WEAVE SPRINT
PAPER I · VOLUME TWO

MD and DNB psychiatry, theory revision

Foundations of Psychiatry

Inheritance and the Developing Mind

How psychiatric risk is inherited and where it sits in the genome. Then the mind as theory: perception, memory, thought, and how children become who they are.

Dr. Wilfred D'souza · Dr. Niharika Reddy

WEAVE
CENTRE FOR INTEGRATIVE PSYCHIATRY

Weave
Centre for Integrative Psychiatry

WEAVE SPRINT
PSYCHIATRY OUTREACH PROGRAMME

Psychiatry that listens before it prescribes.

Therapy-informed psychiatry for adults, children, couples and families. Online across India, in person in Mumbai.





Assessments

ADHD, autism and developmental. Anxiety, mood, attention and personality patterns.



Consultations and sessions

Psychiatric consultations, therapy sessions, medication review and couples sessions.



Family Library

Free plain-language guides for families, in five languages.

`weave.clinic/family`

REFER, OR SEND SOMEONE OUR WAY

Your patient contacts Weave directly and decides whether to book.

You remain the referring clinician. Any coordination between clinicians happens with the patient's permission.

CONTACT

`weave.clinic/contact`
`WhatsApp +91 7625004229`

Dr. Niharika Reddy and Dr. Wilfred D'souza, Consultant Psychiatrists. Runwal Forests Clinic, Kanjurmarg West, Mumbai, and online.

WEAVE.CLINIC

Routine referrals only. This is not an emergency route.

WEAVE SPRINT · PAPER I

Foundations of Psychiatry

THE WEAVE SPRINT SERIES

TITLE

Weave Sprint, Paper I, Volume Two: Inheritance and the Developing Mind

Part of the Weave Sprint series, MD and DNB psychiatry theory revision.

WRITTEN BY

Dr. Wilfred D'souza and Dr. Niharika Reddy

PUBLISHED BY

Weave, Centre for Integrative Psychiatry · weave.clinic

EDITION

First compiled 2026. Free to read, share and print for study.

The clinical content is written for doctors and doctors in training. It is a study and revision aid, not a substitute for current guidelines or clinical judgement. Verify doses and thresholds against the current references and your local protocols before any clinical use.

For every resident who has ever sat up the night before,
afraid it will not be enough.

ACKNOWLEDGEMENT

A word of thanks

I want to begin by thanking something I cannot quite name. Call it whatever you like. I have never been certain what to call it, and I have stopped needing to be. There is a part of this work that does not feel like mine. The line that arrives before I have thought of it, the connection I did not plan, the steadiness on a morning I had no reason to be steady. I only hold the pen. Something moves through the holding, and I have learned to thank it without asking it for a name.

Someone once asked me why I give all of this away. Why hand out the notes I sat up making, to the very people sitting the same exam beside me. It is a fair question. If I had kept them, I would probably have scored a few marks more than the next person, and I might have been thought of as the better student. I have turned that over honestly, and I have decided it is a small thing to want. What I get instead, by putting the work in your hands, is the chance to take a little of the fear out of a great many nights. That trade is not close. Easing that fear is not a detour on the way to becoming a good psychiatrist. It is the thing itself. I did not come here to be the best student in the room. I came here to be a good psychiatrist.

And to Niharika, who reads everything first and knows when to be honest and when to wait; and to the residents who study from these pages and write back with the corrections and the questions: thank you. The book is better for you, and so am I.

Dr. Wilfred D'souza

Foreword

This second volume turns from the brain to the mind, and it does so through the one chapter that belongs to both. Genetics is inheritance measured, and it sets the limits within which development happens. What follows is development itself: how perception, memory, thought and motivation are studied, and how a child becomes a particular person.

The notes were written to be understood, not just revised. Each chapter is a full account of its subject, from the mechanism up to the point the exam tests, so that you can read to learn the first time and read to recall every time after. Where a fact is worth holding exactly, it is marked. Where a mistake is easy to make, it is named before you make it. The colour code on the next pages tells your eye what kind of fact it is looking at before your mind has to decide, and after a few pages it stops being a key you consult and becomes a sense you carry.

Read it in order if you are meeting the material, or open it anywhere if you are returning to it. The contents at the front and the index at the back both jump to the page you want. However you use it, the hope held in these pages is plain: that one ordered, trustworthy place to study from makes the work a little lighter, and that you walk into the hall steadier than you would have otherwise.

HOW TO USE THIS BOOK

The colour memory code

Every note in this volume speaks one visual language, so once you learn it in the first chapter you read the rest without thinking about it.

