Q14 (identical overlap), Q25 (aggression circuits, amygdala, hypothalamus, PAG, PFC)

Q16: "What are the basic emotions? Discuss briefly the theories of emotion." 10 marks [2+8]

Exam Strategy: Quick list of basic emotions (Ekman), then structured coverage of major theories. A table works well for the theories.

A. Basic Emotions [2]

Paul Ekman (1972) identified **six universal basic emotions** through cross-cultural studies of facial expressions (including isolated Papua New Guinean tribes):

1. **Happiness** (joy)
2. **Sadness**
3. **Fear**
4. **Anger**
5. **Disgust**
6. **Surprise**

Ekman later expanded this to include: contempt, embarrassment, excitement, guilt, shame, pride, satisfaction, and amusement. However, the original six are the most widely recognized as universal.

Other models:

- **Plutchik (1980):** Eight basic emotions arranged in a wheel, joy, trust, fear, surprise, sadness, disgust, anger, anticipation. Opposite emotions are across the wheel. Combinations produce secondary emotions (e.g., joy + trust = love).
- **Jaak Panksepp (2004):** Seven primary emotional systems: SEEKING, RAGE, FEAR, LUST, CARE, PANIC/GRIEF, PLAY (neuroscience-based, mapped to specific brain circuits).

B. Theories of Emotion [8]

1. James-Lange Theory (1884-1885) [1.5]

- **Core idea:** Physiological arousal precedes and CAUSES the emotional experience
- **Sequence:** Stimulus --> Bodily response (autonomic arousal, muscular action) --> Brain interprets bodily changes --> Emotion
- "We do not cry because we are sad; we are sad because we cry"
- **Evidence for:** Facial feedback hypothesis (smiling makes you feel happier); spinal cord injury patients report reduced emotional intensity
- **Evidence against:** Physiological responses are too slow and too similar across emotions to differentiate them; Cannon's critique

2. Cannon-Bard Theory (1927-1938) [1.5]

- **Core idea:** Emotion and physiological arousal occur **simultaneously and independently**
- **Sequence:** Stimulus --> Thalamus --> simultaneously sends signals to cortex (emotional experience) AND hypothalamus/body (physiological response)
- Walter Cannon's critique of James-Lange:
- Visceral changes are too slow to cause emotion

- Same visceral changes occur in different emotions (e.g., tachycardia in both fear and anger)
- Artificial induction of visceral changes (adrenaline injection) doesn't reliably produce specific emotions
- **Clinical relevance:** Explains why patients with spinal cord injuries can still experience emotions (though possibly with reduced intensity)

3. Schachter-Singer Two-Factor Theory (1962) [1.5]

- **Core idea:** Emotion = physiological arousal + cognitive label (interpretation)
- **Sequence:** Stimulus --> Physiological arousal (nonspecific) --> Cognitive appraisal of the situation --> Emotion
- **Classic experiment:** Participants injected with adrenaline. Those uninformed about side effects attributed their arousal to the situation (happy / angry confederate) and reported corresponding emotions. Those informed correctly attributed arousal to the injection.
- **Key insight:** The SAME physiological arousal can be experienced as different emotions depending on cognitive context
- **Clinical relevance:** Explains misattribution of arousal (e.g., Dutton & Aron's bridge study, fear arousal misattributed as romantic attraction); relevant to panic disorder (interoceptive misinterpretation)

4. Cognitive Appraisal Theory (Lazarus, 1966) [1]

- **Core idea:** Cognitive evaluation of the stimulus is **primary**, emotion depends on how the situation is appraised, not the stimulus itself
- **Two types of appraisal:**
- **Primary appraisal:** "Is this relevant to me? Is it threatening or beneficial?"
- **Secondary appraisal:** "Can I cope with this? What resources do I have?"
- **Same stimulus, different appraisal, different emotion:** Job loss may produce fear (if appraised as threatening) or relief (if appraised as escape from a bad situation)
- **Clinical relevance:** Foundation of CBT, changing cognitive appraisals changes emotional responses; Ellis's ABC model; Beck's cognitive triad

5. Facial Feedback Hypothesis (Darwin, Ekman, Tomkins) [0.5]

- Facial expressions are not just outputs of emotion, they **feed back** to influence emotional experience
- Holding a pen between teeth (mimicking a smile) increases humor ratings
- Botox studies: paralyzing frown muscles reduces depressive symptoms and amygdala reactivity
- Supports the James-Lange direction of causation (body --> emotion)

6. Somatic Marker Hypothesis (Damasio, 1994) [1]

- Emotions generate **somatic markers** (bodily states stored in vmPFC) that guide decision-making
- When facing a decision, the brain reactivates somatic markers from past similar situations
- These "gut feelings" bias choices toward adaptive outcomes
- **Iowa Gambling Task:** Patients with vmPFC damage fail to develop somatic markers and make consistently disadvantageous choices despite intact intellectual reasoning
- **Clinical relevance:** Explains poor decision-making in conditions affecting PFC (substance use disorders, traumatic brain injury, antisocial PD)

7. Constructionist Theory (Barrett, 2017) [1]

- Emotions are not natural kinds with dedicated circuits, they are **constructed** by the brain from more basic ingredients:
- **Core affect** (valence + arousal) + **Conceptual knowledge** (learned emotion categories) + **Contextual cues**
- The brain is a "prediction machine" that constructs emotional experience based on prior learning
- **Clinical relevance:** Explains cultural variation in emotional experience; alexithymia as impaired emotional construction; implications for emotional granularity (people who differentiate emotions more precisely have better mental health)

EXAM PEARL

Cross-reference: Q14-Q15 (neural circuits), Q17-Q18 (emotional intelligence, applications of emotion understanding)

Q17: "What is emotional intelligence? Describe components. Relationship with IQ." 10 marks [2+4+4]

Exam Strategy: Definition (Goleman + Salovey/Mayer), components in a clear list, then a nuanced IQ comparison section.

A. Definition of Emotional Intelligence [2]

Emotional intelligence (EI) is the ability to **perceive, understand, manage, and use emotions** effectively in oneself and others.

The concept was first formally proposed by **Salovey and Mayer (1990)** as a form of intelligence and popularized by **Daniel Goleman (1995)** in his bestselling book *Emotional Intelligence*.

Salovey & Mayer's definition: "The ability to monitor one's own and others' feelings and emotions, to discriminate among them, and to use this information to guide one's thinking and actions."

B. Components of Emotional Intelligence [4]

Goleman's Five-Component Model (1995):

COMPONENT	DEFINITION	EXAMPLE
1. Self-awareness	Recognizing and understanding one's own emotions, strengths, weaknesses, values, and their impact on others	A psychiatrist notices they feel irritated with a patient and recognizes this as countertransference
2. Self-regulation	Managing one's emotions and impulses; adaptability; maintaining standards	Remaining calm during a psychiatric emergency; not reacting impulsively to provocation
3. Motivation	Internal drive to achieve for the sake of achievement; optimism; resilience	Continuing to study for exams despite setbacks; intrinsic motivation for clinical work
4. Empathy	Understanding and sharing the feelings of others; reading emotional cues; sensitivity to cultural and social differences	A therapist accurately perceives a patient's shame beneath expressed anger
5. Social skills	Managing relationships; communication; conflict resolution; leadership; collaboration	Building therapeutic alliance; effective teamwork in a multidisciplinary team

Salovey & Mayer's Four-Branch Model (1997), more academically rigorous:

BRANCH	ABILITY	DEVELOPMENTAL PROGRESSION
1. Perceiving emotions	Accurately identifying emotions in faces, voices, images, music	Most basic ability
2. Using emotions to facilitate thought	Generating emotions to aid judgment, creativity, and problem-solving	Emotions as cognitive tools
3. Understanding emotions	Comprehending emotional language, transitions, and complex blends	Emotional vocabulary and dynamics
4. Managing emotions	Regulating emotions in self and others; staying open to feelings	Most complex; requires all branches

C. Relationship Between EI and IQ [4]

DIMENSION	IQ (COGNITIVE INTELLIGENCE)	EI (EMOTIONAL INTELLIGENCE)
What it measures	Logical reasoning, verbal ability, spatial processing, working memory	Emotion perception, regulation, empathy, social skills

DIMENSION	IQ (COGNITIVE INTELLIGENCE)	EI (EMOTIONAL INTELLIGENCE)
Stability	Relatively stable after childhood	Can be developed and improved throughout life
Heritability	~50-80% heritable	Less heritable; more influenced by learning and environment
Measurement	Well-validated (WAIS, Stanford-Binet); strong psychometric properties	Less standardized; ability-based (MSCEIT) vs. self-report (EQ-i) measures
Correlation	IQ and EI are weakly correlated ($r \sim 0.1-0.3$), largely independent constructs	
Prediction of success	Strong predictor of academic achievement	Better predictor of workplace performance, leadership, and relationship quality

Key findings on EI vs. IQ:

1. **IQ is necessary but not sufficient**, High IQ without adequate EI leads to poor interpersonal functioning, leadership failure, and career underperformance
2. **EI predicts life outcomes beyond IQ**, Goleman claimed EI accounts for ~80% of success factors, though this is widely considered an overstatement. Meta-analyses suggest EI predicts **5-10% of variance in job performance** beyond IQ and personality
3. **Complementary, not competing**, The most effective individuals score high on both
4. **EI is more trainable**, Programs to improve EI (social-emotional learning in schools, leadership coaching) show moderate effectiveness
5. **Clinical relevance:**
6. **Alexithymia**, Extreme low EI; difficulty identifying and describing emotions; common in psychosomatic disorders, substance use, autism
7. **Physicians with higher EI** show better patient satisfaction, fewer complaints, lower burnout
8. **Psychiatry trainees**, EI predicts therapeutic alliance quality
9. **Psychopathy**, Dissociation between cognitive empathy (intact or enhanced) and affective empathy (impaired); cognitive EI can be weaponized

EXAM PEARL

Cross-reference: Q18 (same topic, different mark split, emphasize applications there)

Q18: "What is emotional intelligence? Discuss different components and applications.": 10 marks [3+3+4]

Exam Strategy: More marks on definition and applications here than Q17. Cover clinical, educational, workplace, and psychiatric applications.

A. Definition [3]

(Expanded from Q17)

Emotional intelligence (EI) refers to a set of abilities involving the **perception, appraisal, expression, and regulation of emotions** in self and others, and the use of emotions to guide adaptive behavior.

Historical development:

- **Thorndike (1920)**, Described "social intelligence", the ability to understand and manage people
- **Gardner (1983)**, Proposed **interpersonal** and **intrapersonal intelligence** as part of multiple intelligences theory
- **Salovey & Mayer (1990)**, First formal definition; proposed EI as a genuine form of intelligence
- **Goleman (1995)**, Popularized the concept; broadened it to include personality traits like motivation and social skills

Measurement:

- **Ability-based:** MSCEIT (Mayer-Salovey-Caruso Emotional Intelligence Test), tests actual ability; considered more valid
- **Self-report:** EQ-i (Bar-On Emotional Quotient Inventory); correlates more with personality than true ability
- **360-degree assessment:** Observer-rated EI; useful in organizational settings

B. Components [3]

(See Q17 for detailed tables.)

Goleman's 5 components: Self-awareness, Self-regulation, Motivation, Empathy, Social skills

Salovey & Mayer's 4 branches: Perceiving emotions, Using emotions, Understanding emotions, Managing emotions

Bar-On's model (1997), five meta-factors:

1. **Intrapersonal**, Self-regard, emotional self-awareness, assertiveness, independence, self-actualization
2. **Interpersonal**, Empathy, social responsibility, interpersonal relationships
3. **Adaptability**, Reality testing, flexibility, problem-solving

4. **Stress management**, Stress tolerance, impulse control
5. **General mood**, Optimism, happiness

C. Applications [4]

1. Clinical Psychiatry [1]

- **Alexithymia** (deficient EI): Core feature of psychosomatic disorders, substance use, PTSD, eating disorders, autism. Measured by the Toronto Alexithymia Scale (TAS-20)
- **Therapeutic alliance**: Therapist EI predicts stronger alliances and better outcomes
- **Psychopathy**: Intact cognitive empathy with impaired affective empathy, manipulative use of emotional knowledge
- **Burnout prevention**: Physicians and mental health professionals with higher EI have lower burnout rates
- **Group therapy**: EI-building is an explicit goal; interpersonal learning and universality enhance EI

2. Education [1]

- **Social-Emotional Learning (SEL) programs** in schools (CASEL framework) teach emotion recognition, regulation, and prosocial behavior
- Meta-analyses show SEL programs improve academic achievement by 11 percentile points, reduce behavioral problems, and increase prosocial behavior
- **Bullying prevention**: Building empathy reduces perpetration; building emotion regulation reduces victimization

3. Workplace and Leadership [1]

- Leaders with high EI create more positive organizational climates
- EI predicts job performance in roles requiring interpersonal interaction (sales, management, healthcare)
- **Organizational EI**: Teams with higher collective EI perform better
- **Conflict resolution**: EI enables perspective-taking and de-escalation
- **Selection and training**: Increasingly used in hiring decisions and executive coaching

4. Medical Education and Patient Care [1]

- Communication skills training incorporates EI principles
- **Patient satisfaction** correlates with physician empathy (cognitive + affective)
- **Medical error reduction**: Emotionally intelligent teams communicate better in high-stakes environments
- **Residency training**: EI-based curricula improve resident well-being and reduce interpersonal conflict

- **Psychiatric residency specifically:** Empathic attunement with patients is a trainable EI skill

EXAM PEARL

Cross-reference: Q17 (EI vs. IQ comparison), Q14-Q15 (neural basis of emotion, EI depends on intact prefrontal-amygdala circuits)

Q19: "What is bereavement? Stages of normal bereavement. Complicated bereavement.": 10 marks [2+4+4]

Exam Strategy: Clear definitions first, then stages (Kubler-Ross + Bowlby + Worden), then complicated grief with DSM-5-TR criteria.

A. Definition of Bereavement [2]

Bereavement is the **state of having experienced the death** of a significant person (or, more broadly, any significant loss). It is the **objective situation** of loss.

Related terms:

- **Grief**, The **emotional response** to bereavement; the subjective experience of loss (sadness, yearning, anger, guilt)
- **Mourning**, The **social expression** of grief; culturally shaped rituals and behaviors (funerals, wearing black, shiva)

B. Stages/Phases of Normal Bereavement [4]

1. Kubler-Ross's Five Stages (1969) [1.5]

Originally described for patients facing their own death (*On Death and Dying*), widely applied to grief:

STAGE · DESCRIPTION

1. Denial "This can't be true." Shock and disbelief; emotional numbness; protective function

2. Anger "Why me? This is unfair." Directed at deceased, God, doctors, self; frustration and helplessness

3. Bargaining "If only I had..." Attempts to negotiate reversal; guilt-driven; often involves religious/spiritual thinking

4. Depression Awareness of the full impact of loss; withdrawal, sadness, tearfulness; "preparatory grief"

5. Acceptance Coming to terms with reality; not "being okay" but acknowledging the loss; reinvestment in life

Caveat: These stages are **not sequential or universal**. Modern grief research emphasizes that grief is non-linear and highly individual. The stage model is criticized for being prescriptive.

2. Bowlby's Four Phases of Grief (1961, 1980) [1]

Derived from **attachment theory** (loss of attachment figure activates the attachment system):

PHASE	DURATION	DESCRIPTION
1. Numbing	Hours to 1 week	Shock, disbelief, emotional blunting; may have bursts of intense distress or anger
2. Yearning and Searching	Weeks to months	Intense longing for deceased; restlessness; preoccupation with the lost person; "searching" behavior; misperceptions (hearing their voice)
3. Disorganization and Despair	Months	Realization that the person will not return; apathy, withdrawal, difficulty functioning; depression-like state
4. Reorganization	Variable	Gradual reorientation to life without the deceased; formation of new relationships; the lost person is internalized

3. Worden's Four Tasks of Mourning (1991) [1.5]

An active, task-based model (the bereaved must DO something, not just pass through stages):

TASK	DESCRIPTION	CLINICAL RELEVANCE
1. Accept the reality of the loss	Overcome denial; both intellectual and emotional acceptance	Viewing the body, attending the funeral facilitates this
2. Process the pain of grief	Experience and work through the emotional pain; not suppress or avoid it	Suppression leads to complicated grief; cultures that encourage emotional expression show better outcomes
3. Adjust to the environment without the deceased	Practical adjustments (finances, household) + emotional adjustments (identity without the person) + spiritual adjustments (meaning-making)	Support groups, practical assistance help

TASK	DESCRIPTION	CLINICAL RELEVANCE
4. Find an enduring connection while embarking on a new life	Maintain a bond with the deceased while reinvesting emotional energy in living	"Continuing bonds" model, healthy grief does not require "letting go" but rather integrating the loss

C. Complicated Bereavement [4]

DSM-5-TR: Prolonged Grief Disorder (PGD), newly added in 2022:

Diagnostic criteria:

- Death of someone close to the bereaved **at least 12 months ago** (6 months for children)
- Since the death, persistent and pervasive **grief response** characterized by intense **yearning/longing** for the deceased OR **preoccupation** with the deceased
- **At least 3 of the following** (experienced to a clinically significant degree nearly every day for at least the last month):
 - Identity disruption (feeling as if part of oneself has died)
 - Marked sense of disbelief about the death
 - Avoidance of reminders that the person is dead
 - Intense emotional pain (anger, bitterness, sorrow)
 - Difficulty reintegrating into relationships and activities
 - Emotional numbness
 - Feeling that life is meaningless
 - Intense loneliness
- Causes clinically significant distress or impairment
- Duration/severity exceeds expected social, cultural, or religious norms
- Not better explained by MDD, PTSD, or substance use

Risk factors for complicated grief:

- **Relationship:** Loss of child, loss of spouse, highly dependent or ambivalent relationship
- **Circumstances:** Sudden, violent, or traumatic death; suicide; multiple losses
- **Personal:** History of psychiatric illness (especially depression, anxiety), insecure attachment, prior losses, social isolation
- **Social:** Lack of social support; disenfranchised grief (loss not socially acknowledged)

Types of abnormal grief:

TYPE · DESCRIPTION

Prolonged/Chronic grief Normal grief that persists beyond expected duration without resolution

Delayed grief Minimal initial reaction; grief emerges later, sometimes triggered by another loss

Inhibited grief Emotional expression is blocked; may present as somatic symptoms

Distorted grief Extreme intensity of one grief component (e.g., overwhelming anger or guilt)

Absent grief No apparent grief response; may indicate denial or dissociation

EXAM PEARL

Cross-reference: Q20-Q23 (overlapping grief questions, vary emphasis per mark split), Q12 (attachment theory, Bowlby's grief model originates from attachment theory)

Q20: "Bereavement, grief and mourning? Describe stages of grief and clinical relevance.": 10 marks [3+7]

Exam Strategy: More marks on definitions here (3). Stages + clinical relevance section should be the bulk. Emphasize clinical application.

A. Bereavement, Grief, and Mourning, Definitions [3]

TERM	DEFINITION	NATURE	EXAMPLE
Bereavement	The objective state of having experienced the death of a significant person	Situational; external event	A woman whose husband died last month is "bereaved"
Grief	The emotional, cognitive, physical, and behavioral response to the loss	Internal experience; multidimensional	Sadness, yearning, insomnia, appetite loss, difficulty concentrating, social withdrawal
Mourning	The outward, socially and culturally shaped expression of grief	External expression; culturally determined	Wearing black, funeral rites, sitting shiva, chanting prayers, wailing ceremonies

Relationship: Bereavement is the **situation**, grief is the **reaction**, mourning is the **expression**. All three are normal and necessary. Problems arise when grief is prolonged, absent, or distorted.

Dimensions of normal grief:

- **Emotional:** Sadness, anger, guilt, anxiety, loneliness, yearning, relief
- **Cognitive:** Disbelief, confusion, preoccupation with deceased, sense of presence

- **Physical:** Sleep disturbance, appetite change, fatigue, somatic complaints, immune suppression
- **Behavioral:** Crying, social withdrawal, restlessness, searching behavior, visiting places of significance

B. Stages of Grief and Clinical Relevance [7]

Stages of Grief:

(See Q19 for detailed Kubler-Ross, Bowlby, and Worden models.)

Brief summary:

- **Kubler-Ross (1969):** Denial --> Anger --> Bargaining --> Depression --> Acceptance
- **Bowlby (1980):** Numbing --> Yearning/Searching --> Disorganization/Despair --> Reorganization
- **Worden (1991):** Four tasks: Accept reality --> Process pain --> Adjust to environment --> Find enduring connection
- **Dual Process Model (Stroebe & Schut, 1999):** The bereaved oscillates between **loss-oriented coping** (confronting grief) and **restoration-oriented coping** (attending to life changes, taking breaks from grief). Healthy grief involves oscillation between both.

Clinical Relevance [4]

1. Differentiating normal grief from Major Depressive Disorder [1.5]

FEATURE	NORMAL GRIEF	MAJOR DEPRESSION
Predominant affect	Emptiness, longing, waves of sadness	Persistent depressed mood, anhedonia
Self-esteem	Generally preserved	Pervasive worthlessness, self-loathing
Guilt content	About things done/not done for the deceased	Global, pervasive guilt
Suicidal ideation	Desire to join the deceased (passive)	Active wish to die; hopelessness
Psychomotor changes	Variable; may function normally between waves	Persistent retardation or agitation
Duration	Waves that diminish over months	Persistent, unrelenting
Response to comfort	Can be consoled; capacity for positive emotions	Minimal response to comfort
Psychotic features	Auditory/visual experiences of deceased (normal)	Mood-congruent delusions, hallucinations

Important: DSM-5 removed the "bereavement exclusion", MDD can now be diagnosed during bereavement if criteria are met. However, clinical judgment is essential.

2. Complicated grief as a clinical entity [1]

- **Prolonged Grief Disorder** (DSM-5-TR), distinct from depression and PTSD
- Prevalence: ~10% of bereaved individuals
- Higher risk: traumatic death, loss of child, insecure attachment, social isolation
- Responds to specific grief-focused interventions (see below)

3. Treatment of complicated grief [1.5]

- **Complicated Grief Treatment (CGT, Shear):** Evidence-based; combines exposure (to reminders of loss and avoided situations) with interpersonal therapy techniques. Integrates dual process model. Superior to standard IPT.
- **Pharmacotherapy:** SSRIs may help comorbid depression but do not specifically treat grief; some evidence for combination SSRI + CGT
- **CBT for grief:** Addresses maladaptive cognitions (guilt, self-blame, catastrophizing about the future)
- **Support groups:** Particularly effective for shared experience (e.g., bereaved parents groups)
- **Life review and meaning-making:** Narrative therapy approaches; helping the person construct meaning from the loss

4. Special populations [1]

- **Children:** Grief is developmentally variable; may not show "adult" grief; behavioral regression, school problems
- **Elderly:** "Bereavement overload", multiple losses in rapid succession; increased mortality in bereaved spouses ("broken heart syndrome")
- **Disenfranchised grief:** Grief from losses not socially recognized (miscarriage, pet death, death of ex-partner, death of same-sex partner in unsupportive environments)
- **Healthcare workers:** Occupational grief; cumulative loss exposure; moral injury

EXAM PEARL

Cross-reference: Q19, Q21-Q23 (overlapping content), Q12 (attachment theory underlies grief models)

Q21: "Define grief, bereavement and mourning. Describe relationship between them.": 10 marks [3+7]

Exam Strategy: This question wants the relationship between the three concepts, not just definitions side by side. Spend 3 marks on definitions, then explore how they interconnect.

A. Definitions [3]

Grief: The **internal, multidimensional response** to the loss of someone or something significant. Encompasses emotional (sadness, anger, guilt, yearning), cognitive (disbelief, confusion, preoccupation), physical (insomnia, fatigue, immune suppression), behavioral (crying, withdrawal, searching), and spiritual dimensions.

Bereavement: The **objective state** of having suffered a loss, particularly the death of a significant person. It describes the **situation**, not the reaction. A person is "in bereavement" or "bereaved."

Mourning: The **external expression** of grief, shaped by **social, cultural, and religious** norms. Mourning provides the rituals and frameworks through which grief is expressed and communicated to others (funerals, memorial services, wearing specific clothing, observing specific time periods).

B. Relationship Between Grief, Bereavement, and Mourning [7]

1. Sequential and Causal Relationship [2]

The relationship follows a logical sequence:

- **Bereavement** (the event) --> triggers **Grief** (the reaction) --> expressed through **Mourning** (the social behavior)

However, this is not a simple linear chain:

- Grief can occur **before** bereavement (**anticipatory grief**, grieving before the death, as in terminal illness)
- Grief can occur **without** bereavement in the traditional sense (loss of relationship, loss of health, loss of homeland)
- Mourning practices can **facilitate or inhibit** grief processing
- Cultural mourning norms can **mismatch** with individual grief (e.g., pressure to "move on" too quickly, or to grieve in a specific way)

2. Grief Without Mourning, Disenfranchised Grief [1]

Kenneth Doka (1989) described **disenfranchised grief**: grief that is not openly acknowledged, socially validated, or publicly mourned.

Examples:

- Loss of a same-sex partner in a community that does not recognize the relationship
- Miscarriage or stillbirth (often minimized: "You can have another")
- Death of an ex-spouse, friend, or pet
- Loss of a person to dementia ("ambiguous loss", the person is alive but psychologically absent)

Clinical significance: When mourning is unavailable, grief has no container. This increases the risk of complicated grief, somatization, and depression.

3. Cultural Variation in Mourning, Same Grief, Different Expression [1.5]

Grief is considered **universal** (all humans grieve), but mourning is **culturally specific**:

CULTURE	MOURNING PRACTICE	FUNCTIONAL SIGNIFICANCE
Hindu (Indian)	13-day mourning period; cremation; specific rituals by eldest son; annual shraddha ceremony	Provides structure; community support; spiritual meaning
Jewish	Shiva (7 days), Shloshim (30 days), Yahrzeit (annual)	Graduated return to normal life; community obligation to visit
Muslim	3-day mourning; Iddah (4 months 10 days for widow)	Rapid burial; community-oriented grief
Western secular	Funeral / memorial; no prescribed mourning period	Less community structure; individual must create their own mourning

Clinical implication: Clinicians must assess grief within the individual's cultural mourning framework. What looks like "complicated grief" may be culturally normative mourning, and vice versa.

4. Mourning as Facilitator of Grief [1]

Mourning rituals serve several psychological functions:

- **Reality confirmation:** Viewing the body, attending the funeral confirms the death (Worden's Task 1)
- **Social support:** Funeral gatherings provide the bereaved with community presence
- **Permission to grieve:** Culturally sanctioned mourning gives "permission" to express emotion
- **Meaning-making:** Religious/spiritual mourning provides a framework for understanding death
- **Graduated re-entry:** Prescribed mourning periods (shiva, 13-day Hindu mourning) provide a structured timeline for returning to normal life

5. When the Triad Breaks Down [1.5]

DISRUPTION	MECHANISM	CLINICAL PRESENTATION
Bereavement without grief	Absent or inhibited grief response (denial, emotional numbness, alexithymia)	Somatic symptoms, delayed grief, alcohol use, work addiction

DISRUPTION	MECHANISM	CLINICAL PRESENTATION
Grief without bereavement	Non-death losses: divorce, migration, disability, "ambiguous loss" (Boss)	Often unrecognized and untreated; patient may not identify as "grieving"
Grief without mourning	Disenfranchised grief; no social support or cultural framework	Complicated grief, isolation, shame
Mourning without grief	Social performance of grief without internal experience	May be adaptive (not everyone grieves intensely) or may mask suppression
Prolonged mourning	Cultural expectation or personal inability to relinquish the mourning role	Chronic grief, depression, social disability

Clinical approach:

- Assess all three: What happened (bereavement)? How is the person feeling (grief)? What support and expression is available (mourning)?
- The therapeutic relationship can function as a "mourning space" when cultural mourning is absent

EXAM PEARL

Cross-reference: Q19-Q20, Q22-Q23 (overlapping grief content), Q12 (attachment theory)

Q22: "Define grief. Features of complicated grief. Management.": 10 marks [2+3+5]

Exam Strategy: Brief definition, then DSM-5-TR criteria for Prolonged Grief Disorder, then detailed management (5 marks, this is the bulk).

A. Definition of Grief [2]

Grief is the **multidimensional response** to loss, particularly the death of a significant person. It encompasses:

- **Emotional:** Sadness, yearning, anger, guilt, anxiety, loneliness, shock, relief
- **Cognitive:** Disbelief, confusion, preoccupation with the deceased, sense of presence
- **Physical:** Sleep and appetite disturbance, fatigue, somatic complaints, immune suppression
- **Behavioral:** Crying, social withdrawal, restlessness, searching, sighing
- **Spiritual:** Questioning meaning, anger at God, existential crisis, or deepened faith

Normal grief is **self-limiting**, it diminishes in intensity over weeks to months. It occurs in waves triggered by reminders (anniversaries, places, songs). Capacity for positive emotions is preserved between waves.

B. Features of Complicated Grief [3]

Prolonged Grief Disorder (DSM-5-TR, 2022):

Core features (at least one required):

1. Intense **yearning/longing** for the deceased, pervasive, daily
2. **Preoccupation** with the deceased (constant thoughts, memories, images)

Associated symptoms (at least 3 of 8):

1. **Identity disruption**, "Part of me died with them"
2. **Disbelief** about the death, even after 12+ months
3. **Avoidance** of reminders that the person is dead
4. **Intense emotional pain**, bitterness, anger, sorrow related to the death
5. **Difficulty reintegrating** into life, relationships, activities, plans
6. **Emotional numbness**, feeling detached, unable to feel positive emotions
7. **Meaninglessness**, life feels pointless without the person
8. **Intense loneliness**, feeling alone even with others

Temporal criterion: Symptoms persist for **at least 12 months** after the death (6 months for children/adolescents)

Differentiating features:

- Distinguished from **MDD**: Grief is focused on the loss; depression is pervasive. Self-esteem preserved in grief. Suicidal ideation (if present) is about reuniting with deceased, not self-worthlessness.
- Distinguished from **PTSD**: PTSD involves re-experiencing the traumatic circumstances of death; complicated grief involves yearning and searching for the deceased.
- **Comorbidity**: Complicated grief frequently co-occurs with MDD (~50%), PTSD (especially after violent death), and substance use.

C. Management of Complicated Grief [5]

1. Complicated Grief Treatment (CGT, Katherine Shear) [2]

- **Gold standard** evidence-based treatment (RCT-validated; superior to standard IPT)
- **16-session protocol** combining elements of:
 - **Attachment theory**, Understanding the lost bond and building new connections
 - **Cognitive-behavioral techniques**, Exposure to grief-related stimuli; cognitive restructuring
 - **Dual Process Model**, Oscillation between loss-oriented and restoration-oriented work
- **Key components:**

- **Revisiting exercise:** Patient narrates the story of the death in session (recorded, listened to between sessions), analogous to imaginal exposure in PTSD
- **Situational exposure:** Graded exposure to avoided places, activities, and reminders
- **Imaginal conversation:** Patient "talks to" the deceased in session; addresses unfinished business
- **Personal goals and aspirations:** Restoration-oriented work; rebuilding life
- **Grief monitoring diary:** Tracks grief intensity and functioning

2. Pharmacotherapy [1]

- **SSRIs** (particularly escitalopram): May reduce comorbid depression and anxiety; do not specifically treat grief yearning
- **Combination:** CGT + citalopram showed better outcomes than either alone in one RCT (Shear et al., 2016)
- **Benzodiazepines:** Generally avoided, may inhibit emotional processing and delay grief work. Short-term use only for severe insomnia or acute distress.
- **No specific pharmacotherapy for grief itself,** medication targets comorbid symptoms

3. Psychotherapy Approaches [1]

- **IPT modified for grief:** Focus on role transitions and interpersonal disputes related to the loss
- **CBT for grief:** Targets maladaptive cognitions (self-blame, catastrophizing, "I should be over this")
- **Meaning-making therapy (Neimeyer):** Narrative reconstruction; finding meaning in the loss
- **Mindfulness-based interventions:** Acceptance of grief waves; non-judgmental observation of emotions
- **EMDR:** For traumatic grief (violent or sudden death), targets traumatic imagery

4. Support-Based Interventions [0.5]

- **Support groups:** Bereaved parents groups, widows / widowers groups, suicide survivor groups
- **Online support:** Growing evidence for internet-based grief interventions
- **Peer support:** Particularly valuable for disenfranchised grief

5. Preventive and Early Interventions [0.5]

- **Identify at-risk individuals early:** Screen for risk factors (sudden death, loss of child, insecure attachment, psychiatric history, social isolation)
- **Anticipatory guidance:** Normalize grief reactions; psychoeducation about the grief process

- **Palliative care teams:** Support caregivers before and after death
- **Follow-up:** Brief check-in by GP / primary care at 6 months and 12 months post-bereavement

EXAM PEARL

Cross-reference: Q19-Q21, Q23 (overlapping grief content)

Q23: "Define grief. Phases and different types of grief.": 10 marks [2+4+4] -- LONG ESSAY CANDIDATE

Exam Strategy: This is the comprehensive grief question. For 20-mark: expand phases (multiple models), expand types extensively, add clinical applications.

10-MARK VERSION

A. Definition of Grief [2]

Grief is the **natural, multidimensional response** to the loss of a significant person, relationship, or object. It manifests across emotional (sadness, yearning, anger, guilt), cognitive (disbelief, preoccupation, confusion), physical (fatigue, insomnia, appetite change, immune suppression), behavioral (crying, withdrawal, searching), and spiritual (questioning meaning) dimensions.

Grief is **universal** but its expression is shaped by culture, personality, the nature of the relationship, and circumstances of the loss. Normal grief is self-limiting and occurs in waves of decreasing frequency and intensity.

B. Phases of Grief [4]

1. Bowlby's Four Phases (1961, 1980) [1.5]

PHASE	DURATION	DESCRIPTION
Numbing	Hours-1 week	Shock, disbelief, emotional blunting; may be interrupted by bursts of intense distress
Yearning & Searching	Weeks-months	Intense pining; restlessness; preoccupation; perceptual experiences (hearing voice, seeing the deceased)
Disorganization & Despair	Months	Full realization of loss; apathy, withdrawal, purposelessness; depression-like state
Reorganization	Variable	Reinvestment in life; new identity without the deceased; internalization of the relationship

2. Kubler-Ross's Five Stages (1969) [1]

Denial --> Anger --> Bargaining --> Depression --> Acceptance

(Non-sequential, non-universal; widely critiqued but culturally influential)

3. Dual Process Model (Stroebe & Schut, 1999) [1]

- Not stages but an **oscillation** between two orientations:
- **Loss-oriented coping:** Confronting grief; processing the pain; yearning
- **Restoration-oriented coping:** Attending to life changes; new roles; taking a break from grief
- Healthy grief involves **dynamic oscillation** between both
- Getting stuck in either orientation = pathological: all loss-oriented = chronic grief; all restoration-oriented = delayed/absent grief

4. Worden's Tasks (1991) [0.5]

Accept reality --> Process pain --> Adjust to environment --> Find enduring connection

(Active, task-based, the bereaved has agency in their grief process)

C. Types of Grief [4]

TYPE	DESCRIPTION	CLINICAL SIGNIFICANCE
Normal/Uncomplicated grief	Expected emotional response; waves of sadness, yearning; gradually resolves over months; positive emotions preserved	Self-limiting; support is usually sufficient
Anticipatory grief	Grief that occurs before the death, during terminal illness	Allows preparation; may reduce post-death grief intensity; but does not eliminate it
Prolonged/Complicated grief	Grief that persists >12 months with unremitting intensity; meets PGD criteria (DSM-5-TR)	Affects ~10% of bereaved; requires specific treatment (CGT)
Delayed grief	Minimal initial grief reaction; grief emerges weeks to months later, often triggered by another loss or reminder	May be mistaken for resilience; sudden onset can be disorienting
Inhibited grief	Emotional expression of grief is blocked; grief manifests as somatic symptoms, behavioral changes, or functional impairment	Associated with alexithymia, masculine gender norms, cultural prohibitions on crying

TYPE	DESCRIPTION	CLINICAL SIGNIFICANCE
Distorted grief	One component of grief is exaggerated (overwhelming anger, guilt, or hostility) while others are suppressed	The distorted emotion may be more tolerable than the underlying sadness
Absent grief	No apparent grief response at all	May represent pathological denial, dissociation, or (rarely) genuine resilience
Disenfranchised grief	Grief that is not socially recognized or validated	Miscarriage, pet loss, loss of ex-partner, loss of incarcerated person, loss of same-sex partner
Chronic grief	Continuous, intense grief that does not diminish; life remains centered on the loss	Overlaps with prolonged grief disorder
Traumatic grief	Grief complicated by traumatic circumstances of death (murder, suicide, accident, disaster)	Features of PTSD + grief; requires integrated treatment (EMDR, prolonged exposure + grief work)
Collective grief	Shared grief after a community loss (disaster, pandemic, national tragedy)	COVID-19 produced unprecedented collective grief with restricted mourning
Ambiguous loss (Boss)	Loss without closure, person is physically present but psychologically absent (dementia) or physically absent but status unknown (missing person)	Among the most difficult to resolve; no death certificate, no mourning rituals
Cumulative grief	Multiple losses in rapid succession before processing of earlier losses is complete	Common in elderly ("bereavement overload"), healthcare workers, marginalized communities

20-MARK EXPANDED VERSION

A. Definition of Grief [3]

(Same as 10-mark version, expanded)

Grief was described by Freud (1917, *Mourning and Melancholia*) as the process of withdrawing **libido** (psychic energy) from the lost object. This "grief work" is painful because each memory and expectation linked to the lost person must be individually confronted and detached. Bowlby (1969, 1980) reframed grief through **attachment theory**, grief is the activation of the attachment system when the attachment figure is lost. The searching, yearning, and protest of grief are the same behaviors that an infant shows during separation.

Modern models (Stroebe & Schut, Neimeyer) emphasize grief as a process of **meaning reconstruction**, the bereaved must rebuild their assumptive world (their beliefs about themselves, others, and the future) after it has been shattered by loss.

B. Phases of Grief, Detailed [7]

1. Bowlby's Four Phases (1980) [2]

PHASE	DURATION	FEATURES	ATTACHMENT MECHANISM
Numbing	Hours-1 week	Shock; emotional anesthesia; denial; may function on "autopilot"; occasional bursts of intense distress or anger	Attachment system overwhelmed; defensive exclusion of painful information
Yearning & Searching	Weeks-months	Intense pining; preoccupation with the deceased; restlessness; perceptual experiences (hearing voice, feeling presence); anger ("Why did you leave me?"); directed searching (visiting grave, looking for the person in crowds)	Attachment system fully activated; proximity-seeking behavior directed at the absent figure
Disorganization & Despair	Months	Full realization that the person will not return; withdrawal, apathy, purposelessness; "giving up" the search; resembles clinical depression; may include identity confusion	Attachment system deactivates; the internal working model must be updated; this is the most painful transition
Reorganization	Variable	Reorientation to life; new roles, relationships, and identity; the deceased is internalized as a continuing bond; capacity for joy returns	New internal working model formed; the relationship with the deceased is transformed, not severed

2. Kubler-Ross Five Stages (1969) [1.5]

(See Q19 for detailed table)

Modern critique:

- Originally described for the dying person's own process, not bereavement

- No empirical evidence that people progress through discrete stages
- Can be harmful if used prescriptively ("you should be past denial by now")
- Useful as a vocabulary for common grief experiences, not as a roadmap
- Maciejewski et al. (2007) provided partial support: yearning was the dominant negative emotion (not depression), and acceptance was the dominant positive experience from the beginning

3. Dual Process Model (Stroebe & Schut, 1999) [2]

The most empirically supported contemporary model:

LOSS-ORIENTED · RESTORATION-ORIENTED

Grief work Attending to life changes

Intrusion of grief Distraction from grief

Relinquishing bonds Forming new relationships

Denial of restoration Denial/avoidance of grief

Processing the loss Doing new things

Yearning, crying Learning new skills

Oscillation: The bereaved person moves back and forth between these orientations, sometimes within the same day. This is **healthy and necessary**.

Pathological patterns:

- **Stuck in loss-orientation** --> Chronic grief, prolonged grief disorder
- **Stuck in restoration-orientation** --> Delayed/inhibited grief; may appear resilient but grief is unprocessed

4. Worden's Four Tasks (1991) [1]

(See Q19 for table)

Key point: Tasks can be worked on simultaneously; they are not sequential. Therapy can target whichever task is stalled.

5. Continuing Bonds Model (Klass, Silverman, Nickman, 1996) [0.5]

- Challenged Freud's "detachment" model, healthy grief does not require "letting go"
- The bereaved maintains an **ongoing, evolving relationship** with the deceased
- Maladaptive only when the bond prevents engagement with the living

C. Types of Grief, Detailed [7]

1. Normal/Uncomplicated Grief [1]

- The expected, adaptive response to loss
- **Features:** Waves of intense sadness, yearning, anger, guilt; these waves become less frequent and less intense over time; capacity for positive emotions preserved; functional impairment is temporary
- **Duration:** Most bereaved individuals show significant improvement by 6-12 months, though anniversary reactions and triggered waves continue indefinitely
- **Resilience:** Bonanno's research showed that ~50-60% of bereaved individuals show a **resilient trajectory**, they are sad but never develop clinical symptoms

2. Complicated/Prolonged Grief [1.5]

- ~10% of bereaved individuals develop prolonged grief disorder (DSM-5-TR)
- **Core features:** Persistent, intense yearning/longing; preoccupation with the deceased; identity disruption; avoidance of reminders; emotional numbness; meaninglessness; loneliness
- **Risk factors:** Sudden/violent death, loss of child, insecure attachment, prior psychiatric illness, social isolation, dependent relationship
- **Neurobiology:** Functional imaging shows activation of **reward circuitry** (nucleus accumbens) in complicated grief, the yearning has a craving-like quality; also amygdala hyperactivation and PFC hypofunction
- **Treatment:** CGT (Shear), sometimes with SSRI augmentation

3. Anticipatory Grief [0.5]

- Grief experienced before the actual death, during terminal illness
- Allows emotional preparation, practical planning, and saying goodbye
- **Ambiguous finding:** Does not necessarily reduce post-death grief intensity
- Risk of "premature detachment", emotionally withdrawing from the dying person too early

4. Traumatic Grief [1]

- Loss complicated by traumatic circumstances: homicide, suicide, accident, disaster, witnessing the death
- Features of **PTSD + grief:** intrusive images of the death, avoidance of trauma reminders AND grief reminders, hyperarousal
- **Distinction from uncomplicated grief:** The traumatic imagery "blocks" the normal grief process, the person cannot access their grief because they are overwhelmed by the trauma
- **Treatment:** Phase-based, stabilize first, then process trauma (EMDR, prolonged exposure), THEN grief work (CGT)

5. Disenfranchised Grief (Doka, 1989) [1]

- Grief from a loss that is **not socially acknowledged, publicly mourned, or validated**
- **Types of disenfranchisement:**
- Relationship not recognized (ex-spouse, same-sex partner, affair partner, friend)
- Loss not recognized (miscarriage, perinatal death, pet, job, homeland)
- Griever not recognized (children, elderly with dementia, intellectually disabled)
- Circumstances stigmatized (suicide, overdose, AIDS)
- Way of grieving not recognized ("Men don't cry")
- **Clinical impact:** No social support, no rituals, no permission, increased risk of complicated grief
- **Treatment:** Validate the grief; create mourning rituals; support groups

6. Ambiguous Loss (Pauline Boss, 1999) [0.5]

- Loss without clarity or closure:
- **Type 1:** Physical absence with psychological presence (MIA soldier, missing person, kidnapping)
- **Type 2:** Physical presence with psychological absence (dementia, severe TBI, catatonia, addiction)
- Cannot be fully resolved because the loss is ongoing; traditional grief models don't fit
- **Treatment:** Increase tolerance of ambiguity; both/and thinking; maintain hope without waiting

7. Cumulative/Bereavement Overload [0.5]

- Multiple losses before previous grief is processed
- Common in: elderly (serial loss of spouse, siblings, friends), healthcare workers, marginalized communities, pandemics
- Each new loss reactivates and amplifies previous unresolved grief
- **Treatment:** Acknowledge each loss separately; prevent "stacking" of unprocessed grief

8. Collective Grief [0.5]

- Shared grief after community-level loss (natural disaster, pandemic, mass shooting, national tragedy)
- COVID-19 pandemic: unprecedented scale of collective grief with restricted mourning (no funerals, no physical contact, dying alone)
- **Treatment:** Community-level interventions; public memorials; narrative sharing; policy-level support

Clinical Application of Grief Typology [0.5]

1. **Assessment:** Determine the type of grief to guide intervention

2. **Normalize:** Psychoeducation about grief types reduces self-blame ("There must be something wrong with me")
3. **Tailor treatment:** CGT for prolonged grief; EMDR for traumatic grief; validation for disenfranchised grief; tolerance-building for ambiguous loss
4. **Cultural competence:** Assess mourning practices; avoid pathologizing cultural norms

EXAM PEARL

Cross-reference: Q19-Q22 (overlapping content), Q12 (attachment theory, Bowlby)

**Q24: "Define aggression. Predictors. Psychological and social theories of aggression.":
10 marks [1+3+3+3]**

Exam Strategy: Four-part answer. Quick definition, predictors list, then psychological and social theories separately.

A. Definition of Aggression [1]

Aggression is any **behavior** intended to **harm** another individual who is **motivated to avoid** that harm (Baron & Richardson, 1994). It may be physical (hitting, assaulting), verbal (threatening, insulting), relational (social exclusion), or indirect (property destruction).

Types:

- **Hostile/Reactive aggression:** Impulsive, anger-driven, response to perceived provocation
- **Instrumental/Proactive aggression:** Planned, goal-directed, used to achieve a purpose (e.g., robbery)

B. Predictors of Aggression [3]

Individual predictors:

- **Past history of violence,** The single strongest predictor
- **Male sex,** Higher rates of physical aggression (though relational aggression may be equal across sexes)
- **Young age** (15-30 years)
- **Substance use,** Particularly alcohol (disinhibition), stimulants, PCP
- **Psychiatric illness,** Psychosis with threat/control override symptoms, mania, personality disorders (antisocial, borderline), intermittent explosive disorder, PTSD
- **Low IQ and cognitive impairment** (dementia, intellectual disability, delirium)
- **Childhood conduct disorder,** Strongest predictor of adult antisocial behavior
- **Neurological damage,** Especially frontal lobe lesions (orbitofrontal cortex)
- **Low serotonin,** CSF 5-HIAA inversely correlated with impulsive aggression

Situational predictors:

- **Provocation**, Most common immediate trigger
- **Frustration** (blocked goal attainment)
- **Crowding** and environmental stress
- **Heat**, Temperature-aggression relationship is robust
- **Weapons availability** ("weapons effect", Berkowitz)
- **Social exclusion** and perceived injustice

Social/demographic predictors:

- **Low socioeconomic status**
- **Childhood abuse and neglect**, Both victimization and exposure to domestic violence
- **Peer group**, Association with antisocial peers
- **Media violence exposure**, Modest but consistent effect

C. Psychological Theories of Aggression [3]

1. Psychoanalytic Theory (Freud) [0.75]

- Aggression is a manifestation of **Thanatos** (death instinct)
- Originally, aggression was a component of the libido; later (1920, *Beyond the Pleasure Principle*), Freud proposed Thanatos as an independent drive
- Aggression is inevitable; it can be **sublimated** (channeled into sports, work) or **displaced** (directed toward substitute targets)
- If not expressed, aggression turns inward --> depression, self-harm

2. Frustration-Aggression Hypothesis (Dollard et al., 1939) [0.75]

- **Original formulation:** Frustration (blocking of goal-directed behavior) always leads to aggression; aggression always presupposes frustration
- **Revised version (Berkowitz, 1989):** Frustration produces **negative affect** (anger, irritation); aggression is one possible response, mediated by:
 - Aggressive cues in the environment ("weapons effect")
 - Learned aggressive scripts
 - Cognitive appraisal of the frustration
- **Clinical relevance:** Explains aggression in settings of resource scarcity, social inequality, and institutional frustration

3. Social Learning Theory (Bandura, 1961, 1977) [0.75]

- Aggression is **learned** through:
 - **Observation** (modeling), Children who observe aggressive behavior are more likely to reproduce it (Bobo doll experiment)

- **Reinforcement**, Aggression that is rewarded (achieves goals, gains status) is more likely to be repeated
- **Vicarious reinforcement**, Observing others being rewarded for aggression increases one's own aggressive behavior
- **Key moderators**: Self-efficacy for aggression, outcome expectations, self-regulation capacity
- **Clinical relevance**: Children exposed to domestic violence model aggressive behavior; media violence debate; gang socialization

4. Cognitive Neoassociation Theory (Berkowitz, 1989) [0.75]

- Aversive events (frustration, pain, heat, bad odors) produce **negative affect**
- Negative affect automatically activates both **fight** (aggression-related thoughts, memories, behaviors) and **flight** (escape-related) tendencies
- Higher-order cognitive processing then determines whether aggression is expressed
- Explains why diverse aversive stimuli (not just frustration) can trigger aggression

D. Social Theories of Aggression [3]

1. General Aggression Model (GAM, Anderson & Bushman, 2002) [1]

- Integrative framework combining all previous theories
- **Person factors** (traits, attitudes, beliefs, scripts) + **Situation factors** (provocation, frustration, drugs, cues) -->
- Influence **internal state** (cognition, affect, arousal) -->
- Which undergoes **appraisal and decision processes** (automatic vs. controlled) -->
- Leading to **thoughtful or impulsive action**
- Repeated cycles build aggressive **knowledge structures** (hostile attribution bias, aggressive scripts)

2. Social Information Processing Model (Dodge, 1986) [1]

- Children process social situations through a series of steps:
- Encoding of cues
- Interpretation of cues
- Clarification of goals
- Response access / construction
- Response decision
- Behavioral enactment
- **Hostile attribution bias**: Aggressive children tend to interpret ambiguous social cues as hostile (Step 2 distortion)
- This bias is stable and predicts chronic aggression

- **Clinical relevance:** Social skills training targets these processing steps; CBT addresses hostile attribution bias

3. Strain Theory (Agnew, 1992) [0.5]

- Aggression and criminal behavior result from **strain** (stress and negative life events)
- Three sources of strain: failure to achieve goals, removal of positive stimuli, introduction of negative stimuli
- Strain produces negative emotions (anger, frustration) that may be expressed as aggression when coping resources are inadequate

4. Deindividuation Theory (Zimbardo, 1969) [0.5]

- Loss of individual identity in a group leads to reduced self-awareness, reduced inhibition, and increased aggression
- Explains mob violence, online aggression, and institutional abuse
- Conditions: anonymity, group membership, arousal, reduced accountability

EXAM PEARL

Cross-reference: Q25 (biological basis of aggression), Q14-Q15 (emotion circuits, overlapping amygdala/PFC pathways)

Q25: "What is aggression? Biological basis of aggression.": 10 marks

Exam Strategy: Brief definition (2), then comprehensive biological basis (8). Cover neuroanatomy, neurotransmitters, hormones, genetics.

A. Definition of Aggression [2]

Aggression is **behavior directed toward another individual with the intent to cause harm**, where the target is motivated to avoid being harmed. It is a heterogeneous construct:

TYPE	FEATURES	NEURAL CORRELATE
Reactive/Hostile/Impulsive	Anger-driven, response to threat or provocation, "hot" aggression	Amygdala-mediated; serotonin deficit
Proactive/Instrumental/Predatory	Goal-directed, planned, "cold" aggression, no emotional arousal required	Prefrontal planning; intact in psychopathy

Aggression is distinguished from **violence** (a severe form of physical aggression) and **hostility** (an attitude or cognitive set, not behavior).

B. Biological Basis of Aggression [8]

1. Neuroanatomical Basis [2.5]

STRUCTURE	ROLE IN AGGRESSION	EVIDENCE
Amygdala	Threat detection, fear conditioning, emotional memory; activates aggressive responses to perceived threat	Stimulation produces rage (Kluver-Bucy = bilateral damage = docility); hyperactivation in reactive aggression
Hypothalamus	Ventromedial hypothalamus: defensive aggression; lateral hypothalamus: predatory aggression; coordinates autonomic and behavioral attack responses	Animal studies: stimulation produces attack behavior; sham rage after decortication
Prefrontal cortex (PFC)	Inhibitory control over aggressive impulses; decision-making; empathy; consequence evaluation	PFC damage (esp. orbitofrontal and ventromedial PFC) = increased impulsive aggression; Phineas Gage (1848): personality change, aggression after frontal lobe injury
Anterior cingulate cortex (ACC)	Conflict monitoring; error detection; emotional regulation	Hypofunction in aggressive individuals; reduced gray matter in violent offenders
Periaqueductal gray (PAG)	Coordinates defensive behaviors (fight, flight, freeze)	Stimulation produces rage-like behavior in animals
Septal nuclei	Modulate aggression; lesions increase aggression ("septal rage")	Septal damage in animals produces hyperaggression

Key circuit: The **medial hypothalamus-PAG pathway** drives defensive rage; the **lateral hypothalamus-PAG pathway** drives predatory aggression. Both are modulated by the **PFC** (top-down inhibition) and **amygdala** (threat detection and emotional tagging).

2. Neurotransmitter Basis [2.5]

NEUROTRANSMITTER	ROLE	EVIDENCE
Serotonin (5-HT)	Inhibitory , Low serotonin = disinhibition of aggressive impulses	CSF 5-HIAA (serotonin metabolite) is inversely correlated with impulsive aggression and violent suicide (Brown et al., Linnoila et al.); Tryptophan depletion increases aggression; SSRIs reduce impulsive aggression; 5-HT1B knockout mice = hyperaggressive

NEUROTRANSMITTER	ROLE	EVIDENCE
Dopamine	Facilitatory , Increases reward-seeking and approach behavior, including aggressive reward-seeking	Stimulants (amphetamine, cocaine) increase aggression; dopamine agonists can increase aggression; predatory aggression involves dopaminergic reward circuits
Noradrenaline (NA)	Facilitatory , Increases arousal, alertness, and readiness for action	Beta-blockers (propranolol) reduce aggressive behavior in brain injury and developmental disability; NA increases in response to threat
GABA	Inhibitory , Primary inhibitory neurotransmitter modulates aggression	GABA-A agonists (benzodiazepines) generally reduce aggression (but paradoxical aggression can occur); GABA-B knockout mice show increased aggression
Acetylcholine	Facilitatory in septal-hippocampal system	Cholinergic stimulation in animal studies increases aggression
Nitric oxide (NO)	Inhibitory , nNOS knockout mice show increased aggression	Emerging evidence
Glutamate	Facilitatory , NMDA receptor involvement in aggressive circuits	Ketamine and PCP (NMDA antagonists) can increase aggression

The serotonin deficiency hypothesis is the most robust finding in aggression neurobiology. It applies specifically to **impulsive/reactive aggression**, not instrumental / proactive aggression.

3. Hormonal and Neuroendocrine Basis [1.5]

HORMONE	ROLE	EVIDENCE
Testosterone	Facilitatory , Increases dominance-seeking, status competition, and aggression	Males commit ~90% of violent crime; testosterone peaks in adolescence / young adulthood (peak violence years); castration reduces aggression in animals; anabolic steroid use increases aggression ("roid rage"); BUT the relationship is bidirectional, winning increases testosterone

HORMONE	ROLE	EVIDENCE
Cortisol	Inhibitory at normal levels; complex , Low basal cortisol associated with chronic aggression (HPA axis blunting in anti-social individuals)	Low cortisol + high testosterone = highest aggression risk; stress-induced cortisol normally triggers withdrawal, but chronic stress may impair this inhibitory function
Vasopressin	Facilitatory , Promotes territorial aggression, particularly in males	V1a receptor knockout mice show reduced aggression; vasopressin in anterior hypothalamus increases aggression
Oxytocin	Complex , Promotes ingroup bonding but can increase out-group aggression	"Tend and defend" rather than purely prosocial; may increase aggression toward perceived threats to ingroup
Estrogen	Modulates aggression through interaction with serotonin system; premenstrual aggression linked to estrogen-progesterone fluctuations	Less studied than testosterone but significant

4. Genetic Basis [1.5]

- **Heritability:** Twin studies estimate ~50% heritability for aggressive behavior (Rhee & Waldman, 2002)
- **MAOA gene ("warrior gene"):**
 - MAOA (monoamine oxidase A) metabolizes serotonin, noradrenaline, and dopamine
 - **Low-activity MAOA variant** + childhood maltreatment = significantly increased risk of antisocial and aggressive behavior (Caspi et al., 2002, landmark gene-environment interaction study)
 - Low MAOA alone does NOT cause aggression, the gene-environment interaction is key
 - Brunner syndrome: rare complete MAOA deficiency = intellectual disability + impulsive aggression
- **5-HTTLPR (serotonin transporter polymorphism):**
 - Short allele associated with increased amygdala reactivity and reduced emotional regulation
 - Interacts with childhood adversity to increase aggression risk
- **COMT (catechol-O-methyltransferase):**
 - Val158Met polymorphism; Met/Met = higher PFC dopamine = better executive function (less impulsive aggression)

- **CDH13** and **MAOA**, Finnish study of violent offenders found association with both genes
- **Epigenetics**: Childhood adversity produces **epigenetic modifications** (DNA methylation of glucocorticoid receptor gene, NR3C1) that alter HPA axis function and increase aggression risk

Summary, Integrated Biological Model:

Aggression results from an imbalance between **excitatory drives** (amygdala, hypothalamus, testosterone, dopamine, noradrenaline) and **inhibitory controls** (PFC, serotonin, GABA, cortisol). Genetic factors (MAOA, 5-HTTLPR) create vulnerability, which is activated or buffered by early environment (attachment, abuse, modeling). The **serotonin-PFC axis** is the most important modifiable target for pharmacological management of impulsive aggression.

Pharmacological implications:

- **SSRIs**, First-line for impulsive aggression (fluoxetine, sertraline)
- **Mood stabilizers** (lithium, valproate, carbamazepine), Reduce aggression across diagnoses
- **Beta-blockers** (propranolol), Useful in brain injury and developmental disability
- **Atypical antipsychotics** (risperidone, clozapine), Reduce aggression in psychosis and developmental disability
- **Anti-androgens** (cyproterone acetate), Used in sexual aggression (forensic setting)

EXAM PEARL

Cross-reference: Q24 (psychological and social theories), Q14-Q15 (emotion circuits, same amygdala-PFC architecture)

CROSS-REFERENCE MAP

TOPIC	RELATED QUESTIONS	KEY OVERLAP
Defense mechanism classification	Q1, Q2, Q3, Q6, Q7	Same classification system; vary examples and emphasis
OCD defenses	Q4, Q5	Same defenses; Q4 adds treatment, Q5 has more marks on defenses
Phobia defenses	Q2	Displacement-dominant (contrast with OCD: isolation-dominant)
Mature defenses	Q3, Q6	Choose different 3-4 in each to avoid repetition

TOPIC	RELATED QUESTIONS	KEY OVERLAP
Defenses in treatment	Q7	Comprehensive; subsumes Q2, Q4-Q5 content
Erikson's stages	Q8, Q11	Q8 = basic listing; Q11 = psychopathology focus
Piaget's stages	Q9, Q10, Q13	Q9 = sensorimotor detail; Q10 = theory emphasis; Q13 = neurocognitive
Emotion definition + circuits	Q14, Q15	Near-identical; Q15 has more marks on neural pathways
Emotion theories	Q16	Standalone; builds on circuits in Q14-Q15
Emotional intelligence	Q17, Q18	Q17 = EI vs. IQ; Q18 = applications
Grief	Q19, Q20, Q21, Q22, Q23	Heavy overlap; Q19 = bereavement+stages+complicated; Q20 = definitions+clinical relevance; Q21 = relationship between terms; Q22 = management focus; Q23 = comprehensive phases+types
Aggression	Q24, Q25	Q24 = psychological/social theories; Q25 = biological basis

Mnemonics & Memory Tricks

EXAM PEARL

Last updated: March 2026

1. Vaillant's Defense Mechanism Hierarchy

- **Mnemonic:** "MNI", Mature, Neurotic, Immature (top to bottom)
- **Encodes:** The three levels of Vaillant's hierarchy of adaptive defense mechanisms
- **Expansion:**
 - Mature, healthiest, seen in well-adjusted adults (sublimation, humor, altruism, suppression, anticipation)
 - Neurotic, intermediate, common in anxiety / OCD (displacement, isolation, intellectualization, reaction formation, repression, undoing)
 - Immature, primitive, seen in personality disorders and psychosis (projection, denial, splitting, acting out, regression, somatization, passive aggression, projective identification)
- **Why this works:** Three letters, three tiers, like a building. Mature on top, Immature at the foundation. Think of it as a mental health "floor level."