Concept and rule	The core idea and the principle that follows from it. When a line is petrol, it is the thing to understand, and the thing worth being able to state.
Key number	A figure to hold exactly: a dose, a threshold, a prevalence, a cut-off. Amber means memorise this number, not just the shape of it.
Trap	The mistake the exam is waiting for. When a line is coral, it is warning you off an error that looks right until it costs you the mark.

Hold this is the single line from a topic you must carry out of it. **Good to remember** gathers, for each named thing, what it is, when it matters, and the one number or formula worth keeping. Both help a tired brain find the centre of a dense page fast.

The contents at the front is clickable, and so is the index at the back: every entry jumps to its page. Read to learn once, and to recall as often as you need.

Contents

FRONT MATTER

Foreword 7

How to use this book 8

PART III **Psychiatric Genetics** 11

- Foundations 11
- Methods: locating the risk 33
- Mechanisms 54
- Findings in the clinic 76
- Discriminate 98
- Apply and consolidate 105

PART IV **General & Developmental Psychology** 132

- Foundations 132
- General psychology 137
- The three depth-psychology schools 208
- Developmental psychology 226
- Discriminate 268
- Apply and consolidate 274

BACK MATTER

Subject index 293

About the authors 295

PART III

III

Psychiatric Genetics

How psychiatric risk is inherited, how it is located in the genome, and what the clinic does with it.

01 Foundations

02 Methods: locating the risk

03 Mechanisms

04 Findings in the clinic

05 Discriminate

06 Apply and consolidate

Psychiatric Genetics

Six sections · 16 topics · one complete notes document

Psychiatric disorders are among the most heritable conditions in medicine, yet almost none of them obey Mendel. This chapter is built as a toolkit: each method answers one question about where the risk lives. **Learn the tool, not just the result.** The order runs the way the field itself moved: first establish that a disorder is familial and heritable (family, twin, adoption studies), then locate the risk (linkage, then genome-wide association, then rare variants and sequencing), then read it back as mechanism (epigenetics, endophenotypes, neurodevelopment), as clinical fact (heritability figures, the schizophrenia story, pharmacogenetics), and finally as something you can apply in a counselling room. Almost every answer here rewards the candidate who names the right study design and the key finding together, rather than reciting a list of genes.

HOW TO USE THESE NOTES

Every figure declares one axis and codes it in colour and shape, with a small legend. The colours are consistent throughout: **petrol** marks the method, the structure and the neutral relay; **coral** marks risk, pathology or a rare large-effect variant; and **marigold** highlights the key finding or the common-variant signal. Watch for the boxes marked **Good to remember**: they gather every named gene, locus, allele and hard number in one place so the reference facts sit apart from the reasoning.

Foundations

1 · Orientation and the genetics toolkit

Before the detail, the frame. Psychiatric disorders sit on a paradox you have to hold throughout: they are among the *most heritable* conditions in medicine, yet almost none of them are inherited in a clean Mendelian way. There is no single gene for schizophrenia the way there is one for Huntington disease. Instead, risk is **polygenic and complex**: thousands of common variants each add a sliver of liability, a minority of rare large-effect variants (copy-number variants and de novo mutations) shove a few individuals hard toward illness, and the whole thing plays out on a developing brain over time. The single move that runs through this material, repeated in the margin: **heritable but not Mendelian, common-variant-mostly but rare-variant-punchy, and read out through neurodevelopment**. Hold that and every method below has a job to do.