2. Mature Defense Mechanisms: "SHASA"

- **Mnemonic:** SHASA (like "shasha", sounds like the Hindi word for rabbit, *shashak*)
- **Encodes:** The 5 mature defense mechanisms in Vaillant's hierarchy
- **Expansion:**
 - Sublimation, channeling unacceptable impulses into socially valued activities
 - Humor, using comedy to express feelings without discomfort
 - Altruism, serving others to manage own internal conflicts
 - Suppression, consciously postponing attention to a conflict
 - Anticipation, planning ahead for future discomfort
- **Why this works:** SHASA is easy to say, rhymes naturally, and the rabbit association makes it sticky, the mature mind is quick and adaptive, like a *shashak*.

3. Defense Mechanisms in OCD: "I URI"

- **Mnemonic:** I URI (think: "I, URI", like addressing someone named Uri, or the urinary frequency in anxious OCD patients)
 - **Encodes:** The 4 classic defense mechanisms in Obsessive-Compulsive Disorder
 - **Expansion:**
 - Isolation (of affect), separating the thought from its emotional content
 - Undoing, performing an act to symbolically reverse a prior thought or action
 - Reaction formation, adopting feelings/behaviors opposite to the true impulse
 - Intellectualization, using abstract thinking to distance from emotional reality
 - **Why this works:** The "I" bookends capture the OCD patient's experience, isolated from their own feelings (Isolation) yet trapped in excessive cerebral processing (Intellectualization), with Undoing and Reaction Formation sandwiched between.
-

4. Defense Mechanisms in Phobia: "DiP"

- **Mnemonic:** DiP, "Phobia makes you DiP (dodge)"
 - **Encodes:** The 2 primary defense mechanisms in phobic disorders
 - **Expansion:**
 - Displacement, anxiety is shifted from the original source to a symbolic substitute (e.g., fear of father becomes fear of dogs)
 - Projection, internal danger is perceived as external threat
 - **Why this works:** When you're phobic, you "dip", you dodge and avoid. Displacement + Projection = the phobic maneuver.
-

5. Erikson's 8 Stages: "Trust the Initiative, Ride the Identity, Love the Integrity"

- **Mnemonic:** "Trust the Initiative, Ride the Identity, Love the Integrity"
- **Encodes:** Erikson's 8 psychosocial stages with crisis at each
- **Expansion:**

#	STAGE	CRISIS	MNEMONIC ANCHOR
1	Infancy (0-1)	Trust vs Mistrust	Trust
2	Early Childhood (1-3)	Autonomy vs Shame/Doubt	the (Autonomy, toddler says "the world is mine")
3	Play Age (3-6)	Initiative vs Guilt	Initiative

#	STAGE	CRISIS	MNEMONIC ANCHOR
4	School Age (6-12)	Industry vs Inferiority	(implicit, Ride = industrious)
5	Adolescence (12-18)	Identity vs Role Confusion	Identity
6	Young Adult (18-35)	Intimacy vs Isolation	Love
7	Middle Adult (35-65)	Generativity vs Stagnation	(implicit, the generative years)
8	Late Adult (65+)	Integrity vs Despair	Integrity

Alternative ordered mnemonic: "TAS I-I IGI", Trust, Autonomy, iNitiative (Shame), Industry, Identity, Intimacy, Generativity, Integrity

- **Why this works:** The sentence flows naturally and hits the 3 most-tested crises (Trust, Identity, Integrity) as the anchor words.

6. Piaget's 4 Stages: "Some People Can't Focus"

- **Mnemonic:** SPCF, "Some People Can't Focus"
- **Encodes:** Piaget's 4 stages of cognitive development + key concept at each
- **Expansion:**

LETTER	STAGE	AGE	KEY CONCEPT
S	Sensorimotor	0-2 yrs	Object permanence (develops ~8 months)
P	Preoperational	2-7 yrs	Egocentrism, symbolic play, animism, no conservation
C	Concrete Operational	7-11 yrs	Conservation, reversibility, seriation, classification
F	Formal Operational	11+ yrs	Abstract reasoning, hypothetical-deductive thinking

- **Why this works:** The sentence is ironic, "Some People Can't Focus" is literally what happens without formal operational thinking. Also memorable for anyone with ADHD.

7. Piaget's 6 Sensorimotor Substages: "Really Pretty Children Carefully Create New Stuff"

- **Mnemonic:** "Really Pretty Children Carefully Create New Stuff"
- **Encodes:** The 6 substages of the sensorimotor period (0-2 years)
- **Expansion:**

#	SUBSTAGE	AGE	MNEMONIC ANCHOR
1	Reflex activity	0-1 month	Really
2	Primary circular reactions	1-4 months	Pretty
3	Secondary Circular reactions	4-8 months	Children
4	Coordination of secondary schemes	8-12 months	Carefully (object permanence emerges here)
5	Tertiary Circular reactions	12-18 months	Create (trial-and-error experimentation)
6	Mental representation / New means through mental combinations	18-24 months	New Stuff (symbolic thought begins)

- **Why this works:** The sentence tells a developmental story, children start with reflexes (really), progress through reactions (pretty, children), coordinate (carefully), experiment (create), then think symbolically (new stuff).

8. Ainsworth's Attachment Types: "SAAD Baby"

- **Mnemonic:** SAAD Baby (a sad baby needs secure attachment)
- **Encodes:** Ainsworth's 4 attachment types from the Strange Situation
- **Expansion:**
 - Secure, distressed on separation, comforted on reunion, uses caregiver as safe base
 - Anxious-Ambivalent (resistant), highly distressed, not comforted on reunion, clingy yet angry
 - Avoidant, minimal distress, ignores caregiver on reunion
 - Disorganized (Main & Hesse, added later), contradictory behaviors, freezing, fear of caregiver
- **Why this works:** A "SAAD baby" is one who didn't get secure attachment, the acronym itself encodes the emotional cost of insecure attachment. Plus "saad" means simple/straightforward in Hindi, and the classification IS straightforward.

9. Kubler-Ross 5 Stages of Grief: "DABDA"

- **Mnemonic:** DABDA (like a "dab" of tears, then "da", yes, acceptance)
 - **Encodes:** Kubler-Ross's 5 stages of grief (1969, *On Death and Dying*)
 - **Expansion:**
 - Denial, "This can't be happening"
 - Anger, "Why me?"
 - Bargaining, "If only I had..."
 - Depression, "I can't go on"
 - Acceptance, "I will be okay"
 - **Why this works:** DABDA is universally used. The "dab" evokes wiping tears; "da" in Hindi/Marathi means "yes", final acceptance. Note: these are NOT sequential/universal; Kubler-Ross herself clarified this. Exam trap.
-

10. Worden's 4 Tasks of Mourning: "RAPE" (Accept, Process, Adjust, Endure)

- **Mnemonic:** A-P-A-E, "Accept, Process, Adjust, Endure" (or the tasks as a sentence: "Accept the Pain, Adjust, and Endure the connection")
 - **Encodes:** Worden's 4 tasks of mourning (active tasks, not passive stages)
 - **Expansion:**
 - Task 1: Accept the reality of the loss
 - Task 2: Process the pain of grief (work through the grief)
 - Task 3: Adjust to a world without the deceased (external, internal, and spiritual adjustments)
 - Task 4: Find an Enduring connection with the deceased while Embarking on a new life
 - **Why this works:** Unlike Kubler-Ross stages (passive), Worden's are TASKS, things the mourner must actively DO. The verb-first format (Accept, Process, Adjust, Endure) captures this active nature. Exam favorite: "How does Worden differ from Kubler-Ross?" Answer: tasks vs stages.
-

11. Bowlby's 4 Phases of Grief: "NYPD" (Numbness, Yearning, Disorganization, Reorganization)

- **Mnemonic:** NYPD, "Numbness, Yearning, Protest/Despair, (re)Organization"
- **Encodes:** Bowlby's 4 phases of grief/mourning
- **Expansion:**
 - Numbness and protest, initial shock, disbelief (hours to weeks)
 - Yearning and searching, pining for the deceased, searching behavior, waves of grief

- Disorganization and despair, reality sets in, withdrawal, purposelessness
- **Reorganization**, (implied) gradual reintegration, forming new identity
- **Why this works**: NYPD is instantly memorable. Think of it as: the "police" of grief, the mind's own law-enforcement process to restore order after a devastating event.

12. Ekman's 6 Basic Emotions: "SHE FAD"

- **Mnemonic**: SHE FAD (emotions are fashionable, they come and go like a fad)
- **Encodes**: Ekman's 6 universal basic emotions (cross-cultural facial expression research)
- **Expansion**:
 - Sadness
 - Happiness
 - Emotion (placeholder), actually Surprise (alternate: **SHAFDS**, Sadness, Happiness, Anger, Fear, Disgust, Surprise)
 - Fear
 - Anger
 - Disgust

Better alternative: "SHAFDS", "SHAFTs of DiSgust" or simply **SADFISH**, Sadness, Anger, Disgust, Fear, Interest (surprise), Happiness

- **Mnemonic (cleaner)**: DASHFS, "DASH For Safety"
- Disgust, Anger, Sadness, Happiness, Fear, Surprise
- **Why this works**: DASH For Safety, when overwhelmed by emotion, you dash for safety. Captures the survival function of basic emotions.

13. Theories of Emotion: Chronological, "JC SuPaM-D"

- **Mnemonic**: "James Called Schachter, Papez called MacLean, Damasio finished" or JC-SPM-D
- **Encodes**: Major theories of emotion in chronological order
- **Expansion**:

LETTER	THEORY	THEORIST	YEAR	CORE IDEA
J	James-Lange	James, Lange	1884	Body first, then emotion (I tremble, therefore I fear)

LETTER	THEORY	THEORIST	YEAR	CORE IDEA
C	Cannon-Bard	Cannon, Bard	1927	Simultaneous, thalamus sends signal to cortex AND body at same time
S	Schachter-Singer	Schachter, Singer	1962	Two-factor: arousal + cognitive label = emotion
P	Papez Circuit	Papez	1937	Hippocampus-cingulate-hypothalamus circuit = emotional brain
M	MacLean Triune Brain	MacLean	1952	Limbic system concept; reptilian-limbic-neocortical triad
D	Somatic Marker	Damasio	1994	Body states guide decision-making; emotions are rational

- **Why this works:** JC-SPM-D follows the chronological order. "James Called Schachter, Papez called MacLean" is a phone chain, each built on the previous. Damasio finishes the conversation.

14. Goleman's 5 Components of Emotional Intelligence: "SEEMS"

- **Mnemonic:** SEEMS, "Emotional intelligence SEEMS easy but isn't"
- **Encodes:** Goleman's 5 components of emotional intelligence (1995)
- **Expansion:**
 - Self-awareness, knowing one's emotions, strengths, weaknesses
 - Empathy, understanding others' emotions
 - Emotion regulation (self-regulation), managing disruptive emotions
 - Motivation, intrinsic drive, resilience, optimism
 - Social skills, managing relationships, influence, teamwork
- **Why this works:** EI "SEEMS" straightforward but requires deep development. The first three are intrapersonal (Self-awareness, Emotion regulation, Motivation), the last two are interpersonal (Empathy, Social skills). Think: master yourself first, then others.

15. Biological Basis of Aggression: "FAST"

- **Mnemonic:** FAST, "Aggression is FAST, it bypasses thought"
- **Encodes:** The 4 key biological substrates of aggression
- **Expansion:**
 - Frontal lobe, prefrontal cortex inhibits aggression; damage (e.g., Phineas Gage) = disinhibition
 - Amygdala, threat detection, fear conditioning; Kluver-Bucy syndrome (bilateral lesions) = placidity
 - Serotonin, LOW serotonin = HIGH aggression (inverse relationship); CSF 5-HIAA levels inversely correlate with violence
 - Testosterone, higher levels correlate with dominance and aggression; castration studies; BUT correlation is not causation
- **Why this works:** Aggression IS fast, the amygdala fires before the frontal lobe can evaluate. The mnemonic mirrors the neurobiology. Plus: Frontal-Amygdala-Serotonin-Testosterone captures the complete exam answer for "biological basis of aggression."

Quick-Reference Summary Table

#	TOPIC	MNEMONIC	WHAT IT ENCODES
1	Vaillant's Hierarchy	MNI	Mature > Neurotic > Immature
2	Mature DMs	SHASA	Sublimation, Humor, Altruism, Suppression, Anticipation
3	OCD DMs	I URI	Isolation, Undoing, Reaction formation, Intellectualization
4	Phobia DMs	DiP	Displacement, Projection
5	Erikson's 8 Stages	Trust the Initiative...	8 psychosocial crises in order
6	Piaget's 4 Stages	SPCF	Sensorimotor, Preoperational, Concrete, Formal
7	Sensorimotor Substages	Really Pretty Children...	6 substages, 0-2 years
8	Attachment Types	SAAD Baby	Secure, Anxious-Ambivalent, Avoidant, Disorganized

#	TOPIC	MNEMONIC	WHAT IT ENCODES
9	Kubler-Ross Grief	DABDA	Denial, Anger, Bargaining, Depression, Acceptance
10	Worden's Tasks	A-P-A-E	Accept, Process, Adjust, Endure
11	Bowlby's Phases	NYPD	Numbness, Yearning, Despair, Reorganization
12	Ekman's Emotions	DASH For Safety	Disgust, Anger, Sadness, Happiness, Fear, Surprise
13	Theories of Emotion	JC-SPM-D	James-Lange, Cannon-Bard, Schachter-Singer, Papez, MacLean, Damasio
14	Emotional Intelligence	SEEMS	Self-awareness, Empathy, Emotion regulation, Motivation, Social skills
15	Aggression Biology	FAST	Frontal lobe, Amygdala, Serotonin, Testosterone

High-Yield Comparisons

EXAM PEARL

Last updated: March 2026

1. Mature vs Neurotic vs Immature Defense Mechanisms (Vaillant)

FEATURE	MATURE	NEUROTIC	IMMATURE
Examples	Sublimation, humor, altruism, suppression, anticipation	Displacement, isolation, intellectualization, reaction formation, repression, undoing	Projection, denial, splitting, acting out, regression, somatization, passive aggression, projective identification
Characteristics	Conscious or near-conscious; integrative; socially constructive; flexible	Partly conscious; anxiety-reducing but distorting; rigid patterns	Unconscious; reality-distorting; primitive; relationship-damaging
Typically Seen In	Well-adjusted adults; healthy coping	Neurotic disorders (OCD, anxiety disorders, phobias)	Personality disorders, psychosis, severe stress, children
Effect on Reality Testing	Preserved	Mildly impaired	Significantly impaired
Prognosis	Best, associated with psychological health and resilience	Intermediate, amenable to therapy (insight-oriented)	Poorest, harder to treat; requires long-term work (Schema Therapy, MBT, DBT)

Exam pearl: Vaillant's hierarchy is ADAPTIVE, it ranks defenses by how well they help the person function, NOT by whether they are "good" or "bad." Sublimation is the MOST adaptive single defense.

2. Erikson vs Piaget: Developmental Stages Side-by-Side

AGE RANGE	ERIKSON STAGE / CRISIS	PIAGET STAGE	KEY CONCEPT (PIAGET)	IF UNRESOLVED (ERIKSON)
0-1 yr	Trust vs Mistrust	Sensorimotor (0-2)	Object permanence developing	Suspicion, withdrawal, difficulty in relationships

AGE RANGE	ERIKSON STAGE / CRISIS	PIAGET STAGE	KEY CONCEPT (PIAGET)	IF UNRESOLVED (ERIKSON)
1-3 yrs	Autonomy vs Shame/Doubt	Sensorimotor → Preoperational	Symbolic play begins (~2 yrs)	Compulsive self-doubt, OCD traits, excessive shame
3-6 yrs	Initiative vs Guilt	Preoperational	Egocentrism, animism, centration, no conservation	Inhibition, psychosomatic complaints, excessive guilt
6-12 yrs	Industry vs Inferiority	Concrete Operational (7-11)	Conservation, reversibility, seriation, classification	Low self-esteem, work paralysis, inferiority complex
12-18 yrs	Identity vs Role Confusion	Formal Operational (11+)	Abstract reasoning, hypothetical-deductive thinking	Identity diffusion, "negative identity," susceptibility to cults
18-35 yrs	Intimacy vs Isolation	(Post-Piaget)	N/A	Avoidance of relationships, isolation, character pathology
35-65 yrs	Generativity vs Stagnation	(Post-Piaget)	N/A	Self-absorption, midlife crisis, interpersonal impoverishment
65+ yrs	Integrity vs Despair	(Post-Piaget)	N/A	Despair, fear of death, bitterness, regret

Exam pearl: Erikson is psychoSOCIAL (relationships drive development). Piaget is COGNITIVE (thinking drives development). They are complementary, not competing.

3. Erikson's 8 Stages: Full Table

STAGE	AGE	CRISIS	VIRTUE GAINED	SIGNIFICANT RELATIONSHIP	PSYCHOPATHOLOGY IF UNRESOLVED
1	0-1 yr	Trust vs Mistrust	Hope	Mother/primary caregiver	Depression, paranoid traits, attachment disorders

STAGE	AGE	CRISIS	VIRTUE GAINED	SIGNIFICANT RELATIONSHIP	PSYCHOPATHOLOGY IF UNRESOLVED
2	1-3 yrs	Autonomy vs Shame/Doubt	Will	Parents	OCD, compulsive doubt, excessive shame, dependent PD
3	3-6 yrs	Initiative vs Guilt	Purpose	Family	Conversion disorder, phobias, inhibition, psychosomatic illness
4	6-12 yrs	Industry vs Inferiority	Competence	School, peers	Work paralysis, inferiority complex, ADHD complications
5	12-18 yrs	Identity vs Role Confusion	Fidelity	Peers, role models	Identity diffusion, borderline traits, delinquency, cult susceptibility
6	18-35 yrs	Intimacy vs Isolation	Love	Partners, friends	Avoidant PD, social isolation, character pathology
7	35-65 yrs	Generativity vs Stagnation	Care	Family, community	Midlife crisis, self-absorption, narcissistic traits
8	65+ yrs	Integrity vs Despair	Wisdom	Humanity, life review	Despair, depression in elderly, fear of death

Exam pearl: The VIRTUE at each stage is the positive outcome of successfully resolving the crisis. "Hope, Will, Purpose, Competence, Fidelity, Love, Care, Wisdom", these are testable.

4. Piaget's 4 Stages: Full Table

STAGE	AGE	KEY ACHIEVEMENTS	LIMITATIONS	CLINICAL RELEVANCE
Sensorimotor	0-2 yrs	Object permanence (~8 mo), goal-directed behavior, mental representation (end), stranger anxiety (~8 mo)	No symbolic thought (until ~18 mo), no language-based reasoning	Separation anxiety onset; failure = intellectual disability markers; A-not-B error = frontal immaturity
Preoperational	2-7 yrs	Symbolic play, language explosion, intuitive reasoning	Egocentrism (three-mountain task), centration, animism, no conservation, irreversibility	Magical thinking in childhood anxiety; "my fault" thinking in abuse survivors; difficulty with CBT (no abstract thought yet)
Concrete Operational	7-11 yrs	Conservation, reversibility, seriation, classification, decentration	Cannot think abstractly or hypothetically; bound to concrete examples	Can begin structured behavioral therapy; school refusal assessment; ADHD functional impact peaks
Formal Operational	11+ yrs	Abstract reasoning, hypothetical-deductive thinking, metacognition, propositional logic	Not all adults reach this stage; culture/education-dependent	Required for insight-oriented therapy and CBT; adolescent existential crises; risk-taking (imaginary audience, personal fable)

Exam pearl: Object permanence = sensorimotor. Conservation = concrete operational. Abstract thinking = formal operational. These three concepts are the most tested.

5. Attachment Styles (Ainsworth)

STYLE	CHILD BEHAVIOR (STRANGE SITUATION)	CAREGIVER STYLE	ADULT OUTCOME (HAZAN & SHAVER)	ASSOCIATED DISORDERS
Secure (~60%)	Explores freely; distressed on separation; comforted on reunion; uses caregiver as safe base	Sensitive, responsive, consistent, attuned	Comfortable with intimacy; trusting; balanced self-esteem	Resilience factor, protective against psychopathology
Anxious-Ambivalent (~15%)	Clingy, limited exploration; VERY distressed on separation; NOT comforted on reunion; angry + clingy simultaneously	Inconsistent, sometimes responsive, sometimes unavailable	Preoccupied; jealous; fears abandonment; emotional reactivity	BPD, dependent PD, anxiety disorders, eating disorders
Anxious-Avoidant (~20%)	Minimal exploration anxiety; little distress on separation; IGNORES caregiver on reunion	Emotionally unavailable, rejecting, dismissive	Dismissive; uncomfortable with closeness; values independence excessively	Avoidant PD, schizoid traits, substance use, alexithymia
Disorganized (~5%)	Contradictory behaviors (approach + freeze); fear/apprehension toward caregiver; "fright without solution"	Frightening OR frightened; often history of abuse, unresolved trauma, dissociation	Fearful-avoidant; chaotic relationships; dissociative tendencies	Dissociative disorders, complex PTSD, severe BPD, disorganized attachment in offspring (intergenerational)

Exam pearl: Disorganized attachment was added by Main & Hesse (1990), NOT Ainsworth. Ainsworth's original study (1978) identified only the first three. Disorganized is the strongest predictor of later psychopathology.

6. Grief Models Comparison

FEATURE	KUBLER-ROSS (1969)	WORDEN (1991)	BOWLBY (1980)	DUAL PROCESS MODEL (STROEBE & SCHUT, 1999)
Framework	5 Stages	4 Tasks	4 Phases	Oscillation between 2 orientations

FEATURE	KUBLER-ROSS (1969)	WORDEN (1991)	BOWLBY (1980)	DUAL PROCESS MODEL (STROEBE & SCHUT, 1999)
Components	Denial, Anger, Bargaining, Depression, Acceptance	Accept reality, Process pain, Adjust to world, Find enduring connection	Numbness, Yearning/Searching, Disorganization/Despair, Reorganization	Loss-oriented (grief work) vs Restoration-oriented (new roles, identity)
Key Concept	Grief as a sequence (though non-linear)	Grief as ACTIVE WORK, mourner must DO tasks	Grief as attachment behavior, searching for the lost figure	Healthy grief = oscillation; pathology = getting stuck in one orientation
Process Type	Passive (stages happen TO you)	Active (tasks done BY you)	Biological/ethological (attachment system drives grief)	Dynamic (constant movement between loss and restoration)
Limitation	Often misapplied as rigid sequence; originally for DYING patients, not bereaved; limited empirical support	Implies linear progression through tasks; Western-centric	Less attention to cultural variation; ethological model may be reductive	Relatively newer; less clinical application literature; can be abstract

Exam pearl: Kubler-Ross stages were originally described for DYING patients, NOT the bereaved, this is one of the most common exam traps. Worden's tasks are the most clinically useful model for grief counseling.

7. Normal Grief vs Major Depression vs Prolonged Grief Disorder

FEATURE	NORMAL GRIEF	MAJOR DEPRESSIVE DISORDER	PROLONGED GRIEF DISORDER (ICD-11/DSM-5-TR)
Duration	Acute grief weeks-months; gradual adaptation over 6-12 months	At least 2 weeks (DSM-5); persistent	At least 6 months (DSM-5-TR) / 6 months (ICD-11) after bereavement
Core Affect	Waves of grief; periods of positive emotion possible ("pangs of grief")	Persistent pervasive low mood; anhedonia; inability to experience pleasure	Persistent, pervasive longing/yearning for the deceased; preoccupation with the deceased

FEATURE	NORMAL GRIEF	MAJOR DEPRESSIVE DISORDER	PROLONGED GRIEF DISORDER (ICD-11/DSM-5-TR)
Guilt Focus	Related to the DECEASED, "I wish I had said goodbye"	Generalized self-blame, "I am worthless"	Related to the LOSS, guilt about moving on, feeling disconnected from deceased
Self-Image	Preserved; may feel empty temporarily	Worthlessness, self-loathing, pervasive low self-esteem	Preserved BUT identity disruption, "part of me died with them"
Suicidality	Transient wishes to "join" the deceased; no sustained plan	Active suicidal ideation, plans, intent	May have passive death wishes; risk increases with severity
Functioning	Impaired acutely but gradually improves; can engage when distracted	Pervasively impaired across domains	Functionally impaired specifically in domains connected to the loss
Response to Context	Mood REACTIVE, can laugh, enjoy moments	Mood often NON-reactive (melancholic) or partially reactive	Reactive to reminders of the deceased specifically
Treatment	Support, psychoeducation; "watchful waiting"	Antidepressants + psychotherapy (CBT, IPT)	Complicated grief treatment (Shear); prolonged exposure elements; NOT standard antidepressants as first-line

Exam pearl: The key differentiator between normal grief and MDD is the FOCUS of distress: grief = focused on the LOSS; MDD = focused on the SELF. PGD was added to DSM-5-TR (2022) and ICD-11, expect this in recent exams.

8. Theories of Emotion

THEORY	THEORIST(S)	YEAR	MECHANISM	KEY EVIDENCE / CONTRIBUTION	CRITICISM
James-Lange	William James, Carl Lange	1884	Stimulus → bodily response → THEN conscious emotion ("I tremble, therefore I fear")	Emphasizes body in emotion; basis for interoception research	Cannon's critique: same visceral changes in different emotions; emotions faster than visceral feedback
Cannon-Bard	Walter Cannon, Philip Bard	1927	Stimulus → thalamus → SIMULTANEOUS cortical (emotion) + bodily (arousal) response	Thalamus as relay center; challenged peripheral theory	Oversimplifies thalamic role; emotions DO differ in bodily patterns (later research)
Schachter-Singer (Two-Factor)	Stanley Schachter, Jerome Singer	1962	Emotion = physiological arousal + cognitive LABEL; arousal is undifferentiated	Bridge study (Dutton & Aron); misattribution of arousal	Replication issues; arousal is NOT fully undifferentiated; cognitive appraisal may not always be needed
Papez Circuit	James Papez	1937	Hippocampus → fornix → mammillary bodies → anterior thalamus → cingulate → back to hippocampus	First neural circuit model of emotion; foundational for limbic system	Hippocampus is more memory than emotion; circuit is incomplete

THEORY	THEORIST(S)	YEAR	MECHANISM	KEY EVIDENCE / CONTRIBUTION	CRITICISM
Triune Brain	Paul MacLean	1952	Limbic system (coined by MacLean) mediates emotion; reptilian (brain-stem) → paleomammalian (limbic) → neomammalian (neocortex)	Named the limbic system; integrated evolutionary and neuroanatomical thinking	Overly simplistic; neat tripartite division doesn't hold neuroanatomically; brains didn't evolve in layers
Somatic Marker	Antonio Damasio	1994	Body states ("somatic markers") tag experiences; emotions guide rational decision-making; "emotions are rational"	Iowa Gambling Task (ventromedial PFC patients); reversed emotion-cognition hierarchy	Hard to empirically test the full hypothesis; somatic markers may be one of many inputs

Exam pearl: James-Lange = body FIRST. Cannon-Bard = SIMULTANEOUS. Schachter-Singer = arousal + LABEL. These three contrasts are the most tested. Papez circuit components are asked in anatomy-based questions.

9. Biological vs Psychological Theories of Aggression

ASPECT	BIOLOGICAL THEORIES	PSYCHOLOGICAL THEORIES
Key Factors	Serotonin (low 5-HT = high aggression), testosterone, prefrontal cortex dysfunction, amygdala hyperreactivity, genetics (MAOA "warrior gene"), temporal lobe epilepsy	Frustration-aggression hypothesis (Dollard), social learning theory (Bandura, Bobo doll), cognitive neoassociation (Berkowitz), general aggression model (Anderson), psychoanalytic (Thanatos/death drive)
Core Mechanism	Neurochemical imbalance or structural deficit → reduced inhibition OR heightened threat reactivity	Learned behavior (modeling, reinforcement), cognitive appraisal, displaced frustration, unconscious drives

ASPECT	BIOLOGICAL THEORIES	PSYCHOLOGICAL THEORIES
Key Evidence	CSF 5-HIAA inversely correlates with violence; Phineas Gage (frontal damage); castration reduces aggression; Kluver-Bucy (amygdala); XYY controversy (debunked)	Bobo doll experiment; frustration studies; media violence research; social deprivation studies
Clinical Relevance	Antisocial PD with low serotonin; IED (intermittent explosive disorder); substance-induced aggression; traumatic brain injury	Conduct disorder (modeling); domestic violence cycles; gang behavior; post-traumatic aggression
Management Implications	SSRIs/mood stabilizers (valproate, lithium); antipsychotics for acute aggression; treat underlying neurological cause; hormonal interventions (rare)	CBT-based anger management; ART (Aggression Replacement Training); behavioral parent training; social skills training; environmental modification

Exam pearl: The exam loves "biological basis of aggression" as a standalone question. Hit all 4: serotonin (inverse), testosterone (positive correlation), frontal lobe (inhibition), amygdala (threat detection). Then mention Phineas Gage and CSF 5-HIAA for bonus marks.

10. Goleman's Emotional Intelligence vs IQ

FEATURE	EMOTIONAL INTELLIGENCE (EI)	INTELLIGENCE QUOTIENT (IQ)
Nature	Ability to perceive, use, understand, and manage emotions (self and others)	General cognitive ability, reasoning, problem-solving, abstract thinking
Modifiability	Highly modifiable, can be trained and developed throughout life (Goleman's central claim)	Relatively stable after early adulthood; genetic component ~50-80%
Predictive Value	Better predictor of workplace SUCCESS, leadership, relationship quality, and life satisfaction (per Goleman)	Better predictor of ACADEMIC performance, professional entry, and task-specific cognitive performance
Components	Self-awareness, self-regulation, motivation, empathy, social skills (Goleman's 5)	Verbal comprehension, perceptual reasoning, working memory, processing speed (Wechsler)
Measurement	MSCEIT (Mayer-Salovey), EQ-i (Bar-On), self-report scales; less standardized	WAIS, WISC, Stanford-Binet; highly standardized, reliable

FEATURE	EMOTIONAL INTELLIGENCE (EI)	INTELLIGENCE QUOTIENT (IQ)
Distribution	Not normally distributed in the same way; culturally variable	Normally distributed (mean 100, SD 15)
Criticism	Poorly defined construct; overlaps with personality traits; "EI predicts success" claim is overstated; publication bias	Culture-bound; narrow definition of intelligence; doesn't capture creativity, practical intelligence

Exam pearl: Goleman popularized EI (1995) but the scientific construct was developed by Salovey & Mayer (1990). Bar-On coined "EQ" (1988). The exam may ask about all three names. Goleman's model is a MIXED model (ability + personality traits); Mayer-Salovey is a pure ABILITY model.

PYQ Frequency Analysis

EXAM PEARL

Source: PG exams Psychiatry Papers Dec 2011, Jun 2025 (~28 exam sessions) + PG exams 2013-2022 **Last updated:** March 2026

Executive Summary

Psychology-Core is a **reliably tested cluster** in Paper I. Defense mechanisms, developmental psychology, and emotion/aggression/grief questions appear with a combined frequency of **~28 mentions** across 28 sessions, approximately one question per exam from this cluster.

Key insight: Defense mechanisms are the most predictable (asked almost identically each time). Grief/bereavement is the sleeper hit, asked 5+ times and often overlooked in prep.

Topic-Level Frequency

TOPIC	EXAM MENTIONS	AVG PER EXAM	VERDICT
Defense Mechanisms	7	~0.25	Appears every 3-4 exams
Developmental Psychology (Erikson, Piaget, Attachment)	6	~0.21	Appears every 4-5 exams
Emotion/Aggression/Grief	15+	~0.54	Appears every other exam
Combined cluster	~28	~1.0	~1 question per exam

Sub-Topic Breakdown

Defense Mechanisms (7 mentions)

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Classify defense mechanisms	4	"Define and classify", "How do you classify"
Mature defense mechanisms	2	"Discuss four mature defense mechanisms with examples"

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Defense mechanisms in specific disorders (OCD, phobia)	3	"Defense mechanisms used in phobia/OCD"
Psychodynamic theories + defense mechanisms	1	"Psychodynamic theories for personality disorders"

Pattern: The question is almost always: "**Define, classify, give examples.**" The twist varies, sometimes it's disorder-specific (OCD, phobia), sometimes it's maturity-level (mature vs immature). Prepare ONE comprehensive answer that covers all variants.

Developmental Psychology (6 mentions)

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Piaget's cognitive development	3	"Stages of cognitive development", "Sensory-motor stages"
Erikson's psychosocial stages	2	"Eight stages of life cycle", "Psychopathological outcomes"
Attachment theory	1	"Attachment theory and implications for psychiatry"

Pattern: Piaget appears slightly more than Erikson. The Erikson question often asks for **psychopathological outcomes**, not just listing stages but linking each to what goes wrong. Attachment theory is rarer but has appeared.

Emotion / Aggression / Grief (15+ mentions)

SUB-TOPIC	FREQUENCY	QUESTION PATTERNS
Grief/Bereavement/Mourning	6	"Define grief. Stages. Complicated grief. Management."
Define emotion + neural circuits	3	"Define emotion. Neural pathways with diagram"
Theories of emotion	1	"Basic emotions. Discuss theories of emotion"
Emotional intelligence	2	"Define EI. Components. Applications."
Aggression (define, theories, biological basis)	3	"Define aggression. Predictors. Theories."

Sleeper hit: Grief/bereavement is asked **6 times**, more than defense mechanisms! Yet students under-prepare it. The question almost always asks: define grief/bereavement/mourning → stages → complicated grief → management.

Long Essay Candidates (20-mark format)

RANK	TOPIC	WHY	EST. PROBABILITY
1	"Classify defense mechanisms. Describe mature and immature types with examples. Discuss their role in specific psychiatric disorders."	Asked in various forms 7 times; perfect long essay topic	High
2	"Describe Erikson's eight stages of psychosocial development. Discuss psychopathological outcomes when stages are not mastered."	Comprehensive, well-structured for 20-mark format	High
3	"Define grief, bereavement, and mourning. Describe stages of grief. Discuss complicated grief and its management."	Asked 6 times; a natural 20-mark question	High
4	"Describe Piaget's stages of cognitive development. Discuss their clinical relevance in child psychiatry."	Reliable perennial	Medium-High
5	"Define emotion. Describe the neural circuit of emotion with a diagram. Discuss theories of emotion."	Combines neuroscience + psychology	Medium

Year-by-Year Highlights

YEAR	QUESTION	TOPIC
Dec 2011	Defense mechanisms + personality disorders	DM
Dec 2011	Bereavement, stages, complicated	Grief

YEAR	QUESTION	TOPIC
Dec 2011	Define emotion, neuronal circuit	Emotion
Dec 2012	Define defense mechanisms, classify, phobia	DM
Dec 2012	Attachment theory and implications	Dev Psych
Dec 2012	Define aggression, predictors, theories	Aggression
Jun 2013	Erikson's eight stages	Dev Psych
Apr 2016	Piaget's stages, sensory-motor	Dev Psych
Oct 2016	DM and purposes, DM in OCD	DM
Dec 2016	Ego functions, mature DMs	DM
Oct 2017	Erikson's eight stages + psychopathology	Dev Psych
Apr 2018	Define emotion, neural pathways, diagram	Emotion
Oct 2018	Emotional intelligence, components, IQ	Emotion
Oct 2019	Aggression, define, biological basis	Aggression
Apr 2020	Piaget's theory, stages	Dev Psych
Apr 2023	Grief, define, complicated, management	Grief
Oct 2023	Theories of emotion	Emotion
Jun 2025	Classify defense mechanisms, use in treatment	DM
Jun 2025	Emotional intelligence, components + applications	Emotion

Exam Strategy Recommendations

Must-Prepare

1. **Defense mechanisms**, ONE master answer: define, classify (Vaillant's mature/neurotic/immature), 3-4 examples of each level, specific DMs in OCD (isolation, undoing, reaction formation) and phobia (displacement, projection)

2. **Grief/bereavement**, Define all three terms, Kubler-Ross stages vs Worden's tasks vs Bowlby's phases, complicated grief (DSM-5 Prolonged Grief Disorder), management
3. **Erikson's 8 stages**, Table format: stage, age, psychosocial crisis, virtue, psychopathology if unresolved

Should-Prepare

1. **Piaget's stages**, Sensorimotor (object permanence), preoperational (egocentrism), concrete operational, formal operational
2. **Emotion circuits**, Papez circuit, amygdala role, James-Lange vs Cannon-Bard vs Schachter-Singer
3. **Aggression**, Biological (serotonin, testosterone, frontal lobe), psychological (frustration-aggression, social learning), predictors

Nice-to-Know

1. Emotional intelligence (Goleman's model, components, clinical relevance)
2. Attachment theory (Bowlby, Ainsworth's Strange Situation, secure/insecure types)

Cross-References

- Defense mechanisms overlap with NB-06 (Schizophrenia, primitive DMs like projection, splitting)
- Attachment theory overlaps with NB-02 developmental and NB-07 depression (insecure attachment as risk factor)
- Grief overlaps with Paper II mood disorders (differential from major depression)
- Aggression overlaps with Paper III forensic questions

Analysis based on PG exams Psychiatry Question Papers Dec 2011, Jun 2025 + PG exams MD Psychiatry Papers 2013-2022.

Quick Review

EXAM PEARL

40 Rapid-Fire Q&A | Distribution: 12 Defense Mechanisms, 14 Developmental, 14 Emotion/Grief/Aggression **Last updated:** March 2026

Defense Mechanisms (12 Questions)

Q1: Name the 5 mature defense mechanisms in Vaillant's hierarchy.

A: Sublimation, Humor, Altruism, Suppression, Anticipation (mnemonic: SHASA). These are the most adaptive defenses, associated with psychological health and preserved reality testing.

Q2: What are the 3 levels of Vaillant's defense mechanism hierarchy, from most to least adaptive?

A: Mature → Neurotic → Immature. Mature defenses are integrative and conscious. Neurotic defenses reduce anxiety but distort reality mildly. Immature defenses are primitive, unconscious, and significantly distort reality.

Q3: A patient with OCD extensively explains the logical reasons for their handwashing but shows no emotional distress about it. Which defense mechanism is this?

A: Intellectualization, using abstract, logical thinking to distance from the emotional content of the obsession. The patient understands the act cognitively but has detached from its emotional significance. This differs from **isolation of affect**, where the thought is conscious but stripped of its associated emotion.

Q4: A man who secretly hates his boss brings him coffee every morning and praises him publicly. Which defense mechanism is this?

A: Reaction formation, adopting feelings and behaviors that are the **direct opposite** of the true unconscious impulse. Common in OCD and seen in neurotic-level functioning. The excessiveness and rigidity of the behavior is the clinical clue.

Q5: A patient performs a ritual of tapping the doorknob 3 times after having an intrusive thought about harming their child. Which defense mechanism?

A: Undoing, performing a symbolic act to "reverse" or neutralize an unacceptable thought or impulse. One of the 4 classic OCD defenses (Isolation, Undoing, Reaction Formation, Intellectualization).

Q6: What are the 2 primary defense mechanisms in phobic disorders?

A: Displacement (anxiety shifted from the true source to a symbolic substitute) and **Projection** (internal danger perceived as external threat). Example: fear of father → displaced onto fear of dogs; internal aggression → projected as "the dog will attack me."

Q7: Differentiate suppression from repression.

A: Suppression is **conscious** and **voluntary**, deliberately postponing attention to a conflict ("I'll deal with this after the exam"). It is a **mature** defense. **Repression** is **unconscious** and **involuntary**, the memory/impulse is pushed out of awareness entirely. It is a **neurotic** defense. Suppression = you know but choose to delay. Repression = you don't know at all.

Q8: A surgeon channels her aggressive impulses into performing complex operations with precision and skill. Which defense mechanism?

A: Sublimation, channeling unacceptable impulses into socially valued, constructive activities. Considered the **most adaptive** single defense mechanism in Vaillant's hierarchy. The key: the original impulse is transformed, not merely redirected.

Q9: A patient with borderline personality disorder says "You're the best doctor I've ever had" one week and "You're completely useless and don't care about me" the next. Which defense mechanism?

A: Splitting, an **immature** defense mechanism where people/objects are seen as entirely good OR entirely bad, with no integration. Hallmark of **BPD** and other Cluster B presentations. Represents failure of object constancy.

Q10: A mother who unconsciously resents her child becomes excessively overprotective and smothering. Which defense mechanism, and at what level?

A: Reaction formation at the **neurotic** level. The hostile impulse is converted into its opposite (overprotection). Clinical clue: the behavior is **excessive, rigid, and compulsive**, genuine care would be flexible and responsive to the child's actual needs.

Q11: Classify these defenses by Vaillant's level: projection, sublimation, displacement, denial, humor, isolation of affect.

A:

- **Mature:** Sublimation, Humor
 - **Neurotic:** Displacement, Isolation of affect
 - **Immature:** Projection, Denial
-

Q12: A patient in therapy discusses a traumatic event in a calm, detached manner, describing facts without any emotional response. Which defense mechanism?

A: Isolation of affect, the thought/memory is conscious, but the **emotion** associated with it is separated and repressed. Common in OCD and obsessional personality. Differs from intellectualization (which uses abstract reasoning to distance) and from alexithymia (which is a trait, not a defense).

Developmental Psychology (14 Questions)

Q13: Name all 8 of Erikson's psychosocial stages with their crises.

A:

1. **Trust vs Mistrust** (0-1 yr)
 2. **Autonomy vs Shame/Doubt** (1-3 yrs)
 3. **Initiative vs Guilt** (3-6 yrs)
 4. **Industry vs Inferiority** (6-12 yrs)
 5. **Identity vs Role Confusion** (12-18 yrs)
 6. **Intimacy vs Isolation** (18-35 yrs)
 7. **Generativity vs Stagnation** (35-65 yrs)
 8. **Integrity vs Despair** (65+ yrs)
-

Q14: What virtue is gained at each of Erikson's stages?

A: Hope (Trust), **Will** (Autonomy), **Purpose** (Initiative), **Competence** (Industry), **Fidelity** (Identity), **Love** (Intimacy), **Care** (Generativity), **Wisdom** (Integrity).

Q15: At what Piagetian stage does object permanence develop, and at what age?

A: Sensorimotor stage, specifically at substage 4 (**Coordination of secondary schemes**), around **8-12 months**. Object permanence = understanding that objects continue to exist even when not visible. Its emergence coincides with **stranger anxiety** and **separation anxiety**.

Q16: A 4-year-old insists that the taller glass has more water, even after watching the same volume being poured from a shorter, wider glass. Which Piagetian concept explains this?

A: Lack of conservation, the hallmark limitation of the **preoperational stage** (2-7 years). The child shows **centration** (focusing on one dimension, height, while ignoring width). Conservation is not achieved until the **concrete operational stage** (7-11 years).

Q17: Describe the 4 attachment types identified through the Strange Situation. Which was NOT part of Ainsworth's original classification?

A:

1. **Secure**, distressed on separation, comforted on reunion (~60%)
2. **Anxious-Ambivalent**, highly distressed, NOT comforted on reunion, clingy + angry (~15%)
3. **Anxious-Avoidant**, minimal distress, ignores caregiver on reunion (~20%)
4. **Disorganized**, contradictory behaviors, freezing, approach-avoidance (~5%)

Disorganized was NOT part of Ainsworth's original 1978 study, it was added by **Main & Hesse in 1990**.

Q18: Which attachment style is most strongly associated with borderline personality disorder?

A: Disorganized attachment (also called fearful-avoidant in adult classification). Associated with caregivers who are simultaneously the source of fear and the source of comfort, "fright without solution." Also associated with **anxious-ambivalent** attachment (preoccupied adult style). Both involve fear of abandonment + chaotic relational patterns.

Q19: A 10-month-old searches for a toy hidden under blanket A, even after watching it being moved to blanket B. Name this error and its Piagetian significance.

A: A-not-B error (perseverative search error). Occurs in **sensorimotor substage 4** (8-12 months). The infant has emerging but incomplete object permanence, they can search for hidden objects but cannot yet account for **visible displacements**. Full object permanence with invisible displacement is achieved by substage 6 (18-24 months).

Q20: How does Erikson's theory fundamentally differ from Freud's psychosexual stages?

A: Three key differences:

1. **Scope:** Erikson covers the **entire lifespan** (8 stages, birth to death); Freud stops at adolescence (5 stages)
2. **Focus:** Erikson is **psychoSOCIAL** (relationships and society drive development); Freud is **psychoSEXUAL** (libidinal drives)
3. **Nature:** Erikson frames each stage as a **crisis with a positive resolution possible**; Freud frames development around **fixation and pathology**

Q21: Name the key cognitive achievement and limitation at each of Piaget's 4 stages.

A:

STAGE	ACHIEVEMENT	LIMITATION
Sensorimotor	Object permanence	No symbolic thought
Preoperational	Symbolic play, language	No conservation, egocentrism
Concrete Operational	Conservation, reversibility	Cannot think abstractly
Formal Operational	Abstract/hypothetical reasoning	Not universally achieved

Q22: What is "egocentrism" in Piaget's theory, and which task demonstrates it?

A: Egocentrism = the inability to take **another person's perspective**. It is a limitation of the **preoperational stage** (2-7 years). Demonstrated by the **Three Mountain Task**, the child selects their own view when asked what the doll sees from a different position. Not the same as selfishness, it is a cognitive limitation, not a moral one.

Q23: At what Erikson stage would failure lead to "identity diffusion," and what does this look like clinically?

A: Stage 5: Identity vs Role Confusion (adolescence, 12-18 years). Identity diffusion manifests as: inability to commit to roles/ values/ goals, susceptibility to **peer pressure and cults**, adoption of a "**negative identity**" (defining self by opposition), occupational paralysis, and chaotic relationships. Marcia's identity statuses (diffusion, foreclosure, moratorium, achievement) expand on this concept.

Q24: Which attachment style is associated with a caregiver who is emotionally unavailable and dismissive?

A: Anxious-Avoidant attachment. The child learns to suppress attachment needs because signaling distress leads to rejection. In the Strange Situation, the child shows **minimal distress on separation and ignores the caregiver on reunion**, a learned self-reliance that masks insecurity. Adult outcome: **dismissive-avoidant** style.

Q25: Name Piaget's 6 sensorimotor substages in order.

A:

1. **Reflex activity** (0-1 month), innate reflexes
2. **Primary circular reactions** (1-4 months), repeating pleasurable body-centered acts
3. **Secondary circular reactions** (4-8 months), repeating acts that affect the environment

4. **Coordination of secondary schemes** (8-12 months), goal-directed behavior, object permanence emerges
 5. **Tertiary circular reactions** (12-18 months), trial-and-error experimentation, "little scientist"
 6. **Mental representation** (18-24 months), symbolic thought, deferred imitation, invisible displacement
-

Q26: A 14-year-old believes that everyone in the school cafeteria is watching and judging them. Which Piagetian concept explains this?

A: Imaginary audience, a feature of adolescent egocentrism in the **formal operational stage**. The adolescent assumes others are as preoccupied with their appearance/behavior as they are themselves. Related concept: **personal fable**, the belief that one's experiences are unique and that one is invulnerable ("it won't happen to me").

Emotion, Grief, and Aggression (14 Questions)

Q27: Contrast James-Lange, Cannon-Bard, and Schachter-Singer theories of emotion.

A:

- **James-Lange (1884):** Body FIRST → emotion. "I tremble, therefore I am afraid." Stimulus triggers physiological response; brain interprets the body state as emotion.
 - **Cannon-Bard (1927):** SIMULTANEOUS. Thalamus sends signals to cortex (emotion) and body (arousal) at the same time. Challenged James-Lange.
 - **Schachter-Singer (1962):** TWO-FACTOR. Undifferentiated arousal + cognitive LABEL = emotion. Same arousal can be labeled as different emotions depending on context.
-

Q28: Name the components of the Papez circuit.

A: Hippocampus → Fornix → Mammillary bodies → Anterior thalamic nucleus → Cingulate gyrus → Parahippocampal gyrus → back to Hippocampus. Proposed by James Papez (1937) as the neural substrate of emotion. It was the first anatomical circuit model of emotion and laid the groundwork for MacLean's limbic system concept.

Q29: What are the 5 components of Goleman's emotional intelligence?

A:

1. **Self-awareness**, recognizing one's own emotions
2. **Self-regulation**, managing disruptive emotions and impulses
3. **Motivation**, intrinsic drive, resilience, optimism
4. **Empathy**, understanding others' emotional states

5. **Social skills**, managing relationships, influence, collaboration

(Mnemonic: SEEMS)

Q30: What 4 biological factors are most associated with aggression?

A:

1. **Serotonin**, LOW 5-HT = HIGH aggression (inverse relationship; CSF 5-HIAA is the marker)
2. **Testosterone**, positive correlation with dominance and aggression
3. **Frontal lobe**, prefrontal cortex inhibits aggression; damage = disinhibition (Phineas Gage)
4. **Amygdala**, threat detection and fear conditioning; bilateral lesions → Kluver-Bucy syndrome (placidity)

(Mnemonic: FAST)

Q31: Differentiate Kubler-Ross stages from Worden's tasks of mourning. Why does the distinction matter clinically?

A: **Kubler-Ross** describes 5 **stages** (DABDA), they are **passive** experiences that happen TO the bereaved. **Worden** describes 4 **tasks**, they are **active** work the mourner must DO (accept reality, process pain, adjust to world, find enduring connection).

Clinical significance: Worden's model is more useful therapeutically because it frames grief as something the patient can **work on**, it empowers agency. Kubler-Ross can inadvertently pathologize patients who don't follow the "correct" sequence. Also, Kubler-Ross was originally described for **dying patients**, not the bereaved.

Q32: Name Bowlby's 4 phases of grief and their approximate durations.

A:

1. **Numbness**, hours to days / weeks; shock, disbelief, emotional blunting
2. **Yearning and searching**, weeks to months; pining, searching behavior, restlessness, illusions of the deceased
3. **Disorganization and despair**, months; withdrawal, purposelessness, cognitive disruption
4. **Reorganization**, gradual; forming new identity, reinvesting in life

Bowlby grounded grief in **attachment theory**, grief IS attachment behavior directed at a figure who cannot return.

Q33: Why is grief NOT classified as a depressive disorder despite overlapping symptoms?

A: Several critical distinctions:

1. **Focus:** Grief is focused on the **loss**; MDD is focused on the **self** (worthlessness, self-loathing)
2. **Reactivity:** Grief mood is **context-reactive** (can laugh at a joke, enjoy a meal); MDD mood is often **pervasive and non-reactive**
3. **Self-image:** Preserved in grief; impaired in MDD
4. **Course:** Grief **fluctuates** in waves; MDD is **persistent**
5. **Evolutionary function:** Grief is an **adaptive response** to attachment loss; MDD represents a **failure of adaptive systems**
6. **Treatment:** Grief resolves with support and time; MDD typically requires pharmacotherapy + psychotherapy

The addition of **Prolonged Grief Disorder** (DSM-5-TR) acknowledges that grief CAN become pathological, but the pathological form is distinct from MDD.

Q34: Name Ekman's 6 basic emotions. What makes them "basic"?

A: Happiness, Sadness, Anger, Fear, Disgust, Surprise (mnemonic: DASH For Safety).

They are "basic" because they are:

1. **Universal** across cultures (demonstrated through cross-cultural facial expression studies, including isolated tribes)
 2. Each has a **distinct facial expression**
 3. Each has a **distinct physiological signature**
 4. Each has an **evolutionary function** (e.g., disgust = contamination avoidance, fear = threat response)
-

Q35: A patient reports feeling intensely anxious while crossing a bridge. Their heart is racing. Using Schachter-Singer's theory, explain why they feel anxiety rather than excitement.

A: According to the **two-factor theory**, the physiological arousal (racing heart, sweating) is **undifferentiated**, it is the same whether you're anxious or excited. The emotion you EXPERIENCE depends on the **cognitive label** you assign based on context. On a bridge with a fear of heights, the label is "anxiety." In Dutton & Aron's famous bridge study, men on a scary bridge who met an attractive researcher **misattributed** their arousal to attraction. The arousal is identical; the label is contextual.

Q36: What is the Dual Process Model of grief, and how does it improve on Kubler-Ross?

A: Stroebe & Schut (1999). Healthy grief involves **oscillation** between two orientations:

1. **Loss-oriented**, confronting the loss, grief work, rumination about the deceased
2. **Restoration-oriented**, attending to life changes, new roles, identity reconstruction, taking breaks from grief

Improvement over Kubler-Ross:

- Not a linear sequence, oscillation is the healthy norm
 - Explains why bereaved people can laugh one moment and cry the next (normal oscillation)
 - Pathological grief = getting **stuck** in one orientation (only loss = chronic grief; only restoration = absent grief/avoidance)
-

Q37: Describe the frustration-aggression hypothesis. Who proposed it, and what is its main limitation?

A: Proposed by **Dollard et al. (1939)**. Original claim: **frustration ALWAYS leads to aggression, and aggression is ALWAYS the result of frustration**. Later revised by **Berkowitz (1989)**, frustration creates a **READINESS** for aggression (cognitive neoassociation model), but the actual aggressive response depends on environmental cues, learning, and cognitive appraisal.

Main limitation: The original formulation is too absolute. Not all frustration leads to aggression (people may cry, withdraw, problem-solve), and not all aggression stems from frustration (instrumental aggression, predatory aggression, sadistic aggression exist independently).

Q38: What is the somatic marker hypothesis, and who proposed it?

A: Proposed by **Antonio Damasio (1994)**. Body states ("somatic markers") from previous emotional experiences **tag** decision options as good or bad, guiding rapid decision-making below conscious awareness. Key evidence: the **Iowa Gambling Task**, patients with **ventromedial prefrontal cortex** damage made disadvantageous choices because they lacked somatic markers. Central claim: **emotions are not irrational, they are essential for rational decision-making**.

Q39: A 45-year-old man whose wife died 8 months ago reports persistent yearning, inability to accept the death, feeling that life is meaningless without her, avoidance of reminders, and emotional numbness. He cannot return to work. Diagnosis?

A: Prolonged Grief Disorder (DSM-5-TR / ICD-11). Criteria met:

- **Duration:** >6 months post-bereavement
- **Core symptoms:** Persistent yearning/longing, preoccupation with the deceased

- **Additional symptoms:** Difficulty accepting death, emotional numbness, feeling life is meaningless, avoidance of reminders
- **Functional impairment:** Cannot work
- **Distinguishing from MDD:** Focus is on the LOSS (not generalized self-worthlessness); not pervasive anhedonia across all domains

Treatment: **Complicated Grief Treatment** (Shear), combines elements of IPT and prolonged exposure, NOT standard antidepressants alone.

Q40: Compare Bandura's social learning theory and the biological model of aggression. A child witnesses domestic violence at home and becomes aggressive at school, which theory best explains this, and why?

A: Bandura's social learning theory best explains this scenario. The child learns aggression through **observational learning (modeling)**, witnessing the aggressor being reinforced (getting compliance through violence) makes aggression a **viable behavioral strategy**. Key mechanisms: attention → retention → reproduction → motivation (vicarious reinforcement).

The biological model (serotonin, testosterone, frontal lobe, amygdala) would explain aggression as neurochemical/structural, which may contribute but doesn't account for the **specificity** of the behavior (aggressive at school, same pattern as witnessed at home).

In reality, both interact: The child's exposure (social learning) may alter neurobiological stress responses (epigenetic changes, HPA axis dysregulation, amygdala hyperreactivity), creating a biological vulnerability ON TOP of the learned behavior. This is the **biosocial model**, nature AND nurture, not nature vs nurture.

GUIDE 03 · PART I

Assessment Testing

Paper I · Basic Sciences. Six study modes, from notes to quick review.

Study Notes

SECTION A: INTELLIGENCE TESTS

A1. Theories of Intelligence

THEORY	AUTHOR	CORE IDEA	KEY TERMS
General Intelligence (g)	Charles Spearman (1904)	All cognitive abilities share a single underlying factor g ; task-specific abilities are s factors	Two-factor theory, g-loading
Fluid vs Crystallised	Raymond Cattell (1963)	Gf = novel problem-solving, pattern recognition (declines with age). Gc = accumulated knowledge, vocabulary (stable / increases)	Gf-Gc theory, Horn-Cattell
Multiple Intelligences	Howard Gardner (1983)	8 independent intelligences: linguistic, logical-mathematical, spatial, musical, bodily-kinesthetic, interpersonal, intrapersonal, naturalistic	MI theory, no single g
Triarchic Theory	Robert Sternberg (1985)	3 components: Analytical (componential), Creative (experiential), Practical (contextual)	Successful intelligence

CLINICAL ANCHOR

Cattell's Gf-Gc distinction is directly relevant to neuropsychological assessment. Gf declines early in dementia; Gc is preserved longer.

EXAM PEARL

Spearman and Cattell appear most frequently. Know two-factor theory vs Gf-Gc.

A2. IQ Classification (Wechsler System)

IQ RANGE	CLASSIFICATION	POPULATION %
130+	Very Superior	2.2%
120-129	Superior	6.7%
110-119	High Average	16.1%
90-109	Average	50%
80-89	Low Average	16.1%
70-79	Borderline	6.7%
69 and below	Extremely Low (Intellectual Disability)	2.2%

EXAM PEARL

IQ = (Mental Age / Chronological Age) x 100, this is the **ratio IQ** (Binet's original). Modern tests use **deviation IQ** (mean = 100, SD = 15 for Wechsler, SD = 16 for Stanford-Binet).

Intellectual Disability classification (ICD-11):

- **Mild:** IQ 50-69 (85% of ID population)
- **Moderate:** IQ 35-49
- **Severe:** IQ 20-34
- **Profound:** IQ < 20

A3. Wechsler Scales

The gold standard for intelligence testing worldwide. Three versions by age group:

SCALE	AGE RANGE	CURRENT EDITION	SUBTESTS
WAIS-IV	16-90 years	4th edition (2008)	10 core + 5 supplemental
WISC-V	6-16 years	5th edition (2014)	10 core + 6 supplemental
WPPSI-IV	2:6-7:7 years	4th edition (2012)	Varies by age band

WAIS-IV INDEX SCORES AND SUBTESTS

INDEX	ABBREVIATION	CORE SUBTESTS	MEASURES
Verbal Comprehension	VCI	Similarities, Vocabulary, Information	Crystallised ability, verbal reasoning, word knowledge

INDEX	ABBREVIATION	CORE SUBTESTS	MEASURES
Perceptual Reasoning	PRI	Block Design, Matrix Reasoning, Visual Puzzles	Fluid reasoning, spatial processing, visual-motor
Working Memory	WMI	Digit Span, Arithmetic	Attention, concentration, mental manipulation
Processing Speed	PSI	Symbol Search, Coding	Speed of mental operations, visual scanning

Full Scale IQ (FSIQ) = composite of all four indices.

EXAM PEARL

VCI-PRI discrepancy > 15 points is clinically significant. Low WMI = suspect ADHD, anxiety, or frontal dysfunction. Low PSI = suspect depression, medication effects, subcortical pathology. Digit Span has 3 components: Forward (attention), Backward (working memory), Sequencing (executive function).

WISC-V (FOR CHILDREN)

WISC-V adds a **5th index: Visual Spatial Index (VSI)**, separating it from Fluid Reasoning Index (FRI). This is the key structural difference from WAIS-IV.

Five WISC-V indices: VCI, VSI, FRI, WMI, PSI.

WPPSI-IV (PRESCHOOL)

Used for ages 2:6 to 7:7. Two age bands with different subtests. Useful for early identification of intellectual disability and giftedness.

A4. Stanford-Binet Intelligence Scales (5th Edition: SB5)

- **Author:** Originally Alfred Binet and Theodore Simon (1905, France); revised by Lewis Terman at Stanford (1916)
- **Current edition:** SB5 (2003)
- **Age range:** 2-85+ years
- **Structure:** 5 factor indices, Fluid Reasoning, Knowledge, Quantitative Reasoning, Visual-Spatial Processing, Working Memory
- **Each factor has:** Verbal and Nonverbal subtests (10 subtests total)
- **Scoring:** Mean = 100, SD = 16 (note: slightly different from Wechsler's SD = 15)
- **Unique feature:** Routing subtests (Vocabulary + Nonverbal Fluid Reasoning) determine starting point

EXAM PEARL

First standardised intelligence test. Introduced the concept of **Mental Age (MA)**.

A5. Binet-Kamat Test (BKT): VERY IMPORTANT FOR PG exams

- **Indian adaptation** of the Stanford-Binet by **C.H. Rice** and later standardised by **V.V. Kamat (1934, revised 1967)**
- **Age range:** 3-22 years
- **Language:** Available in Kannada, Marathi, Hindi, and English
- **Structure:** Age-graded scale, items arranged by difficulty corresponding to age levels
- **Scoring:** Yields **Mental Age (MA)** and **ratio IQ** ($MA/CA \times 100$)
- **Administration:** Individual, verbal-performance mixed
- **Indian norms:** Standardised on Indian population, this is its primary advantage over Western tests

Key items by age level (commonly tested):

- **Age 3:** Naming objects, repeating sentences, telling sex
- **Age 5:** Counting 4 objects, copying square, answering comprehension questions
- **Age 7:** Copying diamond, repeating 5 digits, detecting absurdities
- **Age 9:** Making change, arranging weights, rhyming
- **Age 12:** Defining abstract words, repeating 5 digits backward

Limitations:

- Ratio IQ (not deviation IQ), less statistically robust
- Older norms (1967 standardisation)
- Heavily verbal, disadvantages non-verbal populations
- No separate factor scores like Wechsler

EXAM PEARL

BKT is the most commonly used Indian-adapted intelligence test and frequently appears in exam questions. Know the author (V.V. Kamat), Indian norms, ratio IQ, and age-level examples.

A6. Culture-Fair Tests

Tests designed to minimise cultural and linguistic bias:

RAVEN'S PROGRESSIVE MATRICES (RPM)

- **Author:** John C. Raven (1938)
- **Types:**

- **Standard Progressive Matrices (SPM):** Ages 6-80, 60 items in 5 sets (A-E)
- **Coloured Progressive Matrices (CPM):** Ages 5-11 and elderly/ID, 36 items in 3 sets
- **Advanced Progressive Matrices (APM):** Above-average adults, 48 items
- **Format:** Visual patterns with a missing piece; choose correct option from 6-8 alternatives
- **Measures:** Primarily Spearman's **g** and Cattell's **Gf** (fluid intelligence)
- **Administration:** Individual or group; can be untimed or timed
- **Advantages:** Non-verbal, culture-fair, easy to administer, no reading required
- **Limitations:** Measures only one aspect of intelligence (not comprehensive)

CULTURE-FAIR INTELLIGENCE TEST (CFIT)

- **Author:** Raymond Cattell
- **Structure:** 3 scales by age/ability level
- **Subtests:** Series completion, classification, matrices, conditions (topology)
- **Measures:** Fluid intelligence (Gf)
- **Advantage:** Minimal cultural/verbal loading

A7. Developmental Quotient (DQ) vs IQ

FEATURE	DQ	IQ
Age group	Infants and toddlers (0-3 years)	Children 3+ and adults
Measures	Developmental milestones (motor, language, social, adaptive)	Cognitive abilities (reasoning, memory, processing)
Key test	Gesell Developmental Schedules , Bayley Scales (BSID-III)	Wechsler, Stanford-Binet, BKT
Formula	$DQ = (DA / CA) \times 100$	Deviation IQ or Ratio IQ
Predictive value	Poor predictor of later IQ (especially in typical range)	Stable after age 6-7
Clinical use	Screening for developmental delay	Diagnosis of ID, giftedness, cognitive decline

A8. Vineland Adaptive Behavior Scales (VABS-3)

- **Author:** Sara Sparrow, David Balla, Domenic Cicchetti (original); currently 3rd edition
- **Purpose:** Measures **adaptive functioning**, essential for ID diagnosis (ICD-11 and DSM-5 require BOTH low IQ AND impaired adaptive functioning)
- **Domains:**

- **Communication** (receptive, expressive, written)
- **Daily Living Skills** (personal, domestic, community)
- **Socialisation** (interpersonal, play /leisure, coping)
- **Motor Skills** (gross, fine), for ages < 7 only
- **Adaptive Behavior Composite (ABC)**, overall score
- **Administration:** Semi-structured interview with caregiver (parent/ teacher)
- **Scoring:** Standard scores (mean = 100, SD = 15) and age equivalents
- **Age range:** Birth to 90 years
- **Clinical use:** Intellectual disability diagnosis, ASD assessment, treatment planning

A9. Seguin Form Board

- **Author:** Edouard Seguin (1866)
- **Type:** Performance / non-verbal test
- **Description:** 10 differently shaped blocks must be placed into corresponding recesses on a wooden board
- **Measures:** Visual-motor coordination, form discrimination, psychomotor speed
- **Scoring:** Time to completion (3 trials; best time used)
- **Age range:** 2+ years
- **Clinical use:** Screening for intellectual disability, especially in non-verbal or culturally diverse populations
- **Advantage:** No language required, quick to administer
- **Indian context:** Widely used in Indian clinical settings as a quick screening tool

A10. Cognitive Screening Instruments

FEATURE	MMSE	MOCA	ACE-III
Full name	Mini-Mental State Examination	Montreal Cognitive Assessment	Addenbrooke's Cognitive Examination-III
Authors	Folstein et al. (1975)	Nasreddine et al. (2005)	Hsieh et al. (2013)
Max score	30	30	100
Cut-off	< 24 (dementia screen)	< 26 (MCI screen)	< 88 (dementia); < 82 (frontotemporal)
Time	5-10 min	10 min	15-20 min

FEATURE	MMSE	MOCA	ACE-III
Domains	Orientation, registration, attention/calculation, recall, language, visuospatial	Visuospatial/executive, naming, memory, attention, language, abstraction, orientation	Attention, memory, fluency, language, visuospatial
Strengths	Most widely used, quick	Better sensitivity for MCI, tests executive function	Most comprehensive, good for differentiating AD vs FTD
Weaknesses	Ceiling effect, poor for MCI, copyright issues, low executive testing	Harder, may over-detect in low education	Longer, less suitable for bedside screening
Education correction	No formal correction	+1 point if education $\leq$ 12 years	Available but varies

EXAM PEARL

MMSE misses executive dysfunction and MCI. If you suspect either, use MoCA. For differentiating dementia subtypes (AD vs FTD), ACE-III is superior.

Frontal Assessment Battery (FAB):

- 6 subtests: conceptualisation, mental flexibility, motor programming (Luria), sensitivity to interference, inhibitory control, environmental autonomy
- Score: 0-18, < 12 suggests frontal dysfunction
- Quick bedside test (10 min)

SECTION B: PROJECTIVE TESTS

B1. Projective Hypothesis: Definition and Rationale

Definition: Projective tests present **ambiguous, unstructured stimuli** to the examinee, who projects their unconscious needs, conflicts, desires, and personality characteristics onto the stimulus through their responses.

Projective hypothesis (Frank, 1939): When confronted with an ambiguous stimulus, a person's responses reveal their inner psychological world, their personality structure, unconscious conflicts, defence mechanisms, and emotional functioning, because the lack of structure in the stimulus forces them to impose their own meaning.

Theoretical basis: Psychoanalytic/psychodynamic theory, the concept of **projection** as a defence mechanism (Freud). The person attributes their own unacceptable thoughts, feelings, or motives to external stimuli.

Rationale:

- Structured tests (objective questionnaires) allow conscious control of responses, people can fake good/bad
- Ambiguous stimuli bypass conscious defences
- Responses are less susceptible to deliberate distortion
- Access deeper personality layers than self-report measures

Key characteristics of projective tests:

1. **Ambiguous stimuli**, inkblots, pictures, incomplete sentences
 2. **Freedom of response**, no right or wrong answers
 3. **Indirect assessment**, person doesn't know what's being measured
 4. **Holistic interpretation**, qualitative analysis of response patterns
 5. **Assumed connection** between response and personality
-

B2. Rorschach Inkblot Test

Author: Hermann Rorschach (1921), Swiss psychiatrist

Publication: *Psychodiagnostik* (1921)

Stimulus: 10 bilaterally symmetrical inkblot cards (5 achromatic, 2 red-black, 3 multicoloured)

EXNER'S COMPREHENSIVE SYSTEM (CS)

The **standardised scoring system** developed by John Exner (1974), made the Rorschach scientifically respectable by providing:

- Standardised administration
- Standardised scoring
- Normative data
- Empirically derived interpretation

ADMINISTRATION (2 PHASES)

Phase 1: Free Association (Response Phase)

- Present each card with: "What might this be?"
- Record all responses verbatim (including latency, card rotation, exclamations)
- No prompting, no time limit
- If only 1 response to Card I, prompt: "Most people see more than one thing"
- Aim: ≥ 14 responses across all 10 cards (if < 14 , re-administer)

Phase 2: Inquiry Phase

- After all 10 cards, go back through each response
- Ask: "Where did you see it?" and "What about it made it look like that?"

- Purpose: Determine **location** and **determinants** (what features of the blot were used)
- Do NOT introduce new responses during inquiry

SCORING CATEGORIES (4 MAIN + 1)

CATEGORY	WHAT IT MEASURES	KEY CODES
Location	Where on the blot the response is seen	W (whole), D (common detail), Dd (unusual detail), S (white space)
Determinants	What features of the blot shaped the response	F (form), M (human movement), FM (animal movement), C (colour), C' (achromatic colour), T (texture/shading), Y (diffuse shading), V (vista/dimensionality), FD (form dimension)
Content	What the response is about	H (whole human), Hd (human detail), A (whole animal), Ad (animal detail), An (anatomy), Bl (blood), Sx (sex), etc.
Popular responses (P)	Responses given by $\geq 1/3$ of population	Specific to each card (e.g., Card I = bat/butterfly, Card III = two people, Card V = bat/butterfly)
Organisational Activity (Z)	Cognitive effort in organising responses	Z-scores for integrating parts of the blot

KEY RATIOS AND INDICES FOR INTERPRETATION

RATIO/INDEX · CLINICAL MEANING

Lambda (L) Simplification of stimulus; high L = defensive/avoidant

Erlebnistypus (EB) Sum M : Weighted Sum C = introversive vs extratensive coping style

EA (Experience Actual) Sum M + WSumC = available coping resources

es (experienced stimulation) Sum FM+m : Sum C'+T+V+Y = experienced stress

D score EA - es = stress tolerance

X+% Conventional form quality, reality testing

X-% Distorted form quality, perceptual distortion

SCZI (Schizophrenia Index) Now replaced by PTI (Perceptual Thinking Index)

DEPI (Depression Index) Screens for affective disturbance

S-CON (Suicide Constellation) 8+ of 12 variables = suicide risk (validated)

STRENGTHS

- Rich personality data
- Difficult to fake
- Standardised scoring (Exner CS)
- Cross-cultural applicability (non-verbal stimuli)
- Validated for psychosis detection, thought disorder, personality structure

LIMITATIONS

- Time-consuming (administration + scoring: 45-90 min)
 - Requires extensive training
 - Inter-rater reliability concerns (outside CS)
 - Limited incremental validity over self-report for many constructs
 - Normative data debates
 - Not useful as a standalone diagnostic tool
-

B3. Thematic Apperception Test (TAT)

Authors: Henry Murray and Christiana Morgan (1935), Harvard Psychological Clinic

Publication: *Explorations in Personality* (Murray, 1938)

Stimulus: 31 picture cards (30 with pictures + 1 blank), showing ambiguous social scenes

ADMINISTRATION

- Select 10-12 cards appropriate for the examinee's age and sex (cards coded M, F, B, G, BM, GF, etc.)
- **Instruction:** "Tell me a story about this picture, what is happening, what led up to it, what are the characters feeling and thinking, and what will the outcome be?"
- Cards presented one at a time
- Session can be split across two sittings
- Blank card (Card 16): "Imagine a picture and tell a story", most revealing

MURRAY'S NEED-PRESS SCORING SYSTEM

Need (n): Internal drives/motives of the **hero** (character the examinee identifies with)

- n Achievement, n Affiliation, n Aggression, n Dominance, n Nurturance, n Order, n Succorance, n Abasement, n Autonomy

Press (p): Environmental forces acting on the hero

- p Affiliation, p Aggression, p Dominance, p Loss, p Rejection, p Nurturance

Thema: Need + Press interaction = the core conflict/ theme of the story

Other scoring elements:

- **Hero:** Who the examinee identifies with
- **Outcome:** Happy, sad, ambiguous, indicates optimism/ pessimism
- **Emotional tone:** Overall mood of stories
- **Unusual responses:** Omissions, distortions, card rejection

INTERPRETATION PRINCIPLES

1. The hero represents the examinee
2. Needs expressed by the hero = examinee's needs
3. Environmental forces (press) = how the examinee perceives the world
4. Recurring themes across stories = dominant personality patterns
5. Outcomes = expectancies about the world
6. Stories reflect both conscious and unconscious material

STRENGTHS

- Rich narrative data about interpersonal patterns
- Difficult to fake
- Good for identifying themes, conflicts, object relations
- Useful in psychotherapy assessment

LIMITATIONS

- Poor psychometric properties (reliability, validity)
- Subjective interpretation
- No widely accepted standardised scoring system
- Time-consuming
- Cultural bias in pictures (predominantly Western, white figures)

B4. Other Projective Tests

SENTENCE COMPLETION TEST (SCT)

- **Key version:** Rotter Incomplete Sentences Blank (RISB; Rotter, 1950)
- **Format:** 40 sentence stems (e.g., "I wish...", "My mother...", "I am afraid...")
- **Scoring:** Each response scored 0-6 on conflict-positive continuum; total score indicates adjustment level
- **Measures:** Attitudes, conflicts, personality themes
- **Advantages:** Quick, easy to administer, can be group-administered, semi-projective
- **Clinical use:** Screening, therapy planning, identifying specific conflict areas

DRAW-A-PERSON TEST (DAP)

- **Author:** Karen Machover (1949)
- **Instructions:** "Draw a person" → then "Draw a person of the opposite sex"
- **Interpretation:** Body image, self-concept, interpersonal attitudes
- Size of drawing = self-esteem
- Placement = mood (top = optimistic, bottom = depressed)
- Detail emphasis = preoccupation
- Omissions = avoidance / conflict
- **Goodenough-Harris version:** Scored for cognitive development (Draw-a-Man test for IQ estimation in children)
- **Limitations:** Poor reliability and validity; interpretation highly subjective

CHILDREN'S APPERCEPTION TEST (CAT)

- **Authors:** Leopold Bellak and Sonya Sorel Bellak (1949)
- **Stimulus:** 10 cards with **animal figures** in human-like situations
- **Age range:** 3-10 years
- **Rationale:** Children identify more readily with animal characters than human figures
- **CAT-H (Human):** Same situations but with human figures (for older children)
- **Scoring:** Similar to TAT, themes, defences, identification figures

WORD ASSOCIATION TEST (WAT)

- **Original:** Francis Galton (1879); systematised by Carl Jung
- **Procedure:** Examiner reads a list of stimulus words; examinee responds with first word that comes to mind
- **Scoring:** Reaction time, content of response, unusual associations, repetitions, blocking
- **Clinical use:** Identifying emotional complexes (Jung), forensic assessment

HOUSE-TREE-PERSON (HTP)

- **Author:** John Buck (1948)
- **Procedure:** Draw a house, a tree, and a person (separate drawings)
- **Interpretation:**
- **House** = home life, family relationships
- **Tree** = deeper unconscious self, growth, environmental relationships
- **Person** = self-concept, body image, interpersonal attitudes
- **Chromatic phase:** Repeat with coloured crayons, adds emotional dimension

BENDER VISUAL MOTOR GESTALT TEST (BENDER GESTALT / BGT)

- **Author:** Laretta Bender (1938), based on Wertheimer's Gestalt principles

- **Stimulus:** 9 geometric designs (cards A, 1-8)
- **Procedure:** Copy each design on blank paper
- **Measures:** Visual-motor integration, neurological impairment, developmental maturity
- **Scoring errors (Koppitz system for children):**
- **Distortion of shape**
- **Rotation** (> 45 degrees)
- **Integration failure** (parts not properly joined)
- **Perseveration** (repeating elements beyond stimulus)
- **Clinical use:** Screening for organic brain damage, developmental delay
- **Bender Gestalt II (2003):** Updated norms, added recall phase (memory component)
- **Note:** Primarily a neuropsychological screening tool, not a personality test, but has projective elements

SECTION C: PERSONALITY ASSESSMENT

C1. Objective Tests: MMPI-2

Full name: Minnesota Multiphasic Personality Inventory-2

Authors: Starke Hathaway and J.C. McKinley (original 1943); MMPI-2 by James Butcher et al. (1989)

Items: 567 true/false items

Age range: 18+ years (MMPI-A for adolescents 14-18)

Administration: Individual or group; self-report; 60-90 minutes

VALIDITY SCALES

SCALE	NAME	DETECTS	HIGH SCORE MEANS
L	Lie	Deliberate faking good	Naive defensiveness, presenting unrealistically positive self-image
F	Infrequency	Faking bad / random responding	Exaggeration, malin-gering, severe psy-chopathology, random responding
K	Correction/Defensive-ness	Subtle defensiveness	Denial of problems, guarded, psychologi-cally sophisticated defensiveness
?	Cannot Say	Unanswered items	> 30 invalidates profile

SCALE	NAME	DETECTS	HIGH SCORE MEANS
VRIN	Variable Response Inconsistency	Random responding	Inconsistent, random answering pattern
TRIN	True Response Inconsistency	Acquiescence / naysaying	Fixed "true" or "false" responding
Fb	Back-page Infrequency	Faking bad on latter half	Changed attitude mid-way through test
Fp	Infrequency-Psychopathology	Differentiates malingering from genuine pathology	Malingering (even genuine patients rarely endorse these items)

EXAM STRATEGY

Always interpret validity scales FIRST. If profile is invalid, clinical scales cannot be trusted.

10 CLINICAL SCALES

SCALE #	ABBREVIATION	NAME	HIGH SCORE INTERPRETATION
1	Hs	Hypochondriasis	Somatic preoccupation, vague physical complaints
2	D	Depression	Sadness, pessimism, psychomotor retardation, dissatisfaction
3	Hy	Hysteria (Conversion)	Somatic symptoms under stress, denial of psychological problems, la belle indifference
4	Pd	Psychopathic Deviate	Authority conflicts, impulsivity, antisocial behaviour, family discord
5	Mf	Masculinity-Femininity	Non-traditional gender role interests (interpretation varies by sex)
6	Pa	Paranoia	Suspiciousness, persecutory ideation, rigidity, hypersensitivity

SCALE #	ABBREVIATION	NAME	HIGH SCORE INTERPRETATION
7	Pt	Psychasthenia	Anxiety, obsessive-ness, rumination, indecisiveness, guilt
8	Sc	Schizophrenia	Bizarre thinking, social alienation, unusual experiences, poor reality testing
9	Ma	Hypomania	Elevated mood, grandiosity, hyperactivity, flight of ideas, impulsivity
0	Si	Social Introversion	Social withdrawal, shyness, discomfort in social situations

Profile interpretation:

- T-score ≥ 65 = clinically significant elevation
- **2-point code types:** Most common interpretive approach (e.g., 2-7 code = anxiety + depression; 4-9 code = antisocial + impulsive)
- **Spike profiles:** Single elevated scale
- **Conversion V:** Scales 1 and 3 elevated, Scale 2 low = conversion disorder pattern
- **Paranoid valley:** Scales 6 and 8 elevated, Scale 7 low = paranoid pattern

MMPI-2-RF (Restructured Form): 338 items, 51 scales; designed to address overlap between original clinical scales. Uses RC (Restructured Clinical) scales. More psychometrically sound but less clinical tradition.

C2. Cattell's 16 Personality Factor Questionnaire (16PF)

- **Author:** Raymond Cattell (1949, currently 5th edition)
- **Basis:** Factor analysis of language (lexical hypothesis)
- **Structure:** 16 primary personality factors measured by 185 items
- **Key factors include:** Warmth (A), Reasoning (B), Emotional Stability (C), Dominance (E), Liveliness (F), Rule-Consciousness (G), Social Boldness (H), Sensitivity (I), Vigilance (L), Abstractedness (M), Privateness (N), Apprehension (O), Openness to Change (Q1), Self-Reliance (Q2), Perfectionism (Q3), Tension (Q4)
- **5 Global Factors** (second-order): Extraversion, Anxiety, Tough-Mindedness, Independence, Self-Control
- **Scoring:** Bipolar scales (e.g., Reserved vs Warm)

- **Use:** Personality profiling, career counselling, research

C3. NEO-PI-R and the Big Five (OCEAN)

Authors: Paul Costa and Robert McCrae

Full name: NEO Personality Inventory-Revised (1992)

Items: 240 items, 5-point Likert scale

Structure: 5 domains, each with 6 facets (30 facets total)

DOMAIN	HIGH POLE	LOW POLE	FACETS
O, Openness	Imaginative, curious, open to experience	Practical, conventional, narrow interests	Fantasy, Aesthetics, Feelings, Actions, Ideas, Values
C, Conscientiousness	Organised, disciplined, reliable	Careless, disorganised, impulsive	Competence, Order, Dutifulness, Achievement-striving, Self-discipline, Deliberation
E, Extraversion	Sociable, assertive, active	Reserved, solitary, quiet	Warmth, Gregariousness, Assertiveness, Activity, Excitement-seeking, Positive emotions
A, Agreeableness	Trusting, cooperative, altruistic	Suspicious, competitive, antagonistic	Trust, Straightforwardness, Altruism, Compliance, Modesty, Tender-mindedness
N, Neuroticism	Anxious, moody, vulnerable	Calm, stable, resilient	Anxiety, Angry hostility, Depression, Self-consciousness, Impulsiveness, Vulnerability

CLINICAL ANCHOR

Big Five and personality disorders: High N + Low A + Low C = antisocial PD pattern. High N + Low E = avoidant PD pattern. High N + High A = dependent PD pattern. Low A + Low N = narcissistic pattern.

C4. Eysenck Personality Questionnaire (EPQ)

- **Author:** Hans Eysenck (original: Maudsley Personality Inventory → EPI → EPQ)

- **Model:** 3 superfactors:
- **Extraversion (E)**, sociable, lively, active vs reserved, quiet
- **Neuroticism (N)**, emotional instability, anxiety vs stability, calm
- **Psychoticism (P)**, tough-minded, aggressive, antisocial vs empathic, conventional
- **Lie scale (L):** Social desirability
- **Biological basis:** Eysenck proposed cortical arousal levels (introverts = chronically over-aroused; extraverts = under-aroused, seek stimulation)
- **EPQ-R (Revised):** 100 items, yes/no format

C5. Millon Clinical Multiaxial Inventory (MCMI-IV)

- **Author:** Theodore Millon
- **Current edition:** MCMI-IV (2015)
- **Items:** 195 true/false items
- **Purpose:** Specifically designed to assess **personality disorders** and **clinical syndromes** (aligned with DSM)
- **Scales:**
- **15 Personality Pattern scales** (e.g., Schizoid, Avoidant, Dependent, Histrionic, Narcissistic, Antisocial, Compulsive, Negativistic, Masochistic, Sadistic, Schizotypal, Borderline, Paranoid)
- **10 Clinical Syndrome scales** (Anxiety, Somatoform, Bipolar: Manic, Dysthymia, Alcohol Dependence, Drug Dependence, PTSD, Thought Disorder, Major Depression, Delusional Disorder)
- **3 Modifier indices + 2 Validity scales**
- **Base Rate (BR) scores:** Uses prevalence-based scoring (BR ≥ 75 = trait present; BR ≥ 85 = disorder prominent)
- **Key advantage over MMPI:** Designed specifically for personality pathology; shorter; aligned with DSM personality disorder categories
- **Limitation:** Should only be used with clinical/psychiatric populations (not normals)

C6. Objective vs Projective Tests: Summary Comparison

FEATURE	OBJECTIVE TESTS	PROJECTIVE TESTS
Stimuli	Structured, specific questions	Ambiguous, unstructured stimuli
Response format	Fixed choice (true/false, Likert)	Free response
Scoring	Standardised, objective	Subjective, requires trained examiner

FEATURE	OBJECTIVE TESTS	PROJECTIVE TESTS
Reliability	Generally high	Variable, often lower
Validity	Well-established (criterion, construct)	Debated; some evidence for specific uses
Faking	Easier to fake (but validity scales help)	Harder to fake (less transparent)
Theoretical basis	Empirical / trait theory	Psychodynamic / psychoanalytic
Administration	Quick, can be group-administered	Time-consuming, individual only
Examples	MMPI-2, 16PF, NEO-PI-R, EPQ	Rorschach, TAT, SCT, DAP
Best for	Screening, diagnosis, research	Personality dynamics, unconscious processes, therapy planning

C7. Types of Validity in Psychological Testing

TYPE	DEFINITION	EXAMPLE
Face validity	Test appears to measure what it claims (surface level; not true validity)	Depression questionnaire has items about sadness
Content validity	Items adequately sample the full domain of the construct	IQ test covers verbal, spatial, memory, speed
Criterion validity	Test correlates with an external criterion	IQ score predicts academic performance
<i>Concurrent</i>	Criterion measured at same time	New depression scale correlates with BDI
<i>Predictive</i>	Criterion measured in the future	SAT score predicts college GPA
Construct validity	Test measures the theoretical construct it claims to	IQ test correlates with other IQ tests (convergent) and does NOT correlate with unrelated measures (discriminant)

C8. Types of Reliability

TYPE	METHOD	QUESTION ANSWERED
Test-retest	Same test, same people, two occasions	Is the score stable over time?

TYPE	METHOD	QUESTION ANSWERED
Inter-rater	Different scorers, same responses	Do different raters agree?
Internal consistency	Single administration (Cronbach's alpha, split-half)	Do items within the test measure the same construct?
Parallel forms	Two equivalent versions of the test	Are alternate forms equivalent?

KEY EXAM THEMES AND HIGH-YIELD CONNECTIONS

EXAM PEARL

Binet-Kamat Test, the most frequently asked intelligence test in PG exams. Know: author (V.V. Kamat), Indian norms, ratio IQ, age-level items, strengths/limitations.

EXAM PEARL

Rorschach, the most frequently asked projective test. Know: Exner's Comprehensive System, two phases of administration, the four scoring categories (location, determinants, content, popular), key indices (EB, X+%, SCZI/PTI, S-CON).

EXAM STRATEGY

Projective tests is THE repeat question. Appears almost every other year. Always define projection, list 5-6 tests, describe Rorschach in detail.

EXAM PEARL

MMPI-2, know validity scales (L, F, K) and all 10 clinical scales with their numbers.

EXAM PEARL

Theories of intelligence, Spearman, Cattell, Gardner, Sternberg. These form the opening paragraph of any intelligence essay.

EXAM PEARL

Objective vs Projective, comparison table is high-yield for short notes and discussion questions.

EXAM PEARL

Frontal lobe tests, FAB, Wisconsin Card Sorting Test, Trail Making Test, Stroop Test, verbal fluency, go/no-go tasks. These get asked as a standalone question.

Model Answers

Q1. "Projective tests." [10 marks]

Answer:

EXAM STRATEGY

This is the single most repeated question in this topic. Write a clean define-list-describe structure. Define projective tests and the projective hypothesis (2 marks), list 6-8 tests (2 marks), describe Rorschach in detail (6 marks). If time permits, add a brief comparison with objective tests.

Definition [2 marks]

Projective tests are psychological assessment instruments that present **ambiguous, unstructured stimuli** to the examinee. The underlying rationale is the **projective hypothesis** (Frank, 1939): when confronted with ambiguous stimuli, individuals **project** their unconscious needs, conflicts, desires, defence mechanisms, and personality characteristics onto the stimulus material, thereby revealing aspects of personality that may not be accessible through structured self-report measures.

The theoretical foundation derives from psychoanalytic theory and the concept of projection as a defence mechanism. The ambiguity of the stimulus forces the examinee to impose their own psychological structure and meaning.

Key characteristics:

- Ambiguous stimuli with no correct response
- Freedom of response
- Indirect assessment, the examinee is unaware of what is being measured
- Responses are qualitatively interpreted
- Access deeper personality layers than self-report

Enumeration of Projective Tests [2 marks]

1. **Rorschach Inkblot Test** (Hermann Rorschach, 1921)
2. **Thematic Apperception Test (TAT)** (Henry Murray, 1935)
3. **Sentence Completion Test** (Rotter Incomplete Sentences Blank)
4. **Draw-a-Person Test** (Karen Machover, 1949)
5. **Children's Apperception Test (CAT)** (Leopold Bellak, 1949)
6. **Word Association Test** (Carl Jung)

7. **House-Tree-Person Test** (John Buck, 1948)

8. **Bender Visual Motor Gestalt Test** (Lauretta Bender, 1938)

Rorschach Inkblot Test: Detailed Description [6 marks]

Author and history: Developed by Hermann Rorschach, a Swiss psychiatrist, in 1921. Published in *Psychodiagnostik*. Currently standardised under **Exner's Comprehensive System** (John Exner, 1974), which provides standardised administration, scoring, normative data, and empirically derived interpretation.

Stimulus material: 10 bilaterally symmetrical inkblot cards, 5 achromatic (black and grey), 2 with red highlights, 3 multicoloured.

Administration, Two phases:

Phase 1: Free Association (Response Phase)

- Each card presented with the instruction: "What might this be?"
- All responses recorded verbatim, including reaction time, card rotation, and spontaneous comments
- No prompting or time limit imposed
- Minimum of 14 responses across all 10 cards expected

Phase 2: Inquiry Phase

- After completion of all 10 cards, the examiner reviews each response
- Questions: "Where on the card did you see it?" and "What about it made it look like that?"
- Purpose: to determine **location** and **determinants** used

Scoring (four main categories):

1. **Location:** Where on the blot, W (whole), D (common detail), Dd (unusual detail), S (white space)
2. **Determinants:** What features used, F (form), M (human movement), FM (animal movement), C (colour), T (texture), Y (shading), V (vista)
3. **Content:** What is seen, H (human), A (animal), An (anatomy), Bl (blood), Na (nature), etc.
4. **Popular responses (P):** Responses given by $\geq$ one-third of the population for specific cards

Interpretation, Key indices:

- **Erlebnistypus (EB):** Ratio of M to weighted sum of colour responses, determines introversive vs extroversive coping style
- **Experience Actual (EA):** Total coping resources
- **X+% and X-%:** Reality testing (form quality)

- **Perceptual Thinking Index (PTI):** Screens for thought disorder
- **Suicide Constellation (S-CON):** 8+ of 12 variables indicates elevated suicide risk
- **Depression Index (DEPI):** Screens for affective disturbance

Strengths:

- Difficult to fake
- Standardised scoring with Exner's system
- Cross-cultural applicability
- Validated for psychosis detection and thought disorder assessment

Limitations:

- Time-consuming (45-90 minutes)
- Requires extensive training
- Inter-rater reliability concerns outside standardised systems
- Limited incremental validity over self-report for many constructs
- Normative data controversies

Q2. "What is Projection? Name different projective tests and describe one in detail." [10 marks]

Answer:

EXAM STRATEGY

This overlaps heavily with Q1 but explicitly asks for the defence mechanism definition.

Allocate 2 marks to defining projection, 2 marks to listing tests, 6 marks to detailed description.

Describe Rorschach (safest) or TAT (if you want variety).

Projection: Definition [2 marks]

Projection is a **defence mechanism** first described by Sigmund Freud in which an individual attributes their own unacceptable thoughts, feelings, impulses, or traits to another person or to external stimuli. It operates unconsciously to reduce anxiety arising from internal conflicts.

In the context of psychological assessment, the **projective hypothesis** (Frank, 1939) extends this concept: when presented with ambiguous, unstructured stimuli, individuals project their internal psychological world, including unconscious needs, conflicts, desires, and personality dynamics, onto the stimulus material through their responses. This forms the theoretical basis for all projective tests.

Enumeration of Projective Tests [2 marks]

1. Rorschach Inkblot Test (Hermann Rorschach, 1921)
2. Thematic Apperception Test (Henry Murray, 1935)
3. Sentence Completion Test (Rotter, 1950)
4. Draw-a-Person Test (Karen Machover, 1949)
5. Children's Apperception Test (Leopold Bellak, 1949)
6. Word Association Test (Carl Jung)
7. House-Tree-Person Test (John Buck, 1948)
8. Bender Visual Motor Gestalt Test (Lauretta Bender, 1938)

Detailed Description: Thematic Apperception Test (TAT) [6 marks]

Author and history: Developed by **Henry Murray** and Christiana Morgan at the Harvard Psychological Clinic in 1935. Published in *Explorations in Personality* (1938). Based on Murray's theory of personality needs.

Stimulus material: 31 picture cards (30 with pictures depicting ambiguous social scenes + 1 blank card). Cards are coded for specific demographics (M = male, F = female, B = boy, G = girl).

Administration:

- 10-12 cards selected appropriate to the examinee's age and sex
- Instruction: "Tell me a story about this picture. What is happening now? What led up to this situation? What are the characters thinking and feeling? What will the outcome be?"
- Cards presented one at a time; stories recorded verbatim
- Blank card (Card 16): "Imagine any picture and tell a story about it", considered most projectively revealing

Murray's Need-Press Scoring System:

Need (n): The internal drives, motives, and desires of the **hero**, the character with whom the examinee identifies:

- n Achievement, n Affiliation, n Aggression, n Dominance, n Nurturance, n Succorance, n Autonomy, n Abasement, n Order

Press (p): Environmental forces acting on the hero:

- p Affiliation, p Aggression, p Dominance, p Loss, p Rejection, p Nurturance

Thema: The interaction between need and press, represents the core conflict or theme.

Interpretation principles:

- The hero represents the examinee
- Recurring needs = dominant personality patterns

- Environmental forces (press) = how the examinee perceives the world
- Story outcomes = expectations and optimism/pessimism
- Emotional tone, omissions, and card rejections provide additional data

Clinical applications:

- Identifying unconscious interpersonal patterns and object relations
- Assessing motivation, conflict areas, and coping styles
- Useful in therapy planning and progress monitoring
- Applied in forensic, organizational, and clinical settings

Strengths: Rich narrative data, difficult to fake, reveals interpersonal patterns

Limitations: Poor psychometric properties, subjective interpretation, no universally accepted scoring system, cultural bias in picture content

Q3. "What do you understand by projective tests? Name them and describe any one in detail." [10, split 2+2+6]

Answer:

EXAM STRATEGY

Near-identical to Q1 and Q2. The split marking (2+2+6) confirms the structure. Use the same content as Q1, define (2), list (2), describe Rorschach (6). Cross-reference Q1 above for full content.

Answer: Same structure and content as Q1. Allocate exactly as marked, 2 marks for understanding/definition of projective tests including the projective hypothesis, 2 marks for naming 6-8 tests with authors, 6 marks for Rorschach detailed description covering history, stimulus, administration (two phases), scoring (four categories), interpretation (key indices), and strengths/limitations.

Q4. "Projective tests in psychiatry." [10 marks]

Answer:

EXAM STRATEGY

This phrasing demands a clinical psychiatry focus rather than pure psychometrics. Same define-list-describe structure as Q1, but add a section on clinical applications and limitations in psychiatric practice. Consider covering psychiatric-specific uses (psychosis detection, personality assessment, forensic).

Definition and Rationale [2 marks]

Projective tests present ambiguous stimuli that elicit responses revealing the examinee's unconscious personality dynamics, conflicts, and psychological functioning. In psychiatry, they complement clinical interviews and objective tests by accessing aspects of personality and psychopathology that patients may not report directly, particularly unconscious material, defence mechanisms, and thought organisation.

Enumeration [2 marks]

(Same list as Q1, 8 tests with authors)

Rorschach: Detailed Description [4 marks]

(Condensed version of Q1's Rorschach section, administration, scoring categories, key indices)

Clinical Applications in Psychiatry [2 marks]

Psychotic disorders:

- Rorschach PTI (Perceptual Thinking Index) detects thought disorder
- Deviant verbalizations, contaminations, confabulations on Rorschach indicate formal thought disorder
- Poor form quality (X-%) indicates impaired reality testing
- TAT: Bizarre, fragmented, or overly concrete stories suggest psychosis

Mood disorders:

- DEPI (Depression Index) on Rorschach
- TAT: Themes of loss, hopelessness, helplessness; negative outcomes

Personality disorders:

- Mode of relating to stimuli reveals personality structure
- Rorschach texture responses (T), attachment style
- TAT interpersonal themes, object relations quality

Suicide risk:

- S-CON (Suicide Constellation) on Rorschach, validated predictor

Forensic psychiatry:

- Difficult to fake (advantage over self-report)
- Assessment of malingering, competency, dangerousness

Limitations in psychiatric practice:

- Should never be used as sole diagnostic tool
- Require trained clinical psychologists

- Time-consuming in busy clinical settings
 - Questionable incremental validity over structured interviews for diagnosis
 - Better suited for personality dynamics than categorical diagnosis
-

Q5. "Describe projective tests in psychoses." [10 marks]

Answer:

EXAM STRATEGY

Highly specific, they want projective test findings IN psychotic patients. Define projective tests briefly (2 marks), then focus on Rorschach and TAT findings in psychosis (8 marks). This is a clinical application question.

Introduction [2 marks]

Projective tests, by presenting ambiguous stimuli, are particularly valuable in psychotic disorders because they can reveal **thought disorder, perceptual distortion, and impaired reality testing**, often more sensitively than structured clinical interviews. The Rorschach Inkblot Test is the most validated projective instrument for psychosis assessment.

Rorschach Findings in Psychosis [5 marks]

Perceptual-Thinking Index (PTI):

The PTI (replacing the older Schizophrenia Index, SCZI) is a composite of 5 variables that detects disordered thinking and perceptual accuracy problems. Elevated PTI suggests:

- Impaired reality testing
- Disordered thought processes
- Perceptual distortion

Specific Rorschach indicators of psychosis:

FINDING · SIGNIFICANCE

Poor form quality (X-% elevated, X+% low) Impaired reality testing, the patient sees things that don't match the blot's actual form

Deviant verbalizations (DV, DR) Mild thought slippage, unusual word use, circumstantial reasoning

Deviant responses (INCOM, FABCOM, CONTAM) Severe thought disorder, impossible combinations, fabulized combinations, contaminations

Contamination responses Pathognomonic of psychosis, two images fused into one (e.g., "a butterfly-man")

Confabulation (DW) Overgeneralisation from detail to whole, indicates poor reasoning

Perseveration Same response across multiple cards, indicates cognitive rigidity

High M- (human movement with poor form) Distorted internal representations of human interaction

Color-form (CF > FC) Emotional dysregulation, poor modulation of affect

Elevated S (white space) Oppositional, negativistic stance

Low Popular responses (P) Inability to see conventionally, social disconnection

Reality testing summary:

- $X+\% < 70\%$ = poor conventional accuracy
- $X-\% > 20\%$ = significant perceptual distortion
- Both together strongly indicate psychosis

TAT Findings in Psychosis [2 marks]

- **Bizarre, fragmented stories**, loss of narrative coherence
- **Concrete responses**, inability to generate imaginative narratives ("I see two people")
- **Card rejection**, inability to engage with ambiguous stimuli
- **Autistic logic**, idiosyncratic connections not shared by others
- **Persecutory themes**, in paranoid psychosis
- **Loss of hero identification**, multiple shifting identifications, boundary confusion
- **Deviant story structure**, no clear beginning, middle, end

Other Projective Tests in Psychosis [1 mark]

- **Sentence Completion:** Bizarre completions, thought disorder evident in written responses
 - **DAP:** Bizarre, fragmented, or transparently drawn bodies; unusual emphasis on eyes (paranoia)
 - **Bender Gestalt:** Fragmentation, rotation, and severe distortion beyond organic patterns
-

Q6. "Name some projective tests. Discuss development, administration and assessment of any one." [10, split 2+8]

Answer:

EXAM STRATEGY

The 2+8 split means brief listing then deep dive. This is asking for the most detailed possible description of ONE test. Choose Rorschach, it has the most to write about.

Enumeration of Projective Tests [2 marks]

1. Rorschach Inkblot Test (Hermann Rorschach, 1921)
2. Thematic Apperception Test (Henry Murray, 1935)
3. Sentence Completion Test (Rotter, 1950)
4. Draw-a-Person Test (Karen Machover, 1949)
5. Children's Apperception Test (Leopold Bellak, 1949)
6. Word Association Test (Carl Jung)
7. House-Tree-Person Test (John Buck, 1948)
8. Bender Visual Motor Gestalt Test (Lauretta Bender, 1938)

Rorschach Inkblot Test: Development, Administration, and Assessment [8 marks]

DEVELOPMENT [2 MARKS]

Hermann Rorschach (1884-1922), a Swiss psychiatrist, noticed that psychiatric patients responded differently to inkblots compared to healthy individuals. He developed his test through systematic experimentation with hundreds of inkblots, eventually selecting **10 cards** that best discriminated between diagnostic groups. His work was published in *Psychodiagnostik* (1921).

After Rorschach's early death in 1922, several competing scoring systems developed:

- **Beck system** (Samuel Beck), empirical approach
- **Klopfer system** (Bruno Klopfer), more interpretive
- **Piotrowski system**, neuropsychological emphasis
- **Rapaport-Schafer system**, psychoanalytic approach

John Exner (1974) integrated the best elements of all systems into the **Comprehensive System (CS)**, which became the standard. It provided:

- Standardised administration procedures
- Standardised scoring criteria with normative data
- Empirically validated interpretive guidelines
- Structural Summary for quantitative analysis

The **Rorschach Performance Assessment System (R-PAS; 2011)** by Meyer et al. is the most recent update, addressing normative data issues.

ADMINISTRATION [3 MARKS]

Setting: Quiet, distraction-free room. Examiner and examinee seated side by side (not face to face) to minimise examiner influence.

Materials: 10 inkblot cards (numbered I-X on the back), response sheets, location sheets.

Phase 1, Free Association (Response Phase):

- Hand card to examinee in standard upright position
- Standard instruction: "What might this be?" (for Card I); subsequently just hand the card
- Record ALL responses verbatim, including:
 - Reaction time (latency to first response)
 - Total time per card
 - Card rotations
 - Spontaneous comments and exclamations
- No time limit, no prompting
- If only ONE response to Card I, prompt: "Take your time; most people see more than one thing"
- If total responses across all 10 cards < 14, consider re-administration
- If examinee tries to hand back the card, say: "Take your time"

Phase 2, Inquiry:

- After ALL 10 cards completed, return to Card I
- For each response: "I want to make sure I see it the way you did. Where on the card did you see [response]?" and "What about it made it look like [response]?"
- Purpose: determine the EXACT location and the determinants (form, colour, movement, shading, etc.)
- Do NOT suggest or introduce new determinants
- Use a location sheet to mark areas

Phase 3 (optional), Testing the Limits:

- Only after inquiry is complete
- Used if Popular responses are absent, present the card and ask "Some people see [popular response] here; can you see it?"
- Not part of standard scoring

ASSESSMENT / SCORING [3 MARKS]

Every response is scored on multiple dimensions:

1. Location:

- **W** = Whole blot used

- **D** = Common detail area
- **Dd** = Unusual detail area
- **S** = White space used (with or without blot area)

2. Determinants:

- **F** = Form only (shape of the blot)
- **M** = Human movement (people doing something)
- **FM** = Animal movement
- **m** = Inanimate movement
- **C** = Pure colour (no form); **CF** = colour-form; **FC** = form-colour
- **C'** = Achromatic colour
- **T** = Texture (shading as tactile)
- **Y** = Diffuse shading
- **V** = Vista (3D depth from shading)
- **FD** = Form-based dimensionality
- Multiple determinants can be coded as **blends** (e.g., M.FC)

3. Form Quality:

- **+** (**superior**): Exceptionally articulated
- **o** (**ordinary**): Commonly seen, good match
- **u** (**unusual**): Uncommon but adequate match
- **-** (**minus**): Poor match, distorted

4. Content: H, Hd, A, Ad, An, Bl, Bt (botany), Cg (clothing), Ex (explosion), Fi (fire), Fd (food), Ge (geography), Hh (household), Ls (landscape), Na (nature), Sc (science), Sx (sex), Art, Ay (anthropology), Id (ideograph)

5. Popular (P): Specific responses seen in $\geq 1/3$ of protocols for each card

6. Organisational Activity (Z): Score for organising multiple areas of the blot into a meaningful relationship

Structural Summary: All scores compiled into a quantitative summary including:

- Core ratios: EB (Erlebnistypus), EA (Experience Actual), es
- Affect section: FC:CF+C, Afr (Affective Ratio)
- Interpersonal section: COP (Cooperative Movement), AG (Aggressive Movement)
- Self-perception: Fr+rF (Reflection), Egocentricity Index
- Processing: W:D:Dd, Zf, PSV
- Cognitive mediation: X+%, X-%, Xu%
- Ideation: M-, Special Scores (DV, INCOM, DR, FABCOM, ALOG, CONTAM)

- Special indices: S-CON, PTL, DEPI, CDI, HVI, OBS

Q7. "Psychological tests of intelligence: enumerate with a note on Binet Kamat test." [10 marks]

Answer:

EXAM STRATEGY

This is the most commonly asked intelligence question. Quick enumeration (3 marks), then detailed Binet-Kamat (7 marks). PG exams loves Indian adaptations.

Enumeration of Intelligence Tests [3 marks]

Individual tests:

1. Wechsler Adult Intelligence Scale (WAIS-IV), ages 16-90
2. Wechsler Intelligence Scale for Children (WISC-V), ages 6-16
3. Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV), ages 2:6-7:7
4. Stanford-Binet Intelligence Scales (SB5), ages 2-85+
5. Binet-Kamat Test, Indian adaptation, ages 3-22

Group tests:

1. Raven's Progressive Matrices, ages 5-80+
2. Culture-Fair Intelligence Test (CFIT), Cattell

Performance/non-verbal:

1. Seguin Form Board
2. Kohs Block Design Test

Developmental/adaptive:

1. Vineland Adaptive Behavior Scales (VABS-3)
2. Bayley Scales of Infant Development (BSID-III)

Cognitive screening:

1. MMSE, MoCA, ACE-III

Binet-Kamat Test: Detailed Note [7 marks]

BACKGROUND AND DEVELOPMENT

The Binet-Kamat Test (BKT) is the **Indian adaptation** of the Stanford-Binet Intelligence Scale. It was originally adapted by **C.H. Rice** for Indian populations and later systematically standardised by **V.V. Kamat** in **1934**, with a revision in **1967**.

The original Stanford-Binet was developed by Alfred Binet and Theodore Simon in France (1905) to identify children needing special education, and was later revised by Lewis Terman at Stanford University (1916). Kamat adapted it specifically for Indian children, modifying items for cultural relevance and standardising norms on Indian samples.

TEST STRUCTURE

- **Type:** Individual intelligence test
- **Age range:** 3 to 22 years
- **Languages:** Available in Kannada, Marathi, Hindi, and English
- **Structure:** Age-graded scale, test items are arranged by difficulty level corresponding to specific age levels (from age 3 to Superior Adult level)
- **Item types:** Mixed verbal and performance items including vocabulary, comprehension, memory (digit span), reasoning, visual-motor tasks, and abstract thinking

KEY TEST ITEMS BY AGE LEVEL

AGE LEVEL · SAMPLE ITEMS

Age 3 Naming objects in pictures, repeating sentences (6-7 syllables), telling own sex

Age 4 Naming objects from memory, opposite analogies, picture completion

Age 5 Counting 4 objects, copying a square, answering comprehension questions

Age 6 Defining simple words, finding missing parts, repeating sentences

Age 7 Copying a diamond, repeating 5 digits forward, detecting absurdities in pictures

Age 8 Verbal absurdities, defining words, memory for stories

Age 9 Making change (arithmetic), arranging weights, rhyming

Age 10 Giving reasons, vocabulary items, memory tasks

Age 12 Defining abstract words, repeating 5 digits backward, picture interpretation

Age 14 Induction test, reasoning tasks, vocabulary

Average Adult Vocabulary, interpretation of proverbs, differences and similarities

Superior Adult Advanced vocabulary, complex reasoning, abstract thinking

ADMINISTRATION

- Administered **individually** by a trained clinical psychologist
- Begin at the age level **BELOW** the child's chronological age (to ensure initial success)
- **Basal age:** The highest age level at which **ALL** items are passed

- **Ceiling age:** The lowest age level at which ALL items are failed
- Testing continues from basal to ceiling
- Time: 30-60 minutes depending on the child's age and ability

SCORING

- **Mental Age (MA):** Basal age + credit for items passed above basal (each item = a fraction of a year, depending on the number of items at each level)
- **Intelligence Quotient (IQ):** Calculated as the **ratio IQ**:

$$\text{IQ} = (\text{Mental Age} / \text{Chronological Age}) \times 100$$

- This is a **ratio IQ** (not a deviation IQ like Wechsler)

IQ CLASSIFICATION (BINET-KAMAT)

IQ RANGE · CLASSIFICATION

140+ Genius or near genius

120-139 Very superior

110-119 Superior

90-109 Normal / Average

80-89 Dull normal

70-79 Borderline

50-69 Mild intellectual disability (moron)

25-49 Moderate ID (imbecile)

< 25 Severe / Profound ID (idiot)

(Note: Older terminology in original classification; current ICD-11/DSM-5 terminology preferred in clinical practice)

ADVANTAGES

1. **Indian norms**, standardised on Indian population (most important advantage)
2. Culturally adapted items relevant to Indian context
3. Available in multiple Indian languages (Kannada, Marathi, Hindi, English)
4. Wide age range (3-22 years)
5. Well-established in Indian clinical and educational settings
6. Individual administration allows clinical observation

LIMITATIONS

1. **Ratio IQ**, less statistically robust than deviation IQ; IQ scores not directly comparable across ages
2. **Outdated norms**, 1967 standardisation; Flynn effect means current population scores higher
3. **Heavily verbal**, disadvantages non-verbal, hearing-impaired, or culturally different populations
4. **No separate factor scores**, provides only a global IQ, not index scores like Wechsler (VCI, PRI, WMI, PSI)
5. **Single examiner required**, not suitable for group testing
6. **Limited adult utility**, norms only up to age 22

CLINICAL SIGNIFICANCE

The Binet-Kamat Test remains the most commonly used individually administered intelligence test in India, particularly for:

- Diagnosis of intellectual disability
- Educational placement decisions
- Medico-legal assessments (disability certification)
- Baseline cognitive assessment in child psychiatry

Q8. "Describe theories of intelligence. Describe two standard tests. Describe executive functions and clinical relevance." [10 marks: LONG ESSAY CANDIDATE]

Answer:

EXAM STRATEGY

This is a 3-part question that could appear as a 20-mark long essay. Structure it clearly with subheadings for each section. Allocate marks as: theories (4), two tests (8), executive functions (8) for the 20-mark version. For 10-mark version: theories (3), tests (4), executive functions (3).

20-MARK VERSION

Part A: Theories of Intelligence [4 marks]

1. SPEARMAN'S TWO-FACTOR THEORY (1904)

Charles Spearman proposed that intelligence consists of a **general factor (g)**, a single underlying cognitive ability that influences performance across all intellectual tasks, and multiple **specific factors (s)** that are unique to individual tasks. The g factor is measured by

the common variance shared by different cognitive tests. This theory was derived from factor analysis of test intercorrelations.

CLINICAL ANCHOR

The concept of g underlies the Full Scale IQ in modern intelligence tests.

2. CATTELL'S FLUID-CRYSTALLISED THEORY (1963)

Raymond Cattell, building on Spearman, proposed that g consists of two broad components:

- **Fluid intelligence (Gf):** Ability to solve novel problems, identify patterns, and reason abstractly, independent of prior knowledge. Measured by tasks like matrix reasoning and pattern recognition. Declines with age, especially after 60.
- **Crystallised intelligence (Gc):** Accumulated knowledge, vocabulary, and skills acquired through education and experience. Remains stable or increases with age.

CLINICAL ANCHOR

Gf declines early in neurodegenerative disorders (especially frontotemporal dementia), while Gc is preserved longer (especially in Alzheimer's disease).

3. GARDNER'S MULTIPLE INTELLIGENCES (1983)

Howard Gardner proposed that intelligence is not a single construct but comprises 8 **independent intelligences**: Linguistic, Logical-Mathematical, Spatial, Musical, Bodily-Kinaesthetic, Interpersonal, Intrapersonal, and Naturalistic. Each intelligence has its own neural substrate and developmental trajectory.

Criticism: Difficult to operationalise and measure; some "intelligences" may be better described as talents or aptitudes.

4. STERNBERG'S TRIARCHIC THEORY (1985)

Robert Sternberg proposed three interacting components of intelligence:

- **Analytical (Componential):** Academic problem-solving, critical thinking, what traditional IQ tests measure
- **Creative (Experiential):** Ability to deal with novel situations and automatise processes
- **Practical (Contextual):** "Street smarts", adapting to, shaping, or selecting real-world environments

CLINICAL ANCHOR

Explains why some patients with low IQ function well in daily life (high practical intelligence) and vice versa.

Part B: Two Standard Intelligence Tests [8 marks]

TEST 1: WECHSLER ADULT INTELLIGENCE SCALE-IV (WAIS-IV) [4 MARKS]

Author: David Wechsler (original 1955; WAIS-IV published 2008)

Age range: 16-90 years

Type: Individual, comprehensive intelligence test

Time: 60-90 minutes

Structure, Four Index Scores:

INDEX	ABBREVIATION	CORE SUBTESTS	WHAT IT MEASURES
Verbal Comprehension	VCI	Similarities, Vocabulary, Information	Crystallised ability, verbal reasoning
Perceptual Reasoning	PIRI	Block Design, Matrix Reasoning, Visual Puzzles	Fluid reasoning, spatial processing
Working Memory	WMI	Digit Span, Arithmetic	Attention, mental manipulation
Processing Speed	PSI	Symbol Search, Coding	Speed of cognitive processing

Full Scale IQ (FSIQ): Composite of all four indices. Mean = 100, SD = 15. Deviation IQ.

Clinical applications:

- VCI-PIRI discrepancy > 15 points = clinically significant (lateralised brain damage, learning disabilities)
- Low WMI = ADHD, anxiety, frontal dysfunction
- Low PSI = depression, subcortical pathology, medication effects
- Scatter analysis across subtests = specific cognitive profiles

Strengths: Gold standard, excellent norms, deviation IQ, provides both global and specific cognitive profiles

Limitations: Expensive, requires trained administration, long, culture-bound

TEST 2: BINET-KAMAT TEST [4 MARKS]

(Refer to Q7 for full content, Development, structure, age-level items, administration, ratio IQ formula, classification, advantages, limitations)

Key points for comparison with WAIS-IV:

- Indian standardisation (WAIS norms are Western)
- Ratio IQ vs deviation IQ

- Global score only vs four index scores
- 1967 norms vs 2008 norms

Part C: Executive Functions and Clinical Relevance [8 marks]

DEFINITION

Executive functions (EFs) are a set of higher-order cognitive processes mediated primarily by the **prefrontal cortex** (especially dorsolateral prefrontal cortex, orbitofrontal cortex, and anterior cingulate cortex) that enable goal-directed behaviour. They are the "CEO of the brain", they control, regulate, and manage other cognitive processes.

COMPONENTS OF EXECUTIVE FUNCTION

COMPONENT	DEFINITION	TEST
Planning and organisation	Formulating a strategy, sequencing steps	Tower of London, Tower of Hanoi
Cognitive flexibility (set-shifting)	Switching between mental sets or strategies	Wisconsin Card Sorting Test (WCST), Trail Making Test B
Inhibitory control	Suppressing prepotent/automatic responses	Stroop Colour-Word Test, Go/No-Go tasks
Working memory	Holding and manipulating information online	Digit Span Backward, N-back task
Abstract reasoning	Forming concepts, identifying rules	WCST (categories), Similarities subtest
Verbal fluency	Generating words under constraints	Phonemic (FAS) and Semantic (animals) fluency
Decision-making	Evaluating outcomes and making choices	Iowa Gambling Task
Error monitoring	Detecting and correcting mistakes	Part of all EF tasks

TESTS OF EXECUTIVE FUNCTION

1. Wisconsin Card Sorting Test (WCST):

- Measures: Cognitive flexibility, abstract reasoning, perseveration
- Procedure: Sort cards by colour, form, or number; sorting rule changes without warning
- Key scores: Categories achieved, perseverative errors, total errors
- Perseverative errors = frontal dysfunction (inability to shift set)

2. Trail Making Test (TMT):

- **Part A:** Connect numbered circles in order (1-2-3...), measures processing speed, visual scanning

- **Part B:** Alternate between numbers and letters (1-A-2-B-3-C...), measures cognitive flexibility, set-shifting
- B-A difference = executive component
- Sensitive to frontal dysfunction

3. Stroop Colour-Word Test:

- Read colour words printed in incongruent ink colours (word "RED" printed in blue ink)
- Measures: Inhibitory control (suppressing automatic reading response)
- Stroop interference effect = increased time/errors
- Sensitive to anterior cingulate and prefrontal dysfunction

4. Frontal Assessment Battery (FAB):

- 6 subtests: conceptualisation (similarities), mental flexibility (phonemic fluency), motor programming (Luria sequence: fist-edge-palm), sensitivity to interference (conflicting instructions), inhibitory control (go/no-go), environmental autonomy (prehension behaviour)
- Score: 0-18; < 12 suggests frontal dysfunction
- Quick bedside test (10 minutes)

5. Verbal Fluency Tests:

- Phonemic (letter fluency): "Name as many words starting with F as you can in 60 seconds"
- Semantic (category fluency): "Name as many animals as you can in 60 seconds"
- Normal: 12-15 words per minute for phonemic; 15-20 for semantic
- Reduced fluency = frontal/temporal dysfunction

CLINICAL RELEVANCE OF EXECUTIVE DYSFUNCTION

CONDITION · EXECUTIVE DYSFUNCTION PATTERN

Frontal lobe lesions Global EF impairment, planning, inhibition, flexibility, personality change

Schizophrenia WCST perseveration, poor verbal fluency, planning deficits (dorsolateral prefrontal hypofunction)

ADHD Inhibitory control deficits, poor working memory, planning difficulties

Bipolar disorder EF deficits persist even in euthymia, set-shifting, verbal fluency, working memory

Frontotemporal dementia Early and severe EF impairment with relative memory preservation (vs Alzheimer's)

Alzheimer's disease EF affected later; memory and language affected first

Traumatic brain injury Frontal lobes vulnerable to contrecoup injury, disinhibition, poor planning

Substance use disorders Orbitofrontal dysfunction, impaired decision-making, impulsivity

OCD Set-shifting deficits (WCST), difficulty with cognitive flexibility

Antisocial personality Orbitofrontal dysfunction, poor decision-making, impaired response inhibition

EXAM PEARL

Executive dysfunction is transdiagnostic, it appears across most psychiatric disorders but is most prominent and earliest in conditions affecting the frontal lobes (FTD, TBI, schizophrenia, ADHD).