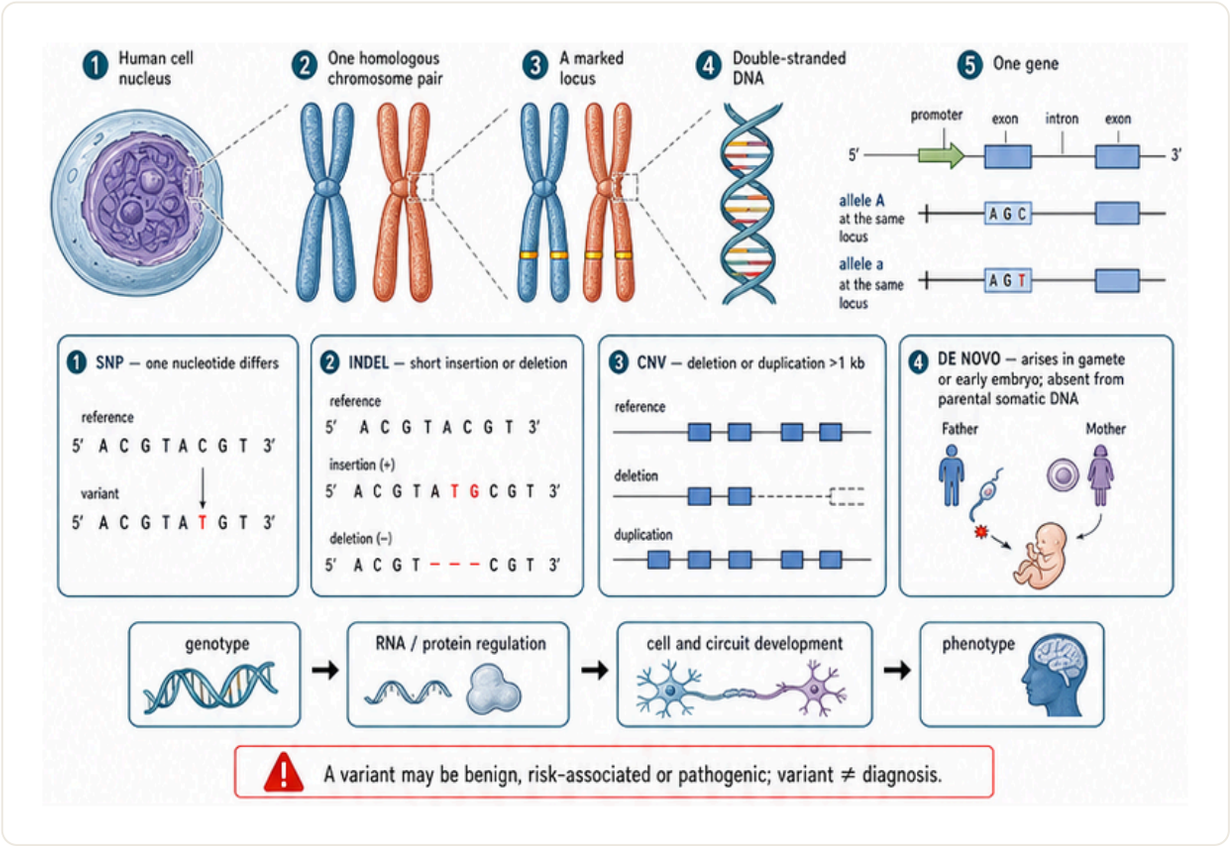


Fig 3.1 From chromosome to variant.

The reason genetics is a Paper-1 staple is that examiners test the *logic of the toolkit*, not just facts: each study design answers exactly one question, and the designs form a ladder from the crudest (does it run in families?) to the most granular (which base changed?). The classic epidemiological trio (Kaplan & Sadock 2024) establishes *that* genes matter and roughly how much; the molecular methods then ask *which* genes, and the modern aggregate methods ask *how much of one person's risk* we can now read from their genome. This topic lays out the whole map so that when a later topic drills into schizophrenia or pharmacogenomics, you already know which rung of the ladder it is standing on.

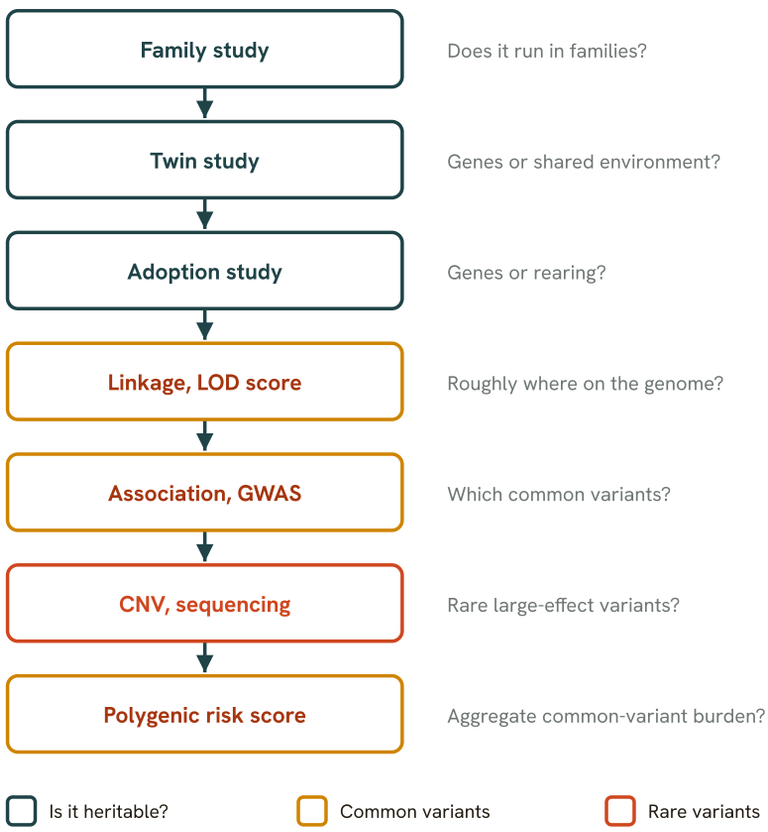


Fig 3.2 The psychiatric genetics toolkit as an evidence hierarchy. Each method answers one question, and the field moved down the ladder in this order: family, twin and adoption studies first establish that risk is heritable and separate genes from environment; linkage then genome-wide association locate the risk with rising resolution; copy-number and sequencing methods catch the rare large-effect variants; and the polygenic risk score aggregates the common-variant burden. Colour marks the job: petrol establishes heritability, marigold locates common variants, coral flags rare variants.