Q9. "Frontal lobe function tests." [10 marks]

Answer:

EXAM STRATEGY

Focused question, they want specific tests. Brief intro on frontal lobe functions (2 marks), then detailed description of tests (8 marks). Overlap with Q8 Part C.

Introduction [2 marks]

The frontal lobes, particularly the prefrontal cortex, mediate **executive functions**, higher-order cognitive processes including planning, cognitive flexibility, inhibitory control, working memory, abstract reasoning, decision-making, and social cognition. Frontal lobe dysfunction manifests across multiple psychiatric and neurological conditions including frontotemporal dementia, schizophrenia, ADHD, TBI, and substance use disorders.

Frontal lobe function tests assess these executive capacities. No single test captures all frontal functions; a battery approach is recommended.

Specific Tests [8 marks]

1. FRONTAL ASSESSMENT BATTERY (FAB)

- **Authors:** Dubois et al. (2000)
- **Time:** 10 minutes (bedside-friendly)
- **6 subtests:**

- **Conceptualisation (Similarities):** "In what way are a banana and an orange alike?", abstract reasoning (dorsolateral PFC)
- **Mental flexibility (Lexical fluency):** "Say as many words as you can beginning with S in 60 seconds", (dorsolateral PFC)
- **Motor programming (Luria sequence):** Fist-Edge-Palm sequence, motor planning and sequencing (supplementary motor area)
- **Sensitivity to interference (Conflicting instructions):** Tap once when examiner taps twice and vice versa, (medial PFC)
- **Inhibitory control (Go/No-Go):** Tap once when examiner taps once, do NOT tap when examiner taps twice, (medial/orbital PFC)
- **Environmental autonomy (Prehension behaviour):** "Do not take my hands" while placing hands in patient's, grasp reflex indicates frontal release (orbital PFC)
- **Scoring:** Each subtest 0-3; total 0-18; < 12 = **frontal dysfunction**

2. WISCONSIN CARD SORTING TEST (WCST)

- **Measures:** Cognitive flexibility, concept formation, set-shifting, perseveration
- **Procedure:** 128 response cards sorted to 4 stimulus cards by colour, form, or number. Rule changes after 10 correct sorts without warning.
- **Key scores:**
 - Categories completed (max 6), concept formation
 - Perseverative errors, failure to shift set (key frontal indicator)
 - Total errors
- **Clinical significance:** Perseverative errors are the hallmark of dorsolateral prefrontal dysfunction. Elevated in schizophrenia, FTD, and ADHD.

3. TRAIL MAKING TEST (TMT)

- **Part A:** Connect numbered circles in order (1→2→3...), processing speed, visual scanning
- **Part B:** Alternate numbers and letters (1→A→2→B→3→C...), **cognitive flexibility, set-shifting**
- **Scoring:** Time to completion; B-A difference = executive component
- **Cut-offs:** Part A > 78 sec, Part B > 273 sec = impaired
- **Sensitivity:** Part B is sensitive to frontal dysfunction; Part A alone is not specific to frontal lobes

4. STROOP COLOUR-WORD TEST

- **Three conditions:** Word reading, colour naming, interference (read colour of ink, not the word)
- **Stroop effect:** Increased time and errors when word and ink colour conflict

- **Measures: Inhibitory control**, ability to suppress automatic (reading) response in favour of controlled (colour naming) response
- **Neural basis:** Anterior cingulate cortex, dorsolateral PFC
- **Clinical use:** Impaired in ADHD, schizophrenia, TBI, FTD

5. VERBAL FLUENCY TESTS

- **Phonemic (letter fluency):** Generate words starting with F, A, S (1 minute each)
- **Semantic (category fluency):** Generate animal names in 1 minute
- **Normal:** Phonemic ~12-15/min; Semantic ~15-20/min
- **Phonemic fluency**, primarily frontal (dorsolateral PFC)
- **Semantic fluency**, temporal + frontal
- **Clinical pattern:** Phonemic < Semantic = frontal dysfunction; Semantic < Phonemic = temporal lobe dysfunction (Alzheimer's pattern)

6. TOWER OF LONDON / TOWER OF HANOI

- **Measures:** Planning, problem-solving, sequencing
- **Procedure:** Move coloured beads/ discs from initial position to target position in minimum moves
- **Scoring:** Number of moves to solution, planning time
- **Neural basis:** Dorsolateral PFC

7. IOWA GAMBLING TASK

- **Measures:** Decision-making under ambiguity, reward processing
- **Procedure:** Choose cards from 4 decks, 2 advantageous (small gains, smaller losses) and 2 disadvantageous (large gains, larger losses). Normal individuals learn to prefer advantageous decks.
- **Neural basis:** Ventromedial/ orbitofrontal cortex
- **Clinical use:** Impaired in patients with orbitofrontal lesions (Damasio's somatic marker hypothesis), substance use disorders, antisocial personality

8. GO/NO-GO TASKS

- **Measures:** Response inhibition
- **Procedure:** Respond to one stimulus (Go), withhold response to another (No-Go)
- **Neural basis:** Right inferior frontal gyrus, pre-supplementary motor area
- **Commission errors** (responding on No-Go trials) = poor inhibitory control

9. LURIA'S TESTS

- **Fist-Edge-Palm:** Motor sequencing (supplementary motor area)

- **Alternating sequences:** Draw alternating patterns (e.g., triangle-square-triangle...), perseveration if unable to alternate
- **Graphic sequencing:** Continue a pattern, tests motor programming

SUMMARY TABLE

TEST	PRIMARY EF DOMAIN	FRONTAL REGION
FAB	Multiple (screening)	Multiple frontal
WCST	Cognitive flexibility	Dorsolateral PFC
TMT-B	Set-shifting	Dorsolateral PFC
Stroop	Inhibitory control	Anterior cingulate, DLPFC
Verbal Fluency	Generativity	DLPFC (phonemic), temporal (semantic)
Tower of London	Planning	Dorsolateral PFC
Iowa Gambling	Decision-making	Orbitofrontal / ventromedial PFC
Go/No-Go	Response inhibition	Right inferior frontal gyrus

CROSS-REFERENCE MAP

QUESTION	OVERLAPPING CONTENT	NOTES
Q1, Q2, Q3, Q4, Q6	All ask about projective tests, define, list, describe	Same core structure. Q4 adds clinical psychiatry angle. Q5 is psychosis-specific. Q6 demands deepest Rorschach detail.
Q5	Rorschach in psychosis	Unique, focus on PTI, contamination, form quality, thought disorder indicators
Q7, Q8	Intelligence tests	Q7 focuses on BKT. Q8 is broader, theories + 2 tests + executive function.
Q8, Q9	Executive functions and frontal lobe tests	Q8 embeds EF within an intelligence essay. Q9 is standalone. Same content, different framing.

Mnemonics & Memory Tricks

Mnemonic 1: WAIS-IV Index Scores

Very Patient Women Prevail

MNEMONIC

Very Patient Women Prevail
EXAM PEARL: Encodes the 4 WAIS-IV Index Scores in order

LETTER	INDEX	CORE SUBTESTS
V	Verbal Comprehension Index (VCI)	Similarities, Vocabulary, Information
P	Perceptual Reasoning Index (PRI)	Block Design, Matrix Reasoning, Visual Puzzles
W	Working Memory Index (WMI)	Digit Span, Arithmetic
P	Processing Speed Index (PSI)	Symbol Search, Coding

The phrase "Very Patient Women Prevail" is a complete sentence with vivid imagery, easy to hold in working memory. The alliterative P-W-P pattern mirrors the actual index structure.

Mnemonic 2: WAIS-IV VCI Subtests

SVI

MNEMONIC

SVI
EXAM PEARL: Encodes the 3 core subtests of VCI

- S = Similarities
- V = Vocabulary
- I = Information

Three-letter abbreviation, reads like a word. Simple and tight.

Mnemonic 3: Rorschach Scoring Categories: LDCP

Look Deep, Check Popularity

MNEMONIC

Look Deep, Check Popularity

EXAM PEARL: Encodes the 4 main Rorschach scoring categories (in scoring order)

LETTER	CATEGORY	QUESTION IT ANSWERS
L	Location (W, D, Dd, S)	WHERE on the blot?
D	Determinants (F, M, C, T, Y, V)	WHAT features shaped the response?
C	Content (H, A, An, Bl, etc.)	WHAT did they see?
P	Popular responses	Is this commonly seen?

"Look Deep, Check Popularity" mirrors exactly what you do when scoring, first look at WHERE, then go DEEP into what features they used, then CHECK the content, and finally see if it's POPULAR. The mnemonic describes the scoring process itself.

Mnemonic 4: Rorschach Determinants: "For Many, Colour Tells You Vast Feelings"

F-M-C-T-Y-V-FD

MNEMONIC

For Many, Colour Tells You Vast Feelings

EXAM PEARL: Encodes the 7 major determinant categories

CODE	DETERMINANT	WHAT IT MEANS
F	Form	Shape of the blot only
M	Movement (human)	People doing something
C	Colour (chromatic)	Colour influenced perception (FC, CF, C)
T	Texture	Shading perceived as tactile (soft, rough)
Y	Diffuse shading	General dark/light shading
V	Vista	3D depth from shading

CODE	DETERMINANT	WHAT IT MEANS
FD	Form Dimension	Depth from form (not shading)

The sentence has natural rhythm and each word starts with the code letter. "Colour Tells You Vast Feelings" captures the interpretive spirit, colour = emotion, texture = attachment need, vista = self-reflection.

Mnemonic 5: TAT Need-Press Themes: "AAAD NAOS"

AAAD NAOS

MNEMONIC

AAAD NAOS

EXAM PEARL: Encodes the 8 most commonly scored Murray needs in TAT: Achievement, Affiliation, Aggression, Dominance, Nurturance, Autonomy, Order, Succorance

NEED · MEANING

n Achievement Drive to accomplish, excel

n Affiliation Need to belong, be close to others

n Aggression Hostility, dominance through force

n Dominance Need to control, lead, influence

n Nurturance Need to care for, help others

n Autonomy Need for independence, freedom

n Order Need for organisation, tidiness

n Succorance Need to be helped, supported, comforted

"AAAD NAOS" splits into two chunks of 4, which is within the working memory span. The word "NAOS" happens to mean the inner chamber of a Greek temple, fitting for accessing the inner chamber of personality through TAT.

Mnemonic 6: MMPI-2 Validity Scales: "Lying Fakers get K-orrected"

Lying Fakers get K-orrected

MNEMONIC

Lying Fakers get K-orrected
EXAM PEARL: Encodes the 3 primary MMPI-2 validity scales and what they detect

SCALE	NAME	WHAT HIGH SCORE MEANS
L	Lie	Faking good, naive defensiveness, unrealistic virtue
F	Infrequency	Faking bad, exaggeration, malingering, random responding
K	Correction	Subtle defensiveness, psychologically sophisticated denial

The sentence tells you exactly what each scale detects. L = lying (faking good), F = faking (bad), K = correction (subtle). The misspelling "K-orrected" cues the K scale while embedding its function. Also: order L-F-K matches standard MMPI profile order.

Mnemonic 7: MMPI-2 Clinical Scales 1-0: "Healthy Deeds Help People Make Positive Progress; Seek Happiness Socially"

Healthy Deeds Help People Make Positive Progress; Seek Happiness Socially

MNEMONIC

Healthy Deeds Help People Make Positive Progress; Seek Happiness Socially
EXAM PEARL: Encodes all 10 MMPI-2 clinical scales in order (1-0)

#	LETTER	SCALE	ABBREVIATION
1	Healthy	Hypochondriasis	Hs
2	Deeds	Depression	D
3	Help	Hysteria	Hy
4	People	Psychopathic Deviate	Pd
5	Make	Masculinity-Femininity	Mf
6	Positive	Paranoia	Pa
7	Progress	Psychasthenia	Pt

#	LETTER	SCALE	ABBREVIATION
8	Seek	Schizophrenia	Sc
9	Happiness	Hypomania	Ma
0	Socially	Social Introversion	Si

The sentence is a positive, memorable statement. The semicolon splits it into 7+3, matching the natural grouping (scales 1-7 are "clinical core"; 8-0 are the final three). Each first letter matches the scale abbreviation's first letter (H-D-H-P-M-P-P-S-H-S).

Mnemonic 8: Big Five (OCEAN)

Open Conscientious Extraverts Agree Neurotically

MNEMONIC

Open Conscientious Extraverts Agree Neurotically

EXAM PEARL: Encodes the 5 NEO-PI-R / Big Five personality domains

LETTER	DOMAIN	HIGH POLE	LOW POLE
O	Openness to Experience	Imaginative, curious	Conventional, narrow
C	Conscientiousness	Organised, disciplined	Careless, impulsive
E	Extraversion	Sociable, assertive	Reserved, quiet
A	Agreeableness	Trusting, cooperative	Suspicious, competitive
N	Neuroticism	Anxious, moody	Calm, stable

OCEAN is already a mnemonic, but the sentence adds meaning. "Open Conscientious Extraverts Agree Neurotically" describes a specific personality profile, someone who is open and disciplined and social and agreeable but also neurotic. This vivid personality picture makes it stickier than the bare acronym.

Mnemonic 9: Types of Validity: "Face the Content of the Criterion Construct"

Face the Content of the Criterion Construct

MNEMONIC

Face the Content of the Criterion Construct

EXAM PEARL: Encodes the 4 types of validity in psychological testing

TYPE	DEFINITION	HOW TO ASSESS
Face validity	Appears to measure what it claims (surface level)	Subjective judgment
Content validity	Items adequately sample the construct domain	Expert panel review
Criterion validity	Test correlates with external criterion (concurrent + predictive)	Correlation with criterion measure
Construct validity	Measures the theoretical construct (convergent + discriminant)	Factor analysis, multitrait-multimethod

The sentence reads as an instruction: "Face the Content of the Criterion Construct." It flows naturally and preserves the order from weakest (face) to strongest (construct) validity.

Mnemonic 10: Projective vs Objective Tests: "SURF vs SHORE"

SURF vs SHORE

MNEMONIC

SURF (projective) vs SHORE (objective)

EXAM PEARL: Encodes key differences between projective and objective tests

SURF (Projective tests):

- **S** = Stimuli are ambiguous/unstructured
- **U** = Unconscious material accessed
- **R** = Responses are free/open-ended
- **F** = Faking is harder

SHORE (Objective tests):

- **S** = Stimuli are structured/specific

- **H** = High reliability
- **O** = Objective scoring (standardised)
- **R** = Responses are fixed-choice
- **E** = Easy to administer (group, quick)

Surf = deep, unpredictable, hard to control (like projective tests). Shore = solid, structured, reliable (like objective tests). The metaphor mirrors the psychometric properties.

Mnemonic 11: Bender Gestalt Errors (Koppitz): "DRIP"

DRIP

MNEMONIC

DRIP

EXAM PEARL: Encodes the 4 categories of errors scored on the Bender Gestalt Test (Koppitz system)

ERROR	DESCRIPTION	EXAMPLE
D, Distortion	Shape is altered beyond recognition	Circle drawn as oval, angles wrong
R, Rotation	Design rotated > 45 degrees	Horizontal design drawn vertically
I, Integration failure	Parts not properly joined / aligned	Circles don't overlap where they should
P, Perseveration	Repeating elements beyond the stimulus	Drawing 15 dots when stimulus shows 8

"DRIP" is a single word, easy to recall under exam pressure. Visualise ink dripping on a page (messing up the Bender drawings).

Mnemonic 12: Intelligence Classification (Wechsler): The 15-Point Ladder

The 15-Point Ladder

MNEMONIC

Start at 100 (Average), go up or down in steps of ~15 (1 SD)

EXAM PEARL: Encodes the full Wechsler IQ classification system

IQ	CLASSIFICATION	STEPS FROM MEAN
130+	Very Superior	+2 SD
115-129	Superior / High Average	+1 to +2 SD
90-109	Average	-0.67 to +0.67 SD
80-89	Low Average	-0.67 to -1.33 SD
70-79	Borderline	-1.33 to -2 SD
< 70	Extremely Low (ID)	< -2 SD

The "15-point ladder" leverages the fact that Wechsler uses SD = 15. Each classification boundary is approximately 1 SD apart. Start at 100, go up by 15s (115, 130) or down by 15s (85, 70). The anchor points 70 and 130 are the clinical cut-offs (ID and gifted).

Mnemonic 13: Rorschach Card Popular Responses: "Bats Play Hard Ball"

Bats Play Hard Ball

MNEMONIC

Bats Play Hard Ball

EXAM PEARL: Encodes the most commonly tested Popular responses

CARD · POPULAR RESPONSE

Card I Bat or butterfly (whole blot)

Card II Two human figures

Card III Two people (most common P)

Card V Bat or butterfly (easiest card)

Card VIII Animals (bears / dogs on sides)

Card X Crabs or spiders (blue areas)

"Bats Play Hard Ball" gives you the most frequently examined populars. Card V = easiest card (almost everyone sees a bat), absence of P here is significant. Card III's two people is the single most commonly given popular response in the entire test.

Mnemonic 14: Frontal Lobe Tests: "WEST of the Frontal Lobe, Go FAB"

WEST of the Frontal Lobe, Go FAB

MNEMONIC

WEST of the Frontal Lobe, Go FAB
EXAM PEARL: Encodes the major frontal lobe / executive function tests

LETTER	TEST	MEASURES
W	Wisconsin Card Sorting Test	Cognitive flexibility, perseveration
E	Executive function tests (Tower of London, Iowa Gambling)	Planning, decision-making
S	Stroop Colour-Word Test	Inhibitory control
T	Trail Making Test (Part B)	Set-shifting
FAB	Frontal Assessment Battery	Bedside screening (6 subtests)
Go	Go/No-Go task	Response inhibition

"WEST of the Frontal Lobe, Go FAB", the frontal lobe IS the westernmost (anteriormost) part of the brain. And FAB is literally the Frontal Assessment Battery. The command "Go FAB" cues the Go/No-Go task too.

Mnemonic 15: Cattell's Gf vs Gc: "Fluid Falls, Crystal Climbs"

Fluid Falls, Crystal Climbs

MNEMONIC

Fluid Falls, Crystal Climbs
EXAM PEARL: Encodes the ageing trajectory of fluid vs crystallised intelligence

TYPE	TRAJECTORY WITH AGE	MEASURES	TEST EXAMPLE
Fluid (Gf)	Falls, peaks in 20s, declines after 60	Novel problem-solving, pattern recognition	Raven's Matrices, WAIS Matrix Reasoning
Crystallised (Gc)	Climbs, stable or increases through life	Accumulated knowledge, vocabulary	WAIS Vocabulary, Information subtests

Perfect alliterative pairing. "Fluid Falls", both start with F, and fluid literally falls (declines). "Crystal Climbs", both start with C, and crystals grow upward. The mnemonic encodes the single most clinically important fact about the Gf-Gc distinction: their opposite trajectories with ageing. This is critical for interpreting cognitive testing in elderly patients and differentiating normal ageing from dementia.

QUICK REFERENCE TABLE

#	MNEMONIC	ENCODES
1	Very Patient Women Prevail	WAIS-IV 4 indices (VCI, PRI, WMI, PSI)
2	SVI	VCI subtests
3	Look Deep, Check Popularity	Rorschach scoring categories (LDCP)
4	For Many, Colour Tells You Vast Feelings	Rorschach determinants (F-M-C-T-Y-V-FD)
5	AAAD NAOS	TAT Murray needs
6	Lying Fakers get K-orrected	MMPI validity scales (L, F, K)
7	Healthy Deeds Help People Make Positive Progress; Seek Happiness Socially	MMPI 10 clinical scales
8	Open Conscientious Extraverts Agree Neurotically	Big Five (OCEAN)
9	Face the Content of the Criterion Construct	4 types of validity
10	SURF vs SHORE	Projective vs objective tests
11	DRIP	Bender Gestalt errors
12	15-Point Ladder	Wechsler IQ classification
13	Bats Play Hard Ball	Rorschach popular responses
14	WEST of the Frontal Lobe, Go FAB	Frontal lobe tests
15	Fluid Falls, Crystal Climbs	Gf vs Gc ageing trajectory

High-Yield Comparisons

Table 1: Objective vs Projective Tests

FEATURE	OBJECTIVE TESTS	PROJECTIVE TESTS
Stimuli	Structured, specific questions with fixed options	Ambiguous, unstructured stimuli (inkblots, pictures, drawings)
Response format	Fixed-choice (true / false, Likert scale, multiple choice)	Free, open-ended (no right or wrong answer)
Scoring	Standardised, objective, computer-scorable	Requires trained examiner; subjective interpretation
Reliability	Generally high (test-retest, internal consistency)	Variable; often lower, especially inter-rater
Validity	Well-established criterion and construct validity	Debated; some evidence for specific applications (Rorschach for psychosis)
Faking	Easier to fake (but validity scales like L, F, K help detect)	Harder to fake (purpose less transparent)
Theoretical basis	Empirical / trait theory (factor analysis, criterion keying)	Psychodynamic / psychoanalytic (projection, unconscious)
Administration	Quick (30-90 min); can be group-administered	Time-consuming (45-120 min); individual only
Training required	Minimal, can be administered by technicians	Extensive, clinical psychologist with specialised training
What they measure	Conscious self-report of symptoms, traits, attitudes	Unconscious personality dynamics, defences, conflicts
Best for	Screening, diagnosis, research, treatment monitoring	Personality structure, therapy planning, forensic assessment
Examples	MMPI-2, 16PF, NEO-PI-R, EPQ, BDI, BAI	Rorschach, TAT, SCT, DAP, CAT, WAT, HTP

Table 2: Intelligence Tests: WAIS-IV vs WISC-V vs Stanford-Binet vs Binet-Kamat

FEATURE	WAIS-IV	WISC-V	STANFORD-BINET 5	BINET-KAMAT
Author	David Wechsler	David Wechsler	Binet/Terman (Roid, 2003)	V.V. Kamat (1934, rev. 1967)
Age range	16-90 years	6-16 years	2-85+ years	3-22 years
IQ type	Deviation IQ (M=100, SD=15)	Deviation IQ (M=100, SD=15)	Deviation IQ (M=100, SD=16)	Ratio IQ (MA/CA x 100)
Indices	4: VCI, PRI, WMI, PSI	5: VCI, VSI, FRI, WMI, PSI	5: FR, Kn, QR, VS, WM	None (global IQ only)
Core subtests	10	10	10 (5 verbal + 5 nonverbal)	Mixed verbal-performance, age-graded
Population norms	Western (US)	Western (US)	Western (US)	Indian
Languages available	English (adaptations available)	English (adaptations)	English	Kannada, Marathi, Hindi, English
Standardisation	2008 norms	2014 norms	2003 norms	1967 norms (outdated)
Administration	Individual; 60-90 min	Individual; 65-80 min	Individual; 50-75 min	Individual; 30-60 min
Key strength	Gold standard for adults; index scores allow profile analysis	5th index (VSI) separates visual-spatial from fluid reasoning	Wide age range; routing subtests	Indian norms; culturally adapted
Key limitation	Western norms; lengthy	Western norms	SD=16 (not directly comparable with Wechsler)	Ratio IQ; outdated norms; no factor scores
Clinical use	Adult cognitive assessment, ID diagnosis, neuropsychology	Child cognitive assessment, LD diagnosis, ADHD	Lifespan assessment, ID, giftedness	Most common IQ test in India; ID diagnosis, medico-legal

Table 3: Rorschach vs TAT vs Sentence Completion

FEATURE	RORSCHACH INKBLOT TEST	TAT	SENTENCE COMPLETION (RISB)
Author	Hermann Rorschach (1921)	Henry Murray (1935)	Julian Rotter (1950)
Stimulus	10 inkblot cards (5 achromatic, 5 chromatic)	31 picture cards (ambiguous social scenes)	40 sentence stems
Response type	What the person sees in the blot	Story about the picture (narrative)	Complete the sentence
Administration	Individual; 45-90 min (2 phases)	Individual; 60-120 min	Individual or group; 20-40 min
Scoring system	Exner Comprehensive System (standardised)	Murray Need-Press (not standardised universally)	0-6 conflict scale per response (total score)
What it measures	Personality structure, reality testing, thought disorder, coping style, affect regulation	Interpersonal themes, needs, press, object relations, unconscious conflicts	Attitudes, conflicts, adjustment level, specific problem areas
Psychometric properties	Better after Exner; adequate reliability, some validity evidence	Poor reliability and validity; no universally accepted system	Moderate reliability; reasonable validity for screening
Strengths	Standardised scoring; re-validated for psychosis; difficult to fake	Rich narrative data; reveals interpersonal patterns; reveals motivation	Quick; easy to administer; can be group-administered; quantifiable
Limitations	Time-consuming; extensive training needed; normative debates	Subjective; poor psychometrics; culturally biased pictures	Easier to fake than Rorschach/TAT; limited depth
Best for	Psychosis detection, personality structure, forensic	Interpersonal dynamics, therapy planning, motivation	Screening, identifying conflict areas, pre-therapy assessment

Table 4: MMPI-2 vs 16PF vs NEO-PI-R

FEATURE	MMPI-2	16PF (5TH ED.)	NEO-PI-R
Author	Hathaway & McKinley (1943/1989)	Raymond Cattell (1949/2003)	Costa & McCrae (1992)
Items	567 true/false	185 three-choice	240 five-point Likert
Time	60-90 minutes	35-50 minutes	35-45 minutes

FEATURE	MMPI-2	16PF (5TH ED.)	NEO-PI-R
Scales	10 clinical + 4 validity + supplementary	16 primary factors + 5 global factors	5 domains x 6 facets = 30 facets
Theoretical basis	Empirical criterion keying (atheoretical)	Factor analysis of trait descriptors (lexical)	Five-factor model (Big Five)
Population	Clinical/ psychiatric	Normal + clinical	Normal + clinical
Scoring approach	T-scores (M=50, SD=10); T≥65 = clinical	Sten scores (1-10); M=5.5, SD=2	T-scores (M=50, SD=10)
Validity scales	Yes, L, F, K, VRIN, TRIN, Fb, Fp	Yes, Impression Management, Infrequency, Acquiescence	Yes, 3 validity items
Best for	Psychopathology screening, personality disorder patterns, forensic	Personality profiling, career counselling, normal personality	Personality research, dimensional personality, trait description
Key strength	Most researched personality test; extensive validity data; good malingering detection	Comprehensive normal personality; useful for occupational settings	Gold standard for Big Five; excellent psychometrics; facet-level detail
Key limitation	Very long; outdated clinical scale names; item overlap between scales	Less clinical utility than MMPI	Less useful for detecting psychopathology

Table 5: IQ Classification (Wechsler System)

IQ RANGE	CLASSIFICATION	SD FROM MEAN	POPULATION %	CLINICAL SIGNIFICANCE
130+	Very Superior	> +2 SD	2.2%	Gifted; consider if academic underachievement present
120-129	Superior	+1.33 to +2 SD	6.7%	Above average; expected high academic performance
110-119	High Average	+0.67 to +1.33 SD	16.1%	Above average; competent
90-109	Average	-0.67 to +0.67 SD	50%	Population norm

IQ RANGE	CLASSIFICATION	SD FROM MEAN	POPULATION %	CLINICAL SIGNIFICANCE
80-89	Low Average	-0.67 to -1.33 SD	16.1%	May struggle with complex tasks; not ID
70-79	Borderline	-1.33 to -2 SD	6.7%	Borderline intellectual functioning; needs adaptive function check
69 and below	Extremely Low	< -2 SD	2.2%	Intellectual Disability (requires adaptive impairment also)

EXAM PEARL

Mean = 100, SD = 15 (Wechsler) or SD = 16 (Stanford-Binet). ID diagnosis requires BOTH IQ < 70 AND impaired adaptive functioning (Vineland). IQ alone does not determine severity of ID, adaptive functioning is the primary determinant in ICD-11.

Table 6: Projective Tests Overview

TEST	AUTHOR (YEAR)	STIMULUS	WHAT IT MEASURES	AGE RANGE
Rorschach Inkblot	Hermann Rorschach (1921)	10 inkblot cards	Personality structure, reality testing, thought disorder, coping	All ages (norms 5-90+)
TAT	Henry Murray (1935)	31 picture cards (social scenes)	Interpersonal themes, needs, press, object relations	Adolescents and adults
CAT	Leopold Bellak (1949)	10 cards with animal figures	Themes, defenses, identification (children)	Ages 3-10
Sentence Completion (RISB)	Julian Rotter (1950)	40 sentence stems	Attitudes, conflicts, adjustment level	Adolescents and adults
Draw-a-Person	Karen Machover (1949)	Blank paper + pencil	Body image, self-concept, interpersonal attitudes	All ages

TEST	AUTHOR (YEAR)	STIMULUS	WHAT IT MEASURES	AGE RANGE
House-Tree-Person	John Buck (1948)	Blank paper + pencil (draw H, T, P)	Home life (H), unconscious self (T), self-concept (P)	All ages
Word Association	Carl Jung (systematised)	List of stimulus words	Emotional complexes, reaction times, associations	Adolescents and adults
Bender Gestalt	Lauretta Bender (1938)	9 geometric designs to copy	Visual-motor integration, organic impairment, development	Ages 3+

Table 7: Cognitive Screening Tools: MMSE vs MoCA vs ACE-III

FEATURE	MMSE	MOCA	ACE-III
Full name	Mini-Mental State Examination	Montreal Cognitive Assessment	Addenbrooke's Cognitive Examination-III
Authors	Folstein et al. (1975)	Nasreddine et al. (2005)	Hsieh et al. (2013)
Max score	30	30	100
Cut-off (dementia)	< 24	< 26 (also MCI screen)	< 88 (dementia); < 82 (FTD specific)
Time	5-10 min	10 min	15-20 min
Domains tested	Orientation (10), Registration (3), Attention/Calculation (5), Recall (3), Language (8), Visuospatial (1)	Visuospatial/Executive (5), Naming (3), Memory (5, delayed), Attention (6), Language (3), Abstraction (2), Orientation (6)	Attention (18), Memory (26), Fluency (14), Language (26), Visuospatial (16)
Executive function testing	Minimal (serial 7s only)	Good (Trail B adaptation, clock drawing, abstraction)	Good (letter + category fluency)
MCI sensitivity	Poor (high ceiling effect)	Good , designed for MCI detection	Moderate

FEATURE	MMSE	MOCA	ACE-III
Dementia subtype differentiation	No	No	Yes , VLOM ratio differentiates AD (memory-dominant) vs FTD (fluency / language-dominant)
Education correction	No standard correction	+1 point if education $\leq$ 12 years	Available
Copyright	Yes (restrictive)	Free to use clinically	Free to use
Best for	Quick dementia screening in moderate-severe cases	MCI screening ; first-line cognitive screen	Differentiating AD vs FTD ; comprehensive cognitive profiling
Key limitation	Ceiling effect; misses MCI and executive dysfunction	May over-detect in low education	Longer; less suitable as bedside screen

EXAM STRATEGY

Routine screening / busy clinic: MoCA (best balance of sensitivity and time). Suspected MCI: MoCA (designed for this). AD vs FTD differentiation: ACE-III (VLOM ratio). Moderate-severe dementia tracking: MMSE (adequate; wide familiarity). Frontal dysfunction specifically: FAB (10 min, 6 subtests, bedside).

BONUS: Quick Comparison: Ratio IQ vs Deviation IQ

FEATURE	RATIO IQ	DEVIATION IQ
Formula	$(MA / CA) \times 100$	Based on normal distribution (M=100, SD=15 or 16)
Tests that use it	Binet-Kamat, original Stanford-Binet	WAIS-IV, WISC-V, SB5
Problem	IQ changes meaning with age (MA growth slows after ~16)	Comparable across ages (same meaning at any age)
Comparability	Not directly comparable across ages	Directly comparable
Statistical properties	SD varies by age	SD fixed (15 for Wechsler, 16 for SB)

PYQ Frequency Analysis

Executive Summary

Assessment and testing is a **moderately tested** cluster. Projective tests are the clear star, asked repeatedly in nearly identical form. Intelligence tests appear less often but when they do, they're substantial questions. Personality assessment (MMPI, 16PF) is rarely asked directly but appears embedded in other questions.

Topic-Level Frequency

TOPIC	EXAM MENTIONS	AVG PER EXAM	VERDICT
Projective tests	7-8	~0.28	Every 3-4 exams
Intelligence tests	3-4	~0.14	Every 6-7 exams
Personality assessment (MMPI, 16PF, NEO-PI)	1-2	~0.07	Rare but can appear
Frontal lobe function tests	2	~0.07	Often appears in neuroanatomy context
Combined cluster	~14	~0.5	~1 question every 2 exams

Key PYQs Identified

Projective Tests (most predictable)

1. "Projective tests." [10 marks], asked at least 4 times in identical form
2. "What is Projection? Name the different projective tests and describe one in detail." [10 marks]
3. "What do you understand by projective tests? Name different projective tests and describe any one in detail." [10 marks, split 2+2+6]
4. "Projective tests in psychiatry." [10 marks]
5. "Describe projective tests in psychoses." [10 marks]
6. "Name some projective tests. Discuss development, administration and assessment procedure of any one." [10 marks, split 2+8]

Intelligence Tests

1. "Psychological tests of intelligence, enumerate with a note on Binet Kamat test." [10 marks]
2. "Describe theories of intelligence. Describe any two standard tests. Describe executive functions, brain substrates and clinical relevance." [10 marks]
3. "Frontal lobe function tests." [10 marks], 2 appearances

Personality Assessment

1. "Define personality.", usually combined with Erikson or other topics
2. MMPI/16PF rarely asked as standalone

Long Essay Candidates

RANK	TOPIC	PROBABILITY
1	"Name projective tests. Describe Rorschach/TAT in detail."	High, asked 6+ times
2	"Enumerate intelligence tests. Describe Wechsler/Binet-Kamat in detail."	Medium
3	"Describe personality assessment tools in psychiatry."	Low-Medium

Exam Strategy

Must-Prepare

EXAM STRATEGY

Projective tests, ONE master answer: define projection, list all tests (Rorschach, TAT, SCT, draw-a-person, word association), then describe Rorschach AND TAT in detail (administration, scoring, interpretation, strengths, limitations).

EXAM STRATEGY

Binet-Kamat test, Indian adaptation, PG exams-specific favourite. Know author (V.V. Kamat), ratio IQ, Indian norms, age-level items, advantages over Western tests.

Should-Prepare

EXAM STRATEGY

Wechsler scales (WAIS, WISC, WPPSI), subtests, VIQ vs PIQ vs FSIQ. Know the 4 WAIS-IV indices and their core subtests.

EXAM STRATEGY

Frontal lobe tests (WCST, TMT, Stroop, verbal fluency), frequently appears embedded in neuroscience questions. Have the FAB 6-subtest list ready.

Nice-to-Know

EXAM PEARL

MMPI-2, know validity scales (L, F, K) and all 10 clinical scales with their numbers. Conversion V and paranoid valley patterns are favourites if personality assessment is asked.

EXAM PEARL

16PF, NEO-PI-R, Big Five model, rarely standalone but may appear in comparison questions alongside MMPI.

Analysis based on PG exams Dec 2011, Jun 2025 + PG exams 2013-2022.

Quick Review

SECTION A: INTELLIGENCE TESTS (Q1-Q10)

Q1. Name the four index scores of the WAIS-IV and one core subtest for each. [Recall]

Answer:

1. **Verbal Comprehension Index (VCI)**, Similarities
 2. **Perceptual Reasoning Index (PRI)**, Block Design
 3. **Working Memory Index (WMI)**, Digit Span
 4. **Processing Speed Index (PSI)**, Coding
-

Q2. Who developed the Binet-Kamat Test, when was it standardised, and what type of IQ does it yield? [Recall]

Answer: Developed by **V.V. Kamat** (originally adapted by C.H. Rice). Standardised in **1934**, revised **1967**. Yields a **ratio IQ** ($\text{Mental Age} / \text{Chronological Age} \times 100$). Available in Kannada, Marathi, Hindi, and English. Age range 3-22 years.

Q3. A 72-year-old retired professor scores 28/30 on MMSE but his family reports significant personality change and poor planning. What cognitive screening tool would be more appropriate and why? [Application]

Answer: **MoCA** or **ACE-III** would be more appropriate. The MMSE has a **ceiling effect**, it is insensitive to mild cognitive impairment and executive dysfunction. This patient likely has **frontal lobe pathology** (personality change + poor planning suggests possible frontotemporal dementia). MoCA includes executive tasks (Trail B adaptation, clock drawing, abstraction). ACE-III is even better for differentiating AD from FTD using the **VLOM ratio** (Verbal fluency + Language vs Orientation + Memory). The **Frontal Assessment Battery (FAB)** would also be indicated for direct frontal lobe assessment.

CLINICAL ANCHOR

MMSE ceiling effect is the classic trap question. Any score near 30/30 with cognitive or behavioural concerns, reach for MoCA or ACE-III.

Q4. You need to assess the intelligence of a 5-year-old child from a rural Kannada-speaking family who has never attended school. Which intelligence test would you choose and why? [Application]

Answer: Binet-Kamat Test, it is the most appropriate because:

1. Available in **Kannada** (child's language)
2. **Indian norms** (standardised on Indian population, unlike WISC or Stanford-Binet)
3. Age range covers 3-22 years (includes this child)
4. Has age-level items appropriate for a 5-year-old (counting objects, copying square, comprehension)

If a non-verbal measure is also needed (given no schooling), supplement with **Seguin Form Board** (no language required, quick) or **Raven's Coloured Progressive Matrices** (culture-fair, no reading).

Q5. What are Cattell's two types of intelligence, and how do they change with age? [Recall]

Answer:

- **Fluid intelligence (Gf):** Novel problem-solving, pattern recognition, abstract reasoning. **Peaks in the 20s, declines after 60.** Measured by Raven's Matrices, WAIS Matrix Reasoning.
- **Crystallised intelligence (Gc):** Accumulated knowledge, vocabulary, learned skills. **Remains stable or increases throughout life.** Measured by WAIS Vocabulary, Information subtests.

EXAM PEARL

Mnemonic: **Fluid Falls, Crystal Climbs.**

Q6. A patient's WAIS-IV shows VCI = 112, PRI = 108, WMI = 78, PSI = 75. FSIQ = 94. What does this profile suggest clinically? [Analysis]

Answer: This profile shows **intact verbal and perceptual abilities** (VCI and PRI in the High Average/ Average range) but **significantly impaired Working Memory and Processing Speed** (both in the Borderline range). The VCI/PRI vs WMI/PSI discrepancy is > 30 points, which is highly clinically significant.

This pattern is characteristic of:

- **ADHD**, poor sustained attention and working memory with preserved reasoning
- **Depression**, psychomotor slowing affecting PSI; poor concentration affecting WMI
- **Subcortical pathology**, PSI is sensitive to subcortical (white matter) dysfunction
- **Medication effects**, sedating medications suppress processing speed

The FSIQ of 94 (Average) **masks** the significant intra-individual variability. Reporting only FSIQ would be misleading, the index-level profile is essential for accurate clinical interpretation.

Q7. Compare Raven's Progressive Matrices and WAIS-IV. When would you use each?
[Analysis]

Answer:

Raven's measures primarily **fluid intelligence (Gf)** / Spearman's g using non-verbal visual patterns. It is culture-fair, requires no reading, can be group-administered, and takes 20-40 minutes. However, it provides only a single score, no profile analysis.

WAIS-IV is a comprehensive individual test measuring verbal comprehension, perceptual reasoning, working memory, and processing speed. It yields 4 index scores and FSIQ, enabling profile analysis and clinical inference. Takes 60-90 minutes and requires trained administration.

Use Raven's when:

- Screening large groups (school, military, employment)
- Assessing non-English speakers or culturally different populations
- Need a quick, culture-fair estimate of intellectual potential
- Research requiring a brief g measure

Use WAIS-IV when:

- Full clinical assessment is needed (diagnostic workup)
- ID diagnosis requires comprehensive cognitive profile
- Neuropsychological assessment (need index discrepancy analysis)
- Medico-legal evaluation requiring detailed documentation

Q8. What are the three components of Sternberg's Triarchic Theory of Intelligence? [Recall]

Answer:

1. **Analytical (Componential):** Academic problem-solving, critical thinking, what traditional IQ tests measure
2. **Creative (Experiential):** Ability to deal with novelty, generate new ideas, automatise processes
3. **Practical (Contextual):** Adaptation to real-world environments, "street smarts," knowing how to navigate social and practical situations

Q9. A 4-year-old is brought for developmental assessment. The developmental paediatrician reports DQ = 68 using the Bayley Scales. Does this confirm intellectual disability? [Application]

Answer: No. A DQ of 68 does NOT confirm intellectual disability for several reasons:

1. **DQ is not IQ**, Developmental Quotient measures motor, language, social, and adaptive milestones, not cognitive ability as measured by intelligence tests
2. **Predictive validity of DQ for later IQ is poor** in the normal-to-borderline range, especially at age 4
3. ID diagnosis requires both **IQ < 70 AND impaired adaptive functioning** (ICD-11, DSM-5)
4. A formal IQ test (Binet-Kamat for Indian setting, or WPPSI-IV) should be administered, along with **Vineland Adaptive Behavior Scales** for adaptive functioning
5. Serial assessments are needed, cognitive trajectory may change with intervention

The DQ raises concern and warrants further evaluation, but it is a screening indicator, not a diagnostic confirmation.

Q10. Why is the Vineland Adaptive Behavior Scale essential for diagnosing intellectual disability, even when IQ is clearly below 70? [Analysis]

Answer: Because both ICD-11 and DSM-5 require **impairment in adaptive functioning** in addition to low IQ for an ID diagnosis. IQ alone is insufficient because:

1. **Adaptive functioning determines real-world impact**, some individuals with IQ < 70 function independently in daily life, while others with IQ in the borderline range cannot
 2. **IQ tests have measurement error**, confidence intervals mean a score of 68 could represent true IQ of 63-73
 3. **Severity classification in ICD-11 is based on adaptive functioning, NOT IQ**, mild, moderate, severe, and profound are determined by how independently the person functions, not their IQ number
 4. **The Vineland measures what IQ cannot**, Communication, Daily Living Skills, Socialisation, and Motor Skills in real-world contexts, as reported by a caregiver
 5. **Cultural and linguistic factors** may artificially lower IQ scores (especially on verbally loaded tests) without reflecting true adaptive capacity
-

SECTION B: PROJECTIVE TESTS (Q11-Q20)

Q11. What is the projective hypothesis and who first articulated it? [Recall]

Answer: The **projective hypothesis** was articulated by **Lawrence Frank (1939)**. It states that when an individual is confronted with an **ambiguous, unstructured stimulus**, they project their unconscious needs, conflicts, desires, defence mechanisms, and personality characteristics onto the stimulus through their responses. The lack of structure forces the person to impose their own psychological meaning, thereby revealing inner personality dynamics that may not be accessible through structured self-report measures. Theoretical basis: psychoanalytic concept of projection (Freud).

Q12. Name the four main scoring categories in the Rorschach (Exner's Comprehensive System) and give one example code for each. [Recall]

Answer:

1. **Location**, W (whole blot), D (common detail), Dd (unusual detail), S (white space)
2. **Determinants**, F (form), M (human movement), C (colour), T (texture), Y (shading), V (vista)
3. **Content**, H (whole human), A (whole animal), An (anatomy), Bl (blood)
4. **Popular (P)**, Responses given by $\geq 1/3$ of population (e.g., Card V = bat/butterfly)

EXAM PEARL

Mnemonic: **Look Deep, Check Popularity (LDCP)**

Q13. A patient's Rorschach protocol shows $X+\% = 45\%$, $X-\% = 35\%$, elevated PTI score, and 3 contamination responses. What does this indicate? [Application]

Answer: This indicates **severely impaired reality testing and thought disorder**, highly suggestive of a **psychotic process**:

- **$X+\% = 45\%$** (normal $> 70\%$): Only 45% of responses match conventional form, the patient frequently perceives things that don't match the actual blot shape
- **$X-\% = 35\%$** (normal $< 15\%$): 35% of responses show distorted form quality, significant perceptual distortion
- **Elevated PTI (Perceptual Thinking Index)**: Composite index screening for thought disorder, replaces the older SCZI
- **Contamination responses**: Two images fused into one (e.g., "a butterfly-man"), considered **pathognomonic of psychosis** in Rorschach interpretation; reflects breakdown of conceptual boundaries

This profile is consistent with schizophrenia or another psychotic disorder with active thought disorder and impaired reality testing.

Q14. In a TAT administration, a patient consistently tells stories where the hero is abandoned by authority figures, seeks help but is rejected, and outcomes are uniformly negative. Using Murray's framework, what needs and press dominate? [Application]

Answer:

Dominant needs:

- **n Succorance**, the hero consistently seeks help and support from others
- **n Affiliation**, desire for closeness, belonging

- **n Abasement**, submissive, self-blaming positioning

Dominant press:

- **p Rejection**, authority figures consistently abandon and reject
- **p Loss**, repeated themes of loss and deprivation
- **p Aggression (dominant)**, hostile, controlling environment

Thema: Succorance-Rejection, the hero needs help but the world rejects them.

Clinical interpretation: This pattern suggests:

- **Insecure/anxious attachment** (possibly disorganised)
 - **Depressive/pessimistic worldview** (uniformly negative outcomes)
 - **Possible early maladaptive schemas** (Abandonment/Instability, Emotional Deprivation, Mistrust/Abuse in Schema Therapy terms)
 - **Object relations:** Expectation that caregiving figures are unreliable and rejecting
-

Q15. What are the two phases of Rorschach administration and what is the purpose of each? [Recall]

Answer:

1. **Free Association (Response Phase):** Each card presented with "What might this be?" All responses recorded verbatim. Purpose: **collect spontaneous responses** without influencing the examinee. No prompting, no time limit.
 1. **Inquiry Phase:** After all 10 cards, return to each response and ask "Where did you see it?" and "What about it made it look like that?" Purpose: **determine the location and determinants** used in each response, essential for accurate scoring. No new responses should be introduced.
-

Q16. A defence attorney argues that the Rorschach should not be admitted as evidence because it is "subjective and unscientific." How would you respond as an expert witness? [Analysis]

Answer: When administered and scored using **Exner's Comprehensive System (CS)** or the newer **R-PAS**, the Rorschach has adequate psychometric properties for forensic use:

In support of admissibility:

- The CS provides **standardised administration, scoring, and normative data**, it is not purely subjective
- **Inter-rater reliability** for major scoring categories (location, determinants, popular responses) is generally adequate ($\kappa > 0.80$ for most variables)

- Specific indices have **demonstrated validity**: the Suicide Constellation (S-CON) is a validated predictor of suicide risk; the PTI has validity for detecting thought disorder
- It is **difficult to fake**, a significant advantage over self-report measures in forensic settings
- The Rorschach is included in major forensic assessment batteries and has survived Daubert challenges

Concessions:

- Inter-rater reliability drops for complex scoring decisions
- Normative data has been debated (Exner norms vs international norms)
- It should **never be used as the sole basis** for forensic opinions, it is one component of a comprehensive assessment battery
- Incremental validity over self-report measures is limited for many constructs

The key distinction: the Rorschach scored with CS/R-PAS is a standardised instrument with empirical support for specific applications; the Rorschach scored "intuitively" without a formal system is indeed problematic.

Q17. You are assessing a 7-year-old child and want to use a projective test. The child is shy and non-verbal in the assessment setting. Which projective test would you choose and why? [Application]

Answer: Draw-a-Person (DAP) or House-Tree-Person (HTP) would be the best choice because:

1. **No verbal response required**, the child draws rather than speaks
2. **Non-threatening**, drawing feels like play, not testing
3. **Developmentally appropriate**, children this age are comfortable with drawing tasks
4. **Minimal instructions**, "Draw a person" requires no complex comprehension

Alternative: The **Children's Apperception Test (CAT)** uses animal figures (less threatening than human figures) but requires verbal storytelling, which this shy child may not provide.

Bender Gestalt Test could also be used, copying geometric designs requires no verbal output and provides information about visual-motor integration and developmental maturity.

The DAP can be scored for both **projective interpretation** (Machover) and **cognitive development** (Goodenough-Harris), giving dual value from a single brief task.

Q18. Why are projective tests considered more useful for personality assessment than for categorical psychiatric diagnosis? [Analysis]

Answer: Projective tests are better suited for personality assessment than diagnosis because of their fundamental design and psychometric properties:

Why they work for personality:

- They access **unconscious personality dynamics**, defences, conflicts, object relations, coping styles, which are dimensional and stable
- They provide **rich qualitative data** about HOW a person perceives and organises experience, not just WHAT symptoms they report
- They reveal **personality structure** (e.g., Rorschach EB reveals introversive vs extratensive style; TAT themes reveal interpersonal patterns)
- They are difficult to fake, accessing deeper personality layers

Why they fail for categorical diagnosis:

- Psychiatric diagnoses (DSM/ICD) are based on **observable symptoms and specific criteria**, projective tests do not map directly onto diagnostic checklists
- **Reliability** is insufficient for binary diagnostic decisions, the same protocol may be interpreted differently by different clinicians
- **Base rate problems**, many "diagnostic indicators" have high false-positive rates in the general population
- **Incremental validity** over structured clinical interviews (like SCID) for diagnosis is minimal
- Diagnosis requires **syndromal pattern recognition** that structured instruments do better

Exception: The Rorschach has demonstrated specific validity for detecting **thought disorder in psychosis** (PTI) and **suicide risk** (S-CON), these are narrow, well-validated applications.

Q19. What is the Children's Apperception Test (CAT), who developed it, and how does it differ from the TAT? [Recall]

Answer:

- **Authors:** Leopold Bellak and Sonya Sorel Bellak (1949)
- **Stimulus:** 10 cards with **animal figures** in human-like social situations
- **Age range:** 3-10 years
- **Key difference from TAT:** Uses **animals instead of humans** because children identify more readily with animal characters (based on the psychoanalytic principle that children project more freely onto animals)
- **CAT-H (Human version):** Same situations depicted with human figures, used for older children (7-10) who may find animal figures juvenile

- **Scoring:** Similar to TAT, themes, defences, identification figures, outcomes, emotional tone
 - **Clinical use:** Assessing children's unconscious conflicts, family dynamics, fears, aggression, regression
-

Q20. A colleague says "Projective tests have no evidence base and should be abandoned." Evaluate this claim. [Analysis]

Answer: This claim is **overly simplistic**. The evidence base is mixed, not absent:

What the evidence supports:

- The Rorschach (Exner CS / R-PAS) has demonstrated validity for **specific applications:** thought disorder detection, reality testing assessment, and suicide risk prediction
- Meta-analyses (Mihura et al., 2013) show that some Rorschach variables have validity coefficients comparable to popular medical tests
- The TAT has utility in **psychotherapy process** research and identifying interpersonal themes, even if formal psychometric validity is limited
- Sentence Completion Tests have adequate reliability and validity as screening instruments

What the evidence criticises:

- Many projective test variables have **poor reliability and limited validity** when used outside their validated applications
- **Incremental validity** over self-report measures and clinical interviews is often modest
- Interpretation depends heavily on clinician training and theoretical orientation
- Some claims (e.g., detailed personality interpretation from DAP drawings) have **no empirical support**

Balanced conclusion: Projective tests should not be abandoned wholesale, but their use should be **evidence-based and circumscribed**, Rorschach for thought disorder and personality structure using standardised scoring; TAT for understanding interpersonal dynamics in therapy contexts; other projective tests primarily as clinical hypothesis generators rather than definitive assessment tools. They complement, but do not replace, structured instruments.

SECTION C: PERSONALITY ASSESSMENT (Q21-Q30)

Q21. List the 10 clinical scales of the MMPI-2 with their numbers and abbreviations. [Recall]

Answer:

#	ABBREVIATION	SCALE NAME
1	Hs	Hypochondriasis
2	D	Depression
3	Hy	Hysteria (Conversion)
4	Pd	Psychopathic Deviate
5	Mf	Masculinity-Femininity
6	Pa	Paranoia
7	Pt	Psychasthenia
8	Sc	Schizophrenia
9	Ma	Hypomania
0	Si	Social Introversion

EXAM PEARL

Mnemonic: **Healthy Deeds Help People Make Positive Progress; Seek Happiness Socially**

Q22. What are the three primary MMPI-2 validity scales, and what does each detect?
[Recall]

Answer:

- **L (Lie):** Detects **faking good**, naive defensiveness, presenting an unrealistically positive self-image. People claiming never to have told a lie, never been angry, etc.
- **F (Infrequency):** Detects **faking bad**, exaggeration of symptoms, malingering, random responding. Items rarely endorsed by anyone, even psychiatric patients.
- **K (Correction/Defensiveness):** Detects **subtle defensiveness**, psychologically sophisticated denial of problems. Unlike L, K-elevated individuals appear well-adjusted rather than unrealistically perfect.

EXAM STRATEGY

Always interpret validity scales **FIRST**. If the profile is invalid (e.g., $F > 100T$, $L > 80T$, $? > 30$), clinical scales cannot be meaningfully interpreted.

EXAM PEARL

Mnemonic: **Lying Fakers get K-orrected**

Q23. An MMPI-2 profile shows T-scores: Scale 1 (Hs) = 78, Scale 3 (Hy) = 82, Scale 2 (D) = 52. All validity scales are within normal limits. What is this profile pattern called and what does it suggest? [Application]

Answer: This is the "**Conversion V**" (also called the "V pattern" or "hysteric valley"):

- Scales 1 (Hypochondriasis) and 3 (Hysteria) are **elevated** (T > 65)
- Scale 2 (Depression) is **low/normal**, creating a V-shaped dip between the two elevated scales

Clinical interpretation:

- Classic pattern for **conversion disorder / somatic symptom disorder**
- The person presents with significant somatic complaints (high Hs) and uses **somatisation as a defence** (high Hy) but does NOT report subjective distress or depression (low D)
- Suggests **la belle indifférence**, lack of appropriate concern about physical symptoms
- These patients typically seek medical rather than psychiatric help
- May also be seen in chronic pain presentations and somatoform disorders

Differential: In the 2-point code system, this is a **1-3/3-1 code type**.

Q24. Name the Big Five personality traits (OCEAN) and give the high and low poles of each. [Recall]

Answer:

DOMAIN	HIGH POLE	LOW POLE
O, Openness	Imaginative, curious, open to new experiences	Practical, conventional, narrow interests
C, Conscientiousness	Organised, disciplined, reliable	Careless, disorganised, impulsive
E, Extraversion	Sociable, assertive, active, energetic	Reserved, solitary, quiet
A, Agreeableness	Trusting, cooperative, altruistic	Suspicious, competitive, antagonistic
N, Neuroticism	Anxious, moody, emotionally unstable	Calm, stable, emotionally resilient

Q25. A patient scores very high on Neuroticism and very low on Agreeableness and Conscientiousness on the NEO-PI-R. Which personality disorder pattern does this most closely resemble? [Application]

Answer: This Big Five profile (High N + Low A + Low C) most closely resembles **Antisocial Personality Disorder**:

- **High Neuroticism:** Emotional instability, angry hostility, impulsiveness (facets of N map onto affective instability and irritability)
- **Low Agreeableness:** Antagonistic, manipulative, deceitful, lacking empathy, core features of ASPD
- **Low Conscientiousness:** Impulsive, irresponsible, fails to plan ahead, disregards obligations, maps onto the behavioural component of ASPD

Other associations:

- If Extraversion is also high: more overt, aggressive antisocial pattern
- If Extraversion is low: more covert, detached pattern (may suggest schizoid features)
- High N + Low A alone (with normal C): could be Narcissistic or Paranoid PD
- High N + High A + Low C: Dependent PD pattern

The Big Five dimensional model of personality disorder is supported by significant research and forms the basis of the alternative DSM-5 model (Section III).

Q26. Compare the MMPI-2 and MCMI-IV. When would you prefer one over the other?
[Analysis]

Answer:

FEATURE	MMPI-2	MCMI-IV
Focus	General psychopathology	Personality disorders specifically
Items	567	195
Time	60-90 min	25-30 min
Scoring	T-scores	Base Rate (BR) scores
Population	Clinical + general	Clinical/psychiatric only
Alignment	Empirical (atheoretical)	DSM personality disorder categories

Prefer MMPI-2 when:

- Comprehensive psychopathology screening is needed
- Forensic evaluation (most validated, most legally defensible)
- Need to assess malingering / faking (superior validity scales)
- Research requiring comparison with extensive normative data

Prefer MCMI-IV when:

- Primary question is about personality disorder diagnosis
- Patient is already in psychiatric treatment
- Need a shorter instrument
- Want direct alignment with DSM personality categories
- Millon's theoretical model is relevant to the clinical question

EXAM PEARL

MCMI-IV should **never** be used with non-clinical populations, its base rate scoring assumes a clinical sample and will produce inflated pathology scores in normal individuals.

Q27. A patient's MMPI-2 shows F = 110T, L = 45T, K = 38T. What does this validity profile suggest? Can you interpret the clinical scales? [Application]

Answer: This validity profile shows:

- **F = 110T** (extremely elevated): Very high endorsement of rare/unusual items
- **L = 45T** (normal): Not faking good
- **K = 38T** (low): Not being defensive; possibly over-reporting problems

This profile suggests one of:

1. **Malingering / faking bad**, deliberately exaggerating symptoms (most common forensic explanation)
2. **Severe genuine psychopathology**, a truly disturbed patient may endorse many unusual items
3. **Random responding**, check VRIN/TRIN scales to rule this out
4. **Cry for help**, consciously or unconsciously amplifying distress to ensure being taken seriously

Can you interpret clinical scales? With F = 110T, the profile is likely **invalid** and clinical scales should be interpreted with **extreme caution**. If F > 100T but VRIN is normal (ruling out random responding), and the patient has severe known psychopathology, cautious interpretation may be possible. Otherwise, the clinical scale elevations are unreliable and likely reflect over-reporting rather than true clinical status.

EXAM STRATEGY

Next step: Check Fp (Infrequency-Psychopathology), if Fp is also very high, malingering is more likely (even genuine psychiatric patients rarely endorse Fp items).

Q28. What are Eysenck's three personality superfactors, and what is the biological basis he proposed for extraversion? [Recall]

Answer:

1. **Extraversion (E):** Sociable, lively, active vs reserved, quiet
2. **Neuroticism (N):** Emotional instability, anxiety vs stability, calm
3. **Psychoticism (P):** Tough-minded, aggressive, cold vs empathic, conventional

Biological basis of Extraversion: Eysenck proposed that introverts have **chronically higher cortical arousal** (ascending reticular activating system) than extraverts. Because introverts are already over-aroused, they avoid stimulation (prefer quiet, solitary activities). Extraverts are chronically **under-aroused** and therefore seek external stimulation (social interaction, novelty, risk-taking) to reach an optimal arousal level. This is the **cortical arousal theory** of extraversion.

Q29. A researcher wants to develop a new personality test. She asks you about different test construction strategies. Compare empirical criterion keying (MMPI approach) with factor-analytic (16PF approach) and theoretical (NEO-PI-R approach). [Analysis]

Answer:

STRATEGY	METHOD	EXAMPLE	STRENGTH	WEAKNESS
Empirical criterion keying	Items selected because they statistically discriminate between known groups (e.g., depressed vs non-depressed), regardless of item content	MMPI	Empirically grounded; items work even if content seems unrelated to the construct	Atheoretical; items may lack face validity; overlap between scales
Factor-analytic	Large item pools administered to large samples; factor analysis identifies clusters of co-varying items as "factors"	16PF	Data-driven; identifies natural personality dimensions; reduces redundancy	Factors depend on the items included; different item pools yield different factor structures
Theoretical / rational	Items written to measure specific constructs defined by a theoretical model; factor analysis confirms structure	NEO-PI-R (Big Five model)	Theory-driven; clear construct definitions; facet-level detail	Model may miss important personality dimensions outside the theory; assumes the theory is correct

EXAM PEARL

A modern test development approach combines all three, start with a theoretical model, write rational items, use factor analysis to refine structure, and validate against external criteria. The NEO-PI-R exemplifies this combined approach.

Q30. You are asked to design a comprehensive personality assessment battery for a new patient in a forensic psychiatry setting. Which tests would you include and why? [Analysis]

Answer: A forensic personality assessment battery should include multiple methods to maximise validity and detect response bias:

1. MMPI-2 (or MMPI-2-RF)

- **Why:** Most validated personality test in forensic settings; excellent validity scales (L, F, K, Fp) for detecting malingering and defensiveness; extensive legal precedent; clinical scales identify psychopathology
- **Role:** Objective personality and psychopathology screening

2. MCMI-IV

- **Why:** Specifically designed for personality disorder assessment; aligned with DSM categories; shorter than MMPI; base rate scoring appropriate for clinical populations
- **Role:** Personality disorder characterisation

3. Rorschach (Exner CS or R-PAS)

- **Why:** Difficult to fake (advantage over self-report in forensic settings); provides data on reality testing, thought disorder, personality structure that self-report cannot; cross-validates MMPI findings
- **Role:** Personality structure, reality testing, thought disorder assessment

4. PCL-R (Psychopathy Checklist-Revised)

- **Why:** Gold standard for psychopathy assessment in forensic settings; semi-structured interview + file review; validated predictor of recidivism and violence risk
- **Role:** Psychopathy assessment (if relevant to referral question)

5. Structured interview (e.g., SCID-5-PD or SIDP-IV)

- **Why:** Direct assessment of personality disorder criteria; structured format reduces bias
- **Role:** Personality disorder diagnosis confirmation

Rationale for multi-method approach:

- No single instrument is sufficient for forensic conclusions
- Self-report (MMPI) can be cross-validated with performance-based (Rorschach) measures

- Malingering detected by MMPI validity scales can be corroborated by Rorschach response patterns
 - Convergent findings across methods strengthen conclusions; divergent findings require explanation
-

GUIDE 04 · PART I

Research Methods

Paper I · Basic Sciences. Six study modes, from notes to quick review.

Study Notes

1. VALIDITY

1.1 Definition

Validity = the degree to which a test or instrument measures what it claims to measure. A valid IQ test actually measures intelligence, not reading speed.

1.2 Types of Validity

TYPE	DEFINITION	EXAMPLE IN PSYCHIATRY
Face	Appears to measure what it claims (subjective judgment)	PHQ-9 "looks like" a depression questionnaire
Content	Covers the full domain of the construct	HAM-D covers mood, guilt, insomnia, psychomotor, somatic, the full depression domain
Criterion	Correlates with an external gold standard	MMSE score correlates with clinical dementia diagnosis
Construct	Measures the theoretical construct accurately	BDI correlates with other depression measures (convergent) but not with anxiety measures (discriminant)

1.3 Criterion Validity: Two Subtypes

SUBTYPE	TIMING	EXAMPLE
Concurrent	Test and criterion measured at the same time	New depression scale given alongside HAM-D to same patients
Predictive	Test predicts a future outcome	GRE score predicting future academic performance

1.4 Construct Validity: Two Subtypes

SUBTYPE	DEFINITION	EXAMPLE
Convergent	Correlates with measures of the same construct	BDI correlates highly with PHQ-9 (both measure depression)

SUBTYPE	DEFINITION	EXAMPLE
Discriminant	Does NOT correlate with measures of different constructs	BDI should not correlate highly with a mania scale

1.5 Internal vs External Validity

FEATURE	INTERNAL VALIDITY	EXTERNAL VALIDITY
Definition	Degree to which results are due to the independent variable, not confounders	Degree to which results can be generalised to other populations/settings
Focus	Cause-and-effect accuracy	Applicability beyond the study
Stronger in	RCTs (controlled environment)	Community-based studies, pragmatic trials
Threats	Selection bias, maturation, testing effects, history, attrition, instrumentation, regression to mean	Sampling bias, Hawthorne effect, setting specificity, volunteer bias
Trade-off	Tight control increases internal but may reduce external	Broad inclusion increases external but may reduce internal

1.6 Threats to Internal Validity (Mnemonic: SHRIMP-T)

- **Selection bias**, groups differ at baseline
- **History**, external events during study affect outcome
- **Regression to the mean**, extreme scores regress on retesting
- **Instrumentation**, measurement tool changes during study
- **Maturation**, natural changes over time in participants
- **Practice / testing effects**, repeated testing improves performance
- **Testing attrition**, differential dropout between groups

1.7 Threats to External Validity

- **Sampling bias**, non-representative sample
- **Hawthorne effect**, participants alter behaviour when observed
- **Setting specificity**, results only apply in that setting (e.g., tertiary care ≠ community)
- **Volunteer bias**, volunteers differ systematically from non-volunteers
- **Interaction of treatment and context**, drug works in young males but not elderly females

2. RELIABILITY

2.1 Definition

Reliability = the degree to which a test produces consistent, reproducible results across time, raters, or items. A reliable thermometer gives the same reading each time you measure the same temperature.

2.2 Types of Reliability

TYPE	WHAT IT MEASURES	STATISTIC	ACCEPTABLE VALUE
Test-retest	Stability over time (same test, same people, different times)	Pearson r or ICC	$r > 0.7$
Inter-rater	Agreement between two or more raters	Cohen's kappa (κ)	$\kappa > 0.6$
Split-half	Consistency between two halves of the same test	Spearman-Brown corrected r	$r > 0.7$
Internal consistency	How well items within a test measure the same construct	Cronbach's alpha (α)	$\alpha > 0.7$

2.3 Cohen's Kappa: Interpretation

KAPPA VALUE · INTERPRETATION

< 0.00 Less than chance agreement

0.01–0.20 Slight agreement

0.21–0.40 Fair agreement

0.41–0.60 Moderate agreement

0.61–0.80 Substantial agreement

0.81–1.00 Almost perfect agreement

Why kappa over simple percentage agreement? Kappa accounts for agreement expected by chance alone. Two raters flipping coins would agree 50% of the time, kappa corrects for this.

2.4 Cronbach's Alpha: Key Points

- Measures internal consistency, how well items "hang together"
- Range: 0 to 1 (higher = more consistent)

- If $\alpha < 0.7 \rightarrow$ items are measuring different things or too few items
- If $\alpha > 0.95 \rightarrow$ items may be redundant (item redundancy)
- Affected by number of items (more items $\rightarrow$ higher alpha, even if items are mediocre)

2.5 Reliability vs Validity: The Relationship

STATEMENT · TRUE/FALSE

A test can be reliable but not valid TRUE, a scale can consistently measure the wrong thing

A test can be valid but not reliable FALSE, if it measures the right thing, it must do so consistently

Reliability is necessary but not sufficient for validity TRUE

High reliability guarantees high validity FALSE

Classic analogy: A marksman shooting a tight cluster (reliable) but missing the bullseye (not valid). Scattered shots hitting the bullseye on average are neither reliable nor truly valid for individual measurement.

3. STUDY DESIGNS

3.1 Hierarchy of Evidence (strongest to weakest)

1. Systematic review / Meta-analysis
2. Randomised Controlled Trial (RCT)
3. Cohort study
4. Case-control study
5. Cross-sectional study
6. Ecological study
7. Case series / Case report
8. Expert opinion

3.2 Study Design Comparison Table

FEATURE	CROSS-SECTIONAL	CASE-CONTROL	COHORT	RCT
Direction	Snapshot	Backward (retrospective)	Forward (prospective or retrospective)	Forward (prospective)
Measure	Prevalence	Odds ratio	Relative risk, incidence	Relative risk, NNT

FEATURE	CROSS-SECTIONAL	CASE-CONTROL	COHORT	RCT
Exposure & outcome	Measured simultaneously	Outcome known, exposure sought	Exposure known, outcome awaited	Exposure assigned, outcome awaited
Causation	Cannot establish	Suggests association	Stronger association	Strongest causation
Time	One point	Past exposure recalled	Long follow-up	Fixed duration
Cost	Low	Moderate	High	Very high
Best for	Prevalence estimation, generating hypotheses	Rare diseases	Rare exposures, incidence estimation	Testing interventions

3.3 Cross-sectional Study

- **Design:** Measures exposure and outcome at the same point in time
- **Measure:** Prevalence (not incidence)
- **Strengths:** Quick, cheap, good for generating hypotheses, estimates disease burden
- **Limitations:** Cannot establish temporality (chicken-or-egg problem), prone to prevalence bias (captures long-duration cases)
- **Psychiatry example:** NMHS 2016, national prevalence of mental disorders in India

3.4 Case-Control Study

- **Design:** Start with cases (disease +) and controls (disease -), look backward for exposure
- **Measure: Odds Ratio (OR)** = $(a \times d) / (b \times c)$ from a 2x2 table
- **Strengths:** Efficient for rare diseases, relatively quick, inexpensive
- **Limitations:** Recall bias (cases remember exposures differently), selection bias in choosing controls, cannot calculate incidence or prevalence directly
- **Psychiatry example:** Childhood trauma (exposure) in patients with BPD (cases) vs. healthy controls

Interpreting Odds Ratio:

- OR = 1 → no association
- OR > 1 → exposure increases odds of disease
- OR < 1 → exposure is protective
- OR = 3.5 → the odds of disease are 3.5 times higher in exposed vs. unexposed

3.5 Cohort Study

- **Design:** Start with exposed and unexposed groups, follow forward to see who develops outcome
- **Types:** Prospective (follow from now) or retrospective (use existing records)
- **Measure: Relative Risk (RR)** = incidence in exposed / incidence in unexposed
- **Strengths:** Can establish temporality, calculate incidence, study multiple outcomes of one exposure
- **Limitations:** Expensive, time-consuming, loss to follow-up, not efficient for rare diseases
- **Psychiatry example:** Framingham Heart Study, depressive symptoms and cardiovascular events

Interpreting Relative Risk:

- $RR = 1 \rightarrow$ no association
- $RR > 1 \rightarrow$ exposure increases risk
- $RR < 1 \rightarrow$ exposure is protective
- $RR = 2.0 \rightarrow$ exposed group has twice the risk

RR vs OR: In rare diseases (prevalence $< 10\%$), OR approximates RR. In common diseases, OR overestimates RR.

3.6 Randomised Controlled Trial (RCT)

- **Design:** Participants randomly assigned to intervention or control
- **Gold standard** for establishing causation

Key Components:

COMPONENT · PURPOSE

Randomisation Eliminates selection bias, balances known and unknown confounders

Allocation concealment Prevents foreknowledge of assignment (different from blinding)

Single blinding Participant blinded

Double blinding Participant + assessor blinded

Triple blinding Participant + assessor + statistician blinded

ITT (Intention-to-treat) Analyse all participants in their assigned group regardless of compliance, preserves randomisation, conservative estimate

Per-protocol Analyse only those who completed the protocol, can overestimate treatment effect

- **Strengths:** Highest internal validity, can establish causation, minimises bias
- **Limitations:** Expensive, ethical constraints (can't randomise harmful exposures), Hawthorne effect, low external validity if inclusion criteria too strict
- **Psychiatry example:** STAR*D trial, sequential treatment strategies for depression

3.7 Ecological Study

- **Design:** Uses aggregate data (populations, not individuals)
- **Measure:** Correlation at population level
- **Strengths:** Uses existing data, hypothesis-generating, cheap
- **Limitations:** **Ecological fallacy**, cannot infer individual-level associations from group-level data
- **Psychiatry example:** Countries with higher lithium in drinking water have lower suicide rates

3.8 Case Series and Case Report

FEATURE	CASE REPORT	CASE SERIES
N	1 patient	Multiple patients (no control group)
Use	Novel presentations, rare side effects, new treatment ideas	Describe patterns, generate hypotheses
Strength	First signal of new phenomenon	Identifies emerging patterns
Limitation	No comparison, no generalisability	No controls, no causation
Example	First report of NMS with a new antipsychotic	Series of 20 patients with treatment-resistant depression who responded to ketamine

4. STATISTICAL TESTS

4.1 Key Concepts First

TERM · DEFINITION

p-value Probability of obtaining results as extreme as observed, assuming H_0 is true. $p < 0.05$ = statistically significant

Confidence Interval (CI) Range within which the true population parameter lies with 95% probability. If 95% CI for OR does not include 1 → significant

Effect size Magnitude of the difference (Cohen's d, η^2 , r). Small = 0.2, Medium = 0.5, Large = 0.8

Power Probability of detecting a true effect ($1 - \beta$). Aim for ≥ 0.80

Type I error (α) Rejecting H_0 when it is true (false positive). Threshold typically 0.05

Type II error (β) Failing to reject H_0 when it is false (false negative). Related to power

4.2 The Decision Tree: Which Test When?

Step 1: What type of data?

DATA TYPE	EXAMPLES	TESTS
Continuous (interval/ratio)	HAM-D scores, age, weight	t-test, ANOVA, Pearson r
Categorical (nominal/ordinal)	Diagnosis (yes/no), severity (mild/moderate/severe)	Chi-square, Fisher's exact

Step 2: How many groups?

GROUPS	CONTINUOUS (PARAMETRIC)	CONTINUOUS (NON-PARAMETRIC)	CATEGORICAL
2 groups, unpaired	Independent t-test	Mann-Whitney U	Chi-square
2 groups, paired	Paired t-test	Wilcoxon signed-rank	McNemar's test
3+ groups, unpaired	One-way ANOVA	Kruskal-Wallis	Chi-square
3+ groups, paired	Repeated measures ANOVA	Friedman test	Cochran's Q

Step 3: Parametric or non-parametric?

Use **parametric** tests when:

- Data is normally distributed
- Continuous data (interval/ratio)
- Adequate sample size ($n > 30$ per group as rough guide)
- Homogeneity of variance (Levene's test)

Use **non-parametric** tests when:

- Data is ordinal or skewed
- Small sample size
- Normality assumption violated
- Outliers present

4.3 Individual Tests: Details

T-TEST (STUDENT'S T-TEST)

Independent (unpaired) t-test:

- **Use:** Compare means of **two independent groups**
- **Assumptions:** Normal distribution, continuous data, homogeneity of variance, independent observations
- **Example:** Mean HAM-D score in drug group vs. placebo group

Paired t-test:

- **Use:** Compare means of **same group at two time points** or matched pairs
- **Assumptions:** Normal distribution of differences, continuous data
- **Example:** HAM-D score before and after 6 weeks of treatment in the same patients
- **Key:** Calculates difference for each pair, then tests if mean difference $\neq 0$

ANOVA (ANALYSIS OF VARIANCE)

One-way ANOVA:

- **Use:** Compare means of **3+ independent groups** on one factor
- **Example:** Mean depression scores across three groups: SSRI, SNRI, placebo
- **Post-hoc:** If significant, use Tukey's HSD or Bonferroni to identify which pairs differ

Two-way ANOVA:

- **Use:** Examine effects of **two independent variables** and their interaction
- **Example:** Effect of drug (SSRI vs placebo) AND gender (male vs female) on depression score

Repeated measures ANOVA:

- **Use:** Same subjects measured at **3+ time points**
- **Example:** Depression scores at baseline, 4 weeks, 8 weeks, 12 weeks
- **Assumption:** Sphericity (Mauchly's test), if violated, use Greenhouse-Geisser correction

CHI-SQUARE TEST

Test of Independence:

- **Use:** Test association between **two categorical variables**
- **Example:** Is there an association between gender (male / female) and diagnosis (depression / anxiety)?
- **Requirement:** Expected cell count ≥ 5 in at least 80% of cells

Goodness of Fit:

- **Use:** Test whether observed frequencies match **expected** frequencies

- **Example:** Are psychiatric diagnoses equally distributed across blood groups?

If expected cell count < 5 → use Fisher's exact test

NON-PARAMETRIC TESTS

Mann-Whitney U test:

- Non-parametric alternative to independent t-test
- Compares rank distributions of two independent groups
- Example: Comparing satisfaction scores (ordinal) between two hospitals

Wilcoxon signed-rank test:

- Non-parametric alternative to paired t-test
- Compares two related samples
- Example: Patient-reported severity (ordinal) before and after intervention

Kruskal-Wallis test:

- Non-parametric alternative to one-way ANOVA
- Compares three or more independent groups
- Example: Comparing therapy satisfaction across 4 treatment modalities
- If significant, use Dunn's test for post-hoc pairwise comparisons

CORRELATION

FEATURE	PEARSON R	SPEARMAN P
Data type	Continuous, normally distributed	Ordinal or non-normal continuous
Measures	Linear association	Monotonic association
Range	-1 to +1	-1 to +1
Example	Correlation between HAM-D and BDI scores	Correlation between severity ranking and treatment response ranking

Interpreting r:

- 0–0.3: weak
- 0.3–0.7: moderate
- 0.7–1.0: strong

Correlation ≠ Causation. Two variables may correlate because of a shared confounder.

FISHER'S EXACT TEST

- Used when Chi-square assumptions are violated (expected count < 5)

- Small sample sizes
- Calculates exact probability rather than approximation
- Example: Association between a rare genotype and treatment response in a sample of 15 patients

REGRESSION

TYPE	USE	EXAMPLE
Linear regression	Predict continuous outcome from one or more predictors	Predicting HAM-D score from age, duration of illness, base-line score
Logistic regression	Predict binary outcome from one or more predictors	Predicting treatment response (yes/no) from baseline variables
Multiple regression	Multiple predictors for one outcome	Effect of CBT hours, medication adherence, and social support on depression score

5. SENSITIVITY AND SPECIFICITY

5.1 The 2×2 Table

	DISEASE +	DISEASE –	
Test +	a (True Positive)	b (False Positive)	a + b
Test –	c (False Negative)	d (True Negative)	c + d
	a + c	b + d	N

5.2 Formulae

MEASURE	FORMULA	MEANING
Sensitivity	$a / (a + c)$	Proportion of actual positives correctly identified (true positive rate)
Specificity	$d / (b + d)$	Proportion of actual negatives correctly identified (true negative rate)
PPV	$a / (a + b)$	Probability that a positive test = true disease
NPV	$d / (c + d)$	Probability that a negative test = true absence

MEASURE	FORMULA	MEANING
LR+	$\text{Sensitivity} / (1 - \text{Specificity})$	How much a positive test increases the odds of disease
LR-	$(1 - \text{Sensitivity}) / \text{Specificity}$	How much a negative test decreases the odds of disease

5.3 Clinical Rules

- **SnNOuT** = Sensitive test, Negative result rules OUT disease
- **SpPIn** = Specific test, Positive result rules IN disease

Why? A highly sensitive test catches almost all true cases → very few false negatives → if it's negative, you can be confident the disease is absent.

5.4 Effect of Prevalence on PPV and NPV

PREVALENCE	PPV	NPV
High (common disease)	↑ Higher	↓ Lower
Low (rare disease)	↓ Lower	↑ Higher

Clinical implication: Even a highly sensitive and specific test will have poor PPV in a low-prevalence population because the absolute number of false positives exceeds true positives.

Example: If PHQ-9 sensitivity = 90%, specificity = 85%, and depression prevalence = 2%:

- For every 1000 people: 20 have depression, 980 do not
- True positives = 18 (90% of 20)
- False positives = 147 (15% of 980)
- $\text{PPV} = 18 / (18 + 147) = 10.9\%$, most positive screens are false positives

5.5 ROC Curve

- **ROC** = Receiver Operating Characteristic
 - Plots **sensitivity (y-axis)** vs **1 – specificity (x-axis)** at different cut-off points
 - **AUC (Area Under the Curve):** 0.5 = no better than chance; 0.7–0.8 = acceptable; 0.8–0.9 = excellent; > 0.9 = outstanding
 - **Use:** Compare diagnostic performance of different scales or select optimal cut-off
 - **Psychiatry example:** Comparing PHQ-9 vs BDI-II as screening tools for depression, the one with higher AUC performs better across all thresholds
-

6. EVIDENCE-BASED MEDICINE (EBM)

6.1 Definition

EBM = the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. Integrates:

1. Best available evidence
2. Clinical expertise
3. Patient values and preferences

(David Sackett, 1996)

6.2 Five Steps of EBM (Mnemonic: 5 A's)

STEP	ACTION	EXAMPLE
1. Ask	Formulate a PICO question	In adults with MDD (P), does CBT + SSRI (I) compared to SSRI alone (C) improve remission rates (O)?
2. Acquire	Search for best evidence	PubMed, Cochrane Library, NICE guidelines
3. Appraise	Critically evaluate the evidence	Check study design, bias, applicability
4. Apply	Integrate evidence with clinical expertise and patient preferences	Discuss options with patient considering their values
5. Assess	Evaluate your practice and outcomes	Audit remission rates in your patients

6.3 Levels of Evidence Pyramid

LEVEL	STUDY TYPE	STRENGTH
1a	Systematic review of RCTs	Strongest
1b	Individual RCT with narrow CI	↓
2a	Systematic review of cohort studies	↓
2b	Individual cohort study	↓
3a	Systematic review of case-control studies	↓
3b	Individual case-control study	↓
4	Case series	↓

LEVEL	STUDY TYPE	STRENGTH
5	Expert opinion	Weakest

6.4 NNT and NNH

MEASURE	FORMULA	INTERPRETATION
NNT (Number Needed to Treat)	$1 / \text{ARR}$	Number of patients needed to treat with intervention for one additional good outcome
NNH (Number Needed to Harm)	$1 / \text{ARI}$	Number of patients treated before one additional patient is harmed
ARR (Absolute Risk Reduction)	$\text{CER} - \text{EER}$	Difference in event rates between control and experimental groups

- CER = Control Event Rate
- EER = Experimental Event Rate

Example: If relapse rate is 40% with placebo and 25% with drug:

- $\text{ARR} = 0.40 - 0.25 = 0.15$
- $\text{NNT} = 1 / 0.15 = 6.7 \rightarrow$ treat 7 patients with the drug to prevent one relapse

Clinical rule: Lower NNT = more effective treatment. Higher NNH = safer treatment. Compare NNT to NNH for risk-benefit.

7. META-ANALYSIS AND SYSTEMATIC REVIEW

7.1 Definitions

FEATURE	SYSTEMATIC REVIEW	META-ANALYSIS
Definition	Structured, reproducible synthesis of all available evidence on a question	Statistical pooling of results from multiple studies into a single summary estimate
Statistics	Qualitative synthesis (narrative)	Quantitative synthesis (statistical)
Relationship	Every meta-analysis is within a systematic review	Not every systematic review includes a meta-analysis
When meta-analysis is NOT done	Studies too heterogeneous, different outcomes, insufficient data	

7.2 Steps in a Systematic Review / Meta-analysis

1. **Define research question** (PICO)
2. **Protocol registration** (PROSPERO)
3. **Comprehensive literature search** (multiple databases: PubMed, Cochrane, Embase, PsycINFO)
4. **Study selection** (inclusion/exclusion criteria, PRISMA flowchart)
5. **Data extraction** (standardised forms)
6. **Quality assessment** (Cochrane Risk of Bias tool for RCTs, Newcastle-Ottawa Scale for observational studies)
7. **Data synthesis** (narrative or meta-analytic)
8. **Assess heterogeneity** (I^2 , Q test)
9. **Assess publication bias** (funnel plot, Egger's test)
10. **Report** (PRISMA guidelines)

7.3 Forest Plot Interpretation

A forest plot displays:

- **Each study:** horizontal line (CI) with a square (point estimate). Square size = study weight.
- **Summary diamond:** combined effect estimate; width = CI of the summary
- **Line of no effect:** vertical line at OR/RR = 1 (or mean difference = 0)

How to read:

- If the CI of a study crosses the line of no effect → that study is non-significant
- If the summary diamond does NOT cross the line → overall result is significant
- Wider CI = less precise study (smaller sample)
- Larger square = greater weight in the analysis

7.4 Heterogeneity

MEASURE	DEFINITION	INTERPRETATION
Cochrane Q	Chi-square test for heterogeneity	$p < 0.10$ → significant heterogeneity (liberal threshold because of low power)
I^2	Percentage of variability due to heterogeneity rather than chance	0–25% = low, 25–50% = moderate, 50–75% = substantial, > 75% = considerable

If heterogeneity is high:

- Use **random-effects model** (assumes true effect varies across studies)

- Perform **subgroup analysis** or **meta-regression** to explore sources
- Consider NOT pooling data

If heterogeneity is low:

- **Fixed-effect model** is appropriate (assumes one true effect)

7.5 Publication Bias

- **Problem:** Studies with significant results are more likely to be published → pooled estimate is biased
- **Funnel plot:** Scatter plot of effect size (x-axis) vs study precision/sample size (y-axis). Symmetric = no bias. Asymmetric = possible publication bias.
- **Egger's test:** Statistical test for funnel plot asymmetry
- **Trim and fill method:** Statistical adjustment for missing studies
- **Solutions:** Pre-registration of trials, searching grey literature, contacting authors

7.6 Network Meta-analysis (NMA)

- **Definition:** Extends traditional meta-analysis to compare **multiple treatments** simultaneously, even if they haven't been compared head-to-head
- **Advantage:** Ranks treatments by probability of being best
- **Key concept:** Uses both **direct evidence** (A vs B trials) and **indirect evidence** (if A vs C and B vs C exist, can estimate A vs B)
- **Assumption:** Transitivity, similar study populations across comparisons
- **Psychiatry landmark:** Cipriani et al. (2018), network meta-analysis of 21 antidepressants. Found amitriptyline, mirtazapine, and venlafaxine most effective; fluoxetine, escitalopram most acceptable.

8. RESEARCH METHODOLOGY

8.1 Research Question: PICO Framework

COMPONENT	MEANING	EXAMPLE
P	Population	Adults with treatment-resistant depression
I	Intervention	Ketamine infusion
C	Comparison	Midazolam (active placebo)
O	Outcome	Reduction in MADRS score at 24 hours

8.2 Hypothesis Types

TYPE	DEFINITION	EXAMPLE
Null (H_0)	No difference or no association	There is no difference in HAM-D scores between drug and placebo
Alternative (H_1)	There IS a difference or association	Drug group has lower HAM-D scores than placebo
Directional (one-tailed)	Specifies the direction of difference	Drug group will have LOWER scores (not just different)
Non-directional (two-tailed)	Difference exists but direction unspecified	Scores will DIFFER between groups

8.3 Sampling Methods

PROBABILITY SAMPLING (EVERY MEMBER HAS A KNOWN CHANCE OF SELECTION)

METHOD	HOW IT WORKS	ADVANTAGE	LIMITATION
Simple random	Every individual has equal chance (lottery, random number table)	Unbiased, representative	Needs complete sampling frame
Stratified random	Divide population into strata (e.g., age groups), random sample from each	Ensures representation of subgroups	More complex, needs knowledge of strata
Cluster	Divide population into clusters (e.g., villages), randomly select entire clusters	Practical for large, dispersed populations	Higher sampling error
Systematic	Every kth individual from a list (e.g., every 5th patient)	Simple, quick	Bias if list has a periodic pattern

NON-PROBABILITY SAMPLING (NOT EVERYONE HAS A CHANCE OF SELECTION)

METHOD	HOW IT WORKS	USE CASE
Convenience	Whoever is available	Quick pilot studies
Purposive	Researcher selects based on characteristics	Qualitative research, expert panels
Snowball	Participants recruit other participants	Hard-to-reach populations (IV drug users, sex workers)

METHOD	HOW IT WORKS	USE CASE
Quota	Researcher ensures certain proportions (like stratified but non-random)	Market research

8.4 Sample Size Calculation

Why it matters: Too small → Type II error (miss real effects). Too large → wasteful, ethical concerns (unnecessary exposure).

Factors affecting sample size:

FACTOR · EFFECT ON SAMPLE SIZE

Effect size ↑ ↓ Smaller sample needed

Power ↑ (e.g., 0.80 → 0.90) ↑ Larger sample needed

Alpha level ↓ (e.g., 0.05 → 0.01) ↑ Larger sample needed

Variability ↑ ↑ Larger sample needed

Expected dropout ↑ ↑ Larger sample needed (inflate by 10–20%)

General formula concept: $n = f(Z\alpha, Z\beta, \sigma, \delta)$ where:

- $Z\alpha$ = Z-value for desired significance level (1.96 for $\alpha = 0.05$)
- $Z\beta$ = Z-value for desired power (0.84 for power = 0.80)
- σ = standard deviation
- δ = minimum clinically meaningful difference

8.5 Bias Types

BIAS	DEFINITION	EXAMPLE	HOW TO MINIMISE
Selection bias	Systematic differences in who enters the study	Only including patients from tertiary hospital	Random sampling, clear inclusion criteria
Information bias	Systematic errors in measuring exposure or outcome	Recall bias in case-control studies	Standardised instruments, blinding
Recall bias	Cases remember exposures differently than controls	Mothers of children with birth defects recall medication use more accurately	Prospective design, objective records
Observer bias	Researcher's expectations influence data collection	Unblinded rater scores drug group as improved	Blinding of assessors

BIAS	DEFINITION	EXAMPLE	HOW TO MINIMISE
Performance bias	Unequal care between groups	Intervention group gets more attention	Standardised protocols, blinding
Attrition bias	Differential loss to follow-up	Sicker patients drop out of drug arm → drug looks better	ITT analysis, minimise dropout
Publication bias	Positive results more likely published	Only significant anti-depressant trials published	Trial registries, grey literature search
Confounding	Third variable associated with both exposure and outcome	Coffee drinkers have more lung cancer (confounder: smoking)	Randomisation, restriction, matching, stratification, multivariate analysis
Lead-time bias	Earlier detection inflates survival time without true benefit	Screening detected cancer 2 years earlier but patient dies at same time	Measure mortality, not survival from diagnosis
Berkson bias	Hospital-based studies create spurious associations	Studying depression and diabetes in hospitalised patients, both conditions increase hospitalisation probability	Community-based studies

8.6 Confounding, Effect Modification, and Mediation

CONCEPT	DEFINITION	HOW TO IDENTIFY	HOW TO HANDLE
Confounding	Third variable distorts the true association	Crude and adjusted estimates differ	Randomisation, stratification, multivariate analysis
Effect modification	Effect of exposure on outcome DIFFERS across levels of a third variable	Significant interaction term	Report stratum-specific estimates (do NOT adjust away)
Mediation	Third variable lies on the causal pathway between exposure and outcome	Exposure → Mediator → Outcome	Mediation analysis (Baron & Kenny steps, Sobel test)

8.7 Odds Ratio: Detailed

From a 2×2 table:

	DISEASE +	DISEASE –
Exposed	a	b
Unexposed	c	d

- $OR = (a \times d) / (b \times c)$
- Used in case-control studies (cannot calculate RR because you start with known outcome numbers)
- In cohort studies, RR is preferred; OR overestimates RR when outcome is common

8.8 Qualitative Research Methods

METHOD	FOCUS	APPROACH	EXAMPLE
Phenomenology	Lived experience of a phenomenon	In-depth interviews, meaning analysis	Experience of living with schizophrenia
Grounded theory	Develop theory from data	Iterative coding, constant comparison, theoretical sampling	How families cope with a member's addiction
Ethnography	Culture and social behaviour	Immersive observation in a community	Mental health beliefs in a tribal community
Content analysis	Systematic categorisation of text	Coding themes from transcripts	Themes in suicide notes
Thematic analysis	Identifying patterns across data	6-step Braun & Clarke method	Barriers to mental health treatment in rural India

Qualitative rigour criteria (equivalent to quantitative validity / reliability):

- **Credibility** ($\approx$ internal validity), prolonged engagement, triangulation, member checking
- **Transferability** ($\approx$ external validity), thick description
- **Dependability** ($\approx$ reliability), audit trail
- **Confirmability** ($\approx$ objectivity), reflexivity

8.9 Factor Analysis

- **Definition:** Statistical technique that reduces a large number of variables to fewer underlying dimensions (factors)
- **Types:**
- **Exploratory Factor Analysis (EFA):** No prior assumption about factor structure, "let the data speak"
- **Confirmatory Factor Analysis (CFA):** Tests whether a hypothesised factor structure fits the data

- **Key terms:**
- **Factor loading:** Correlation between a variable and a factor (> 0.3 or > 0.4 is meaningful)
- **Eigenvalue:** Amount of variance explained by a factor (Kaiser criterion: retain factors with eigenvalue > 1)
- **Scree plot:** Graph of eigenvalues, retain factors before the "elbow"
- **Rotation:** Varimax (orthogonal) or oblimin (oblique), simplifies factor structure
- **Psychiatry applications:**
 - Development of PANSS factor structure (positive, negative, general psychopathology)
 - Validation of personality inventories (e.g., five-factor model)
 - Identifying symptom dimensions in depression (cognitive, somatic, affective)

9. ADDITIONAL HIGH-YIELD CONCEPTS

9.1 Normal Distribution

- Bell-shaped, symmetric curve
- Mean = median = mode
- 68% within ± 1 SD, 95% within ± 2 SD, 99.7% within ± 3 SD
- Many statistical tests assume normality
- Test with: Shapiro-Wilk test, Kolmogorov-Smirnov test, Q-Q plot

9.2 Bonferroni Correction

- When doing multiple comparisons, risk of Type I error increases
- Bonferroni: divide α by number of comparisons (e.g., 3 comparisons $\rightarrow \alpha = 0.05/3 = 0.017$)
- Conservative, reduces power
- Alternative: Holm-Bonferroni (step-down, less conservative)

9.3 Intention-to-Treat vs Per-Protocol

FEATURE	ITT	PER-PROTOCOL
Includes	ALL randomised participants	Only those who completed protocol
Preserves	Randomisation	
Bias	Conservative (underestimates effect)	May overestimate effect
Preferred for	Superiority trials (primary analysis)	Complements ITT; preferred for non-inferiority trials

9.4 CONSORT, STROBE, PRISMA

GUIDELINE	FOR WHICH STUDY TYPE	KEY FEATURE
CONSORT	RCTs	Flow diagram of participant progression
STROBE	Observational studies (cohort, case-control, cross-sectional)	22-item checklist
PRISMA	Systematic reviews and meta-analyses	Flow diagram of study selection

KEY TABLES SUMMARY

Master Test Selection Table

SCENARIO	PARAMETRIC TEST	NON-PARAMETRIC ALTERNATIVE
2 independent groups, continuous	Independent t-test	Mann-Whitney U
2 paired groups, continuous	Paired t-test	Wilcoxon signed-rank
3+ independent groups, continuous	One-way ANOVA	Kruskal-Wallis
3+ paired groups, continuous	Repeated measures ANOVA	Friedman test
2 categorical variables	Chi-square test of independence	Fisher's exact test
Correlation (continuous)	Pearson r	Spearman ρ
Predict continuous outcome	Linear regression	
Predict binary outcome	Logistic regression	

Cross-reference: D2 (Model Answers), D3 (Mnemonics), D4 (Comparisons), D6 (Quick Review)

Model Answers

Q1. Define validity. Types. Importance in psychiatry. [10 marks: 2+6+2]

Exam Strategy

Split strictly: 1 para definition (2 marks), 4 types with examples (6 marks, 1.5 each), brief importance section (2 marks). Use a table for types.

Model Answer

Definition (2 marks)

Validity refers to the degree to which a measurement instrument accurately measures the construct it is intended to measure. A valid test measures what it claims to measure. For example, a valid depression scale should measure depression, not general distress or anxiety.

Types of Validity (6 marks)

TYPE	DEFINITION	EXAMPLE
Face validity	The instrument appears to measure the intended construct on superficial examination. Assessed by non-experts.	PHQ-9 "looks like" it measures depression, questions about mood, sleep, appetite. Weakest form of validity.
Content validity	The instrument covers the entire domain of the construct comprehensively. Assessed by expert panel.	HAM-D includes items on depressed mood, guilt, insomnia, psychomotor changes, somatic symptoms, and suicidality, covering the full domain of depression.
Criterion validity	The instrument correlates with an established external standard (gold standard). Two sub-types: (a) Concurrent , new test and criterion measured simultaneously (e.g., comparing a new depression scale with HAM-D in same patients). (b) Predictive , test predicts a future outcome (e.g., MMSE score predicting progression to dementia at 2-year follow-up).	

TYPE	DEFINITION	EXAMPLE
Construct validity	The instrument measures the theoretical construct. Two sub-types: (a) Convergent , correlates with measures of the same construct (BDI correlates with PHQ-9). (b) Discriminant , does not correlate with measures of different constructs (BDI does not correlate with mania rating scale).	

Importance in Psychiatry (2 marks)

- Psychiatry lacks biomarkers, diagnosis and outcome measurement rely heavily on rating scales and clinical interviews. Validity ensures these instruments accurately capture subjective constructs like depression, psychosis, or personality pathology.
- Treatment trials depend on valid outcome measures; invalid instruments lead to erroneous conclusions about drug efficacy.
- Classification systems (ICD, DSM) require construct validity of diagnostic categories.
- Forensic psychiatry: medicolegal opinions must be based on valid assessment tools to be admissible.

Q2. What is validity? Discuss types with examples. [10 marks: 3+7]: LONG ESSAY CANDIDATE

Exam Strategy

This is a long essay candidate, write 3+ pages. Expand each type with psychiatric examples. Include internal vs external validity as bonus types to demonstrate depth.

Model Answer

Definition of Validity (3 marks)

Validity is defined as the degree to which a test or measurement instrument accurately measures the construct it purports to measure. It addresses the fundamental question: "Is this test measuring what we think it is measuring?"

Validity is not a binary property but exists on a continuum. A test may be valid for one purpose but not another. For example, the MMSE is a valid screening tool for cognitive impairment but not a valid diagnostic tool for specific dementia subtypes.

The concept is central to psychiatry because, unlike other medical specialties, psychiatric diagnoses rely primarily on phenomenological assessment rather than laboratory

investigations. The validity of our tools directly determines the quality of our clinical decisions.

Types of Validity (7 marks)

1. Face Validity

Face validity refers to whether an instrument appears, on the surface, to measure what it claims to measure. It is the weakest and most subjective form of validity, typically assessed by non-experts or the target population.

Example: The PHQ-9 has high face validity, questions about feeling down, sleep difficulties, poor appetite, and concentration problems are recognisable as depression symptoms to most patients and clinicians.

Limitation: Face validity can be misleading. A test may "look right" but actually measure a different construct. Conversely, some valid tests may lack face validity (e.g., projective tests like the Rorschach).

Relevance: Important for patient compliance, patients are more likely to complete a questionnaire that appears relevant to their problems.

2. Content Validity

Content validity refers to the degree to which the instrument comprehensively covers all aspects of the construct being measured. It is assessed by expert panels who evaluate whether items represent the full domain.

Example: The HAM-D (Hamilton Depression Rating Scale) has strong content validity because it includes items assessing depressed mood, feelings of guilt, suicidal ideation, insomnia (early, middle, late), work and activities, psychomotor retardation, psychomotor agitation, anxiety, somatic symptoms, loss of insight, and diurnal variation, covering the full syndromal domain of depression.

A scale that only measured mood and sleep would lack content validity for depression because it omits cognitive, psychomotor, and somatic dimensions.

Assessment method: Content Validity Index (CVI), proportion of experts rating each item as relevant.

3. Criterion Validity

Criterion validity is established when the instrument's scores correlate with an external criterion or gold standard. It has two subtypes:

(a) Concurrent validity: The test and criterion are measured at the same time. The new instrument is validated against an established measure.

Example: A newly developed Hindi depression scale is administered alongside the validated HAM-D to the same patients on the same day. If the correlation (r) is > 0.70 , concurrent validity is established.

(b) Predictive validity: The test score predicts a future outcome.

Example: The AUDIT (Alcohol Use Disorders Identification Test) score at admission predicting development of alcohol withdrawal seizures during hospitalisation. A high AUDIT score predicting more severe withdrawal supports predictive validity.

Another example: GCS score predicting functional outcome at 6 months in traumatic brain injury.

4. Construct Validity

Construct validity examines whether the instrument truly measures the theoretical construct it claims to measure. This is the most rigorous and important form of validity.

Two subtypes:

(a) Convergent validity: The instrument correlates positively with other measures of the same construct.

Example: The BDI-II shows high correlation ($r = 0.85$) with the PHQ-9, both measuring depression. This supports convergent validity of both instruments.

(b) Discriminant (divergent) validity: The instrument does NOT correlate with measures of theoretically unrelated constructs.

Example: The BDI-II should show low correlation with the YMRS (Young Mania Rating Scale). If it showed high correlation with a mania scale, its discriminant validity would be questionable, it might be measuring general distress rather than depression specifically.

Other methods: Known-groups validity (instrument distinguishes between groups known to differ, e.g., depression scale scores higher in clinically depressed patients than healthy controls), factorial validity (factor analysis confirms the hypothesised factor structure).

5. Internal Validity (bonus)

Internal validity refers to the degree to which the results of a study can be attributed to the intervention rather than confounding variables. It applies to study designs rather than instruments.

Example: A well-conducted double-blind RCT of an antidepressant has high internal validity because randomisation controls for confounders, and blinding prevents bias.

Threats: Selection bias, maturation, history, testing effects, attrition, regression to the mean.

6. External Validity (bonus)

External validity refers to the generalisability of study results to other populations, settings, and times.

Example: An RCT conducted exclusively in urban tertiary centres with highly selected patients may lack external validity for rural primary care settings.

Relevance to Indian psychiatry: Many psychiatric treatment guidelines are based on Western studies, their external validity for the Indian population (different pharmacogenomics, cultural factors, disease presentation) requires careful consideration.

Q3. Define reliability and validity. Significance. Types. [10 marks: 3+2+5]

Exam Strategy

Balanced coverage needed. Give equal weight to both concepts. Use a comparison table to demonstrate understanding.

Model Answer

Definitions (3 marks)

Reliability is the degree to which a measurement instrument produces consistent and reproducible results when applied repeatedly under similar conditions. A reliable instrument yields the same result each time it measures the same underlying construct, assuming the construct has not changed.

Validity is the degree to which a measurement instrument accurately measures the construct it is intended to measure. A valid instrument measures what it claims to measure.

The relationship between reliability and validity is asymmetric: reliability is a necessary but not sufficient condition for validity. A test can be reliable but not valid (consistently measuring the wrong thing), but a test cannot be valid without being reliable.

Significance (2 marks)

- In psychiatry, where diagnosis depends on clinical assessment and rating scales rather than laboratory tests, both reliability and validity determine the quality of clinical practice, research, and medicolegal work.
- Inter-rater reliability is critical for multisite clinical trials, if raters at different centres score the HAM-D differently, the study results are uninterpretable.
- Validity of diagnostic categories (e.g., DSM-5) directly impacts treatment selection, prognosis estimation, and research classification.
- Reliable and valid instruments are prerequisites for evidence-based practice, guidelines based on studies using unreliable instruments are fundamentally flawed.

Types (5 marks)

Types of Reliability:

TYPE	WHAT IT MEASURES	STATISTIC	EXAMPLE
Test-retest	Stability over time	Pearson r, ICC	Administering BPRS to same patients 2 weeks apart
Inter-rater	Agreement between raters	Cohen's kappa	Two psychiatrists rating same patient on PANSS
Split-half	Internal consistency (two halves)	Spearman-Brown corrected r	Odd-numbered items vs even-numbered items of BDI
Internal consistency	How well items measure same construct	Cronbach's alpha	All 21 items of BDI measuring depression ($\alpha > 0.7$)

Types of Validity:

TYPE	WHAT IT MEASURES	EXAMPLE
Face	Surface appearance	PHQ-9 looks like a depression questionnaire
Content	Domain coverage	HAM-D covers all depression dimensions
Criterion (concurrent + predictive)	Correlation with gold standard	New scale correlates with HAM-D (concurrent); AUDIT predicts withdrawal severity (predictive)
Construct (convergent + discriminant)	Theoretical construct accuracy	BDI correlates with PHQ-9 (convergent); BDI does not correlate with YMRS (discriminant)

Q4. What is reliability? Types with examples. Internal and external validity. [10 marks: 2+4+4]

Exam Strategy

Heavy on reliability (6 marks total with definition). Separate section for internal and external validity with threats.

Model Answer

Definition (2 marks)

Reliability is the extent to which a measurement instrument yields consistent, reproducible, and dependable results across different occasions, raters, or forms. If the underlying

construct has not changed, a reliable instrument will produce the same score on repeated measurement.

Types of Reliability with Examples (4 marks)

1. Test-retest reliability: Measures the stability of scores over time. The same instrument is administered to the same individuals at two different time points, and the correlation between scores is calculated.

Example: The BPRS is administered to 50 patients with schizophrenia at baseline and again 2 weeks later (assuming clinical stability). A Pearson correlation coefficient of $r = 0.85$ indicates good test-retest reliability.

Consideration: The time interval matters, too short risks practice effects; too long risks genuine change in the construct.

2. Inter-rater reliability: Measures agreement between two or more raters assessing the same subject. Quantified using Cohen's kappa (κ) for categorical data or Intraclass Correlation Coefficient (ICC) for continuous data.

Example: Two psychiatrists independently rate the same videotaped clinical interview using the PANSS. Cohen's kappa of 0.75 indicates substantial inter-rater agreement. This is critical for multisite clinical trials where different raters must produce comparable scores.

3. Split-half reliability: The test is divided into two halves (usually odd vs even items), and the correlation between halves is calculated. Corrected using the Spearman-Brown prophecy formula.

Example: The 21-item BDI is split into odd-numbered items and even-numbered items. A corrected correlation of $r = 0.88$ indicates good split-half reliability.

4. Internal consistency (Cronbach's alpha): Measures how well all items in a test measure the same underlying construct. Essentially an average of all possible split-half combinations.

Example: Cronbach's alpha of 0.89 for the PHQ-9 means the 9 items consistently measure the same construct (depression). An alpha > 0.70 is acceptable; > 0.90 may indicate item redundancy.

Internal and External Validity (4 marks)

Internal Validity

Internal validity is the degree to which a study's results accurately reflect the true relationship between the independent and dependent variables, free from confounding influences. It answers: "Did the intervention truly cause the observed effect?"

Threats to internal validity:

- **Selection bias:** Groups differ at baseline (mitigated by randomisation)
- **History:** External events affect outcome during the study period

- **Maturation:** Natural developmental changes in participants
- **Regression to the mean:** Extreme values at baseline tend to move toward the mean on retest
- **Attrition:** Differential dropout between groups
- **Instrumentation:** Changes in measurement tools or observers over time
- **Testing effect:** Repeated measurement itself affects performance

Example: A double-blind, randomised, placebo-controlled trial of a new antipsychotic has high internal validity, randomisation balances confounders, blinding prevents observer and performance bias, and placebo controls for non-specific effects.

External Validity

External validity is the degree to which study findings can be generalised to other populations, settings, and times.

Threats to external validity:

- **Selection bias in recruitment:** Strict inclusion criteria limit generalisability
- **Hawthorne effect:** Participants behave differently because they know they are being observed
- **Setting specificity:** Results from academic centres may not apply to primary care
- **Volunteer bias:** Volunteers may differ systematically from the general population
- **Cultural specificity:** Western-derived treatments or scales may not apply across cultures

Example: The STAR*D trial enrolled patients from both primary care and psychiatric clinics across the US, enhancing external validity. However, it excluded patients with bipolar disorder and active substance dependence, limiting generalisability to those populations.

The tension: RCTs maximise internal validity (controlled conditions) but may sacrifice external validity (strict criteria create unrepresentative samples). Pragmatic trials attempt to balance both.

Q5. What is psychiatric epidemiology? Uses. Types of designs. [10 marks: 2+4+4]

Exam Strategy

Define psychiatric epidemiology, list uses with Indian examples, then cover 4 major study designs.

Model Answer

Definition (2 marks)

Psychiatric epidemiology is the study of the distribution, determinants, and outcomes of mental disorders in defined populations. It applies epidemiological methods to understand the frequency (incidence, prevalence), risk factors, natural history, and burden of psychiatric illnesses, and to evaluate the effectiveness of interventions.

It differs from clinical psychiatry in that its unit of analysis is the population rather than the individual patient.

Uses of Psychiatric Epidemiology (4 marks)

1. **Estimation of disease burden:** Determines prevalence and incidence of mental disorders. The National Mental Health Survey (NMHS) 2016 estimated the lifetime prevalence of mental disorders in India at 13.7%, with a treatment gap of 70–92%.
1. **Identification of risk and protective factors:** Identifying that childhood adversity increases risk of adult depression (ACE studies), or that social support is protective against PTSD after trauma.
1. **Planning mental health services:** Prevalence data guides resource allocation. India's District Mental Health Programme (DMHP) expansion was informed by epidemiological data on service gaps.
1. **Evaluation of interventions:** Community-based studies evaluating the effectiveness of DMHP, or the MANAS trial evaluating collaborative care for depression in primary care in Goa.
1. **Understanding natural history:** Longitudinal studies tracking the course of first-episode psychosis inform treatment duration guidelines.
1. **Policy development:** WHO's Mental Health Atlas, Global Burden of Disease data, and NMHS data inform the Mental Healthcare Act 2017 and National Mental Health Policy.

Types of Study Designs (4 marks)

1. Cross-sectional (Prevalence study)

- Measures exposure and outcome simultaneously
- Provides prevalence estimates
- *Example:* NMHS 2016, surveyed 34,802 individuals to estimate prevalence of mental disorders
- *Limitation:* Cannot establish temporality

2. Case-control study

- Compares individuals with disease (cases) to those without (controls), looks backward for exposure
- Measure: Odds ratio

- *Example:* Study comparing rates of childhood sexual abuse in women with BPD (cases) versus women with other personality disorders (controls)
- *Limitation:* Recall bias, selection of appropriate controls

3. Cohort study

- Follows exposed and unexposed groups forward (prospective) or backward using records (retrospective)
- Measure: Relative risk, incidence rate
- *Example:* Dunedin Multidisciplinary Health and Development Study, followed a birth cohort to study how childhood factors predict adult mental health
- *Limitation:* Expensive, time-consuming, loss to follow-up

4. Randomised Controlled Trial

- Random assignment to intervention or control
- Gold standard for causation
- *Example:* MANAS trial (Patel et al., 2010), collaborative stepped care for depression in primary care in Goa
- *Limitation:* Ethical constraints, cost, limited external validity

Q6. Describe different types of epidemiological studies in Psychiatry. [10 marks]

Exam Strategy

Cover all major types. Use a comparison table. Add psychiatric examples for each.

Model Answer

Introduction

Epidemiological studies in psychiatry can be classified as observational (researcher observes without intervening) or experimental (researcher assigns an intervention). Each design has specific strengths, limitations, and appropriate applications.

Classification of Epidemiological Studies

A. Observational Studies

1. Descriptive Studies

(a) Case report/case series:

- Description of one or more patients with unusual presentation or outcome
- Hypothesis-generating

- *Example:* First reports of neuroleptic malignant syndrome; first case series of catatonia responding to lorazepam
- *Limitation:* No control group, no generalisability

(b) Cross-sectional (Prevalence study):

- Measures exposure and disease status simultaneously in a defined population
- Provides prevalence, not incidence
- *Measure:* Prevalence ratio
- *Example:* WHO World Mental Health Survey (WMHS); National Mental Health Survey of India 2016
- *Strengths:* Quick, inexpensive, useful for health service planning
- *Limitations:* Cannot establish causation (temporal ambiguity), prevalence bias (over-represents chronic conditions)

(c) Ecological study:

- Uses aggregate data for populations, not individuals
- *Example:* Countries with higher lithium in drinking water showing lower suicide rates
- *Limitation:* Ecological fallacy, cannot infer individual-level associations from group-level data

2. Analytical Observational Studies

(a) Case-control study:

- Starts with cases (disease+) and controls (disease–), compares past exposure
- Direction: Retrospective (outcome → exposure)
- *Measure:* Odds Ratio (OR) = ad/bc
- *Example:* Childhood trauma in patients with dissociative identity disorder vs. controls; cannabis use in first-episode psychosis vs. controls
- *Strengths:* Efficient for rare diseases, quick, inexpensive
- *Limitations:* Recall bias, selection bias, cannot calculate incidence

(b) Cohort study:

- Starts with exposed and unexposed groups, follows forward
- Direction: Prospective or retrospective
- *Measure:* Relative Risk (RR), Incidence Rate Ratio
- *Example:* Edinburgh Postnatal Depression Scale at 6 weeks predicting attachment outcomes at 1 year (prospective cohort); Cannabis use in adolescence and risk of psychosis (Dunedin study)
- *Strengths:* Establishes temporality, calculates incidence, multiple outcomes

- *Limitations:* Expensive, time-consuming, loss to follow-up, not efficient for rare outcomes

Comparison of Analytical Observational Designs:

FEATURE	CASE-CONTROL	COHORT
Direction	Backward	Forward
Starts with	Disease status	Exposure status
Measure	Odds Ratio	Relative Risk
Best for	Rare diseases	Rare exposures
Bias risk	Recall bias	Loss to follow-up
Cost	Lower	Higher

B. Experimental Studies

(a) Randomised Controlled Trial (RCT):

- Random assignment to intervention or control group
- Gold standard for establishing causation
- *Features:* Randomisation, blinding (single / double / triple), allocation concealment, ITT analysis
- *Example:* CATIE trial (comparing atypical antipsychotics); STAR*D trial (sequential treatment for depression)
- *Strengths:* Highest internal validity, controls confounders
- *Limitations:* Expensive, ethical constraints, may lack external validity

(b) Quasi-experimental study:

- Intervention without randomisation
- *Example:* Before-after study of suicide rates following media guidelines implementation
- *Limitation:* Lacks randomisation, more vulnerable to confounders

(c) Community trial:

- Intervention applied at the community level
- *Example:* MANAS trial, cluster-randomised trial of collaborative care in Goa primary health centres

Q7. Discuss Non-Parametric Tests. [10 marks]

Exam Strategy

Define, explain when to use, then describe individual tests with examples. Include comparison table.

Model Answer

Definition and Rationale

Non-parametric tests (also called distribution-free tests) are statistical tests that do not assume the data follows a specific probability distribution (typically the normal distribution). They are used when:

- Data is ordinal or ranked
- Data is not normally distributed (skewed)
- Sample size is small
- Outliers are present that would distort parametric results
- Assumptions of parametric tests (normality, homogeneity of variance) are violated

Non-parametric tests work on ranks rather than raw values, making them more robust to outliers and distribution violations.

Individual Non-Parametric Tests

1. Mann-Whitney U Test

- Non-parametric alternative to the independent samples t-test
- Compares two independent groups by ranking all observations
- *Null hypothesis:* The distributions of the two groups are identical
- *Example:* Comparing patient satisfaction scores (ordinal: 1–5 Likert scale) between two hospitals
- *Psychiatry example:* Comparing CGI-Severity scores between patients on clozapine vs. olanzapine

2. Wilcoxon Signed-Rank Test

- Non-parametric alternative to the paired t-test
- Compares two related samples (before-after, matched pairs)
- *Null hypothesis:* The median difference between paired observations is zero
- *Example:* Comparing patient-reported anxiety severity (ordinal scale) before and after a mindfulness intervention in the same patients

3. Kruskal-Wallis Test

- Non-parametric alternative to one-way ANOVA
- Compares three or more independent groups
- *Null hypothesis:* All groups have the same distribution
- *Post-hoc:* If significant, use Dunn's test for pairwise comparisons
- *Example:* Comparing quality of life scores across four treatment groups (SSRI, SNRI, TCA, placebo) when scores are not normally distributed

4. Friedman Test

- Non-parametric alternative to repeated measures ANOVA
- Compares three or more related groups (same subjects at multiple time points)
- *Example:* Comparing symptom severity scores at baseline, 4 weeks, and 8 weeks in the same group of patients

5. Spearman's Rank Correlation (ρ)

- Non-parametric alternative to Pearson's r
- Measures the strength and direction of monotonic relationship between two ranked variables
- *Example:* Correlation between severity ranking on PANSS and level of social functioning (ordinal categories)

6. Fisher's Exact Test

- Used when Chi-square assumptions are violated (expected cell count < 5)
- Calculates exact probability for 2×2 tables with small samples
- *Example:* Association between a rare genetic polymorphism and treatment response in a sample of 12 patients

7. Sign Test

- Simplest non-parametric test for paired data
- Only considers direction of change (positive or negative), not magnitude
- Less powerful than Wilcoxon signed-rank but requires fewer assumptions
- *Example:* Whether more patients improved than worsened after an intervention

Comparison Table: Parametric vs Non-Parametric Equivalents

PARAMETRIC	NON-PARAMETRIC	PURPOSE
Independent t-test	Mann-Whitney U	2 independent groups
Paired t-test	Wilcoxon signed-rank	2 related groups
One-way ANOVA	Kruskal-Wallis	3+ independent groups
Repeated measures ANOVA	Friedman	3+ related groups
Pearson r	Spearman ρ	Correlation
Chi-square	Fisher's exact	Categorical data (small n)

Advantages of Non-Parametric Tests:

- No distribution assumptions required
- Can handle ordinal data and ranked data

- Robust to outliers
- Valid for small sample sizes

Limitations:

- Less statistical power than parametric equivalents (when parametric assumptions are met)
 - Cannot easily handle complex designs (interactions, covariates)
 - May lose information by converting continuous data to ranks
-

Q8. Chi Square test. [10 marks]

Exam Strategy

Define, explain types, give formula, worked example, assumptions, and psychiatric application.

Model Answer

Definition

The Chi-square (χ^2) test is a non-parametric statistical test used to examine the association between two categorical (nominal or ordinal) variables. It compares observed frequencies with expected frequencies under the null hypothesis of no association.

Types of Chi-Square Test

1. Chi-Square Test of Independence

- Tests whether two categorical variables are independent of each other
- Used with contingency tables (2×2 or larger)
- *Null hypothesis:* The two variables are independent (no association)
- *Example:* Is there an association between gender (male/female) and diagnosis (depression/anxiety)?

2. Chi-Square Goodness of Fit

- Tests whether observed frequencies in a single categorical variable match expected frequencies
- *Null hypothesis:* Observed distribution matches expected distribution
- *Example:* Are psychiatric diagnoses equally distributed across four blood groups?

Formula

$$\chi^2 = \sum [(O - E)^2 / E]$$

Where: O = observed frequency, E = expected frequency

For a 2×2 table, E for each cell = (row total × column total) / grand total

Degrees of Freedom: $df = (\text{rows} - 1) \times (\text{columns} - 1)$. For a 2×2 table, $df = 1$.

Worked Example

A study examines whether gender is associated with treatment response:

	RESPONDED	DID NOT RESPOND	TOTAL
Male	30	20	50
Female	40	10	50
Total	70	30	100

Expected frequencies (under H_0):

- Male, responded: $(50 \times 70)/100 = 35$
- Male, not responded: $(50 \times 30)/100 = 15$
- Female, responded: $(50 \times 70)/100 = 35$
- Female, not responded: $(50 \times 30)/100 = 15$

$$\chi^2 = (30-35)^2/35 + (20-15)^2/15 + (40-35)^2/35 + (10-15)^2/15$$

$$\chi^2 = 0.71 + 1.67 + 0.71 + 1.67 = 4.76$$

With $df = 1$, critical value at $\alpha = 0.05$ is 3.84. Since $4.76 > 3.84$, $p < 0.05$. We reject H_0 , there is a significant association between gender and treatment response.

Assumptions and Conditions

1. Data must be categorical (nominal or ordinal)
2. Observations must be independent (each subject contributes to only one cell)
3. Expected frequency ≥ 5 in at least 80% of cells
4. No cell should have an expected frequency < 1
5. If assumptions are violated → use **Fisher's exact test**

Yates' Correction for Continuity

- Applied to 2×2 tables to correct for overestimation of χ^2

- FORMULA: $\chi^2 = \sum [(O - E - 0.5)^2 / E]$

- Makes the test more conservative (reduces Type I error)

Psychiatric Applications

- Association between adherence (yes/no) and relapse (yes/no)
- Comparing proportion of responders across treatment groups
- Association between family history of mental illness and diagnosis

- Comparing categorical outcomes (improved / not improved) across different psychotherapy modalities
-

Q9. Paired t Test. [10 marks]

Exam Strategy

Define, explain when to use, assumptions, formula, worked example with psychiatric data, interpretation.

Model Answer

Definition

The paired t-test (also called dependent samples t-test) is a parametric statistical test used to compare the means of two related measurements from the same subjects or matched pairs. It tests whether the mean difference between paired observations is significantly different from zero.

When to Use

- Same group of subjects measured at two time points (before-after design)
- Matched pairs of subjects (matched on key variables like age, gender)
- Each observation in one group has a natural pairing with an observation in the other group

Assumptions

1. **Continuous data** (interval or ratio scale)
2. **Normal distribution of differences** (not the raw scores, the differences between pairs must be approximately normal)
3. **Random sampling** from the population
4. **Paired observations**, each subject has two measurements
5. No significant outliers in the difference scores

Formula

$$t = \bar{d} / (SD_d / \sqrt{n})$$

Where:

- $\bar{d}$ = mean of the differences ($d = X_1 - X_2$ for each pair)
- SD_d = standard deviation of the differences
- n = number of pairs
- $df = n - 1$

Worked Example

A psychiatrist administers the HAM-D to 8 patients before and after 6 weeks of SSRI treatment:

PATIENT	PRE-TREATMENT	POST-TREATMENT	DIFFERENCE (D)
1	24	18	6
2	20	14	6
3	28	22	6
4	22	20	2
5	26	16	10
6	18	12	6
7	30	24	6
8	24	16	8

Calculations:

- $\bar{d} = (6+6+6+2+10+6+6+8)/8 = 50/8 = 6.25$
- $SD_d = 2.25$ (calculated from deviations)
- $t = 6.25 / (2.25/\sqrt{8}) = 6.25 / 0.796 = 7.85$
- $df = 8 - 1 = 7$
- Critical t at $\alpha = 0.05$, $df = 7$ (two-tailed) = 2.365

Since $7.85 > 2.365$, $p < 0.05$. There is a statistically significant reduction in HAM-D scores after 6 weeks of SSRI treatment.

Interpretation

- The mean reduction in HAM-D score was 6.25 points (95% CI: 4.37–8.13)
- This is both statistically significant ($p < 0.001$) and clinically meaningful (> 3 -point change on HAM-D is considered the MCID)
- Effect size: Cohen's $d = \bar{d}/SD_d = 6.25/2.25 = 2.78$ (very large effect)

Advantages Over Independent t-test

- Controls for individual differences (each subject serves as their own control)
- More powerful because it reduces error variance
- Requires smaller sample sizes

When NOT to Use

- If the differences are not normally distributed → use Wilcoxon signed-rank test
- If data is ordinal → use Wilcoxon signed-rank test
- If more than two time points → use repeated measures ANOVA

Psychiatric Applications

- Pre-post treatment studies (HAM-D before and after ECT, medication, or psychotherapy)
- Comparing two scales administered to the same patient
- Matched case-control studies (matching on age, gender, duration of illness)

Q10. Enumerate statistical tests. Describe t-test with example. [10 marks: 4+6]

Exam Strategy

First part: classify all tests in a table (4 marks). Second part: detailed t-test with both types and an example (6 marks).

Model Answer

Enumeration of Statistical Tests (4 marks)

CATEGORY	PARAMETRIC	NON-PARAMETRIC
2 independent groups	Independent t-test	Mann-Whitney U
2 paired groups	Paired t-test	Wilcoxon signed-rank
3+ independent groups	One-way ANOVA	Kruskal-Wallis
3+ related groups	Repeated measures ANOVA	Friedman test
Correlation	Pearson r	Spearman ρ
Categorical variables		Chi-square, Fisher's exact
Prediction (continuous outcome)	Linear regression	
Prediction (binary outcome)	Logistic regression	

Additional tests: Two-way ANOVA (two factors), ANCOVA (adjusting for covariates), MANOVA (multiple dependent variables), McNemar's test (paired categorical), Cochran's Q (3+ paired categorical).

The t-test, Detailed Description (6 marks)

The t-test is a parametric statistical test that compares the means of one or two groups to determine if there is a statistically significant difference. Developed by William Sealy Gosset (published under the pseudonym "Student" in 1908).

General Assumptions:

- Continuous data (interval or ratio)
- Normal distribution of data (or of differences for paired t-test)

- Homogeneity of variance for independent t-test (assessed by Levene's test)
- Independent observations

Type 1: Independent (Unpaired) t-test

Purpose: Compares means of two independent groups.

Formula: $t = (\bar{X}_1 - \bar{X}_2) / \sqrt{Sp^2 \times (1/n_1 + 1/n_2)}$

Where Sp^2 is the pooled variance.

Example: Comparing mean HAM-D scores between 30 patients receiving fluoxetine and 30 patients receiving placebo after 8 weeks:

- Fluoxetine group: Mean = 10.5, SD = 4.2
- Placebo group: Mean = 16.8, SD = 5.1
- $t = -5.35$, $df = 58$, $p < 0.001$
- Interpretation: Fluoxetine significantly reduces HAM-D scores compared to placebo

When to use Welch's t-test: If Levene's test is significant (unequal variances), use Welch's t-test which does not assume equal variances.

Type 2: Paired (Dependent) t-test

Purpose: Compares means of two related measurements (before-after, matched pairs).

Formula: $t = \bar{d} / (SD_d / \sqrt{n})$

Example: Measuring PANSS scores in 25 patients before and 4 weeks after starting risperidone:

- Mean baseline PANSS: 85.6 (SD 12.3)
- Mean 4-week PANSS: 62.4 (SD 14.1)
- Mean difference: 23.2 (SD 8.7)
- $t = 23.2 / (8.7 / \sqrt{25}) = 23.2 / 1.74 = 13.33$
- $df = 24$, $p < 0.001$
- Interpretation: There is a statistically significant reduction in PANSS scores after 4 weeks of risperidone

Type 3: One-sample t-test

Purpose: Compares a sample mean to a known or hypothesised population mean.

Example: Testing whether the mean IQ of patients with treatment-resistant schizophrenia differs from the population mean of 100.

Reporting Format

"An independent samples t-test revealed a statistically significant difference in HAM-D scores between the fluoxetine group ($M = 10.5$, $SD = 4.2$) and the placebo group ($M = 16.8$,

SD = 5.1), $t(58) = -5.35$, $p < 0.001$, Cohen's $d = 1.35$."

Q11. Enumerate statistical tests. Describe paired t-test. Two non-parametric tests. [10 marks: 4+2+4]

Exam Strategy

Quick enumeration table (4 marks). Concise paired t-test (2 marks). Two non-parametric tests in detail (4 marks).

Model Answer

Enumeration of Statistical Tests (4 marks)

See Q10 for complete table. Briefly:

Parametric tests: Independent t-test, paired t-test, one-way ANOVA, two-way ANOVA, repeated measures ANOVA, Pearson correlation, linear regression, logistic regression, ANCOVA.

Non-parametric tests: Mann-Whitney U, Wilcoxon signed-rank, Kruskal-Wallis, Friedman, Spearman correlation, Chi-square, Fisher's exact test, McNemar's test, Sign test, Cochran's Q.

Paired t-test (2 marks)

The paired t-test compares the means of two related measurements from the same subjects. It calculates the difference (d) for each pair, then tests whether the mean difference ($\bar{d}$) is significantly different from zero.

Formula: $t = \bar{d} / (SD_d / \sqrt{n})$, $df = n - 1$

Assumptions: Continuous data, normal distribution of differences, paired observations.

Example: Comparing BDI scores in 20 patients before and after 12 sessions of CBT. If mean difference = 8.5 (SD = 3.2), $t = 8.5 / (3.2 / \sqrt{20}) = 11.87$, $p < 0.001$, significant improvement after CBT.

Two Non-Parametric Tests (4 marks)

1. Mann-Whitney U Test (2 marks)

The Mann-Whitney U test is the non-parametric alternative to the independent samples t-test. It compares the distributions of two independent groups by ranking all observations from both groups together.

Procedure:

1. Combine all observations and rank them from lowest to highest
2. Sum the ranks for each group
3. Calculate U statistic for each group

4. Compare U to the critical value or calculate z-score for large samples

Assumptions: Ordinal or continuous data, independent observations, similar distribution shapes (tests whether one distribution is shifted relative to the other).

Example: Comparing satisfaction with care (5-point Likert scale: very dissatisfied to very satisfied) between patients in a community mental health centre ($n = 25$) and a tertiary psychiatry department ($n = 30$). Since Likert data is ordinal, the Mann-Whitney U test is appropriate rather than the t-test.

2. Wilcoxon Signed-Rank Test (2 marks)

The Wilcoxon signed-rank test is the non-parametric alternative to the paired t-test. It compares two related measurements by analysing the magnitude and direction of differences.

Procedure:

1. Calculate the difference for each pair
2. Rank the absolute differences (ignoring zeros)
3. Assign the sign (+ or -) of the original difference to each rank
4. Sum the positive ranks ($W+$) and negative ranks ($W-$)
5. The test statistic is the smaller of $W+$ and $W-$

Assumptions: Ordinal or continuous data, paired observations, symmetric distribution of differences.

Example: Comparing self-rated anxiety on a 10-point visual analogue scale before and after a 20-minute relaxation exercise in 15 patients. Since the VAS data may not be normally distributed with a small sample, the Wilcoxon signed-rank test is more appropriate than a paired t-test.

Q12. Describe Factor Analysis and applications in psychiatric research. [10 marks]

Exam Strategy

Define, explain EFA vs CFA, key terms, procedure, then psychiatric applications (the bulk of the marks).

Model Answer

Definition

Factor analysis is a multivariate statistical technique that reduces a large number of observed variables into a smaller number of underlying latent factors (dimensions) that explain the patterns of correlations among the variables. It identifies clusters of intercorrelated variables that are driven by the same underlying construct.

Types

1. Exploratory Factor Analysis (EFA)

- No prior hypothesis about factor structure
- The data determines how many factors exist and which variables load on which factor
- Used during scale development
- "Let the data speak"

2. Confirmatory Factor Analysis (CFA)

- Tests a pre-specified factor structure
- Uses structural equation modelling (SEM) to assess model fit
- Used to validate an existing scale or theoretical model
- Reports fit indices: CFI, RMSEA, SRMR, TLI

Key Concepts

TERM · DEFINITION

Factor Latent (unobserved) variable underlying a group of observed variables

Factor loading Correlation between an observed variable and a factor (> 0.3 or > 0.4 considered meaningful)

Eigenvalue Amount of total variance explained by a factor

Kaiser criterion Retain factors with eigenvalue > 1

Scree plot Graph of eigenvalues; retain factors before the "elbow"

Communality Proportion of a variable's variance explained by extracted factors

Rotation Simplifies factor structure. *Varimax* = orthogonal (factors uncorrelated).
Oblimin/promax = oblique (factors allowed to correlate)

KMO Kaiser-Meyer-Olkin measure of sampling adequacy (> 0.6 acceptable, > 0.8 good)

Bartlett's test Tests whether the correlation matrix is an identity matrix (should be significant)

Procedure of EFA

1. Assess suitability: $KMO > 0.6$, Bartlett's test significant
2. Extract factors: Principal Component Analysis (PCA) or Principal Axis Factoring
3. Determine number of factors: Eigenvalue > 1 (Kaiser), scree plot, parallel analysis
4. Rotate factors: Varimax (orthogonal) or oblimin (oblique)

5. Interpret: Examine factor loadings, name factors based on loading pattern
6. Report: Variance explained, factor loadings, communalities

Applications in Psychiatric Research

1. Scale Development and Validation

- The PANSS (Positive and Negative Syndrome Scale): Factor analysis identified the three-factor model (positive symptoms, negative symptoms, general psychopathology), later analyses have proposed 5-factor models
- The BDI: Factor analysis reveals cognitive-affective and somatic factors of depression
- The PCL-5 (PTSD Checklist): CFA confirms the four-factor DSM-5 model (intrusion, avoidance, negative cognitions/mood, hyperarousal)

2. Symptom Dimension Research

- Schizophrenia: Factor analysis of symptoms identified 5 dimensions, positive, negative, cognitive, affective, and excitement/hostility, influencing classification and treatment approaches
- Depression: Identifying cognitive, somatic, and affective dimensions helps in understanding why SSRIs and TCAs may work differently on different symptom clusters
- OCD: Factor analysis identified 4 symptom dimensions, contamination/cleaning, symmetry/ordering, forbidden thoughts, hoarding, influencing treatment selection

3. Personality Research

- The Five-Factor Model (Big Five: Openness, Conscientiousness, Extraversion, Agreeableness, Neuroticism) was derived through factor analysis of personality descriptors
- Alternative Model of Personality Disorders (AMPD) in DSM-5 Section III uses factor-analytically derived personality trait domains

4. Diagnostic Classification

- Factor analysis of symptom data has informed revisions to ICD and DSM
- The p-factor (general psychopathology factor), analogous to g-factor in intelligence, was identified through bifactor analysis of psychiatric symptoms, suggesting a common liability to all mental disorders

5. Treatment Research

- Identifying which symptom dimensions respond to specific treatments
 - The MATRICS consensus: factor analysis of cognitive tests identified 7 cognitive domains impaired in schizophrenia (speed of processing, attention, working memory, verbal learning, visual learning, reasoning, social cognition)
-

Q13. What is EBM? Steps. Practice with example. [10 marks: 2+2+6]: LONG ESSAY CANDIDATE

Exam Strategy

Long essay. After definition and steps, walk through a COMPLETE clinical example through all 5 steps. This is what earns the 6 marks.

Model Answer

Definition (2 marks)

Evidence-Based Medicine (EBM) is defined as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" (Sackett et al., 1996). It integrates three pillars:

1. **Best available research evidence**
2. **Clinical expertise** of the practitioner
3. **Patient values and preferences**

EBM does not mean blindly following evidence, it means integrating evidence with clinical judgment and the individual patient's context.

Five Steps (2 marks)

1. **ASK**, Formulate a clear clinical question (PICO format)
2. **ACQUIRE**, Search for the best available evidence
3. **APPRAISE**, Critically evaluate the evidence for validity and applicability
4. **APPLY**, Integrate evidence with clinical expertise and patient preferences
5. **ASSESS**, Evaluate the outcome and the process

Practice with a Detailed Clinical Example (6 marks)

Clinical Scenario:

A 35-year-old man with moderate major depressive disorder (MDD) has had partial response to fluoxetine 20 mg for 8 weeks. You are considering augmentation strategies.

Step 1: ASK, Formulate the PICO question

COMPONENT · DETAIL

P (Population) Adults with MDD who have partially responded to an SSRI

I (Intervention) Augmentation with aripiprazole

C (Comparison) Augmentation with lithium

O (Outcome) Remission rate (HAM-D $\leq$ 7) at 8 weeks

PICO question: "In adults with MDD who have partially responded to an SSRI, does augmentation with aripiprazole compared to lithium lead to higher remission rates?"

Step 2: ACQUIRE, Search for evidence

Search strategy:

- PubMed: ("major depressive disorder" OR "depression") AND ("aripiprazole" OR "augmentation") AND ("lithium") AND ("randomised controlled trial")
- Cochrane Library: Search for systematic reviews on antidepressant augmentation
- NICE / APA guidelines on treatment-resistant depression

Key findings:

- Nelson and Papakostas (2009): Meta-analysis of aripiprazole augmentation, NNT = 9 for remission
- STAR*D Level 3: Lithium augmentation showed modest benefit
- Network meta-analysis (Zhou et al., 2015): Atypical antipsychotic augmentation superior to lithium for remission

Step 3: APPRAISE, Critical appraisal

For the network meta-analysis:

- *Design:* Systematic review with network meta-analysis (Level 1a evidence)
- *Internal validity:* Comprehensive search strategy, multiple databases, risk of bias assessment conducted
- *Heterogeneity:* $I^2 = 45\%$ (moderate), some heterogeneity exists
- *Publication bias:* Funnel plot showed mild asymmetry
- *Effect size:* Aripiprazole augmentation: OR for remission = 2.1 (95% CI: 1.5–3.0) vs placebo
- *NNT:* ~9 for remission, NNH for weight gain: ~6
- *Applicability:* Most studies were in Western populations; limited Indian data
- *Limitations:* Industry sponsorship in many aripiprazole trials, short duration (6–8 weeks)

Step 4: APPLY, Integrate evidence with clinical context

- **Evidence says:** Aripiprazole augmentation has modest efficacy (NNT = 9) with metabolic side effects
- **Clinical expertise:** In my experience, lithium augmentation is well-tolerated in younger patients and has anti-suicidal properties
- **Patient factors:** This patient has a family history of bipolar disorder → lithium may serve dual purpose (augmentation + mood stabilisation). He is concerned about weight gain → aripiprazole's metabolic profile is relevant.

- **Decision:** After discussing options with the patient, including benefits (lithium's anti-suicidal properties, potential mood stabiliser benefit given family history) and risks (thyroid, renal monitoring needed), the patient opts for lithium augmentation.

This illustrates that EBM does not dictate a single correct answer, the "best evidence" is integrated with clinical expertise and patient preferences.

Step 5: ASSESS, Evaluate outcomes

- After 8 weeks of lithium augmentation (serum level 0.6–0.8 mEq/L), the patient achieves remission (HAM-D = 5)
- Thyroid and renal function remain normal
- The clinician reflects: Was this the right decision? Would auditing outcomes across all augmentation patients in the clinic provide useful data?
- This feeds back into quality improvement and future clinical questions

Q14. What is EBM? Practice in India? Limitations. [10 marks]

Exam Strategy

Quick definition, then focus on Indian context (unique section) and limitations.

Model Answer

Definition

Evidence-Based Medicine (EBM) is the integration of the best available research evidence with clinical expertise and patient values in making clinical decisions (Sackett, 1996). It follows 5 steps: Ask, Acquire, Appraise, Apply, Assess.

Practice of EBM in India

Current status:

- EBM is increasingly taught in medical curricula following CBME (Competency-Based Medical Education) guidelines
- Indian Psychiatric Society (IPS) publishes clinical practice guidelines adapted from international evidence
- Institutions like PG exams, and PG exams conduct systematic reviews and contribute to the Cochrane Collaboration

Challenges in Indian context:

1. **Limited Indian evidence base:** Most psychiatric RCTs are conducted in Western, educated, industrialised, rich, democratic (WEIRD) populations. Pharmacogenomic differences (e.g., CYP2D6 polymorphisms in South Asians), cultural factors, and disease presentation may differ.

1. **Access to evidence:** Despite Sci-Hub usage, many clinicians lack institutional access to journals. Open-access initiatives (PubMed Central, IJPM) help but coverage is incomplete.
1. **Treatment gap:** With a 70–92% treatment gap (NMHS 2016) and 0.3 psychiatrists per 100,000 population, implementing evidence-based protocols is constrained by workforce shortages.
1. **Cultural applicability:** Psychotherapy protocols (CBT, DBT) developed in Western settings require cultural adaptation for Indian patients (e.g., family involvement, spiritual frameworks, idioms of distress).
1. **Resource constraints:** Evidence-based treatments like clozapine require blood monitoring, not feasible in rural areas. Cost of newer medications limits implementation.
1. **Research quality:** Many Indian psychiatric studies have methodological limitations, small sample sizes, single-centre designs, lack of randomisation.

Positive developments:

- MANAS trial (Patel et al., 2010), a landmark Indian RCT demonstrating effectiveness of collaborative care for depression in Goa
- National Mental Health Survey 2016, first nationally representative psychiatric epidemiological data
- DBT India initiative, SCARF (Schizophrenia Research Foundation) in Chennai
- SPIRIT (South Asian Hub for Advocacy, Research, and Education in Mental Health)

Limitations of EBM

1. **Evidence hierarchy bias:** Over-reliance on RCTs devalues clinical experience, qualitative research, and patient narratives
 2. **Publication bias:** Published evidence is skewed toward positive results
 3. **Lag time:** Evidence takes years to translate into practice (17-year bench-to-bedside gap)
 4. **Not all questions are answerable by RCTs:** Ethical / practical constraints (e.g., randomising to childhood adversity)
 5. **Individual variation:** Evidence provides population-level estimates, the individual patient may respond differently
 6. **Industry influence:** Pharmaceutical industry funding can bias trial design, outcome selection, and reporting
 7. **Cookbook medicine risk:** EBM misapplied becomes rigid algorithm-following, ignoring clinical nuance
 8. **Equity issues:** Evidence generated from privileged populations may not serve marginalised communities
-

Q15. Discuss levels of evidence and role in EBM. [10 marks]

Exam Strategy

Present the full hierarchy, explain each level, then discuss their role in clinical decision-making.

Model Answer

Introduction

Levels of evidence refer to a hierarchical ranking system that grades the quality and reliability of evidence from clinical research. This hierarchy helps clinicians quickly assess the strength of evidence supporting a clinical decision.

Levels of Evidence Hierarchy

LEVEL	STUDY TYPE	DESCRIPTION
1a	Systematic review of RCTs	Pooled analysis of multiple RCTs with meta-analysis. Strongest evidence.
1b	Individual RCT with narrow CI	Single well-designed RCT with adequate power and narrow confidence intervals.
1c	All-or-none studies	Dramatic effects where all patients previously died but now survive (e.g., insulin for DKA).
2a	Systematic review of cohort studies	Pooled analysis of observational cohort studies.
2b	Individual cohort study or low-quality RCT	Single cohort study or an RCT with methodological limitations.
2c	Outcomes research	Ecological studies using large databases.
3a	Systematic review of case-control studies	Pooled analysis of case-control studies.
3b	Individual case-control study	Single well-designed case-control study.
4	Case series	Report of a series of patients without a control group.
5	Expert opinion	Opinion of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

The Evidence Pyramid (Visual Description)

The evidence pyramid has its base as expert opinion (broadest, weakest) and its apex as systematic reviews/meta-analyses (narrowest, strongest). Moving up the pyramid:

- **Base:** Expert opinion, large volume, weakest methodology
- **Case series/reports**, descriptive, no controls
- **Case-control studies**, analytical, retrospective
- **Cohort studies**, analytical, prospective, can establish temporality
- **RCTs**, experimental, can establish causation
- **Apex:** Systematic reviews/meta-analyses, synthesise all available evidence

Role of Levels of Evidence in EBM

1. Guiding treatment decisions

- When Level 1 evidence exists, it should form the foundation of clinical practice
- *Example:* Cochrane review supporting SSRIs for moderate-severe depression (Level 1a), should be first-line treatment

2. Developing clinical guidelines

- Guidelines grade their recommendations based on evidence levels
- NICE, APA, WFSBP, and IPS guidelines use evidence levels to justify recommendations
- Grade A recommendation (based on Level 1 evidence) carries more weight than Grade C (based on Level 4-5)

3. Identifying evidence gaps

- When only Level 4-5 evidence exists for a clinical question, this highlights the need for RCTs
- *Example:* Ketamine for treatment-resistant depression initially had only case series (Level 4); this drove the design of RCTs

4. Clinical decision-making in practice

- Level 1 evidence may not always be available or applicable
- In such cases, clinicians use the best available evidence even if it is lower-level
- *Example:* For ultra-treatment-resistant depression, combination strategies often rely on Level 4-5 evidence because RCTs are lacking

5. Limitations of the hierarchy

- Higher level ≠ always better for all questions
- Qualitative research (not on the hierarchy) is essential for understanding patient experience

- Well-designed observational studies can sometimes provide stronger evidence than flawed RCTs
 - Network meta-analyses depend on the quality of included RCTs
 - The hierarchy works best for treatment questions; questions about prognosis, diagnosis, and harm may need different frameworks
-

Q16. What is quantitative research? Features, strengths, limitations. [10 marks: 3+3+2+2]

Exam Strategy

Define with features (3+3 marks), then strengths and limitations (2+2 marks).

Model Answer

Definition (3 marks)

Quantitative research is a systematic empirical investigation that uses numerical data, statistical analysis, and mathematical models to test hypotheses, establish relationships between variables, and make generalisable inferences about populations. It follows the scientific method of hypothesis formulation, data collection, statistical testing, and interpretation.

The underlying philosophy is positivism, the belief that reality is objective, measurable, and can be understood through systematic observation and experimentation.

Features (3 marks)

1. **Numerical data:** Variables are measured and expressed as numbers (e.g., HAM-D scores, age, number of hospitalisations)
2. **Hypothesis-driven:** Begins with a clear, testable hypothesis (H_0 and H_1)
3. **Structured design:** Follows predetermined protocols, study design, sampling, data collection, and analysis are planned before data collection begins
4. **Large sample sizes:** Aims for adequate statistical power through sample size calculation
5. **Standardised instruments:** Uses validated rating scales, structured interviews, laboratory measures
6. **Statistical analysis:** Uses inferential statistics (t-test, ANOVA, regression) to test hypotheses
7. **Objectivity:** Researcher maintains distance from participants; findings should be reproducible
8. **Generalisability:** Aims to generalise findings from sample to population
9. **Control of variables:** Attempts to control or adjust for confounders
10. **Replicability:** Detailed methodology allows other researchers to replicate the study

Strengths (2 marks)

- **Objectivity and precision:** Numerical data minimises subjective interpretation
- **Generalisability:** Large, representative samples allow population-level inferences
- **Causal inference:** Experimental designs (RCTs) can establish cause-and-effect
- **Statistical power:** Can detect small but meaningful effects
- **Reproducibility:** Standardised methods allow replication
- **Policy influence:** Quantitative evidence (NNT, effect sizes) directly informs treatment guidelines

Limitations (2 marks)

- **Reductionism:** Complex human experiences (e.g., suffering, meaning, therapeutic relationship) are reduced to numbers
- **Context stripping:** Decontextualises findings, a mean HAM-D score doesn't capture the lived experience of depression
- **Assumes measurability:** Not all psychiatric constructs are easily quantifiable (e.g., therapeutic alliance, insight)
- **Researcher bias in design:** Choice of variables, outcome measures, and statistical tests involves subjective decisions
- **Ecological validity:** Controlled laboratory or clinical settings may not reflect real-world conditions
- **Missing "why":** Tells you THAT something works but not WHY or HOW patients experience it

Q17. Qualitative vs quantitative research. [10 marks: 2+5+3]

Exam Strategy

Define both (2 marks), detailed comparison table (5 marks), when to use each in psychiatry (3 marks).

Model Answer

Definitions (2 marks)

Quantitative research uses numerical data and statistical analysis to test hypotheses, measure variables, and generalise findings to populations. It follows a deductive approach (theory → hypothesis → observation).

Qualitative research uses non-numerical data (words, themes, narratives) to explore meaning, experience, and social processes. It follows an inductive approach (observation → patterns → theory).

Detailed Comparison (5 marks)

FEATURE	QUANTITATIVE	QUALITATIVE
Philosophy	Positivism (objective reality)	Constructivism / interpretivism (subjective reality)
Approach	Deductive (theory-driven)	Inductive (data-driven)
Data type	Numbers, measurements	Words, narratives, images
Sample size	Large (powered for statistics)	Small (purposive, data saturation)
Sampling	Random / probability	Purposive, snowball, theoretical
Analysis	Statistical (t-test, ANOVA, regression)	Thematic, content, grounded theory, IPA
Instruments	Standardised scales, questionnaires	Interviews, focus groups, observation
Researcher role	Detached, objective	Embedded, reflexive
Outcome	Generalisable findings, effect sizes	Rich descriptions, themes, theory
Question type	"How much? How many? Is there a difference?"	"What is the experience like? How do people make sense of it?"
Rigour criteria	Validity, reliability	Credibility, transferability, dependability, confirmability
Causation	Can establish (RCTs)	Cannot establish
Replication	High (standardised methods)	Low (context-dependent)

When to Use Each in Psychiatry (3 marks)

Quantitative is preferred when:

- Testing drug efficacy (RCTs)
- Measuring prevalence and incidence (epidemiological surveys)
- Comparing treatment outcomes across groups
- Validating rating scales (psychometric studies)
- *Example:* "Does aripiprazole augmentation improve remission rates in treatment-resistant depression?", requires an RCT

Qualitative is preferred when:

- Exploring lived experience of illness (phenomenology)
- Understanding barriers to treatment adherence
- Developing culturally sensitive interventions

- Generating new hypotheses from patient narratives
- *Example:* "How do patients with schizophrenia experience auditory hallucinations?", requires phenomenological interviews

Mixed methods, integrating both:

- Increasingly used in psychiatric research
- *Example:* MANAS trial used quantitative outcomes (PHQ-9 remission) AND qualitative interviews with patients and health workers to understand implementation
- Sequential explanatory: Quantitative data first → qualitative to explain findings
- Sequential exploratory: Qualitative first → develop instrument → quantitative testing

Q18. What is meta-analysis vs systematic review? Key studies in psychiatry. [10 marks]

Exam Strategy

Define and compare (4 marks), process (3 marks), landmark psychiatric studies (3 marks).

Model Answer

Definitions and Comparison (4 marks)

FEATURE	SYSTEMATIC REVIEW	META-ANALYSIS
Definition	A structured, reproducible method of identifying, evaluating, and synthesising all available evidence relevant to a specific research question	A statistical technique that combines quantitative results from multiple studies into a single pooled estimate
Nature	Qualitative synthesis	Quantitative synthesis
Relationship	May or may not include a meta-analysis	Always part of a systematic review
When meta-analysis is NOT done	When studies are too heterogeneous, use different outcome measures, or have insufficient data for pooling	
Output	Narrative synthesis with tables	Forest plot, pooled effect size, I^2 , funnel plot

A meta-analysis is always nested within a systematic review, but not every systematic review performs a meta-analysis. When study heterogeneity is too high or studies are too clinically diverse, a narrative synthesis is more appropriate.

Process of Conducting a Systematic Review/Meta-analysis (3 marks)

1. **Formulate PICO question** and register protocol (PROSPERO)
2. **Search strategy:** Multiple databases (PubMed, Cochrane, Embase, PsycINFO), grey literature, hand-searching reference lists
3. **Study selection:** Two independent reviewers screen titles/ abstracts, then full texts; PRISMA flow diagram documents this
4. **Data extraction:** Standardised forms extracting sample size, effect sizes, outcomes
5. **Quality assessment:** Cochrane Risk of Bias tool (RCTs), Newcastle-Ottawa Scale (observational)
6. **Data synthesis:**
 7. Fixed-effect model (assumes one true effect across studies)
 8. Random-effects model (assumes true effect varies, used when heterogeneity exists)
9. **Assess heterogeneity:** I^2 statistic, Cochrane Q test
10. **Assess publication bias:** Funnel plot, Egger's test, trim-and-fill
11. **Sensitivity analysis:** Removing one study at a time to test robustness
12. **Report:** Following PRISMA guidelines

Forest plot interpretation: Each study represented by a square (point estimate) with horizontal line (CI). Diamond at bottom = pooled estimate. Vertical line of no effect (OR = 1 or MD = 0). If diamond does not cross this line → overall result is statistically significant.

Key Meta-analyses and Systematic Reviews in Psychiatry (3 marks)

1. **Cipriani et al., Lancet 2018:** Network meta-analysis of 21 antidepressants (522 trials, 116,477 patients). Found all antidepressants more effective than placebo. Amitriptyline, mirtazapine, and venlafaxine most effective; fluoxetine and escitalopram best accepted (lowest dropout).
1. **Leucht et al., Lancet 2012:** Meta-analysis of antipsychotics for schizophrenia (65 RCTs). Found all antipsychotics more effective than placebo; effect sizes were moderate. Clozapine, amisulpride, olanzapine, and risperidone showed largest effects.
1. **Cuijpers et al. (multiple reviews):** Extensive meta-analyses of psychotherapy for depression. CBT, IPT, and behavioural activation all effective; no consistent superiority of one modality over others (Dodo bird verdict). Combined psychotherapy + medication superior to either alone.
1. **Furukawa et al., World Psychiatry 2019:** Network meta-analysis of initial treatment strategies for depression (pharmacotherapy vs psychotherapy vs combined). Combined treatment most effective.
1. **NICE guidelines for schizophrenia, depression, bipolar disorder:** Based on systematic reviews of the evidence.

1. **Cochrane reviews in psychiatry:** Cover topics from ECT for depression to clozapine for treatment-resistant schizophrenia to psychoeducation for bipolar disorder.
-

Q19. Odds ratio. Confounding, effect modification, mediation. [10 marks: 4+2+2+2]

Exam Strategy

Detailed OR section with 2×2 table (4 marks). Then concise but clear explanations of each concept (2 marks each).

Model Answer

Odds Ratio (4 marks)

Definition: The odds ratio (OR) is a measure of association between an exposure and an outcome in case-control and cross-sectional studies. It compares the odds of exposure in cases to the odds of exposure in controls.

2×2 Table:

	DISEASE + (CASES)	DISEASE – (CONTROLS)
Exposed	a	b
Unexposed	c	d

Formula: $OR = (a \times d) / (b \times c)$

Interpretation:

- $OR = 1 \rightarrow$ No association between exposure and outcome
- $OR > 1 \rightarrow$ Exposure is associated with increased odds of disease (risk factor)
- $OR < 1 \rightarrow$ Exposure is associated with decreased odds of disease (protective factor)
- The 95% CI should not include 1 for the OR to be statistically significant

Example: A case-control study of childhood trauma and adult depression:

	DEPRESSION (CASES)	NO DEPRESSION (CONTROLS)
Trauma +	80	40
Trauma –	20	60

$$OR = (80 \times 60) / (40 \times 20) = 4800 / 800 = 6.0$$

Interpretation: Individuals with childhood trauma have 6 times the odds of developing depression compared to those without trauma.

OR vs RR: In case-control studies, we cannot calculate relative risk (because we select by outcome, not by exposure). OR approximates RR when the outcome is rare (< 10%).

Confounding (2 marks)

Definition: Confounding occurs when a third variable (confounder) is associated with both the exposure and the outcome, creating a spurious or distorted association between them.

Criteria for a confounder:

1. Associated with the exposure
2. Independently associated with the outcome
3. Not on the causal pathway between exposure and outcome

Example: A study finds that coffee consumption is associated with lung cancer. However, coffee drinkers are more likely to smoke. Smoking is the confounder, it is associated with both coffee consumption and lung cancer. Once you adjust for smoking, the coffee-lung cancer association disappears.

How to control confounding:

- *At design stage:* Randomisation (best), restriction, matching
- *At analysis stage:* Stratification, multivariate regression, propensity score matching

Detection: If the adjusted (stratified or regression-adjusted) estimate differs from the crude estimate by > 10%, confounding is present.

Effect Modification (Interaction) (2 marks)

Definition: Effect modification occurs when the magnitude of the association between an exposure and an outcome differs across levels of a third variable (the effect modifier). Unlike confounding, effect modification is a real biological or social phenomenon and should be reported, not adjusted away.

Example: A study finds that SSRI treatment reduces depression scores by 8 points in women but only 3 points in men. Gender is an effect modifier, the treatment effect differs by gender.

How to detect:

- Stratified analysis: different effect sizes in different strata
- Regression: significant interaction term (exposure × modifier)

How to handle: Report stratum-specific estimates. Do NOT adjust for effect modifiers (unlike confounders). If SSRIs work better in women, this is clinically important information.

Mediation (2 marks)

Definition: Mediation occurs when a third variable (mediator) lies on the causal pathway between the exposure and the outcome. The exposure causes the mediator, which in turn

causes the outcome.

Causal pathway: Exposure → Mediator → Outcome

Example: Childhood trauma → Maladaptive schemas → Adult depression. Maladaptive schemas mediate the relationship between trauma and depression. Part of the effect of trauma on depression operates through the development of maladaptive schemas.

Testing mediation (Baron & Kenny, 1986):

1. Exposure significantly predicts outcome (path c)
2. Exposure significantly predicts mediator (path a)
3. Mediator significantly predicts outcome when controlling for exposure (path b)
4. The effect of exposure on outcome is reduced (partial mediation) or non-significant (full mediation) when mediator is in the model (path c')

Types:

- **Full mediation:** Exposure effect becomes non-significant after including mediator
 - **Partial mediation:** Exposure effect is reduced but remains significant
-

Q20. Sampling techniques. Sample size. Principles of calculation. [10 marks: 2+2+6]

Exam Strategy

Quick sampling overview (2 marks), define sample size (2 marks), then detailed principles of calculation (6 marks).

Model Answer

Sampling Techniques (2 marks)

Probability sampling (every member has a known chance of selection):

- **Simple random:** Equal chance for all (lottery, random number table)
- **Stratified:** Divide into strata, sample from each (ensures subgroup representation)
- **Cluster:** Randomly select entire clusters (villages, schools)
- **Systematic:** Every kth individual from a list

Non-probability sampling (not everyone has equal chance):

- **Convenience:** Whoever is available
- **Purposive:** Selected by researcher for specific characteristics
- **Snowball:** Participants recruit others (hard-to-reach populations)

Sample Size (2 marks)

Sample size is the number of participants required in a study to detect a clinically meaningful effect with adequate statistical power while maintaining a specified level of significance. An adequate sample size is the ethical minimum, too small wastes resources and cannot answer the question, too large exposes unnecessary participants to experimental conditions.

Principles of Sample Size Calculation (6 marks)

1. Type I Error Rate (α)

- The probability of rejecting the null hypothesis when it is true (false positive)
- Conventionally set at 0.05 (5%)
- Corresponds to $Z\alpha = 1.96$ for two-tailed tests
- Lowering α (e.g., to 0.01) increases the required sample size
- $Z\alpha$ for one-tailed test at 0.05 = 1.645

2. Statistical Power ($1 - \beta$)

- The probability of correctly rejecting the null hypothesis when it is false
- Conventionally set at 0.80 (80%), sometimes 0.90
- β = Type II error rate (false negative)
- $Z\beta = 0.84$ for 80% power; 1.28 for 90% power
- Higher power → larger sample required

3. Effect Size (δ)

- The minimum clinically meaningful difference between groups
- Smaller expected effect sizes require larger samples
- Determined by clinical judgment and prior research
- Cohen's conventions: small = 0.2, medium = 0.5, large = 0.8

4. Variability (σ)

- Standard deviation of the outcome measure
- Greater variability → larger sample needed
- Estimated from pilot data or previous studies

5. Sample Size Formulas

For comparing two means (independent t-test):

$$n \text{ (per group)} = 2 \times [(Z\alpha + Z\beta)^2 \times \sigma^2] / \delta^2$$

Where:

- $Z\alpha = 1.96$ (for $\alpha = 0.05$, two-tailed)
- $Z\beta = 0.84$ (for power = 0.80)

- σ = standard deviation
- δ = minimum clinically meaningful difference

Worked example:

Comparing HAM-D scores between drug and placebo groups:

- Expected difference (δ) = 4 points
- SD (σ) = 6 points (from previous literature)
- $\alpha = 0.05$, power = 0.80

$$n = 2 \times [(1.96 + 0.84)^2 \times 36] / 16 = 2 \times [7.84 \times 36] / 16 = 2 \times 17.64 = 35.3$$

Need approximately 36 per group, 72 total.

For comparing two proportions:

$$n = [(Z_{\alpha}\sqrt{2\bar{p}\bar{q}}) + Z_{\beta}\sqrt{(p_1q_1 + p_2q_2)}]^2 / (p_1 - p_2)^2$$

6. Adjustment for Dropout

Adjusted $n = n / (1 - \text{expected dropout rate})$

If expecting 20% dropout: $72 / 0.80 = 90$ total

7. Other Considerations

- **Study design:** Cluster randomised trials need inflation factor for intra-cluster correlation
- **Multiple comparisons:** Bonferroni or other corrections require larger samples
- **Non-inferiority trials:** Require larger samples than superiority trials (must rule out pre-specified non-inferiority margin)
- **Crossover designs:** Generally require smaller samples than parallel designs (within-subject comparison)
- **Rare events:** Very large samples needed (or alternative designs like case-control)

8. Software and Resources

- G*Power (free software for sample size calculation)
- nQuery, PASS (commercial)
- Online calculators (OpenEpi, Epitools)
- Consulting a biostatistician is standard practice for grant applications

Cross-reference: D1 (Study Notes), D3 (Mnemonics), D4 (Comparisons), D6 (Quick Review)

Mnemonics & Memory Tricks

Mnemonic 1: Types of Validity: "FaCe CoCo"

Fa = Face validity

Ce = Content validity (Experts judge domain coverage)

Co = Criterion validity (Concurrent + Predictive, against a gold standard)

Co = Construct validity (Convergent + Discriminant, theoretical construct)

Memory aid: "FaCe CoCo", like the face of a coconut shell. Face is surface level (weakest), and you crack through to get to the real content, criterion, and construct inside.

Expanded:

- **Face** → Looks right (subjective, weakest)
 - **Content** → Covers everything (experts check the domain)
 - **Criterion** → Correlates with gold standard (**Concurrent** = same time; **Predictive** = future)
 - **Construct** → Measures the right concept (**Convergent** = correlates with same; **Discriminant** = doesn't correlate with different)
-

Mnemonic 2: Types of Reliability: "TISI"

T = Test-retest (Time stability)

I = Inter-rater (Individuals agree)

S = Split-half (Splitting the test)

I = Internal consistency (Items hang together, Cronbach's alpha)

Memory aid: "TISI" sounds like "Tissue", reliability is like a tissue, consistent and uniform throughout. If one part tears easily while the rest is strong, the tissue is not reliable.

Statistics to remember:

- Test-retest → Pearson r or ICC
 - Inter-rater → Cohen's kappa
 - Split-half → Spearman-Brown corrected r
 - Internal consistency → Cronbach's alpha
-

Mnemonic 3: Study Design Hierarchy: "Smart Researchers Can Create Excellent Cases"

From strongest to weakest:

Systematic review / Meta-analysis

Randomised Controlled Trial

Cohort study

Case-control study

Epidemiological cross-sectional study

Case series / Case report

(Expert opinion at the bottom)

Memory aid: "Smart Researchers Can Create Excellent Cases", and the smartest ones (systematic reviews) sit at the top.

Mnemonic 4: Parametric ↔ Non-Parametric Test Pairs: "I Must Pay Willingly, One Keeps Repeating Freely, Plus Spares"

PARAMETRIC	NON-PARAMETRIC	MNEMONIC WORD
Independent t-test	Mann-Whitney U	"I Must"
Paired t-test	Wilcoxon signed-rank	"Pay Willingly"
One-way ANOVA	Kruskal-Wallis	"One Keeps"
Repeated measures ANOVA	Friedman	"Repeating Freely"
Pearson r	Spearman ρ	"Plus Spares"

Memory aid: "I Must Pay Willingly, One Keeps Repeating Freely, Plus Spares", imagine paying your statistician willingly because they keep repeating analyses freely and always have spare tests.

Mnemonic 5: Five Steps of EBM: "5 A's"

Ask → Formulate PICO question

Acquire → Search for evidence

Appraise → Critically evaluate evidence

Apply → Integrate with expertise and patient values

Assess → Evaluate outcomes

Memory aid: Already a built-in mnemonic. The 5 A's. Think "AAAAA", like the five-star rating you're giving to your evidence-based practice.

Mnemonic 6: Levels of Evidence: "Meta Rules Cohorts, Cases Come Last, Experts Guess"

Meta-analysis / Systematic review (Level 1a)

Randomised Controlled Trial (Level 1b)

Cohort study (Level 2)

Case-control study (Level 3)

Case series (Level 4)

Last: Expert opinion (Level 5)

Guess = expert opinion is basically an educated guess

Memory aid: "Meta Rules, Cohorts and Cases Come Last, Experts Guess", meta-analyses rule the hierarchy, and experts at the bottom are basically guessing (educated guessing, but still).

Mnemonic 7: Sensitivity/Specificity: "SnNOut / SpPIn"

SnNOut = **S**ensitive test, **N**egative result, rules **O**ut disease

SpPIn = **S**pecific test, **P**ositive result, rules **I**n disease

Memory aid: "SnNOut", if you're sick and the sensitive test says **No**, you're **Out** (no disease). "SpPIn", the **S**pecific test says **Positive**, you're **In** (have the disease).

Why this works:

- High sensitivity → very few false negatives → negative result is trustworthy
- High specificity → very few false positives → positive result is trustworthy

Bonus, the 2×2 table positions:

- Sensitivity = $a / (a+c)$, **left column** (disease + only)
 - Specificity = $d / (b+d)$, **right column** (disease – only)
 - PPV = $a / (a+b)$, **top row** (test + only)
 - NPV = $d / (c+d)$, **bottom row** (test – only)
-

Mnemonic 8: Bias Types: "SCORES + PB"

Selection bias, who enters the study

Confounding, third variable distorts

Observer bias, researcher sees what they expect

Recall bias, cases remember differently

Equipment/Instrumentation bias, tools change

Survivor/Attrition bias, differential dropout

+PB:

Performance bias, unequal care between groups

Berkson bias, hospital-based studies create false associations

Memory aid: "SCORES + PB", think of "SCORES" like test scores that can be biased in many ways, plus "PB" for publication bias (which you should always mention in any meta-analysis answer).

Mnemonic 9: PICO Framework: "Patient, Intervention, Comparison, Outcome"

P = Patient/Population/Problem

I = Intervention (or Exposure)

C = Comparison (or Control)

O = Outcome

Memory aid: "PICO" already sounds like "pick-o", you PICK your research question elements. For observational studies, some use PECO (E = Exposure).

Quick template: "In [P], does [I] compared to [C] improve [O]?"

Mnemonic 10: Type I vs Type II Errors: "The Boy Who Cried Wolf"

Type I error (α) = False alarm = "Crying wolf when there is no wolf"

- Rejecting H_0 when it is TRUE
- Finding a significant result when there isn't one
- The **p-value** controls this (threshold: 0.05)
- Mnemonic: Type **I** = **I** made it up (false positive)

Type II error (β) = Missed wolf = "Not crying wolf when the wolf is real"

- Failing to reject H_0 when it is FALSE
- Missing a real effect
- **Power** ($1 - \beta$) controls this
- Mnemonic: Type **II** = **II** stupid to miss it (false negative)

Memory aid: "Type I = I see it (but it's not there). Type II = Too blind to see it (but it IS there)."

Mnemonic 11: When to Use Which Test: "The 2-3 Rule"

2 groups?

- Independent → t-test (parametric) / Mann-Whitney (non-parametric)
- Paired → Paired t-test / Wilcoxon

3+ groups?

- Independent → ANOVA / Kruskal-Wallis
- Repeated → RM-ANOVA / Friedman

Categorical?

- 2×2 table → Chi-square (or Fisher if $n < 5$ expected)
- Paired categorical → McNemar's test

Correlation?

- Normal → Pearson
- Non-normal/ordinal → Spearman

Decision flowchart in words:

1. What's the outcome? → Continuous or Categorical?
 2. If continuous: How many groups? → 2 or 3+?
 3. If 2 groups: Paired or Independent?
 4. Normally distributed? → Yes = parametric, No = non-parametric
-

Mnemonic 12: Threats to Internal Validity: "SHRIMP-T"

S = Selection bias

H = History (external events)

R = Regression to the mean

I = Instrumentation changes

M = Maturation (natural changes)

P = Practice/Testing effects

T = Testing attrition (dropout)

Memory aid: "A SHRIMP-T study has many internal validity threats", picture a tiny shrimp of a study, full of holes and threats. A well-designed RCT is the big fish that overcomes

these.

Mnemonic 13: Cohen's Kappa Interpretation: "Slight Fair Moderate Substantial Perfect"

KAPPA	AGREEMENT	MNEMONIC
< 0.20	Slight	Someone barely trying
0.21–0.40	Fair	Fair attempt
0.41–0.60	Moderate	Middle ground
0.61–0.80	Substantial	Solid work
0.81–1.00	Almost perfect	Amazing

Memory aid: "Some Fair Midfielders Score Amazing goals", kappa goes from slight (barely trying) to almost perfect (amazing).

Mnemonic 14: Forest Plot Reading: "SLIDE"

S = Square = individual study point estimate (size = weight)

L = Line through square = confidence interval for that study

I = Invisible vertical line at null ($OR=1$ or $MD=0$) = line of no effect

D = Diamond at bottom = pooled / summary estimate (width = CI)

E = Effect is significant if diamond does NOT cross the line of no effect

Memory aid: "SLIDE", you slide your eyes down the forest plot from individual studies to the summary diamond.

Mnemonic 15: Qualitative Rigour: "CriTDeC"

Qualitative equivalents of quantitative concepts:

Cri = **Credibility** ($\approx$ internal validity)

T = **Transferability** ($\approx$ external validity)

De = **Dependability** ($\approx$ reliability)

C = **Confirmability** ($\approx$ objectivity)

Memory aid: "CriTDeC", say it fast, sounds like "critical deck", your critical deck of cards for evaluating qualitative research quality.

BONUS: Quick Number Anchors

WHAT · NUMBER TO REMEMBER

Acceptable Cronbach's alpha > 0.70

Substantial Cohen's kappa > 0.60

Standard p-value threshold 0.05

Standard power 0.80

Cohen's d: small/medium/large 0.2 / 0.5 / 0.8

Z for $\alpha = 0.05$ (two-tailed) 1.96

Z for power = 0.80 0.84

AUC excellent range 0.80–0.90

Chi-square min expected count ≥ 5

Normal distribution: ± 1 SD 68%

Normal distribution: ± 2 SD 95%

Cross-reference: D1 (Study Notes), D2 (Model Answers), D4 (Comparisons), D6 (Quick Review)

High-Yield Comparisons

Table 1: Parametric vs Non-Parametric Tests (with Paired Equivalents)

PURPOSE	PARAMETRIC TEST	NON-PARAMETRIC TEST	DATA TYPE
2 independent groups	Independent t-test	Mann-Whitney U	Continuous
2 paired/related groups	Paired t-test	Wilcoxon signed-rank	Continuous
3+ independent groups	One-way ANOVA	Kruskal-Wallis	Continuous
3+ related groups	Repeated measures ANOVA	Friedman test	Continuous
Correlation	Pearson r	Spearman ρ	Continuous
2×2 categorical		Chi-square / Fisher's exact	Categorical
Paired categorical (2×2)		McNemar's test	Categorical
3+ paired categorical		Cochran's Q	Categorical

When to use parametric: Normal distribution, continuous data, adequate sample size (n > 30 per group), homogeneity of variance.

When to use non-parametric: Ordinal data, skewed distribution, small sample size, outliers, violated assumptions.

Key distinction: Parametric tests use raw values and assume a specific distribution; non-parametric tests use ranks and are distribution-free.

Table 2: Type I vs Type II Errors

FEATURE	TYPE I ERROR (A)	TYPE II ERROR (B)
Definition	Rejecting H ₀ when it is true	Failing to reject H ₀ when it is false
In plain language	Finding a difference when none exists	Missing a real difference
Analogy	False alarm (crying wolf)	Missed detection (wolf gets in)

FEATURE	TYPE I ERROR (A)	TYPE II ERROR (B)
Consequence	Adopting an ineffective treatment	Missing an effective treatment
Controlled by	Significance level (α), conventionally 0.05	Statistical power ($1 - \beta$), conventionally 0.80
Relationship to sample size	Fixed by α level	↓ as sample size ↑ (more power)
Clinical impact	Patient receives unnecessary / ineffective treatment	Patient misses a beneficial treatment
Multiple comparisons	Risk increases with more tests (Bonferroni correction)	
Exam mnemonic	Type I = I made it up (false positive)	Type II = Too blind to see it (false negative)
Which is worse?	Context-dependent: worse in safety trials (approving a harmful drug)	Context-dependent: worse in screening (missing a treatable cancer)

The trade-off: Reducing α (stricter threshold) decreases Type I error but increases Type II error (and vice versa). The only way to reduce BOTH is to increase sample size.

Table 3: Sensitivity vs Specificity vs PPV vs NPV

MEASURE	FORMULA	QUESTION ANSWERED	AFFECTED BY
Sensitivity	TP / (TP + FN)	Of all DISEASED, how many tested positive?	Intrinsic test property
Specificity	TN / (FP + TN)	Of all HEALTHY, how many tested negative?	Intrinsic test property
PPV	TP / (TP + FP)	Of all TEST POSITIVES, how many truly have disease?	Prevalence ↑ → PPV ↑
NPV	TN / (FN + TN)	Of all TEST NEGATIVES, how many are truly healthy?	Prevalence ↑ → NPV ↓

CLINICAL RULE	MEANING	USE
SnNOut	Sensitive test + Negative result = rules OUT disease	Screening (don't want to miss cases)

CLINICAL RULE	MEANING	USE
SpPIn	Specific test + Positive result = rules IN disease	Confirmation (don't want false positives)

MEASURE	HIGH VALUE MEANS	CLINICAL APPLICATION
LR+ (Sensitivity / (1-Specificity))	Strong positive test performance	LR+ > 10 = very useful positive result
LR- ((1-Sensitivity) / Specificity)	Strong negative test performance	LR- < 0.1 = very useful negative result

Critical insight: PPV and NPV depend on disease prevalence. Even a test with 99% sensitivity and 99% specificity will have poor PPV in a low-prevalence population because the absolute number of false positives will overwhelm true positives.

Table 4: Study Designs Comparison

FEATURE	CROSS-SECTIONAL	CASE-CONTROL	COHORT	RCT
Direction	Snapshot (no time direction)	Retrospective (outcome → exposure)	Prospective or retrospective (exposure → outcome)	Prospective (intervention → outcome)
What it measures	Prevalence	Odds Ratio (OR)	Relative Risk (RR), Incidence	Relative Risk, NNT, NNH
Starting point	Defined population	Cases + Controls selected	Exposed + Unexposed groups identified	Participants randomised
Can establish temporality	No	No (inferred)	Yes	Yes
Can establish causation	No	No (association only)	Stronger association	Yes (strongest)
Best for	Prevalence estimation, generating hypotheses	Rare diseases	Rare exposures, incidence	Testing interventions
Sample size needed	Moderate	Small–moderate	Large	Large
Time required	Short (one point)	Short–moderate	Long (years of follow-up)	Moderate–long
Cost	Low	Low–moderate	High	Very high

FEATURE	CROSS-SECTIONAL	CASE-CONTROL	COHORT	RCT
Key bias risk	Prevalence bias, temporal ambiguity	Recall bias, selection bias	Loss to follow-up, confounding	Hawthorne effect, strict inclusion → low external validity
Psychiatry example	NMHS 2016 prevalence survey	Trauma in BPD vs controls	Dunedin cohort study	STAR*D, CATIE
Level of evidence	Lower (descriptive)	Level 3b	Level 2b	Level 1b
Ethical concern	Minimal	Minimal	Minimal (observational)	Cannot randomise harmful exposures

Table 5: Qualitative vs Quantitative Research

FEATURE	QUANTITATIVE	QUALITATIVE
Philosophy	Positivism (objective, measurable reality)	Constructivism (subjective, multiple realities)
Approach	Deductive (theory → hypothesis → data)	Inductive (data → patterns → theory)
Research question	"How much? How many? Is there a difference?"	"What is the experience? How do people make sense of it?"
Data	Numbers (scores, counts, measurements)	Words (transcripts, field notes, narratives)
Sample size	Large (powered by calculation)	Small (purposive, until data saturation)
Sampling	Probability (random, stratified, cluster)	Non-probability (purposive, snowball, theoretical)
Data collection	Questionnaires, rating scales, structured interviews	In-depth interviews, focus groups, observation
Analysis	Statistical (t-test, ANOVA, regression)	Thematic analysis, grounded theory, IPA, content analysis
Researcher role	Detached, objective observer	Embedded, reflexive participant
Rigour criteria	Validity + Reliability	Credibility + Transferability + Dependability + Confirmability
Output	Effect sizes, p-values, confidence intervals	Themes, narratives, theoretical frameworks

FEATURE	QUANTITATIVE	QUALITATIVE
Generalisability	High (if representative sample)	Low (context-dependent; transferability instead)
Causation	Can establish (experimental designs)	Cannot establish (explores meaning, not causation)
Replication	High (standardised methods)	Low (unique contexts)
Strengths	Precision, generalisability, causal inference	Depth, context, lived experience, "why"
Limitations	Reductionism, misses meaning, decontextualises	Not generalisable, time-consuming, researcher bias
Psychiatry example	RCT of SSRIs for depression	Phenomenological study of voice-hearing experience
Mixed methods	Can combine both: quantitative outcomes + qualitative process evaluation (e.g., MANAS trial)	

Table 6: Systematic Review vs Meta-analysis vs Network Meta-analysis

FEATURE	SYSTEMATIC REVIEW	META-ANALYSIS	NETWORK META-ANALYSIS
Definition	Structured, reproducible synthesis of all evidence on a question	Statistical pooling of results from multiple studies into a single estimate	Extension of meta-analysis comparing multiple treatments simultaneously
Nature of synthesis	Qualitative (narrative)	Quantitative (statistical)	Quantitative (statistical, complex)
Includes statistical pooling	Not necessarily	Yes (always)	Yes (always)
Types of evidence compared	All studies on one question	Direct comparisons (A vs B)	Direct AND indirect comparisons (A vs B, B vs C → infer A vs C)
Key output	Summary tables, quality assessment, narrative conclusion	Pooled effect size, forest plot, I^2	Treatment rankings, league table, network diagram
Heterogeneity assessment	Described qualitatively	I^2 , Cochrane Q	I^2 , inconsistency, node-splitting
Publication bias	Discussed qualitatively	Funnel plot, Egger's test	Comparison-adjusted funnel plot

FEATURE	SYSTEMATIC REVIEW	META-ANALYSIS	NETWORK META-ANALYSIS
When NOT to pool	When heterogeneity is extreme		When transitivity assumption is violated
Key assumption	Comprehensive search, reproducible methods	Studies are sufficiently similar to pool	Transitivity (similar populations across comparisons)
Reporting guideline	PRISMA	PRISMA	PRISMA-NMA
Psychiatry example	Cochrane review of CBT for depression	Cipriani et al., 2018 (antidepressants)	Cipriani et al., 2018 (21 antidepressants ranked)
Level of evidence	1a	1a	1a

Table 7: Probability vs Non-Probability Sampling

FEATURE	PROBABILITY SAMPLING	NON-PROBABILITY SAMPLING
Definition	Every member of the population has a known, non-zero chance of selection	Selection is based on availability, judgment, or other non-random criteria
Basis	Random selection	Convenience, judgment, or self-selection
Generalisability	High (representative of population)	Low (may not represent population)
Bias risk	Lower (randomisation minimises selection bias)	Higher (selection bias inherent)
Sampling frame	Required (complete list of population)	Not required
Cost and effort	Higher (need complete frame, randomisation)	Lower (practical, quick)
Use in research	Quantitative studies, surveys, clinical trials	Qualitative studies, pilot studies, hard-to-reach populations

TYPE	METHOD	EXAMPLE
Simple random	Every individual has equal chance	Random number table to select patients from hospital register
Stratified	Divide into strata, random sample from each	Stratify by age group, randomly sample within each stratum

TYPE	METHOD	EXAMPLE
Cluster	Randomly select entire clusters	Randomly select 10 PHCs from a district, study all patients at those PHCs
Systematic	Every kth individual	Every 5th patient from the OPD register
Convenience	Whoever is available	Patients attending OPD on the day of data collection
Purposive	Researcher selects based on characteristics	Selecting only patients with treatment-resistant depression for qualitative interviews
Snowball	Participants recruit others	Studying IV drug users, each participant refers peers
Quota	Non-random but ensures proportions	Ensuring 50% male and 50% female in sample (non-randomly selected within each group)

Table 8: Types of Bias in Research

BIAS TYPE	DEFINITION	STAGE	EXAMPLE	PREVENTION
Selection bias	Systematic difference between study participants and target population	Design	Only enrolling tertiary hospital patients (sicker, more complex)	Random sampling, clear inclusion criteria
Recall bias	Cases recall exposure differently from controls	Data collection	Mothers of children with defects remember medication use more accurately	Prospective design, objective records
Observer/Detection bias	Assessor's expectations influence measurement	Data collection	Unblinded rater scores drug group as improved	Blinding of assessors
Performance bias	Differential treatment between groups (beyond the intervention)	Conduct	Intervention group receives more clinician attention	Double blinding, standardised protocols
Attrition bias	Differential loss to follow-up between groups	Follow-up	Sicker patients drop out of drug arm	ITT analysis, minimise dropout

BIAS TYPE	DEFINITION	STAGE	EXAMPLE	PREVENTION
Publication bias	Studies with positive results are more likely published	Reporting	Only significant antidepressant trials in literature	Trial registries, grey lit search, funnel plot
Confounding	Third variable associated with both exposure and outcome	Analysis	Coffee → lung cancer (confounder: smoking)	Randomisation, stratification, multivariate analysis
Lead-time bias	Earlier detection inflates apparent survival time	Interpretation	Screening detects cancer 2 years earlier without changing mortality	Measure mortality, not survival from diagnosis
Berkson bias	Spurious association in hospital-based studies	Design	Depression-diabetes association inflated because both increase hospitalisation	Population-based studies
Information bias	Systematic errors in data collection	Data collection	Using an unvalidated questionnaire	Standardised, validated instruments
Reporting bias	Selective reporting of outcomes	Reporting	Reporting only the outcome that was significant	Pre-registration, protocol publication
Hawthorne effect	Participants change behaviour because they are observed	Conduct	Patients adhere better during a trial than in routine care	Naturalistic designs, long follow-up
Volunteer bias	Volunteers differ systematically from non-volunteers	Design	Volunteers are healthier, more motivated, more educated	Random sampling (when possible)

Cross-reference: D1 (Study Notes), D2 (Model Answers), D3 (Mnemonics), D6 (Quick Review)

PYQ Frequency Analysis

EXAM PEARL

Source: PG exams Dec 2011, Jun 2025 + PG exams 2013-2022

Executive Summary

Statistics and research methodology is a **consistently tested** cluster, arguably the most predictable in Paper I after neurotransmitters and sleep. The questions follow a very stable pattern: validity/reliability, study designs, statistical tests, and evidence-based medicine rotate reliably.

Key insight: Unlike clinical topics, statistics questions have almost no variability. The same 5-6 question templates recycle. Master those templates and you're covered.

Topic-Level Frequency

TOPIC	EXAM MENTIONS	AVG PER EXAM	VERDICT
Validity & Reliability	5	~0.18	Every 5-6 exams
Epidemiological study designs	4	~0.14	Every 6-7 exams
Statistical tests (t-test, Chi-square, ANOVA, non-parametric)	5	~0.18	Every 5-6 exams
Evidence-based medicine	5	~0.18	Every 5-6 exams
Qualitative vs Quantitative research	3	~0.11	Every 8-9 exams
Meta-analysis / Systematic review	3	~0.11	Emerging topic
Sampling & Sample size	2	~0.07	Occasional
Combined cluster	~27	~0.96	~1 question per exam

Key PYQs Identified

Validity & Reliability

1. "Define validity. Name different types. Importance in psychiatry." [10 marks, split 2+6+2]
2. "What is validity? Enumerate types. Criterion validity." [10 marks, split 2+3+5]
3. "What is validity? Discuss different types with examples." [10 marks, split 3+7]
4. "Define reliability and validity. Significance. Types." [10 marks, split 3+2+5]
5. "What is reliability? Types with examples. Internal and external validity." [10 marks, split 2+4+4]

Study Designs & Epidemiology

1. "What is psychiatric epidemiology? Uses. Types of designs." [10 marks, split 2+4+4]
2. "Describe different types of epidemiological studies in Psychiatry." [10 marks]
3. "What is genetic epidemiology? Three types of genetic studies." [10 marks]
4. "Define epidemiology. Different types of epidemiological studies." [10 marks]

Statistical Tests

1. "Discuss Non-Parametric Tests." [10 marks]
2. "Chi Square test." [10 marks]
3. "Paired t Test." [10 marks]
4. "Enumerate statistical tests to measure differences. Describe t-test with example." [10 marks, split 4+6]
5. "Describe Factor Analysis and its applications in psychiatric research." [10 marks]
6. "Enumerate statistical tests. Describe paired t-test. Two non-parametric tests for group difference." [10 marks, split 4+2+4]

Evidence-Based Medicine

1. "What is evidence based medicine? How is it practiced? Steps with example." [10 marks, split 2+2+6]
2. "What is EBM? How is it practiced in India? Limitations." [10 marks]
3. "Discuss levels of evidence and their role in EBM." [10 marks]
4. "What is EBM? What is personalized medicine? Pharmacogenetics." [10 marks, split 2+3+5]

Research Methodology

1. "What is quantitative research? Essential features, strengths, limitations." [10 marks]
2. "What is qualitative research? How does it differ from quantitative?" [10 marks, split 2+5+3]

3. "What is meta-analysis? Systematic review? Key meta-analytical studies in psychiatry." [10 marks]
4. "Odds ratio. Confounding, effect modification, mediation." [10 marks, split 4+2+2+2]
5. "How to generate research question? Types of hypothesis. Meta-analysis vs network analysis." [10 marks]
6. "Sampling techniques. Sample size. Principles of sample size calculation." [10 marks, split 2+2+6]

Long Essay Candidates

RANK	TOPIC	PROBABILITY
1	"Define validity and reliability. Types. Clinical importance."	Very High
2	"What is EBM? Steps. Practice in India. Limitations."	Very High
3	"Enumerate statistical tests. Describe t-test/chi-square with examples."	High
4	"Describe different epidemiological study designs in psychiatry."	High
5	"Qualitative vs quantitative research, features, strengths, limitations."	Medium-High

Exam Strategy

Must-Prepare (will be asked)

1. **Validity**, define, 4 types (face, content, criterion [concurrent + predictive], construct [convergent + discriminant]), examples from psychiatry
2. **Reliability**, define, types (test-retest, inter-rater, split-half, internal consistency / Cronbach's alpha), relationship to validity
3. **Statistical tests**, when to use each: t-test (2 means, parametric), ANOVA (>2 groups), Chi-square (categorical data), Mann-Whitney / Wilcoxon (non-parametric equivalents)
4. **EBM**, define, 5 steps (ask, acquire, appraise, apply, assess), levels of evidence pyramid

Should-Prepare

1. **Study designs**, cross-sectional, case-control, cohort, RCT, ecological.
Strengths/limitations table
2. **Meta-analysis**, define, steps, forest plot, heterogeneity (I^2), advantages over narrative review
3. **Sensitivity/Specificity/PPV/NPV**, 2x2 table, formulae, clinical application

Nice-to-Know

1. Factor analysis (exploratory vs confirmatory)
 2. Odds ratio vs relative risk
 3. Confounding and effect modification
 4. Sampling techniques (probability vs non-probability)
-

Emerging Trends (2020+)

- **Network meta-analysis**, appeared Jun 2025
 - **Pharmacogenetics + personalized medicine**, combining EBM with genetics
 - **Yoga in psychiatry + methodological issues**, India-specific
 - **Sample size calculation**, increasingly tested
-

Analysis based on PG exams Dec 2011, Jun 2025 + PG exams 2013-2022.

Quick Review

RECALL Questions (1–12)

Q1. Define face validity and give one limitation.

A: Face validity is the degree to which a test appears, on the surface, to measure what it intends to measure. It is assessed subjectively by non-experts. **Limitation:** It is the weakest form of validity, a test can look right but actually measure a different construct (e.g., a test that appears to measure anxiety might actually be measuring general distress).

Q2. What are the two subtypes of criterion validity?

A: (1) **Concurrent validity**, the test and the gold standard criterion are measured at the same time (e.g., a new depression scale administered alongside the HAM-D). (2) **Predictive validity**, the test predicts a future outcome (e.g., AUDIT score at admission predicting withdrawal severity during hospitalisation).

Q3. Name the four types of reliability and their associated statistics.

A:

1. **Test-retest** → Pearson r or ICC
2. **Inter-rater** → Cohen's kappa (κ)
3. **Split-half** → Spearman-Brown corrected r
4. **Internal consistency** → Cronbach's alpha (α)

Q4. What is the non-parametric alternative to the independent t-test?

A: The **Mann-Whitney U test**. It compares the rank distributions of two independent groups and does not assume normal distribution.

Q5. What is the non-parametric alternative to the paired t-test?

A: The **Wilcoxon signed-rank test**. It compares two related measurements by analysing the magnitude and direction of differences between pairs.

Q6. State the formula for sensitivity and specificity.

A: From a 2×2 table ($a = TP$, $b = FP$, $c = FN$, $d = TN$):

- **Sensitivity** = $a / (a + c)$, proportion of true positives among all diseased
- **Specificity** = $d / (b + d)$, proportion of true negatives among all non-diseased

Q7. What are the 5 steps of EBM?

A: Ask (formulate PICO question), Acquire (search for evidence), Appraise (critically evaluate), Apply (integrate with expertise and patient values), Assess (evaluate outcomes). The "5 A's."

Q8. What is the difference between a systematic review and a meta-analysis?

A: A **systematic review** is a structured, reproducible synthesis of all available evidence on a research question (qualitative/narrative). A **meta-analysis** is the statistical pooling of results from multiple studies into a single quantitative estimate. Every meta-analysis is part of a systematic review, but not every systematic review includes a meta-analysis (e.g., when studies are too heterogeneous to pool).

Q9. Define NNT and give its formula.

A: NNT (**Number Needed to Treat**) = the number of patients who need to be treated with the intervention for one additional patient to benefit compared to the control. **Formula:** $NNT = 1 / ARR$, where ARR (Absolute Risk Reduction) = Control Event Rate – Experimental Event Rate. Lower NNT = more effective treatment.

Q10. What is the PICO framework?

A: A structured format for clinical research questions: **P** = Population/Patient, **I** = Intervention, **C** = Comparison/Control, **O** = Outcome. Example: "In adults with MDD (P), does CBT + SSRI (I) compared to SSRI alone (C) improve remission rates (O)?"

Q11. Name three probability and three non-probability sampling methods.

A: **Probability:** Simple random, stratified random, cluster sampling. **Non-probability:** Convenience, purposive, snowball sampling.

Q12. What does an I^2 of 75% mean in a meta-analysis?

A: $I^2 = 75\%$ indicates **substantial heterogeneity**, 75% of the variability across study results is due to real differences between studies (heterogeneity) rather than chance. This suggests a random-effects model should be used, and sources of heterogeneity should be explored through subgroup analysis or meta-regression. (Interpretation: 0–25% low, 25–50% moderate, 50–75% substantial, >75% considerable.)

APPLICATION Questions (13–25)

Q13. A study finds $p = 0.03$ with a 95% CI of 1.2–3.4 for the odds ratio. Interpret.

A: The result is **statistically significant** ($p < 0.05$). The odds of the outcome are 1.2 to 3.4 times higher in the exposed group compared to the unexposed group (95% confidence). Since the CI does not include 1 (the null value for OR), this confirms statistical significance.

The point estimate of the OR lies at some value between 1.2 and 3.4 (likely around 2.0). The exposure is a significant risk factor for the outcome.

Q14. A researcher wants to compare anxiety scores (normally distributed) before and after a 12-week yoga intervention in the same 40 patients. Which test?

A: Paired t-test. Rationale: The data is continuous, normally distributed, and involves two measurements from the same subjects (before-after design). If normality of differences were violated, use Wilcoxon signed-rank test instead.

Q15. A study compares treatment response (responder/non-responder) across three drug groups. Which test?

A: Chi-square test of independence. Rationale: The outcome is categorical (responder vs non-responder) and there are three independent groups. This creates a 3×2 contingency table. If any expected cell count is < 5, use Fisher's exact test or collapse categories.

Q16. You want to compare depression scores (skewed distribution) across four therapy groups with 12 patients each. Which test?

A: Kruskal-Wallis test. Rationale: Four independent groups, continuous but non-normally distributed data, relatively small sample sizes. This is the non-parametric alternative to one-way ANOVA. If significant, follow up with Dunn's test for pairwise comparisons.

Q17. A case-control study shows OR = 4.5 (crude) for the association between childhood trauma and BPD. After adjusting for parental substance use, the OR becomes 2.1. What happened?

A: Confounding was present. Parental substance use was a confounder, it was associated with both the exposure (childhood trauma) and the outcome (BPD). The crude OR of 4.5 was inflated by the confounding effect. The adjusted OR of 2.1 represents the true association after removing the confounding effect of parental substance use. Since the crude and adjusted estimates differ substantially (> 10% change), confounding is confirmed.

Q18. A screening test has sensitivity = 95% and specificity = 90%. In a population with 1% prevalence of the disease, calculate the approximate PPV.

A: For 10,000 people: 100 have disease, 9,900 do not.

- $TP = 95\% \times 100 = 95$
- $FP = 10\% \times 9,900 = 990$
- $PPV = 95 / (95 + 990) = 95 / 1,085 = 8.8\%$

Despite excellent sensitivity and specificity, the PPV is only 8.8% because the disease is rare. Most positive results are false positives. This is why screening for low-prevalence conditions generates many false alarms.

Q19. In an RCT, 60% of the control group relapsed and 40% of the drug group relapsed. Calculate the NNT.

A:

- $ARR = CER - EER = 0.60 - 0.40 = 0.20$
- $NNT = 1 / 0.20 = 5$

Interpretation: You need to treat 5 patients with the drug to prevent one additional relapse compared to control. This is a clinically meaningful NNT.

Q20. A forest plot shows 8 studies. 5 studies have confidence intervals that cross the line of no effect. The summary diamond does NOT cross the line of no effect. Is the overall result significant?

A: Yes, the overall result is statistically significant. While individual studies may be non-significant (their CIs cross the null line), the pooled estimate (summary diamond) does not cross the line of no effect, indicating that when all evidence is combined, the treatment effect is statistically significant. This demonstrates the power of meta-analysis, pooling data from multiple underpowered individual studies can reveal a significant effect.

Q21. A researcher measures the correlation between BDI scores and hours of sleep per night in 200 patients with depression. BDI scores are normally distributed. Which test?

A: Pearson's correlation coefficient (r). Rationale: Both variables are continuous (BDI score and hours of sleep), data is normally distributed, and the researcher is examining a linear association between two variables. If either variable were non-normally distributed or ordinal, use Spearman's ρ instead.

Q22. A study of an SSRI vs placebo reports: "Treatment group improved by 3 points more on HAM-D ($p = 0.04$, Cohen's $d = 0.15$)." Is this clinically meaningful?

A: Likely not clinically meaningful despite statistical significance. While $p = 0.04$ is statistically significant, Cohen's $d = 0.15$ indicates a **very small effect size** (small = 0.2, medium = 0.5, large = 0.8). The 3-point HAM-D difference is at the borderline of the minimum clinically important difference (MCID, typically 3–4 points). This illustrates that statistical significance does not equal clinical significance, with a large enough sample, even trivially small differences become statistically significant. Clinical decision-making should weigh effect size and MCID, not just p-values.

Q23. A researcher wants to study the experience of living with treatment-resistant depression from the patient's perspective. Which research methodology is most appropriate?

A: **Qualitative phenomenological study** using in-depth semi-structured interviews. Phenomenology focuses on the lived experience of a phenomenon and aims to understand its essential meaning from the participant's perspective. Data would be analysed using interpretative phenomenological analysis (IPA) or Colaizzi's method. The sample would be small (8–15 participants), purposively selected, and data collection would continue until thematic saturation.

Q24. An RCT randomises 200 patients to drug vs placebo. During the trial, 30 patients in the drug arm stop taking the medication due to side effects. How should they be analysed?

A: Under **Intention-to-Treat (ITT) analysis**, all 200 patients are analysed in their originally assigned groups, the 30 who discontinued are still counted in the drug arm. This preserves the benefits of randomisation and provides a conservative estimate of treatment effect. ITT reflects real-world effectiveness (not all patients comply). A **per-protocol analysis** (excluding non-compliers) can be reported as secondary analysis but may overestimate the true treatment effect by excluding those who had side effects.

Q25. A funnel plot in a meta-analysis shows asymmetry, with missing studies in the lower-left region. What does this suggest?

A: This suggests **publication bias**, smaller studies with negative or null results (lower-left region = small sample size + small/negative effect) are missing from the literature, likely because they were never published. This means the pooled estimate may overestimate the true treatment effect. The researcher should: (1) run Egger's test to confirm statistically, (2) apply trim-and-fill method to adjust the estimate, (3) search for grey literature and unpublished data.

ANALYSIS Questions (26–35)

Q26. Why might a highly sensitive test have poor PPV in a low-prevalence population?

A: Because PPV depends on both the test's specificity and the disease prevalence. In a low-prevalence population, the vast majority of people are disease-free. Even with high sensitivity (catching nearly all true cases), the small number of true positives is overwhelmed by false positives from the large healthy population. For example, if sensitivity = 99% and specificity = 95%, and prevalence = 0.1%: in 100,000 people, 100 have disease (99 detected) but 4,995 healthy people test falsely positive. $PPV = 99 / (99 + 4,995) =$

1.9%. The absolute number of false positives is determined by $(1 - \text{specificity}) \times (\text{number of healthy people})$, which is enormous when prevalence is low.

Q27. A researcher reports that Cohen's kappa for their diagnostic interview is 0.45. Is this adequate for clinical use? Why or why not?

A: $\kappa = 0.45$ indicates **moderate agreement**, which is generally **not adequate for clinical use**, especially for high-stakes decisions. In clinical diagnostics, substantial to almost perfect agreement ($\kappa > 0.60$, ideally > 0.80) is expected. A κ of 0.45 means raters disagree on a substantial proportion of cases even after accounting for chance agreement. This could lead to misdiagnosis depending on which clinician the patient sees. The instrument or training protocol needs improvement before clinical deployment. However, for screening purposes (lower stakes, further assessment follows), moderate reliability may be acceptable.

Q28. An RCT of a new antidepressant excludes patients with comorbid substance use, personality disorders, and suicidal ideation. How does this affect the study's validity?

A: This creates a **tension between internal and external validity**:

- **Internal validity increases:** By excluding complex patients, the study reduces confounders (substance use affecting response, personality pathology affecting adherence, suicidality requiring additional interventions). This creates a cleaner test of the drug's efficacy.
- **External validity decreases dramatically:** In real-world psychiatry, comorbidity is the rule, not the exception. Approximately 40–60% of patients with depression have comorbid substance use, personality difficulties, or suicidal ideation. The study sample represents a highly selected, atypical population. Results cannot be confidently generalised to the patients most commonly seen in clinical practice. This is the "efficacy-effectiveness gap", drugs that work in clinical trials may not work as well in routine care.

Q29. A researcher finds a statistically significant correlation ($r = 0.15$, $p = 0.01$) between social media use and depression scores in a sample of 5,000 adolescents. What should you conclude?

A: The finding is **statistically significant but clinically trivial**. $r = 0.15$ is a very weak correlation, it explains only 2.25% of the variance in depression scores ($r^2 = 0.0225$). The statistical significance is driven entirely by the large sample size ($n = 5,000$), which gives power to detect even negligible effects. The 97.75% of variance is explained by other factors. Additionally, this is a **correlation, not causation**, it could be that (a) social media causes depression, (b) depression leads to more social media use, or (c) a third variable (e.g., loneliness, sleep deprivation) drives both. This highlights why effect size and clinical significance matter more than p-values.

Q30. Why is ITT analysis considered more conservative than per-protocol analysis in a superiority trial?

A: ITT analysis includes ALL randomised participants in their assigned groups, regardless of whether they completed the intervention or adhered to the protocol. This is conservative because:

1. **Non-compliers dilute the treatment effect**, patients who stopped the drug (due to side effects, lack of response, etc.) are still counted in the drug group, pulling the drug group's outcome toward the control group's outcome.
2. **Preserves randomisation**, maintaining the original randomised groups ensures that known and unknown confounders remain balanced.
3. **Reflects real-world effectiveness**, in practice, not all patients comply, so ITT gives a more realistic estimate.

Per-protocol analysis, by excluding non-compliers, creates a biased sample (those who tolerated and adhered may be inherently different) and can overestimate the treatment effect. However, in **non-inferiority trials**, per-protocol is actually the primary analysis because ITT (by diluting differences) can falsely support non-inferiority.

Q31. A new psychiatric rating scale has a Cronbach's alpha of 0.97. Is this a problem?

A: Potentially, yes. While $\alpha > 0.70$ indicates acceptable internal consistency, an α of 0.97 suggests **item redundancy**, the items are so highly intercorrelated that they are essentially asking the same thing in slightly different ways. This means the scale is longer than necessary without adding new information. It increases respondent burden, completion time, and the risk of response fatigue without improving measurement. The scale developer should consider reducing items through item-total correlation analysis, removing items with very high inter-item correlations (> 0.90) that are redundant. An optimal Cronbach's alpha is typically 0.80–0.90.

Q32. A case-control study finds that patients with schizophrenia are more likely to have been born in winter months. What type of bias could explain this finding, and what design would strengthen the evidence?

A: This could be a genuine finding (season of birth effect is well-replicated) but could also be affected by **Berkson bias** (if controls were hospital-based with different seasonal admission patterns) or **selection bias** (if the sampling frame introduced seasonal artefacts). **Recall bias** is less relevant here since date of birth is an objective fact from records. To strengthen the evidence: (1) A large **prospective birth cohort study** following individuals from birth would establish temporality without selection bias. (2) Using **population-based controls** rather than hospital controls eliminates Berkson bias. (3) The **ecological fallacy** should be considered if aggregate population-level birth data is used. The Scandinavian birth register studies (e.g., Danish cohort) provide the strongest evidence for this association.

Q33. Why is the random-effects model preferred over the fixed-effect model when heterogeneity is high in a meta-analysis?

A: The **fixed-effect model** assumes there is ONE true effect size and all variation between studies is due to sampling error (chance). The **random-effects model** assumes the true effect varies between studies (because of differences in populations, interventions, settings) and accounts for both within-study and between-study variance.

When heterogeneity is high ($I^2 > 50\%$), the fixed-effect assumption is violated, studies clearly differ in their true effects. Using a fixed-effect model would produce inappropriately narrow confidence intervals (false precision) because it ignores the real variability between studies. The random-effects model produces wider, more honest confidence intervals that reflect the genuine uncertainty. It also weights studies more equally (small studies get relatively more weight compared to fixed-effect), which can be both an advantage (less dominated by large studies) and a limitation (gives more weight to potentially lower-quality small studies).

Q34. A researcher performs 20 independent t-tests on the same dataset comparing treatment vs control on 20 different outcome measures. All are tested at $\alpha = 0.05$. What is the problem and what is the solution?

A: The problem is **multiple comparisons (inflated Type I error)**. With 20 independent tests at $\alpha = 0.05$, the probability of at least one false positive is: $1 - (1 - 0.05)^{20} = 1 - 0.36 = 0.64$ (64%). There is a 64% chance of finding at least one "significant" result by chance alone, even if there is no true effect.

Solutions:

1. **Bonferroni correction:** Adjust α to $0.05/20 = 0.0025$ per test. Simple but very conservative, increases Type II error.
2. **Holm-Bonferroni (step-down):** Less conservative, ranks p-values and applies progressively less strict thresholds.
3. **False Discovery Rate (FDR) control** (Benjamini-Hochberg): Controls the proportion of false positives among significant results rather than the overall error rate. Less conservative than Bonferroni.
4. **Pre-specify a primary outcome:** Designate one primary outcome and treat others as secondary / exploratory, avoids the multiple comparison problem for the primary endpoint.
5. **MANOVA:** Use multivariate ANOVA to test all outcomes simultaneously.

Q35. Explain why the STAR*D trial is considered methodologically important in psychiatric research, linking it to concepts of internal and external validity.

A: The **STAR*D (Sequenced Treatment Alternatives to Relieve Depression)** trial is landmark because it prioritised **external validity** in a field dominated by explanatory RCTs

with strict inclusion criteria.

External validity strengths:

- Enrolled patients from both primary care and psychiatric settings (real-world recruitment)
- Minimal exclusion criteria, included patients with comorbid anxiety, substance use, and medical conditions (unlike most antidepressant trials)
- Sequential treatment design reflecting real clinical decision-making (what to do when first treatment fails)
- Measured remission ($\text{HAM-D} \leq 7$) as primary outcome rather than just response (more clinically meaningful)

Internal validity trade-offs:

- No placebo control in most steps (ethical and practical decision, but limits causal inference about specific treatments)
- Not blinded in all steps (participants chose some treatment options)
- High dropout rate (28% completed all steps), potential attrition bias

Key findings that shaped clinical practice:

- Overall remission rate across all steps was approximately 67% (cumulative)
- Remission rates decreased with each subsequent step (37% → 31% → 14% → 13%)
- Demonstrated that a substantial proportion of patients need treatment modification
- Provided the first large-scale sequential algorithm data for treatment-resistant depression

STAR*D exemplifies the **efficacy vs effectiveness** distinction: it sacrificed some internal validity (no placebo arm, open-label steps) to maximise external validity (generalisable to real patients). This makes its findings more directly applicable to clinical practice than most tightly controlled explanatory RCTs.

Cross-reference: D1 (Study Notes), D2 (Model Answers), D3 (Mnemonics), D4 (Comparisons)

GUIDE 05 · PART I

Genetics Schizophrenia

Paper I · Basic Sciences. Six study modes, from notes to quick review.

Study Notes

Exam: PG exams MD Psychiatry, Sep 2026

1. Basic Genetics Review

1.1 DNA, Genes, and Alleles

- **DNA** = double-stranded helix of nucleotide bases (A, T, G, C)
- **Gene** = functional unit of heredity; a segment of DNA that codes for a protein or regulatory RNA
- **Allele** = one of two or more alternative forms of a gene at the same locus
- **Homozygous** = two identical alleles; **Heterozygous** = two different alleles
- **Genotype** = genetic makeup; **Phenotype** = observable expression

1.2 Types of Mutations

TYPE	MECHANISM	EXAMPLE
Point mutation	Single nucleotide change (missense, nonsense, silent)	Sickle cell (missense)
Frameshift	Insertion or deletion shifts reading frame	Tay-Sachs disease
Trinucleotide repeat	Expansion of 3-base repeats beyond threshold	Huntington (CAG), Fragile X (CGG)
Chromosomal	Aneuploidy, deletions, duplications, translocations	Down syndrome (trisomy 21)

Trinucleotide repeat disorders relevant to psychiatry:

- **Huntington disease** -- CAG repeat on chromosome 4 (>36 repeats); anticipation (worsens across generations)
- **Fragile X** -- CGG repeat on FMR1 gene (>200 = full mutation); most common inherited cause of intellectual disability
- **Myotonic dystrophy** -- CTG repeat; associated with cognitive decline

1.3 Chromosomal Abnormalities

- **Aneuploidy** -- abnormal chromosome number (e.g., trisomy 21, Turner 45,X, Klinefelter 47,XXY)
- **Deletions** -- loss of chromosomal segment (e.g., 22q11.2 deletion in DiGeorge/VCFS)

- **Duplications** -- extra copy of a segment
- **Translocations** -- transfer between non-homologous chromosomes (balanced vs unbalanced)
- **Inversions** -- segment reversal within a chromosome

1.4 Mendelian vs Complex Inheritance

FEATURE	MENDELIAN	COMPLEX (MULTIFACTORIAL)
Genes involved	Single gene	Multiple genes + environment
Pattern	Predictable ratios	No clear ratios
Penetrance	Often high	Variable, often low
Examples	Huntington, PKU	Schizophrenia, bipolar, diabetes

1.5 Key Genetic Concepts

- **Penetrance** = probability a genotype produces the phenotype
- Complete penetrance = 100% of carriers show phenotype
- Incomplete / reduced penetrance = <100% show phenotype
- **Schizophrenia** has incomplete penetrance (MZ concordance ~48%, not 100%)

EXAM PEARL

Schizophrenia's incomplete penetrance (MZ concordance ~48%, not 100%) is the key argument against Mendelian inheritance and supports the polygenic model.

- **Expressivity** = degree to which a phenotype is expressed
 - Variable expressivity = same genotype, different severity
 - **Genetic heterogeneity**
 - **Locus heterogeneity** = different genes produce the same phenotype
 - **Allelic heterogeneity** = different mutations in the same gene produce the same phenotype
 - **Pleiotropy** = one gene affects multiple phenotypes (e.g., 22q11.2 deletion causes cardiac defects + psychosis + learning disability)
 - **Epistasis** = one gene modifies the effect of another
 - **Endophenotype** (intermediate phenotype) = heritable trait closer to the gene than the clinical phenotype
 - Examples in schizophrenia: smooth pursuit eye movements, P50 sensory gating, working memory deficits, prepulse inhibition
-

2. Genetic Study Designs

2.1 Family Studies

- **Purpose:** Determine if a disorder runs in families
- **Method:** Compare prevalence in relatives of affected individuals (proband) vs general population
- **Recurrence risk** = risk of disorder in relatives of an affected individual
- **Relative risk (lambda)** = recurrence risk in relatives / population prevalence

Schizophrenia family data:

RELATIONSHIP	SHARED GENES	RISK
General population		1%
First-degree relative	50%	~10%
Second-degree relative	25%	~3%
MZ twin	100%	~48%
DZ twin	50%	~17%
Child of two affected parents		~46%

Limitation: Cannot separate genetic from environmental factors (shared family environment)

EXAM PEARL

Key conclusion from adoption studies (below): Genetic factors are the primary driver; being raised by a schizophrenic parent alone does not increase risk.

2.2 Twin Studies

- **MZ (monozygotic) twins** = 100% shared DNA
- **DZ (dizygotic) twins** = ~50% shared DNA (like siblings)
- **Concordance rate** = probability that both twins are affected when one is affected

Heritability estimation:

EXAM PEARL

Heritability (h^2) = $2(r_{MZ} - r_{DZ})$

Where r = concordance rate. For schizophrenia:

EXAM PEARL

$h^2 = 2(0.48 - 0.17) = 2(0.31) = 0.62$ (from concordance data) More sophisticated modeling estimates: ~ 0.80

Equal environments assumption: Assumes MZ and DZ twins share environment equally. If violated (MZ treated more similarly), heritability may be overestimated.

2.3 Adoption Studies

Separate genetic from environmental contributions by studying individuals raised away from biological parents.

STUDY	DESIGN	FINDING
Heston (1966)	Children of schizophrenic mothers adopted away	10.6% developed schizophrenia vs 0% controls
Kety (1968, Danish)	Biological vs adoptive relatives of adopted schizophrenics	Higher rates in biological relatives
Cross-fostering	Children of healthy parents raised by schizophrenic parents	No increased risk

Key conclusion: Genetic factors are the primary driver; being raised by a schizophrenic parent alone does not increase risk.

EXAM PEARL

Candidate gene studies were largely underpowered and most findings did not replicate in GWAS. GWAS has superseded this approach.

2.4 Linkage Analysis

- **Purpose:** Locate genes by tracking co-inheritance of genetic markers with the disease in families
- **Method:** Uses **microsatellites** (short tandem repeats) or SNPs as markers
- **LOD score** (logarithm of odds): statistical measure of linkage
- $\text{LOD} \geq 3.0$ = significant linkage (1000:1 odds)
- $\text{LOD} \leq -2.0$ = linkage excluded
- **Best for:** Mendelian disorders with large effect sizes
- **Limitation in psychiatry:** Most psychiatric disorders are polygenic; linkage has low power for small-effect variants

2.5 Association Studies

- **Purpose:** Test if a specific allele is more common in affected vs unaffected individuals

- **Case-control design:** Compare allele frequencies between cases and controls
- **Transmission Disequilibrium Test (TDT):** Family-based; tests if a particular allele is transmitted from heterozygous parents to affected offspring more than expected by chance. Avoids population stratification bias.
- **Candidate gene studies:** Hypothesis-driven; test specific genes based on known biology
- Problem: poor replication, publication bias, underpowered

2.6 GWAS (Genome-Wide Association Studies)

- **Hypothesis-free:** Scans the entire genome (~1 million+ SNPs)
- **SNP** = Single Nucleotide Polymorphism (single base pair variation)
- **Genome-wide significance threshold:** $p < 5 \times 10^{-8}$ (Bonferroni correction for ~1 million tests)
- **Manhattan plot:** Graph of $-\log_{10}(p\text{-value})$ vs chromosomal position; peaks above significance line = associated loci
- **Linkage disequilibrium (LD):** Non-random association of alleles at different loci; explains why a significant SNP may tag a nearby causal variant

Strengths: Unbiased, can discover novel pathways

Limitations: Detects only common variants (MAF >1%), small effect sizes (OR typically 1.05-1.2), requires enormous samples (tens of thousands), explains only a fraction of heritability

2.7 Copy Number Variants (CNVs)

- **Definition:** Deletions or duplications of DNA segments (>1 kb)
- Detected by array comparative genomic hybridization (aCGH) or SNP arrays
- **De novo CNVs:** New mutations not present in parents; enriched in schizophrenia
- Individual CNVs are rare but have larger effect sizes than common SNPs (OR 2-60)

2.8 Whole Exome / Whole Genome Sequencing

- **Whole exome sequencing (WES):** Sequences all protein-coding regions (~1.5% of genome)
 - **Whole genome sequencing (WGS):** Sequences entire genome including non-coding regions
 - Detects rare variants, de novo mutations, structural variants
 - Important for identifying rare, high-penetrance mutations in psychiatric disorders
-

3. Genetics of Schizophrenia (MAIN FOCUS)

3.1 Overview

- **Heritability:** ~80% (from twin and adoption studies)
- **MZ concordance:** ~48%
- **DZ concordance:** ~17%
- **First-degree relative risk:** ~10% (10x general population)
- **Inheritance pattern:** Complex, polygenic, non-Mendelian
- **Missing heritability:** GWAS loci explain only ~7% of variance; rest may be due to rare variants, epistasis, gene-environment interaction, epigenetics

3.2 Candidate Gene Era

These genes were studied based on the dopamine and glutamate hypotheses. Most findings from candidate gene studies have **not replicated** in GWAS, but they remain important for exam answers and understanding neurobiology.

GENE	FULL NAME	CHROMOSOME	FUNCTION	KEY FINDING
DISC1	Disrupted in Schizophrenia 1	1q42	Neurodevelopment, synaptic plasticity	Identified via balanced translocation in Scottish family
NRG1	Neuregulin 1	8p12	Glutamate signaling, myelination	Icelandic linkage study; role in NMDA receptor function
DTNBP1	Dysbindin	6p22	Glutamate release, synaptic function	Reduced expression in schizophrenia post-mortem brains
COMT	Catechol-O-Methyltransferase	22q11	Dopamine metabolism in PFC	Val158Met polymorphism; Val allele = higher activity = lower PFC dopamine
RGS4	Regulator of G-protein Signaling 4	1q23	Signal transduction	Reduced expression in PFC of schizophrenia patients

EXAM PEARL

Candidate gene studies were largely underpowered and most findings did not replicate. GWAS has superseded this approach. Know the five candidate genes (DISC1, NRG1, DTNBP1, COMT, RGS4) for exam answers even though they are not GWAS-confirmed.

3.3 GWAS Findings

Landmark study: Schizophrenia Working Group of the PGC (2014)

- 36,989 cases + 113,075 controls
- Identified 108 genome-wide significant loci
- Implicated dopaminergic, glutamatergic, calcium signaling, and immune pathways

Key GWAS findings:

LOCUS/GENE · SIGNIFICANCE

MHC region / C4 (complement component 4) Strongest association; C4A overexpression leads to excessive synaptic pruning in adolescence -- links genetics to neurodevelopmental model

DRD2 Dopamine D2 receptor; validates dopamine hypothesis; target of all antipsychotics

Glutamate pathway genes (GRM3, GRIN2A, SRR, GRIA1) Support glutamate/NMDA hypofunction hypothesis

Calcium channel genes (CACNA1C, CACNB2) Shared with bipolar disorder; voltage-gated calcium signaling

TCF4 Transcription factor involved in neurodevelopment

C4 and synaptic pruning (Sekar et al., 2016):

- C4A gene in the MHC region
- Higher C4A expression = more complement-mediated synaptic pruning
- Explains: (a) adolescent onset timing (pruning peaks in adolescence), (b) reduced synaptic density in schizophrenia, (c) grey matter volume loss
- Bridges GWAS finding to neurodevelopmental model

EXAM PEARL

The C4/MHC finding (Sekar et al., 2016) is the key bridge between GWAS statistics and a specific neurobiological mechanism (synaptic pruning). It is a high-yield conceptual anchor.

3.4 Copy Number Variants in Schizophrenia

CNV	TYPE	RISK (OR)	KEY FEATURES
22q11.2 deletion	Deletion	25x risk	DiGeorge/VCFS; 25-30% develop psychosis; most robust CNV finding
1q21.1 deletion	Deletion	~3x	Also associated with ASD, ID
15q13.3 deletion	Deletion	~2x	Contains CHRNA7 (nicotinic receptor)
NRXN1 deletion	Deletion	~2x	Neurexin 1; synaptic adhesion molecule
16p11.2 duplication	Duplication	~3x	Also associated with ASD (deletion)
3q29 deletion	Deletion	~40x	Rare but very high penetrance

22q11.2 deletion syndrome (DiGeorge/VCFS) -- HIGH YIELD:

- Prevalence: 1 in 4000 births
- Features: cardiac defects, palatal abnormalities, hypocalcemia, T-cell deficiency, learning difficulties, characteristic facies
- 25-30% develop schizophrenia-like psychosis (highest known genetic risk factor for schizophrenia after having an MZ twin)
- Contains COMT gene (haploinsufficiency may contribute to dopamine dysregulation)

EXAM PEARL

22q11.2 deletion is the single strongest known genetic risk factor for schizophrenia (after MZ twin status). Know the clinical features of DiGeorge/VCFS: cardiac defects, palatal abnormalities, hypocalcemia, T-cell deficiency.

3.5 Polygenic Risk Scores (PRS)

- Aggregate the effects of thousands of common risk variants into a single score
- PRS for schizophrenia can distinguish cases from controls at a population level (AUC ~0.70-0.75)
- Higher PRS associated with: earlier onset, greater symptom severity, poorer response to treatment
- **Not yet clinically useful** for individual prediction (insufficient discrimination)

- Shared PRS between schizophrenia and bipolar disorder supports the genetic overlap between these conditions

3.6 Two-Hit Hypothesis

1. **First hit:** Genetic vulnerability (polygenic risk, CNVs, or rare mutations)
2. **Second hit:** Environmental insult (prenatal infection, obstetric complications, cannabis use, childhood adversity, urban living, migration)

Both hits are necessary for the disorder to manifest. Explains:

- Why MZ concordance is not 100%
- Why some carriers of high-risk CNVs remain unaffected
- Why environmental risk factors alone are insufficient

3.7 Neurodevelopmental Model

- Schizophrenia conceptualized as a disorder of brain development
- **Prenatal insults** (infection, malnutrition, hypoxia) + **genetic vulnerability** disrupt early brain development
- Abnormalities remain latent until adolescence, when:
 - Normal synaptic pruning (now excessive due to C4A) unmasks deficits
 - Prefrontal cortex maturation fails
 - Dopamine system dysregulation emerges
- **Evidence:** premorbid cognitive deficits, minor physical anomalies, obstetric complications, ventricular enlargement at first episode

4. Epigenetics in Psychiatry

4.1 Core Concepts

Epigenetics = heritable changes in gene expression that do NOT involve changes in DNA sequence.

MECHANISM	DESCRIPTION	EFFECT
DNA methylation	Addition of methyl group to cytosine (CpG sites)	Usually silences gene expression
Histone modification	Acetylation, methylation, phosphorylation of histone tails	Alters chromatin structure (open vs closed)
Non-coding RNA	microRNA, long non-coding RNA	Post-transcriptional gene regulation

4.2 Epigenetics in Schizophrenia

- **RELN (Reelin) gene:** Hypermethylation of promoter region in schizophrenia → reduced reelin expression → impaired neuronal migration and synaptic plasticity
- **GAD67 (GAD1) gene:** Promoter hypermethylation → reduced GAD67 → decreased GABA synthesis in cortical interneurons
- Both findings are consistent with the GABAergic deficit hypothesis of schizophrenia

4.3 Environmental Triggers of Epigenetic Change

- **Cannabis:** THC exposure alters DNA methylation patterns at dopamine-related genes
- **Prenatal stress:** Maternal cortisol exposure alters methylation of glucocorticoid receptor (NR3C1)
- **Prenatal infection:** Maternal immune activation → inflammatory cytokines → epigenetic changes in offspring
- **Early life adversity:** Childhood abuse alters NR3C1 methylation (McGowan et al., 2009 - initially in rats, replicated in humans)

4.4 Transgenerational Epigenetic Effects

- Epigenetic marks can be transmitted across generations
- Dutch Hunger Winter: Offspring of famine-exposed mothers had altered DNA methylation decades later
- Relevance: May partly explain familial aggregation beyond DNA sequence variation

5. Gene-Environment Interactions (GxE)

A GxE interaction occurs when the effect of an environmental exposure on a phenotype depends on the individual's genotype (or vice versa).

5.1 Classic GxE Studies

GXE	GENE	ENVIRONMENT	OUTCOME	REFERENCE
MAOA x maltreatment	MAOA-L (low activity)	Childhood maltreatment	Antisocial behavior	Caspi et al., 2002
5-HTTLPR x stress	Short allele	Stressful life events	Depression	Caspi et al., 2003
FKBP5 x trauma	Risk alleles	Childhood trauma	PTSD risk, HPA axis dysregulation	Binder et al., 2008
COMT x cannabis	Val/Val genotype	Cannabis use in adolescence	Psychosis risk	Caspi et al., 2005

GXE	GENE	ENVIRONMENT	OUTCOME	REFERENCE
AKT1 x cannabis	rs2494732 C/C	Cannabis use	7x increased schizophrenia risk	Di Forti et al., 2012

5.2 Important Caveats

- **5-HTTLPR x stress:** Most debated finding in psychiatric genetics. Large collaborative meta-analysis (Culverhouse et al., 2018) found **no support** for the interaction. However, the broader concept of GxE in depression remains valid.
- **MAOA x maltreatment:** Better replicated than 5-HTTLPR; considered a robust GxE finding
- GxE studies require very large samples to have adequate power

5.3 Diathesis-Stress vs Differential Susceptibility

- **Diathesis-stress:** Risk alleles increase vulnerability to negative environments
- **Differential susceptibility** (Belsky): The same alleles that increase vulnerability to negative environments also increase benefit from positive environments ("orchid vs dandelion" or "for better and for worse")
- Example: 5-HTTLPR short allele carriers may have worse outcomes with adversity but better outcomes with supportive environments

EXAM PEARL

5-HTTLPR x stress is the most debated GxE finding, Culverhouse et al. (2018) found no support in >40,000 subjects. Know this for critical analysis questions.

6. Pharmacogenetics and Pharmacogenomics

6.1 Definitions

- **Pharmacogenetics** = study of how **single genes** affect drug response
- **Pharmacogenomics** = study of how the **entire genome** affects drug response
- Goal: **Personalized medicine** -- right drug, right dose, for the right patient

6.2 CYP450 System

The cytochrome P450 enzymes are the primary drug-metabolizing system. Four enzymes metabolize the majority of psychotropic medications.

CYP ENZYME	KEY SUBSTRATES (PSYCHIATRY)	KEY INHIBITORS	KEY INDUCERS
CYP1A2	Clozapine, olanzapine, fluvoxamine, duloxetine, melatonin	Fluvoxamine, ciprofloxacin	Smoking (PAHs), omeprazole, carbamazepine
CYP2D6	Most SSRIs (fluoxetine, paroxetine), venlafaxine, TCAs (nortriptyline, desipramine), risperidone, aripiprazole, haloperidol, codeine, atomoxetine	Fluoxetine, paroxetine, bupropion, quinidine	Not significantly inducible
CYP2C19	Citalopram, escitalopram, sertraline, diazepam, clobazam, proton pump inhibitors	Fluvoxamine, fluoxetine, omeprazole	Rifampin
CYP3A4	Quetiapine, ziprasidone, lurasidone, buspirone, midazolam, alprazolam, carbamazepine	Ketoconazole, itraconazole, erythromycin, grapefruit juice	Carbamazepine, phenytoin, rifampin, St. John's Wort

EXAM PEARL

CYP1A2 and clozapine + smoking: Smoking **induces** CYP1A2 → faster clozapine metabolism → lower levels. If a patient on stable clozapine **stops smoking** (e.g., hospitalization) → CYP1A2 induction lost → clozapine levels **rise** → risk of toxicity (seizures, sedation, neutropenia).
Clinical rule: Reduce clozapine dose by ~25-50% when a patient stops smoking.

6.3 Metabolizer Phenotypes

PHENOTYPE	ENZYME ACTIVITY	CLINICAL IMPLICATION
Poor metabolizer (PM)	No functional copies	Drug accumulates; higher risk of side effects at standard doses
Intermediate metabolizer (IM)	Reduced activity	Mildly elevated drug levels; may need dose reduction
Extensive/Normal metabolizer (NM)	Normal activity	Standard dosing
Ultrarapid metabolizer (UM)	Increased activity (gene duplication)	Drug cleared too fast; therapeutic failure at standard doses

CYP2D6 examples:

- **PM + codeine** → Cannot convert codeine to morphine → No analgesic effect
- **UM + codeine** → Excessive morphine production → Respiratory depression (fatal in neonates via breast milk)
- **PM + TCAs** → Drug accumulation → Cardiotoxicity
- **PM + risperidone** → Elevated levels → EPS

6.4 HLA Pharmacogenetics

HLA ALLELE	DRUG	ADVERSE REACTION	POPULATION
HLA-B*1502	Carbamazepine, oxcarbazepine, phenytoin	Stevens-Johnson Syndrome (SJS) / Toxic Epidermal Necrolysis (TEN)	Southeast Asian, South Asian, East Asian populations
HLA-A*3101	Carbamazepine	Maculopapular rash, SJS, DRESS	European, Japanese populations
HLA-B*5801	Allopurinol	SJS/TEN	Southeast Asian

CLINICAL ANCHOR

FDA recommends **HLA-B*1502 testing before starting carbamazepine** in patients with Asian ancestry. If positive, **do NOT use carbamazepine**.

6.5 Pharmacogenomic Testing in Clinical Practice

- **CPIC (Clinical Pharmacogenetics Implementation Consortium):** Provides evidence-based dosing guidelines based on genotype
- **Genes with CPIC guidelines in psychiatry:** CYP2D6, CYP2C19, HLA-B
- **Current status:** Routine testing not yet standard of care, but gaining traction
- Strongest evidence: CYP2D6 for TCAs, CYP2C19 for citalopram/escitalopram, HLA-B*1502 for carbamazepine
- Growing evidence: Panel-based testing for treatment-resistant depression (GUIDED trial)
- **Limitations:** Testing only covers pharmacokinetics; pharmacodynamic variation (receptor sensitivity) not captured. Cost, turnaround time, and clinician knowledge are barriers.

6.6 Personalized Medicine

- Moving from "one size fits all" to genotype-guided prescribing
- Combines pharmacogenomics with clinical factors (age, renal/hepatic function, drug interactions)

- **Future directions:** Polygenic risk scores for drug response, AI-guided prescribing algorithms, integration of pharmacogenomic data into electronic health records

7. Genetics of Other Psychiatric Disorders (Brief)

7.1 Bipolar Disorder

- **Heritability:** ~85% (highest among psychiatric disorders along with ASD)
- **MZ concordance:** ~40-70%
- **Key GWAS loci:** CACNA1C (shared with schizophrenia), ANK3, ODZ4
- **Significant genetic overlap** with schizophrenia (~60% shared loci)
- This overlap supports the spectrum concept of psychosis

7.2 ADHD

- **Heritability:** ~76%
- **Candidate genes** (historical): DRD4 (7-repeat allele), DAT1/SLC6A3 (dopamine transporter)
- **GWAS (Demontis et al., 2019):** 12 significant loci; enriched for genes expressed in brain, involved in neurodevelopment
- Genetic correlation with educational attainment (negative), substance use disorders

7.3 Autism Spectrum Disorder

- **Heritability:** ~80-90%
- Strong role of **de novo mutations** (new mutations not inherited from parents)
- **Rare variants:** Large effect CNVs, de novo point mutations
- **Fragile X syndrome:** Single most common known genetic cause (2-3% of ASD cases)
- Other associated syndromes: Rett syndrome (MECP2), Tuberous sclerosis (TSC1/TSC2)
- Hundreds of genes implicated; converge on synaptic function and chromatin remodeling pathways

7.4 Alzheimer Disease

GENE	ROLE	INHERITANCE
APOE e4	Risk factor for late-onset AD	Complex; 1 copy = 3x risk, 2 copies = 12x risk
APP (amyloid precursor protein)	Causal for early-onset familial AD	Autosomal dominant
PSEN1 (presenilin 1)	Most common cause of early-onset familial AD	Autosomal dominant

GENE	ROLE	INHERITANCE
PSEN2 (presenilin 2)	Rare cause of early-onset familial AD	Autosomal dominant

- Early-onset familial AD (<65 years) = ~5% of cases; Mendelian (APP, PSEN1, PSEN2)
- Late-onset sporadic AD = ~95% of cases; APOE e4 is the strongest genetic risk factor
- GWAS has identified 75+ loci for late-onset AD (immune system, lipid metabolism, endocytosis)

8. Summary: Key Numbers for Exam

FACT · NUMBER

Schizophrenia heritability ~80%

Schizophrenia MZ concordance ~48%

Schizophrenia DZ concordance ~17%

First-degree relative risk (schizophrenia) ~10% (10x)

Child of two schizophrenic parents ~46%

PGC 2014 GWAS: loci identified 108

GWAS significance threshold $p < 5 \times 10^{-8}$

LOD score for significant linkage ≥ 3.0

22q11.2 deletion risk for psychosis 25-30% (25x OR)

Bipolar heritability ~85%

ADHD heritability ~76%

ASD heritability ~80-90%

APOE e4 homozygous risk for AD ~12x

Heritability formula (twin) $h^2 = 2(r_{MZ} - r_{DZ})$

9. Cross-References

- **Neurobiology of schizophrenia:** NB-04 (dopamine, glutamate, GABA hypotheses)
- **Pharmacology:** NB-03 (antipsychotics, clozapine monitoring, drug interactions)
- **Schizophrenia clinical features and classification:** NB-06

- **Research methodology and statistics:** NB-01 (study designs, epidemiology)
 - **Child psychiatry / ASD / ADHD:** NB-12
 - **Organic psychiatry / Alzheimer:** NB-08
 - **Substance use / Cannabis and psychosis:** NB-10
-

Model Answers

Exam: PG exams MD Psychiatry, Sep 2026

Q1. "Describe the genetics of schizophrenia." (10 marks)

EXAM STRATEGY

Extremely high-yield, repeated multiple times across years. Structure under clear headings: heritability evidence, family / twin / adoption data, molecular genetics (candidate genes, GWAS, CNVs), then conclude with neurodevelopmental model. Mark allocation: Introduction (1) + Family / Twin / Adoption (3) + Molecular genetics (4) + Integration / Model (2).

Answer:

Introduction (1 mark)

Schizophrenia is a complex, polygenic disorder with estimated heritability of approximately 80%. It does not follow Mendelian inheritance but results from the cumulative effect of multiple genetic variants interacting with environmental factors.

Evidence from Genetic Epidemiology (3 marks)

Family studies:

- Risk increases with degree of genetic relatedness to an affected individual
- General population risk: 1%; first-degree relatives: ~10%; offspring of two affected parents: ~46%
- Relative risk for first-degree relatives is approximately 10x the general population

Twin studies:

- MZ twin concordance: ~48%; DZ twin concordance: ~17%
- Heritability estimated using Falconer's formula: $h^2 = 2(r_{MZ} - r_{DZ}) = 2(0.48 - 0.17) = 0.62$
- More sophisticated models estimate heritability at ~80%
- MZ concordance <100% indicates role of non-genetic factors

Adoption studies:

- Heston (1966): Children of schizophrenic mothers adopted at birth showed 10.6% risk vs 0% in controls
- Kety (1968): Danish adoption study found higher rates in biological relatives of adopted schizophrenics than adoptive relatives
- Cross-fostering studies: Children of healthy parents raised by schizophrenic parents show no increased risk

- Conclusion: Genetic factors are the primary driver of familial aggregation

Molecular Genetics (4 marks)

Candidate genes (historical):

- DISC1 (disrupted in schizophrenia 1) -- identified through a balanced translocation in a Scottish family; involved in neurodevelopment
- NRG1 (neuregulin 1) -- role in NMDA receptor function and myelination
- DTNBP1 (dysbindin) -- reduced expression in postmortem schizophrenia brains; glutamate signaling
- COMT (Val158Met) -- catechol-O-methyltransferase; Val allele associated with increased dopamine degradation in PFC
- Most candidate gene findings have not been replicated in GWAS

GWAS findings:

- PGC Schizophrenia Working Group (2014): 36,989 cases; identified 108 genome-wide significant loci
- Key findings: DRD2 (validates dopamine hypothesis), glutamate pathway genes (GRM3, GRIN2A), calcium channel genes (CACNA1C)
- MHC region / C4 complement gene (Sekar et al., 2016): C4A overexpression leads to excessive synaptic pruning in adolescence, connecting GWAS data to the neurodevelopmental model

Copy number variants (CNVs):

- 22q11.2 deletion (DiGeorge / VCFS) -- 25x risk for schizophrenia; strongest single genetic risk factor
- Other CNVs: 1q21.1, 15q13.3, NRXN1, 3q29 deletions
- Individually rare but confer larger effect sizes than common variants

Polygenic risk scores:

- Aggregate thousands of common risk variants into a single predictive score
- Can distinguish cases from controls at population level but not yet clinically useful for individuals

Integrative Model (2 marks)

The current understanding supports a polygenic, multifactorial model:

- **Two-hit hypothesis:** Genetic vulnerability (first hit) + environmental insult (second hit) required for illness expression
- **Neurodevelopmental model:** Prenatal genetic and environmental insults disrupt brain development; abnormalities remain latent until adolescent synaptic pruning (C4-mediated) unmasks them

- Gene-environment interactions (e.g., COMT x cannabis, AKT1 x cannabis) modulate risk
 - Epigenetic mechanisms (DNA methylation of RELN and GAD67 promoters) may mediate environmental effects on gene expression
-

Q1 Extended: 20-Mark Long Essay Version

Introduction (2 marks) -- As above, expanded with: definition, lifetime prevalence 0.7-1%, classification as a complex genetic disorder, contrast with Mendelian disorders.

Genetic Epidemiology (5 marks) -- As above, expanded with:

- Full risk table across all degrees of relatedness
- Equal environments assumption in twin studies and its limitations
- Specific methodology of each adoption study design
- Endophenotypes: smooth pursuit eye movements, P50 gating, working memory deficits

Molecular Genetics (7 marks) -- As above, expanded with:

- Linkage analysis: LOD scores, why it failed for schizophrenia (small effect sizes, locus heterogeneity)
- Detailed description of GWAS methodology: SNPs, Manhattan plots, genome-wide significance threshold ($p < 5 \times 10^{-8}$), LD
- Expanded candidate gene section with chromosomal locations and functional significance
- Whole exome / genome sequencing: role in detecting rare de novo mutations
- Detailed description of 22q11.2 deletion: prevalence (1:4000), clinical features, COMT haploinsufficiency

Neurodevelopmental and Integrative Models (4 marks) -- Expanded:

- Evidence for neurodevelopmental model: premorbid deficits, obstetric complications, minor physical anomalies, ventricular enlargement at first episode
- C4/MHC finding as bridge between genetics and neurodevelopment
- Two-hit hypothesis with specific examples
- Epigenetics: RELN, GAD67, NR3C1 methylation
- GxE interactions: COMT x cannabis, AKT1 x cannabis

Future Directions and Limitations (2 marks)

- Polygenic risk scores: promise and current limitations
 - Missing heritability problem
 - Pharmacogenomics: moving toward personalized treatment
 - Genetic counseling in schizophrenia: challenges of communicating probabilistic risk
-

Q2. "The biological causes of schizophrenia. Genetics of schizophrenia." [5+5 marks]

EXAM STRATEGY

Two distinct sections, do NOT mix them. Part A: broader biological causes (neurochemical, structural, neurodevelopmental, immune). Part B: genetics specifically (compress the Q1 answer into 5 marks).

Answer:

Part A: Biological Causes of Schizophrenia (5 marks)

Neurochemical hypotheses:

- Dopamine hypothesis: Mesolimbic hyperactivity (positive symptoms), mesocortical hypoactivity (negative/cognitive symptoms). Evidence: amphetamine psychosis, D2 receptor blockade by antipsychotics
- Glutamate hypothesis: NMDA receptor hypofunction. Evidence: PCP/ketamine psychosis mimics schizophrenia including negative symptoms
- GABA hypothesis: Reduced GABAergic interneuron function in cortex
- Serotonin: 5-HT_{2A} involvement (atypical antipsychotics)

Structural brain abnormalities:

- Ventricular enlargement (lateral and third ventricles)
- Reduced grey matter volume (PFC, temporal lobe, hippocampus)
- Present at first episode (not progressive medication effects)

Neurodevelopmental factors:

- Obstetric complications (hypoxia, preeclampsia)
- Prenatal infection (influenza, toxoplasmosis)
- Season of birth effect (winter/spring excess)
- Minor physical anomalies

Neuroimmune/neuroinflammation:

- Microglial activation
- Elevated pro-inflammatory cytokines
- C4 complement gene and excessive synaptic pruning

Part B: Genetics of Schizophrenia (5 marks)

- Heritability ~80%; MZ concordance 48%, DZ 17%, first-degree relative risk 10x
- Adoption studies (Heston, Kety) confirm genetic over environmental transmission
- Candidate genes: DISC1, NRG1, DTNBP1, COMT -- mostly not replicated in GWAS

- GWAS (PGC 2014): 108 loci including DRD2, MHC/C4, glutamate genes, calcium channels
- CNVs: 22q11.2 deletion (25x risk), 1q21.1, 15q13.3, NRXN1
- Polygenic inheritance with gene-environment interaction (two-hit model)
- Epigenetic mechanisms: RELN and GAD67 promoter methylation

Cross-reference: D1 sections 3 and 4; NB-04 (neurobiology)

Q3. "Biopsychosocial model of schizophrenia. Recent advances in genetics." [5+5 marks]

EXAM STRATEGY

Part A: cover bio, psycho, social factors systematically. Part B: focus on GWAS, C4, CNVs, PRS, epigenetics, the "recent" angle.

Answer:

Part A: Biopsychosocial Model (5 marks)

Biological factors:

- Genetic: 80% heritability, polygenic risk, CNVs (22q11.2)
- Neurochemical: Dopamine, glutamate, GABA dysregulation
- Structural: Ventricular enlargement, cortical thinning
- Neurodevelopmental: Obstetric complications, prenatal infection

Psychological factors:

- Expressed emotion (EE): High criticism, hostility, overinvolvement in family increases relapse risk
- Cognitive biases: Jumping to conclusions, externalizing attributional style
- Childhood trauma: 2-3x increased risk; dose-response relationship

Social factors:

- Urbanicity: Urban birth/upbringing increases risk 2-3x
- Migration/ethnic minority status: Increased risk, especially in low ethnic density areas
- Social isolation and deprivation
- Cannabis use: Dose-dependent risk, especially adolescent use

Integration: The stress-vulnerability model (Zubin and Spring, 1977) proposes that the disorder emerges when environmental stressors exceed the individual's threshold, which is determined by genetic and neurodevelopmental vulnerability.

Part B: Recent Advances in Genetics (5 marks)

GWAS:

- PGC 2014: 108 loci in ~150,000 subjects; largest psychiatric GWAS at the time
- PGC3 (2022): >270 loci in expanded samples
- Implicates glutamate, dopamine, calcium, and immune pathways

C4 complement gene (Sekar et al., 2016):

- Strongest GWAS signal maps to MHC region
- C4A overexpression leads to excessive complement-mediated synaptic pruning
- Provides a mechanistic link between genetics and the neurodevelopmental model
- Explains adolescent onset and grey matter loss

Copy number variants:

- Rare but large-effect deletions/ duplications
- 22q11.2 deletion: 25x risk; 3q29 deletion: ~40x risk
- De novo CNVs enriched in sporadic schizophrenia

Polygenic risk scores:

- Aggregate effect of thousands of common variants
- Can predict case-control status at population level (AUC ~0.70)
- Shared PRS with bipolar disorder supports dimensional/ spectrum concept

Epigenetics:

- DNA methylation changes at RELN, GAD67 promoters
- Environmental factors (cannabis, stress, infection) mediate effects through epigenetic mechanisms
- Potential for reversibility -- therapeutic implications

Q4. "Genetics of Schizophrenia." (Short note, 10 marks)

EXAM STRATEGY

Identical content to Q1 but written as a short note (slightly more condensed, same structure).
See Q1 answer above, use the 10-mark version directly.

Q5. "What is Genetic mutation and how does it occur?" (10 marks)

EXAM STRATEGY

Definition + classification + mechanisms + examples. Mark allocation: Definition (1) + Types (4) + Mechanisms (3) + Clinical relevance (2).

Answer:

Definition (1 mark)

A genetic mutation is a permanent change in the nucleotide sequence of DNA. Mutations may be neutral, beneficial, or pathogenic depending on their location and functional impact.

Types of Mutations (4 marks)

Point mutations (single nucleotide changes):

- **Missense:** Change in one amino acid (e.g., sickle cell disease: GAG→GTG, Glu→Val)
- **Nonsense:** Creates premature stop codon → truncated, non-functional protein
- **Silent:** No amino acid change due to codon redundancy

Insertions and deletions (indels):

- **Frameshift:** Insertion/deletion of nucleotides not in multiples of 3 shifts the reading frame → completely altered downstream protein
- **In-frame:** Insertion/deletion in multiples of 3 adds/removes amino acids without shifting frame

Trinucleotide repeat expansions:

- Normal alleles have a set number of repeats; expansion beyond threshold causes disease
- **Anticipation:** Repeat number increases across generations → earlier onset, greater severity
- Examples: Huntington (CAG >36), Fragile X (CGG >200), Myotonic dystrophy (CTG)

Chromosomal mutations:

- **Aneuploidy:** Gain/loss of whole chromosomes (nondisjunction)
- **Deletions:** Loss of chromosomal segment (e.g., 22q11.2)
- **Duplications:** Extra copy of a segment
- **Translocations:** Transfer between chromosomes (balanced vs unbalanced)
- **Inversions:** Reversal of a segment

Mechanisms of Mutation (3 marks)

Spontaneous:

- DNA replication errors (base mismatch, slippage during repeat replication)
- Spontaneous depurination and deamination
- Failure of DNA repair mechanisms

Induced:

- Physical mutagens: ionizing radiation (X-rays, UV), causing thymine dimers, strand breaks

- Chemical mutagens: alkylating agents, base analogs, intercalating agents
- Biological: viral insertion, transposable elements

De novo mutations:

- New mutations not present in either parent
- Occur during gametogenesis or early embryonic development
- Paternal age effect: Older fathers have more de novo point mutations (relevant for schizophrenia and autism risk)

Clinical Relevance in Psychiatry (2 marks)

- Schizophrenia: De novo CNVs (22q11.2 deletion), de novo point mutations, trinucleotide repeats in associated conditions
- Autism: High rate of de novo mutations; hundreds of genes implicated
- Huntington disease: Trinucleotide repeat expansion with anticipation
- Fragile X: Most common inherited intellectual disability; CGG expansion
- Pharmacogenetics: CYP2D6 gene duplications / deletions affect metabolizer status

Q6. "What is pharmacogenetics? Describe its research and implications in treatment."
[2+4+4 marks]

EXAM STRATEGY

Long essay candidate, can be expanded to 20 marks. Clear three-part structure matching mark allocation.

Answer:

What is Pharmacogenetics? (2 marks)

Pharmacogenetics is the study of how genetic variation in individual genes influences drug response, including drug efficacy, dosing requirements, and adverse drug reactions. The broader term pharmacogenomics encompasses the influence of the entire genome on drug response. The goal is to move from empirical "trial and error" prescribing to personalized, genotype-guided treatment.

Research in Pharmacogenetics (4 marks)

CYP450 enzyme polymorphisms:

- CYP2D6: Most studied in psychiatry. Metabolizes most SSRIs, TCAs, risperidone, aripiprazole, haloperidol. Over 100 allelic variants identified. Gene duplications (ultrarapid) and null alleles (poor metabolizer) have clear clinical consequences.
- CYP2C19: Metabolizes citalopram, escitalopram, sertraline, diazepam. Poor metabolizers at risk for citalopram toxicity (QTc prolongation).

- CYP1A2: Metabolizes clozapine, olanzapine. Induced by smoking (polycyclic aromatic hydrocarbons, not nicotine). Critical for clozapine monitoring.
- CYP3A4: Metabolizes quetiapine, lurasidone, benzodiazepines. Many drug interactions.

HLA pharmacogenetics:

- HLA-B*1502 and carbamazepine: Strong association with Stevens-Johnson Syndrome/TEN in Asian populations. FDA mandates testing before prescribing.
- HLA-A*3101 and carbamazepine: Associated with hypersensitivity reactions in European and Japanese populations.

Pharmacodynamic targets:

- Serotonin transporter (SLC6A4): 5-HTTLPR variants may influence SSRI response (evidence mixed)
- DRD2/DRD3 polymorphisms: May influence antipsychotic response
- HTR2A variants: Associated with clozapine response

Key research approaches:

- Candidate gene studies of drug-metabolizing enzymes
- GWAS for drug response phenotypes
- Clinical trials incorporating pharmacogenomic testing (GUIDED trial for treatment-resistant depression)

Implications in Treatment (4 marks)

Clinical applications:

- CYP2D6 genotyping before starting TCAs: Poor metabolizers need 50% dose reduction; ultrarapid metabolizers may need higher doses or alternative drug
- CYP2C19 genotyping for citalopram/escitalopram: Poor metabolizers should not exceed 20mg citalopram (QTc risk)
- HLA-B*1502 testing before carbamazepine in Asian populations: Prevents life-threatening SJS/TEN
- CYP1A2 monitoring for clozapine: Smoking cessation requires dose reduction; smoking resumption requires dose increase

Metabolizer phenotype-based dosing:

- Poor metabolizers: Lower starting dose, slower titration, or choose alternative drug not metabolized by that enzyme
- Ultrarapid metabolizers: Higher doses or alternative drug; standard doses may be subtherapeutic
- CPIC guidelines provide specific dosing recommendations based on genotype

Current limitations:

- Cost and accessibility of testing
- Limited clinician knowledge of how to interpret results
- Pharmacokinetic genes (CYP450) are better understood than pharmacodynamic genes
- Most evidence is for avoiding adverse effects rather than predicting efficacy
- Turnaround time may be too slow for acute clinical situations

Future directions:

- Pre-emptive panel testing (test once, use for life)
- Integration into electronic health records with clinical decision support
- Polygenic risk scores for treatment response
- AI-guided prescribing algorithms combining pharmacogenomics with clinical data
- Potential to reduce time to response and number of failed trials, particularly in treatment-resistant illness

Cross-reference: D1 section 6; D4 comparison tables 5 and 6

Q6 Extended: 20-Mark Long Essay Version

Expand each section:

- **Definition (3 marks):** Include distinction between pharmacogenetics vs pharmacogenomics, historical context (genetic variation in drug acetylation, isoniazid in TB), concept of personalized medicine
 - **Research (8 marks):** Detailed CYP450 table with substrates/inhibitors/inducers, full metabolizer phenotype descriptions, HLA associations, pharmacodynamic targets, research methodology (candidate gene vs GWAS), key studies (STAR*D pharmacogenomic analyses, GUIDED trial)
 - **Implications (7 marks):** Clinical decision algorithms, case examples (clozapine + smoking, carbamazepine + HLA), cost-effectiveness data, ethical considerations (genetic discrimination, incidental findings), pharmacogenomic testing panels commercially available
 - **Future directions (2 marks):** As above, expanded
-

Q7. "What is pharmacogenetics? Role in medical disorders with examples." (10 marks)

EXAM STRATEGY

Broader scope than Q6, include non-psychiatric examples. Mark allocation: Definition (2) + Role in medical disorders (4) + Psychiatric examples (4).

Answer:

Definition (2 marks)

Pharmacogenetics is the study of how inherited genetic variation affects individual responses to drugs. It encompasses drug efficacy, required dosing, and susceptibility to adverse drug reactions. It is a key component of personalized/precision medicine.

Role in Medical Disorders (4 marks)

Oncology:

- BRCA1/BRCA2 mutations: Guide use of PARP inhibitors (olaparib) in breast/ovarian cancer
- HER2 amplification: Trastuzumab (Herceptin) for HER2-positive breast cancer
- EGFR mutations: Gefitinib for non-small cell lung cancer
- TPMT polymorphisms: Thiopurine (azathioprine/6-MP) dosing in leukemia and IBD. Poor metabolizers at risk of fatal myelosuppression.

Cardiology:

- CYP2C19 and clopidogrel: Poor metabolizers cannot activate the prodrug → therapeutic failure → increased cardiac events. Alternative: prasugrel or ticagrelor.
- VKORC1 and warfarin: Genetic variants affect warfarin sensitivity. Combined CYP2C9 + VKORC1 genotyping guides dosing.

Infectious disease:

- HLA-B*5701 and abacavir (HIV): Mandatory testing before prescribing. Positive test = do not use (risk of fatal hypersensitivity).

Rheumatology:

- HLA-B*5801 and allopurinol: SJS/TEN risk in Southeast Asian populations

Psychiatric Examples (4 marks)

- CYP2D6: Metabolizer status affects dosing of TCAs, SSRIs, risperidone, aripiprazole. PMs at risk for toxicity; UMs for treatment failure.
 - CYP2C19: Poor metabolizers should have reduced citalopram/escitalopram dosing (QTc prolongation risk).
 - CYP1A2 + smoking + clozapine: Smoking induces CYP1A2; cessation raises clozapine levels; resumption lowers them.
 - HLA-B*1502 + carbamazepine: SJS/TEN in Asian populations. FDA-mandated pre-prescription testing.
 - HLA-A*3101 + carbamazepine: Hypersensitivity in European/Japanese populations.
-

Q8. "What are pharmacogenomics & pharmacogenetics? Relevance in Psychiatry." [4+6 marks]

EXAM STRATEGY

Clear distinction between the two terms in Part A. Part B: focus exclusively on psychiatric applications.

Answer:

Pharmacogenetics and Pharmacogenomics: Definitions and Distinction (4 marks)

Pharmacogenetics:

- Study of how variation in a single gene affects drug response
- Focuses on individual gene polymorphisms (e.g., CYP2D6 variants)
- Historical term; narrower scope
- Example: CYP2D6 poor metabolizer status predicting TCA toxicity

Pharmacogenomics:

- Study of how the entire genome (multiple genes, interactions, regulatory regions) affects drug response
- Uses GWAS, whole-genome approaches
- Broader and more contemporary term
- Example: Polygenic prediction of antidepressant response using genome-wide data

Key distinction: Pharmacogenetics = single gene → drug response. Pharmacogenomics = whole genome → drug response. In practice, the terms are often used interchangeably.

Both fall under the umbrella of **personalized/precision medicine**: selecting the right drug at the right dose for the right patient based on their genetic profile.

Relevance in Psychiatry (6 marks)

Why particularly relevant in psychiatry:

- Psychiatric drug prescribing is largely empirical ("trial and error")
- Time to response is weeks to months
- Adverse effects cause non-adherence (a major problem in psychiatry)
- Treatment-resistant illness is common (30% in depression, 25-30% in schizophrenia)

CYP450 polymorphisms:

- CYP2D6: Metabolizes majority of antidepressants and antipsychotics. Four phenotypes (PM, IM, NM, UM) with distinct dosing implications.
- CYP2C19: Critical for citalopram, escitalopram, sertraline dosing. FDA label for citalopram limits dose in PMs.

- CYP1A2: Clozapine and olanzapine metabolism. Smoking induces CYP1A2. Clinical scenario: hospitalized patient stops smoking → clozapine toxicity.
- CYP3A4: Quetiapine, lurasidone, benzodiazepines. Many drug-drug interactions (e.g., carbamazepine induction).

HLA testing:

- HLA-B*1502: Mandatory before carbamazepine/oxcarbazepine in Asian populations. Prevents SJS/TEN.
- HLA-A*3101: Carbamazepine hypersensitivity in Europeans/Japanese.

Clinical decision support (CPIC guidelines):

- CYP2D6 + TCAs: Dose reduction by 50% in PMs; avoid in UMs or increase dose
- CYP2C19 + SSRIs: Dose adjustment or alternative drug in PMs
- Pre-emptive panel testing: Test multiple genes once, use results throughout lifetime

Evidence from clinical trials:

- GUIDED trial (2019): Pharmacogenomic-guided prescribing improved response and remission rates in treatment-resistant depression compared to treatment as usual

Limitations and future:

- Most evidence relates to pharmacokinetics (drug metabolism) rather than pharmacodynamics (drug target sensitivity)
- Cost-effectiveness still debated
- Future: Integration with EHR, AI-guided prescribing, polygenic scores for treatment response

Q9. "What is pharmacogenetics? Current concept and future use in psychiatry." (10 marks)

EXAM STRATEGY

Overlaps with Q6 and Q8. Emphasize "current concept" = what we know now + "future use" = where the field is heading. Mark allocation: Definition (2) + Current concepts (4) + Future use (4).

Answer:

Definition (2 marks) -- As in Q6/Q8.

Current Concepts (4 marks)

- Pharmacogenetics has moved from theoretical to practical application in specific clinical scenarios
- CYP2D6 and CYP2C19 polymorphisms have the strongest evidence base for guiding psychiatric prescribing

- HLA-B*1502 testing before carbamazepine is now an FDA requirement for Asian patients
- CPIC guidelines provide actionable dosing recommendations based on genotype for TCAs, SSRIs, and carbamazepine
- Commercially available pharmacogenomic panels (e.g., GeneSight, Myriad) test multiple genes simultaneously
- Metabolizer phenotypes (PM, IM, NM, UM) form the basis of clinical decision-making
- CYP1A2 induction by smoking is a critical pharmacogenetic interaction for clozapine management

Future Use in Psychiatry (4 marks)

- **Pre-emptive panel testing:** Genotype patients once early in treatment; store results for lifetime use. Avoids delays when new medications are needed.
- **EHR integration:** Pharmacogenomic results embedded in electronic health records with automated clinical decision support alerts.
- **Pharmacodynamic pharmacogenomics:** Moving beyond drug metabolism to predict which drug will work best (e.g., serotonin transporter variants predicting SSRI response, dopamine receptor variants predicting antipsychotic response).
- **Polygenic risk scores for treatment response:** Aggregate genome-wide data to predict response to specific drugs or drug classes.
- **AI-guided prescribing algorithms:** Combining pharmacogenomic data with clinical variables (age, sex, comorbidities, co-medications) for optimal drug selection.
- **Pharmacoepigonomics:** How epigenetic marks (DNA methylation, histone modification) influence drug response; potential for modifiable targets.
- **Ethical and practical considerations:** Genetic privacy, insurance discrimination, equitable access to testing, need for clinician education.
- **Cost-effectiveness:** As testing costs decrease and evidence grows, routine pharmacogenomic testing may become standard of care, particularly in treatment-resistant illness.

Q10. "What is EBM? What is personalized medicine? Discuss pharmacogenetics." [2+3+5 marks]

EXAM STRATEGY

Three distinct sections with clear mark allocation. EBM: keep concise (definition + levels of evidence). Personalized medicine: bridge concept connecting EBM to pharmacogenetics.

Answer:

Evidence-Based Medicine (2 marks)

Evidence-based medicine (EBM) is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients (Sackett, 1996). It integrates three components:

1. Best available research evidence (systematic reviews, RCTs)
2. Clinical expertise
3. Patient values and preferences

Hierarchy of evidence: Systematic reviews/meta-analyses > RCTs > cohort studies > case-control > case series > expert opinion.

EBM provides population-level treatment guidelines. Its limitation is that it treats patients as homogeneous groups, not accounting for individual biological variation.

Personalized Medicine (3 marks)

Personalized (precision) medicine tailors medical treatment to individual characteristics -- genetic, environmental, and lifestyle -- of each patient. It moves beyond "one size fits all" prescribing.

Key components:

- **Pharmacogenomics:** Genetic testing to guide drug selection and dosing
- **Biomarkers:** Measurable indicators that predict disease course or treatment response
- **Companion diagnostics:** Tests paired with specific therapies (e.g., HER2 testing for trastuzumab)

In psychiatry, personalized medicine addresses the problem that:

- Response to any given psychotropic is only 50-60%
- Time to adequate trial is 4-8 weeks
- Treatment-resistant illness affects 25-30% of patients
- Adverse effects are a leading cause of non-adherence

Personalized medicine is the practical application of EBM at the individual level -- using the best evidence to make the best decision for this specific patient.

Pharmacogenetics (5 marks)

Definition: Study of how genetic variation affects drug response (efficacy, dosing, adverse effects).

Key applications in psychiatry:

- CYP2D6: Guides dosing of TCAs, SSRIs, risperidone, aripiprazole. PMs need dose reduction; UMs may need higher doses or alternative drugs.
- CYP2C19: Guides citalopram/escitalopram dosing. FDA limits citalopram to 20mg in PMs.

- CYP1A2: Clozapine + smoking interaction. Dose adjustment required with smoking changes.
- HLA-B*1502: Prevents SJS/TEN from carbamazepine in Asian patients.

Metabolizer phenotypes: PM, IM, NM, UM -- each with distinct clinical implications.

CPIC guidelines: Evidence-based, gene-drug specific dosing recommendations.

Challenges: Cost, clinician education, limited pharmacodynamic evidence, ethical considerations.

Future: Pre-emptive testing, EHR integration, AI-guided prescribing, polygenic response scores.

Cross-reference: D1 section 6; D4 tables 5 and 6

Q11. "What is genetic epidemiology? Describe three types of genetic studies." (10 marks)

EXAM STRATEGY

Long essay candidate. Definition + three study types in detail. Mark allocation: Definition (2) + Three study types (2.5 each = 7.5) + Summary (0.5). Choose: family, twin, and adoption studies (most commonly expected); OR include one molecular method.

Answer:

Genetic Epidemiology: Definition (2 marks)

Genetic epidemiology is the study of the role of genetic factors and their interaction with environmental factors in the occurrence of disease in populations. It uses epidemiological methods to determine:

1. Whether a disease has a genetic component (familial aggregation)
2. The relative contribution of genetic vs environmental factors (heritability)
3. The mode of inheritance
4. The location and identity of specific genes involved

It bridges classical epidemiology (population-level disease patterns) and molecular genetics (specific genetic variants).

Three Types of Genetic Studies (8 marks)

1. Family Studies (2.5 marks)

Design: Compare the prevalence of a disorder in relatives of affected individuals (probands) with the prevalence in the general population or in relatives of unaffected controls.

Key measures:

- Recurrence risk: Probability of the disorder in a relative of an affected individual

- Relative risk (lambda-R): Recurrence risk / population prevalence
- Risk decreases as genetic distance from the proband increases

Example in schizophrenia:

- General population: 1%
- First-degree relative: ~10% ($\lambda = 10$)
- Second-degree relative: ~3%
- MZ twin: ~48%

Strengths: Simple, demonstrates familial aggregation

Limitation: Cannot distinguish genetic from shared environmental effects (families share both genes and environment)

2. Twin Studies (2.5 marks)

Design: Compare concordance rates between MZ twins (100% shared DNA) and DZ twins (~50% shared DNA). If genetic factors contribute, MZ concordance should exceed DZ concordance.

Key measures:

- Concordance rate: Probability that the co-twin is affected given that one twin is affected
- Heritability: $h^2 = 2(r_{MZ} - r_{DZ})$ (Falconer's formula)

Example:

- Schizophrenia: MZ 48%, DZ 17% $\rightarrow h^2 = 2(0.48 - 0.17) = 0.62$
- Bipolar disorder: MZ ~60%, DZ ~12%
- ADHD: MZ ~80%, DZ ~30%

Strengths: Separates genetic from shared environmental effects (both twin types share family environment)

Limitations:

- Equal environments assumption: Assumes MZ and DZ twins share environment equally (may not hold)
- Ascertainment bias; small sample sizes for rare disorders
- MZ discordance may overestimate environmental contribution (includes stochastic/epigenetic effects)

3. Adoption Studies (2.5 marks)

Design: Study individuals separated from biological parents early in life. Compares rates of disorder in:

- Biological relatives vs adoptive relatives of affected adoptees

- Adopted-away children of affected vs unaffected biological parents
- Cross-fostering: Children of unaffected parents raised by affected adoptive parents

Key studies in schizophrenia:

- Heston (1966): 47 adopted-away children of schizophrenic mothers; 5/47 (10.6%) developed schizophrenia vs 0/50 controls
- Kety (1968): Danish adoption study; rates of schizophrenia spectrum disorders were higher in biological relatives of affected adoptees than in adoptive relatives
- Cross-fostering: No increased risk when raised by schizophrenic adoptive parents

Strengths: Most powerful naturalistic design for separating genetic and environmental effects

Limitations:

- Selective placement (adoption agencies may match families)
- Prenatal environment shared with biological mother
- Limited availability of adoption registries; small samples
- Historical: Adoption practices have changed, limiting replication

Summary (0.5 marks)

Family, twin, and adoption studies together form the foundation of genetic epidemiology in psychiatry. They establish that a disorder has a genetic component and estimate its magnitude (heritability), setting the stage for molecular studies (linkage, association, GWAS) to identify specific genes.

Q11 Extended: 20-Mark Long Essay Version

- **Definition (3 marks):** Expanded with historical development, relationship to other genetic disciplines
 - **Family studies (4 marks):** Full risk tables for schizophrenia, bipolar, ADHD; recurrence risk calculations; lambda calculations
 - **Twin studies (4 marks):** Detailed methodology, concordance vs correlation, heritability across disorders, limitations in detail
 - **Adoption studies (4 marks):** Detailed study designs, all three paradigms, specific studies
 - **Molecular genetic epidemiology (3 marks):** Linkage analysis (LOD scores), association studies (case-control, TDT), GWAS, CNV analysis
 - **Integration and future (2 marks):** How designs complement each other, multi-omics approaches
-

Q12. "Genetic epidemiological studies in Psychiatry." (10 marks)

EXAM STRATEGY

Broader than Q11, cover all study types relevant to psychiatric genetics. Mark allocation: Introduction (1) + Classical designs (4) + Molecular designs (4) + Conclusion (1).

Answer:

Introduction (1 mark)

Genetic epidemiology in psychiatry employs a hierarchy of study designs to determine the genetic architecture of mental disorders. These range from classical designs that establish heritability to molecular approaches that identify specific genetic variants.

Classical Genetic Epidemiological Designs (4 marks)

Family studies: Establish familial aggregation. Example: Schizophrenia risk 10x in first-degree relatives. Limitation: Cannot separate genes from environment.

Twin studies: Compare MZ vs DZ concordance to estimate heritability. Example: Schizophrenia heritability ~80%. Key assumption: Equal environments.

Adoption studies: Separate genetic from environmental transmission. Heston (1966) and Kety (1968) studies confirmed genetic basis of schizophrenia. Most powerful naturalistic design.

Molecular Genetic Epidemiological Designs (4 marks)

Linkage analysis:

- Maps disease genes using co-inheritance of genetic markers in families
- LOD score ≥ 3.0 indicates significant linkage
- Limited success in psychiatry due to small effect sizes and locus heterogeneity

Association studies:

- Case-control design comparing allele frequencies
- TDT: Family-based, avoids population stratification
- Candidate gene studies: Hypothesis-driven but poorly replicated (e.g., COMT, NRG1, DTNBP1)

GWAS:

- Hypothesis-free genome-wide scan of millions of SNPs
- Significance threshold: $p < 5 \times 10^{-8}$
- Key finding: PGC 2014 identified 108 loci for schizophrenia
- Detects common variants with small effects

CNV analysis:

- Identifies rare structural variants (deletions/duplications)

- 22q11.2 deletion: 25x risk for schizophrenia
- Higher effect sizes than common SNPs

Sequencing (WES/WGS):

- Detects rare mutations, de novo variants
- Important for autism (many de novo mutations)
- Emerging role in schizophrenia research

Conclusion (1 mark)

Modern psychiatric genetics integrates classical designs (establishing heritability) with molecular approaches (identifying specific variants) and is increasingly incorporating epigenetic and gene-environment interaction analyses. This multi-layered approach is essential given the polygenic, multifactorial nature of psychiatric disorders.

Q13. "What is gene mapping? How is it different from linkage and association studies?"
[3+7 marks]

EXAM STRATEGY

Part A: define gene mapping and its purpose. Part B: compare linkage and association studies in detail.

Answer:

Gene Mapping (3 marks)

Gene mapping is the process of determining the chromosomal location of a gene and the distance between genes. There are two types:

Genetic mapping:

- Uses recombination frequencies during meiosis to determine relative positions of genes and markers
- Measured in centimorgans (cM); 1 cM $\approx$ 1 million base pairs
- Tools: Linkage analysis using microsatellites or SNPs

Physical mapping:

- Determines actual physical position (base pairs) on a chromosome
- Tools: Fluorescence in situ hybridization (FISH), restriction mapping, sequencing
- Human Genome Project provided the complete physical map

Purpose in psychiatry: Identify specific genes contributing to complex disorders like schizophrenia, bipolar disorder, and depression.

Linkage vs Association Studies (7 marks)

Linkage analysis:

- **Design:** Family-based; tracks co-segregation of genetic markers with disease across generations in pedigrees
- **Markers:** Microsatellites (short tandem repeats), now also SNPs
- **Statistical measure:** LOD score (logarithm of odds ratio). LOD ≥ 3.0 = significant linkage; LOD ≤ -2.0 = excluded
- **Resolution:** Low (~10-20 Mb); identifies broad chromosomal regions, not specific genes
- **Best for:** Mendelian disorders with high penetrance, large effect sizes
- **Limitations in psychiatry:** Most psychiatric disorders are polygenic with small-effect variants; linkage studies have low power for these. Example: Multiple linkage studies in schizophrenia identified candidate regions (6p, 8p, 22q) but with inconsistent replication.

Association studies:

- **Design:** Population-based (case-control) or family-based (TDT)
- **Method:** Compare frequency of a specific allele / genotype between affected and unaffected individuals
- **Resolution:** High (~1 kb); can pinpoint specific SNPs
- **Types:**
 - Candidate gene: Hypothesis-driven, tests specific genes. Example: COMT Val158Met in schizophrenia.
 - GWAS: Hypothesis-free, scans millions of SNPs across genome. Example: PGC 2014 identified 108 loci.
- **Statistical measure:** Odds ratio with p-value (GWAS threshold: $p < 5 \times 10^{-8}$)
- **Strengths:** Detects common variants with small effect sizes; high resolution
- **Limitations:** Population stratification (case-control), need for very large samples, detects association not causation, candidate gene studies suffered from poor replication

FEATURE	LINKAGE	ASSOCIATION
Design	Family-based	Population or family
Sample	Extended pedigrees	Cases vs controls (or trios)
Resolution	Low (10-20 Mb)	High (~1 kb)
Effect size detected	Large	Small to large
Best for	Mendelian traits	Complex traits
Statistical test	LOD score	Chi-square, regression
Significance	LOD ≥ 3.0	$p < 5 \times 10^{-8}$ (GWAS)
Key limitation	Low power for polygenic traits	Population stratification

Key conceptual point: Linkage detects co-segregation within families (are these loci transmitted together?). Association detects co-occurrence in populations (is this allele more common in cases?). They answer different questions and are complementary.

Mnemonics & Memory Tricks

Exam: PG exams MD Psychiatry, Sep 2026

Mnemonic 1: Candidate Genes of Schizophrenia

MNEMONIC

DISC-o NRG Drinks COMT RGS

EXAM PEARL: Picture a "DISCO" club where NRG drinks are served, COMT is the bouncer, and RGS4 is the DJ.

LETTER	GENE	FULL NAME
DISC	DISC1	Disrupted in Schizophrenia 1
NRG	NRG1	Neuregulin 1
D (Drinks)	DTNBP1	Dysbindin
COMT	COMT	Catechol-O-Methyltransferase
RGS	RGS4	Regulator of G-protein Signaling 4

Mnemonic 2: CYP1A2 -- Substrates

MNEMONIC

COD FM

EXAM PEARL: Smoking INDUCES CYP1A2. Stop smoking = clozapine toxicity.

LETTER · SUBSTRATE

C Clozapine

O Olanzapine

D Duloxetine

F Fluvoxamine (also inhibitor)

M Melatonin

Mnemonic 3: CYP2D6 -- Substrates

MNEMONIC

FRIEND-HAV

EXAM PEARL: CYP2D6 is **NOT significantly inducible**. Fluoxetine and paroxetine are potent inhibitors.

LETTER · SUBSTRATE

F Fluoxetine (also inhibitor)

R Risperidone

I Imipramine / TCAs

E (codEine)

N Nortriptyline

D Desipramine

H Haloperidol

A Aripiprazole / Atomoxetine

V Venlafaxine

Mnemonic 4: CYP2D6 Inhibitors

MNEMONIC

FPB-Q

EXAM PEARL: "Fluoxetine and Paroxetine Block Quickly", these two SSRIs are the strongest CYP2D6 inhibitors in psychiatry.

Fluoxetine, Paroxetine, Bupropion, Quinidine

Mnemonic 5: CYP3A4 -- "The Kitchen Sink Enzyme"

MNEMONIC

QLB-MZ / CAPS / KEG

EXAM PEARL: Substrates (psychiatry): Quetiapine, Lurasidone, Buspirone, Midazolam, Ziprasidone EXAM PEARL: Inducers: Carbamazepine, (Ph)Aenytoin, RifamPin, St. John's Wort EXAM PEARL: Inhibitors: Ketoconazole, Erythromycin, Grapefruit juice

Mnemonic 6: Metabolizer Phenotypes

MNEMONIC

PINE

EXAM PEARL: PINE tree, from slowest growth (Poor) to fastest (Extra/Ultrarapid).

PHENOTYPE	COPIES	CLINICAL EFFECT
Poor	0 functional	Drug accumulates -- toxicity risk
Intermediate	1 reduced	Mildly elevated levels
Normal (Extensive)	2 functional	Standard dosing works
Extra (Ultrarapid)	>2 copies	Drug cleared fast -- treatment failure

Mnemonic 7: Heritability Across Psychiatric Disorders

MNEMONIC

ABS are strong

EXAM PEARL: ASD, Bipolar, Schizophrenia all have heritability above 75%. Depression is the outlier at ~37%.

DISORDER	HERITABILITY	MNEMONIC NUMBER
Autism (ASD)	~80-90%	"A is the highest"
Bipolar	~85%	Almost as high as ASD
Schizophrenia	~80%	"S is 8-ty"
ADHD	~76%	"Seven-six"
Depression (MDD)	~37%	"The low one"

Mnemonic 8: Key GWAS Findings in Schizophrenia

MNEMONIC

108-C4-D2-Glut-Cal

EXAM PEARL: "108 soldiers of C4 attacked D2 with Glut and Cal weapons"

- 108 loci identified (PGC 2014)
- C4 complement gene (MHC region) -- synaptic pruning
- D2 -- DRD2 dopamine receptor (validates dopamine hypothesis)
- Glut -- Glutamate pathway genes (GRM3, GRIN2A, SRR, GRIA1)
- Cal -- Calcium channel genes (CACNA1C, CACNB2) shared with bipolar

Mnemonic 9: Genetic Study Design Hierarchy

MNEMONIC

FAT-LAG-WES

EXAM PEARL: "FAT people LAG in WES-tern movies", Classical studies (FAT) come before molecular studies (LAG-WES).

STEP	STUDY TYPE	PURPOSE
F	Family studies	Does it run in families?
A	Adoption studies	Is it genes or environment?
T	Twin studies	How heritable is it?
L	Linkage analysis	Which chromosome region?
A	Association studies	Which specific variant?
G	GWAS	Genome-wide unbiased scan
W	Whole exome sequencing	Rare coding variants?
E	Whole genome sequencing	Everything including non-coding
S	Systems biology	How do variants interact?

Mnemonic 10: Types of Mutations

MNEMONIC

PSF-TCI

LETTER · MUTATION TYPE

P Point (missense, nonsense, silent)

S Substitution (same as point)

F Frameshift (insertion/deletion)

T Trinucleotide repeat expansion

C Chromosomal (aneuploidy, deletion, duplication)

I Inversion / translocation

Mnemonic 11: CNVs in Schizophrenia

MNEMONIC

22-1-15-N-16-3

EXAM PEARL: Think of it as a phone number: 22-1-15 N-16-3. "22 is king (highest yield), 3 is the sleeper (highest penetrance)."

CNV	RISK	KEY FEATURE
22q11.2 del	25x	DiGeorge / VCFS; cardiac + psychosis
1q21.1 del	3x	Also ASD
15q13.3 del	2x	CHRNA7 (nicotinic receptor)
NRXN1 del	2x	Neurexin; synaptic adhesion
16p11.2 dup	3x	ASD (deletion) vs SCZ (duplication)
3q29 del	40x	Rare but highest penetrance

Mnemonic 12: Gene-Environment Interactions (GxE)

MNEMONIC

MAOA-5H-FK-CO-AK

EXAM PEARL: "My Aunt's 5 Friends Keep COming to AKbar's", each friend represents a GxE interaction.

CODE	GENE X ENVIRONMENT	OUTCOME
MAOA	MAOA-L x childhood maltreatment	Antisocial behavior (Caspi 2002)
5H	5-HTTLPR short x life stress	Depression (Caspi 2003, debated)
FK	FKBP5 x childhood trauma	PTSD risk
CO	COMT Val/Val x cannabis	Psychosis
AK	AKT1 x cannabis	7x schizophrenia risk

Mnemonic 13: Trinucleotide Repeat Disorders

MNEMONIC

Hunt My Fragile Friedrich

EXAM PEARL: Key concept: **Anticipation**, repeat number increases across generations, causing earlier onset and greater severity.

DISORDER	REPEAT	GENE/LOCUS	THRESHOLD
Huntington	CAG	Huntingtin (chr 4)	>36 repeats
Myotonic dystrophy	CTG	DMPK (chr 19)	>50 repeats
Fragile X	CGG	FMR1 (X chromosome)	>200 (full mutation)
Friedrich ataxia	GAA	Frataxin (chr 9)	>100 repeats

Mnemonic 14: HLA Pharmacogenetics

MNEMONIC

1502-CBZ-Asian-SJS

EXAM PEARL: "15:02 is the time the Asian patient was admitted for SJS from CBZ"

- HLA-B*1502 + Carbamazepine = SJS/TEN in Asian populations
- HLA-A*3101 + Carbamazepine = Rash/DRESS in European/Japanese
- HLA-B*5701 + Abacavir = Hypersensitivity (HIV -- for comparison)

Mnemonic 15: Schizophrenia Risk by Relatedness

MNEMONIC

1-3-10-17-48

EXAM PEARL: The numbers roughly triple/double as genetic closeness increases. Memorize this sequence cold.

RELATIONSHIP · RISK (%)

General population 1

Second-degree relative 3

First-degree relative 10

DZ twin 17

MZ twin 48

High-Yield Comparisons

Exam: PG exams MD Psychiatry, Sep 2026

Table 1: Linkage vs Association Studies

FEATURE	LINKAGE STUDIES	ASSOCIATION STUDIES
Design	Family-based; tracks co-segregation in pedigrees	Population-based (case-control) or family-based (TDT)
Resolution	Low (~10-20 Mb); identifies broad chromosomal regions	High (~1 kb); can pinpoint specific SNPs
Effect size	Detects large effects (Mendelian)	Detects small to moderate effects (complex traits)
Statistical test	LOD score (≥ 3.0 significant)	Chi-square / regression; $p < 5 \times 10^{-8}$ for GWAS
Best for	Single-gene disorders	Polygenic, multifactorial disorders

EXAM PEARL

Linkage asks "are these loci inherited together within families?" Association asks "is this allele more common in affected individuals in a population?"

Table 2: GWAS vs Candidate Gene Studies

FEATURE	GWAS	CANDIDATE GENE STUDIES
Hypothesis	Hypothesis-free (genome-wide scan)	Hypothesis-driven (tests specific genes)
Coverage	~1 million+ SNPs across entire genome	Selected variants in pre-chosen genes
Sample size	Very large (tens of thousands)	Smaller (hundreds to low thousands)
Significance threshold	$p < 5 \times 10^{-8}$ (Bonferroni correction)	$p < 0.05$ (often uncorrected)
Replication	Generally replicable	Poor replication record

EXAM PEARL

GWAS has largely superseded candidate gene studies. Most candidate gene findings (DISC1, NRG1, DTNBP1) have NOT been confirmed by GWAS. However, GWAS validated some biological pathways that candidate gene studies suggested (e.g., dopamine via DRD2, glutamate via GRIN2A).

Table 3: Twin Studies vs Adoption Studies

FEATURE	TWIN STUDIES	ADOPTION STUDIES
Purpose	Estimate heritability	Separate genetic from environmental factors
Design	Compare MZ vs DZ concordance	Compare biological vs adoptive relatives
Key formula	$h^2 = 2(r_{MZ} - r_{DZ})$	No specific formula; rates compared
Key assumption	Equal environments (MZ = DZ shared environment)	Random placement (no selective matching)
Strength	Quantifies heritability precisely	Cleanest separation of genes vs environment

EXAM PEARL

Twin studies quantify HOW MUCH is genetic. Adoption studies confirm THAT it is genetic (not shared family environment). Together they provide the strongest evidence for genetic contribution.

Table 4: Heritability Across Major Psychiatric Disorders

DISORDER	HERITABILITY	MZ CONCORDANCE	KEY GENETIC FINDINGS
ASD	80-90%	~70-90%	De novo mutations, Fragile X, hundreds of genes
Bipolar disorder	~85%	~40-70%	CACNA1C, ANK3; ~60% genetic overlap with schizophrenia
Schizophrenia	~80%	~48%	108 GWAS loci, C4, 22q11.2 deletion
ADHD	~76%	~80%	DRD4, DAT1; 12 GWAS loci

DISORDER	HERITABILITY	MZ CONCORDANCE	KEY GENETIC FINDINGS
MDD	~37%	~40%	Lower heritability; more environmental contribution

EXAM PEARL

ASD, bipolar, and schizophrenia cluster together with heritability >75%. Depression is notably lower, reflecting greater environmental influence.

Table 5: CYP450 Enzymes in Psychiatry

FEATURE	CYP1A2	CYP2D6	CYP2C19	CYP3A4
Key substrates	Clozapine, olanzapine, duloxetine	Fluoxetine, paroxetine, TCAs, risperidone, aripiprazole, haloperidol	Citalopram, escitalopram, sertraline, diazepam	Quetiapine, lurasidone, buspirone, midazolam
Key inhibitors	Fluvoxamine, ciprofloxacin	Fluoxetine, paroxetine, bupropion	Fluvoxamine, fluoxetine	Ketoconazole, erythromycin, grapefruit juice
Key inducers	Smoking (PAHs), carbamazepine	Not significantly inducible	Rifampin	Carbamazepine, phenytoin, St. John's Wort
High-yield scenario	Smoking cessation raises clozapine levels -- toxicity risk	PM + TCA = cardiotoxicity; UM + codeine = respiratory depression	PM + citalopram = QTc prolongation (FDA 20mg limit)	Carbamazepine induces own metabolism (autoinduction)

Table 6: Metabolizer Phenotypes -- Clinical Implications

FEATURE	POOR METABOLIZER (PM)	NORMAL METABOLIZER (NM)	ULTRARAPID METABOLIZER (UM)
Enzyme activity	None or minimal (0 functional copies)	Normal (2 functional copies)	Increased (gene duplication)
Drug levels	Elevated (accumulation)	Therapeutic at standard dose	Subtherapeutic (rapid clearance)
Clinical effect	Higher ADR risk at standard dose	Expected response	Treatment failure at standard dose
Dose adjustment	Reduce dose by 25-50% or use alternative	Standard dosing	Increase dose or use alternative

FEATURE	POOR METABOLIZER (PM)	NORMAL METABOLIZER (NM)	ULTRARAPID METABOLIZER (UM)
CYP2D6 example	Risperidone accumulates, EPS risk	Normal response to risperidone	Risperidone cleared too fast, inadequate response

CLINICAL ANCHOR

Prodrug caveat, for prodrugs (e.g., codeine converted to morphine by CYP2D6), the pattern reverses: PM cannot activate prodrug (no effect); UM produces excessive active metabolite (respiratory depression, fatal in neonates via breast milk).

Table 7: Copy Number Variants in Schizophrenia

CNV	LOCUS	TYPE	OR / RISK	OTHER ASSOCIATIONS
22q11.2	22q11	Deletion	25x	DiGeorge/VCFS, cardiac defects, hypocalcemia
3q29	3q29	Deletion	~40x	Rare; highest penetrance
1q21.1	1q21	Deletion	~3x	ASD, intellectual disability
15q13.3	15q13	Deletion	~2x	Epilepsy; contains CHRNA7
NRXN1	2p16	Deletion	~2x	ASD; neurexin (synaptic adhesion)

EXAM PEARL

CNVs are individually rare but have large effect sizes (OR 2-40x) compared to common SNPs (OR 1.05-1.2). The 22q11.2 deletion is the **single strongest known genetic risk factor** for schizophrenia (after MZ twin status). Most CNVs are pleiotropic, they confer risk for multiple neurodevelopmental conditions (schizophrenia, ASD, ID, epilepsy). De novo CNVs (not inherited) are enriched in sporadic schizophrenia cases.

Table 8: Epigenetics vs Genetics

FEATURE	GENETICS	EPIGENETICS
Definition	Study of DNA sequence and its inheritance	Study of heritable changes in gene expression WITHOUT DNA sequence change
Mechanism	Mutations, polymorphisms, CNVs	DNA methylation, histone modification, non-coding RNA
Reversibility	Permanent (germline mutations)	Potentially reversible
Environmental sensitivity	DNA sequence generally stable	Highly responsive to environment (stress, diet, toxins, drugs)
Inheritance	Mendelian or complex	Transgenerational (can be transmitted but often reset)
Example in schizophrenia	GWAS: 108 risk loci; CNV: 22q11.2	RELN promoter hypermethylation; GAD67 promoter hypermethylation

CLINICAL ANCHOR

Epigenetic changes may explain: (1) how environmental risk factors (cannabis, prenatal infection, childhood trauma) alter gene expression without changing DNA; (2) why MZ twin concordance is ~48% not 100% (epigenetic divergence); (3) missing heritability (epigenetic variation not captured by GWAS); (4) potential therapeutic targets (epigenetic drugs like HDAC inhibitors are being explored).

PYQ Frequency Analysis

Executive Summary

EXAM PEARL

Genetics is a **moderately tested** but **high-value** topic. When it appears, it usually carries the full 10 marks and requires structured knowledge of study designs + specific findings. Pharmacogenetics is an emerging hot topic that's appeared 5 times and is increasingly combined with EBM/personalized medicine questions.

Topic-Level Frequency

TOPIC	EXAM MENTIONS	AVG PER EXAM	VERDICT
Genetics of schizop- hrenia (specific)	3	~0.11	Every 8-10 exams
Pharmacogenetics/Ph armacogenomics	5	~0.18	Every 5-6 exams (rising)
Genetic epidemiology / study designs	3	~0.11	Every 8-10 exams
Gene mapping / link- age / association	1	~0.04	Rare
Combined cluster	~12	~0.43	~1 question every 2-3 exams

Key PYQs Identified

Genetics of Schizophrenia

1. "The biological causes of schizophrenia. Genetics of schizophrenia." [10, split 5+5]
2. "Biopsychosocial model of schizophrenia. Recent advances in genetics in aetiology." [10, split 5+5]
3. "Describe genetics of schizophrenia." [10] (Notion QB, multiple entries)
4. "Genetics of Schizophrenia." [10] (short note format)
5. "What is Genetic mutation and how does it occur?" [10]

Pharmacogenetics

1. "What is pharmacogenetics? Describe its research and implications in treatment." [10, split 2+4+4]
2. "What is pharmacogenetics? Role in medical disorders with examples." [10]
3. "What are pharmacogenomics & pharmacogenetics? Relevance in Psychiatry." [10, split 4+6]
4. "What is pharmacogenetics? Current concept and future use in psychiatry." [10]
5. "What is EBM? What is personalized medicine? Discuss pharmacogenetics." [10, split 2+3+5]

Genetic Study Designs

1. "What is genetic epidemiology? Describe three types of genetic studies." [10]
2. "Genetic epidemiological studies in Psychiatry." [10]
3. "What is gene mapping? How is it different from linkage analysis and association studies?" [10, split 3+7]

Long Essay Candidates

RANK	TOPIC	PROBABILITY
1	"Describe the genetics of schizophrenia, twin studies, adoption studies, candidate genes, GWAS findings, copy number variants."	Medium-High
2	"What is pharmacogenetics? Discuss its implications and future in psychiatric treatment."	Medium-High (rising trend)
3	"Describe genetic epidemiological study designs in psychiatry, family, twin, adoption, linkage, association, GWAS."	Medium

Exam Strategy

EXAM STRATEGY

Must-Prepare topics listed below, these cover ~90% of likely questions on this cluster.

Must-Prepare

1. **Genetics of schizophrenia**, heritability (~80%), twin concordance (MZ 48%, DZ 17%), adoption studies (Heston, Kety), candidate genes (DISC1, NRG1, DTNBP1, COMT), GWAS findings (108 loci, C4 complement gene), copy number variants (22q11 deletion), polygenic risk scores
2. **Pharmacogenetics**, CYP450 enzymes (2D6, 3A4, 1A2, 2C19), poor/intermediate/extensive/ultrarapid metabolizers, clinical examples (CYP2D6 and codeine/SSRIs, HLA-B*5701 and carbamazepine, CYP1A2 and clozapine/smoking), pharmacogenomic testing in clinical practice
3. **Genetic study designs**, family studies, twin studies (MZ vs DZ, heritability formula), adoption studies, linkage analysis (LOD scores), association studies (case-control), GWAS (Manhattan plots, genome-wide significance), epigenetics

Nice-to-Know

1. Gene-environment interaction (MAOA gene + childhood maltreatment → antisocial behaviour; 5-HTTLPR + stress → depression, though Caspi findings debated)
2. Epigenetics (DNA methylation, histone modification, non-coding RNA)
3. Endophenotypes (conceptual)

Analysis based on PG exams Dec 2011, Jun 2025 + PG exams 2013-2022.

Quick Review

Exam: PG exams MD Psychiatry, Sep 2026

RECALL (Q1-Q10)

Q1. What is the estimated heritability of schizophrenia?

Answer: Approximately 80%, derived from twin and adoption studies.

Q2. What are the MZ and DZ twin concordance rates for schizophrenia?

Answer: MZ: ~48%. DZ: ~17%. Using Falconer's formula: $h^2 = 2(0.48 - 0.17) = 0.62$ (crude estimate; model-based estimates give ~0.80).

Q3. Name five candidate genes historically associated with schizophrenia.

Answer: DISC1 (disrupted in schizophrenia 1), NRG1 (neuregulin 1), DTNBP1 (dysbindin), COMT (catechol-O-methyltransferase), RGS4 (regulator of G-protein signaling 4). Note: Most have NOT been confirmed by GWAS.

Q4. What was the key finding of the PGC Schizophrenia Working Group (2014)?

Answer: Identified 108 genome-wide significant loci in a sample of 36,989 cases and 113,075 controls. Key loci included DRD2, MHC/C4, glutamate pathway genes, and calcium channel genes.

Q5. What is the genome-wide significance threshold for GWAS and why?

Answer: $p < 5 \times 10^{-8}$. This is a Bonferroni correction for approximately 1 million independent SNP tests ($0.05 / 1,000,000 = 5 \times 10^{-8}$).

Q6. What LOD score indicates significant linkage?

Answer: $LOD \geq 3.0$ (indicating 1000:1 odds in favour of linkage). $LOD \leq -2.0$ excludes linkage.

Q7. What is the heritability formula used in twin studies?

Answer: Falconer's formula: $h^2 = 2(r_{MZ} - r_{DZ})$, where r = concordance rate (or correlation) for MZ and DZ twins respectively.

Q8. Name the four CYP450 metabolizer phenotypes.

Answer: Poor metabolizer (PM), intermediate metabolizer (IM), normal/extensive metabolizer (NM), ultrarapid metabolizer (UM).

Q9. What HLA allele must be tested before starting carbamazepine in Asian patients, and what reaction does it predict?

Answer: HLA-B*1502. Predicts Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). FDA mandates testing before carbamazepine in patients of Asian ancestry.

Q10. What is the APOE e4 allele's relationship to Alzheimer disease?

Answer: APOE e4 is the strongest genetic risk factor for late-onset Alzheimer disease. One copy confers ~3x risk; two copies confer ~12x risk. It is a risk factor, not deterministic.

APPLICATION (Q11-Q22)

Q11. A patient of South Asian origin is started on carbamazepine and develops SJS. What genetic test should have been done before prescribing?

Answer: HLA-B*1502 genotyping. This allele is prevalent in South Asian, Southeast Asian, and East Asian populations and is strongly associated with carbamazepine-induced SJS/TEN. FDA guidelines recommend testing before prescribing carbamazepine to patients with Asian ancestry.

Q12. A patient stable on clozapine 400mg/day is admitted to a smoke-free psychiatric unit. After 5 days, they become excessively sedated with drooling. What happened?

Answer: Smoking induces CYP1A2, which metabolizes clozapine. When the patient stopped smoking upon hospitalization, CYP1A2 induction was lost, causing clozapine levels to rise and producing toxicity (sedation, sialorrhea). The clozapine dose should have been reduced by 25-50% upon smoking cessation.

Q13. A CYP2D6 poor metabolizer is prescribed nortriptyline at the standard dose. What clinical problem might arise?

Answer: Nortriptyline (a TCA) is metabolized by CYP2D6. A poor metabolizer cannot clear the drug normally, leading to accumulation and risk of cardiotoxicity (QTc prolongation, arrhythmias), excessive sedation, and anticholinergic toxicity. The dose should be reduced by approximately 50%, or an alternative not metabolized by CYP2D6 should be chosen.

Q14. An ultrarapid CYP2D6 metabolizer is prescribed codeine for pain after a dental procedure. She is also breastfeeding her infant. What is the risk?

Answer: CYP2D6 converts codeine to morphine. An ultrarapid metabolizer produces excessive morphine, which is secreted in breast milk. This can cause respiratory depression and death in the infant. Codeine should be avoided in CYP2D6 ultrarapid metabolizers who are breastfeeding.

Q15. A child is diagnosed with 22q11.2 deletion syndrome (VCFS/DiGeorge). The parents ask about the risk of psychiatric illness. What do you counsel?

Answer: 22q11.2 deletion confers a 25-30% lifetime risk of developing schizophrenia-like psychosis (25x the general population risk). It is the strongest known single genetic risk factor for schizophrenia. The child should be monitored for prodromal symptoms during adolescence. Other psychiatric risks include ADHD, anxiety disorders, and mood disorders.

Q16. A patient on fluoxetine 20mg is started on risperidone 2mg. After one week, the patient develops significant EPS. The dose of risperidone seems low for such side effects. What might explain this?

Answer: Fluoxetine is a potent CYP2D6 inhibitor. Risperidone is metabolized by CYP2D6. Fluoxetine inhibits risperidone metabolism, effectively converting the patient into a pharmacokinetic "poor metabolizer." This causes risperidone levels to rise, producing EPS at what would normally be a low dose. Either reduce risperidone dose, discontinue fluoxetine, or switch to an SSRI that does not inhibit CYP2D6 (e.g., sertraline, escitalopram).

Q17. A researcher finds a LOD score of 2.1 for linkage between a chromosomal region and bipolar disorder. What is the interpretation?

Answer: A LOD score of 2.1 is suggestive but does NOT reach the threshold for significant linkage (LOD $\geq$ 3.0). It warrants further investigation with larger samples but cannot be considered evidence of linkage. LOD $\leq$ -2.0 would exclude linkage.

Q18. A patient with schizophrenia has a family history of schizophrenia in his father and paternal uncle. His GWAS-based polygenic risk score is in the 95th percentile. He asks if his children will definitely develop schizophrenia. How do you counsel?

Answer: A high PRS increases risk but is NOT deterministic. Schizophrenia is polygenic with incomplete penetrance. The baseline risk for a child of one affected parent is ~10%. PRS adds statistical risk at the population level but cannot predict individual outcomes with certainty. Environmental factors (cannabis, stress, obstetric complications) also modulate risk. Genetic counseling should emphasize probabilistic risk, not certainty.

Q19. A researcher wants to study whether a specific SNP is associated with schizophrenia. She has 200 cases and 200 controls. Is this adequate for a GWAS?

Answer: No. GWAS requires very large samples (tens of thousands of cases and controls) to achieve adequate power, because individual SNPs have small effect sizes (OR 1.05-1.2) and the significance threshold is stringent ($p < 5 \times 10^{-8}$). A sample of 200 cases would only be adequate for a candidate gene study (not GWAS) and even then would be underpowered for small effects.

Q20. A patient with schizophrenia who is a heavy smoker (20 cigarettes/day) on stable clozapine is prescribed ciprofloxacin for a urinary tract infection. What drug interaction should you anticipate?

Answer: Ciprofloxacin is a CYP1A2 inhibitor. While smoking induces CYP1A2, ciprofloxacin inhibits it. The net effect is a rise in clozapine levels, potentially causing toxicity. Monitor clozapine levels and consider dose reduction during the ciprofloxacin course.

Q21. The Caspi et al. (2002) study found that MAOA-L allele carriers who experienced childhood maltreatment had higher rates of antisocial behavior. A colleague argues this means the MAOA gene "causes" violence. How do you respond?

Answer: The MAOA-L allele does not "cause" violence. This is a gene-environment interaction: the gene modulates the effect of an environmental exposure (maltreatment). Without maltreatment, MAOA-L carriers do not show increased antisocial behavior. The gene creates a vulnerability that is only expressed under specific environmental conditions. Additionally, the effect size is modest, and many MAOA-L carriers exposed to maltreatment do NOT become antisocial.

Q22. A 45-year-old patient with bipolar disorder on carbamazepine 600mg BD is also started on ketoconazole for a fungal infection. A week later, he develops ataxia, diplopia, and nausea. What is the likely mechanism?

Answer: Carbamazepine is metabolized by CYP3A4. Ketoconazole is a potent CYP3A4 inhibitor. Inhibition of CYP3A4 by ketoconazole causes carbamazepine levels to rise, producing signs of carbamazepine toxicity (ataxia, diplopia, nausea, nystagmus). Carbamazepine levels should be checked and the dose reduced.

ANALYSIS (Q23-Q30)

Q23. Why does the high heritability of schizophrenia (~80%) not translate to simple Mendelian inheritance?

Answer: Because schizophrenia is polygenic (hundreds of genes contribute small effects), exhibits genetic heterogeneity (different genetic variants can produce the same phenotype), has incomplete penetrance (carrying risk alleles does not guarantee illness), and involves gene-environment interaction. High heritability means genetic factors explain most of the variance in liability, but the architecture involves many common variants of small effect plus rare variants of larger effect, rather than a single gene with a clear inheritance pattern.

Q24. The MZ twin concordance for schizophrenia is ~48%. What does the remaining ~52% discordance tell us?

Answer: The 52% discordance in genetically identical individuals indicates that non-genetic factors contribute significantly. These include: (1) environmental factors (prenatal insults, obstetric complications, cannabis, urbanicity, stress), (2) epigenetic divergence (MZ twins accumulate different methylation patterns over time), (3) stochastic developmental variation (random events in brain development), and (4) gene-environment interactions where the same genotype produces different outcomes depending on environmental exposure.

Q25. Why is the C4/MHC finding from GWAS considered such an important advance in schizophrenia genetics?

Answer: The C4/MHC finding (Sekar et al., 2016) is important because it provides a mechanistic bridge between a GWAS statistical signal and a neurobiological process. C4A overexpression leads to excessive complement-mediated synaptic pruning in adolescence. This single finding connects: (1) the strongest GWAS association to (2) a specific molecular mechanism to (3) the neurodevelopmental model of schizophrenia to (4) the clinical observation of adolescent onset and (5) the neuropathological finding of reduced synaptic density and grey matter. It transformed a statistical association into a biologically interpretable and potentially druggable pathway.

Q26. How do common variants (GWAS) and rare variants (CNVs) each contribute to schizophrenia risk, and why do we need to study both?

Answer: Common variants (identified by GWAS) are individually of small effect (OR 1.05-1.2) but collectively explain a substantial portion of genetic risk through polygenic mechanisms. Rare variants (CNVs, de novo mutations) are individually rare but have large effects (OR 2-40x). Studying both is necessary because: (1) they capture different parts of the genetic architecture, (2) rare variants point to specific genes and biological pathways more directly, (3) common variants help build polygenic risk scores, and (4) together they explain more variance than either alone. The "missing heritability" gap may partly lie in rare variants not captured by GWAS.

Q27. Why has the 5-HTTLPR x stress interaction for depression been controversial, and what lesson does this teach about GxE research?

Answer: Caspi et al. (2003) reported that the short allele of 5-HTTLPR interacted with stressful life events to increase depression risk. However, a large collaborative meta-analysis (Culverhouse et al., 2018) with over 40,000 subjects found no support for this interaction. The controversy teaches several lessons: (1) initial GxE findings may be false positives due to small samples and publication bias, (2) environmental measures and genotype categorizations affect replicability, (3) very large samples are needed to detect genuine GxE effects, and (4) replication in well-powered studies is essential before clinical application.

Q28. A colleague says "if schizophrenia is 80% heritable, then environment only contributes 20%." Is this correct?

Answer: This is a common misunderstanding. Heritability is a population-level statistic that describes the proportion of variance in liability attributable to genetic factors in a specific population at a specific time. It does NOT mean the environment contributes only 20% in any individual case. Also: (1) heritability does not account for gene-environment interaction or gene-environment correlation, which may inflate the genetic estimate, (2) epigenetic effects (environmentally induced) may be captured in the "genetic" portion, (3) heritability can change if environmental variance changes (e.g., in a more stressful environment, the environmental contribution increases), and (4) high heritability does not mean the condition is immutable or that environmental interventions are futile.

Q29. Schizophrenia reduces reproductive fitness, yet it persists at ~1% prevalence globally. How can this be explained genetically?

Answer: Several hypotheses explain this paradox: (1) **Balancing selection:** Risk alleles may confer advantages in certain contexts (e.g., creativity, divergent thinking, immune function). (2) **Polygenic mutation-selection balance:** Many variants of small effect are constantly generated by new mutations at a rate that balances selection against them. (3) **De novo mutations:** A substantial fraction of schizophrenia may arise from new mutations (especially CNVs) each generation, replenishing the pool. (4) **Antagonistic pleiotropy:** Variants that increase schizophrenia risk may benefit other traits (e.g., CACNA1C variants may have immune or metabolic benefits). (5) **Relaxed selection in modern environments:** Reduced mortality from other causes allows psychiatric risk alleles to persist.

Q30. What are endophenotypes, why are they important in schizophrenia genetics, and give three examples?

Answer: Endophenotypes (intermediate phenotypes) are heritable, quantifiable traits that lie on the pathway between genes and the clinical phenotype. They are important because:

(1) they are closer to gene action than the complex clinical syndrome, making genetic associations easier to detect, (2) they are present in unaffected relatives (indicating genetic mediation), (3) they are more biologically homogeneous than the clinical diagnosis. Three examples in schizophrenia: (1) **Smooth pursuit eye movement abnormalities** (found in 50-80% of patients and 25-40% of unaffected relatives), (2) **P50 auditory sensory gating deficits** (reduced suppression of the second auditory stimulus; linked to CHRNA7 gene), (3) **Working memory deficits** (related to DLPFC dysfunction and COMT Val158Met polymorphism).

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