1.1 The central paradox: highly heritable, non-Mendelian, mostly polygenic

The frame for the whole set of notes. High **heritability** (the proportion of population variation in a trait attributable to genetic variation) tells you genes matter a great deal, but it says nothing about *how many* genes or *what kind*. Common psychiatric disorders show high heritability yet failed the classical single-gene approaches that cracked Mendelian diseases (Kaplan & Sadock 2024). The resolution is a two-tier architecture (Sullivan; Kaplan & Sadock 2024): the bulk of liability comes from a very large number of **common variants of individually tiny effect** (the polygenic component, odds ratios typically around 1.1 each), plus a smaller contribution from **rare, large-effect variants** (CNVs, de novo mutations) that individually raise risk many-fold but explain illness in only a minority. This is the liability-threshold model: many small risks summed against a threshold.

COMMON TRAP

Do not equate "high heritability" with "genetically determined" or with "inherited in families in a simple pattern." Heritability is a population statistic about variance, not a statement about an individual, and a highly heritable disorder can still be overwhelmingly polygenic with no single causative gene. Equally, a high heritability does not mean environment is irrelevant: it is a partitioning of variance in a particular population, not a fixed biological constant.

RULE **High heritability, non-Mendelian, mostly polygenic.** Common psychiatric disorders are among the most heritable in medicine yet obey no clean single-gene pattern; hold that paradox and every method below has a job.

1.2 The missing heritability, and why development is the read-out

Two loose ends these notes keep returning to. First, **missing heritability**: the variance explained by the variants we can actually measure falls well short of the heritability that twin studies imply (Manolio et al. 2009; Kaplan & Sadock 2024). For schizophrenia, SNP-based heritability captures roughly 17 to 45 percent of variance and a polygenic risk score built from GWAS explains on the order of 7 percent, against twin-study heritability estimates near 80 percent (New Oxford Textbook of Psychiatry). The gap is filled, in part, by rare variants, gene-gene and gene-environment interactions, and structural variation the arrays miss. Second, **neurodevelopment as the mechanism**: genetic risk is largely expressed by shaping how the brain is built, wired, and pruned, so the same risk allele can surface as a childhood neurodevelopmental phenotype or an adult psychosis depending on timing. Genetic risk for a childhood-onset disorder like ADHD does not differ between paediatric and adult samples, underscoring that it indexes a developmental trajectory rather than a discrete adult lesion (Kaplan & Sadock 2024).

~80%	17-45%	~7%
TWIN HERITABILITY, SCHIZOPHRENIA	SNP-BASED HERITABILITY	VARIANCE A PRS EXPLAINS

TRAP Do not read "high heritability" as "genetically determined": a highly heritable disorder can still be overwhelmingly polygenic, and heritability is a population variance ratio, silent about any individual.

1.3 The toolkit as a map: each method answers one question

This is the spine of these notes. The genetics toolkit is a ladder of study designs, and the discriminating exam answer is to bind each method to the *single question it can answer* and no more. Read the definition list as a ladder from crudest to most granular: the first three are the classical epidemiological designs (they establish *that* genes matter), the middle three are molecular localisation and discovery methods (they find *which* variants), and the last is the aggregate clinical read-out (how much of one person's risk we can now quantify).

Family studies

Ask: *does it run in families?* Compare the risk (or relative risk) of the disorder in relatives of an affected proband against the general-population rate, graded by degree of relatedness. Establishes familial

aggregation but cannot separate shared genes from shared upbringing.

Twin studies

Ask: *is the familial resemblance genetic or shared-environmental?* Compare concordance in monozygotic twins (who share effectively 100 percent of their genome) with dizygotic twins (who share on average 50 percent). A higher MZ than DZ concordance points to genetic influence, and the design yields a heritability estimate plus estimates of shared and unique environment (New Oxford Textbook of Psychiatry).

Adoption studies

Ask: *can we physically separate genes from rearing?* Adopted-away children share genes with their biological relatives but environment with their adoptive family, so higher rates in biological than adoptive relatives isolate a genetic contribution. The most rigorous separation of the two, but increasingly infeasible as adoptions decline (New Oxford Textbook of Psychiatry).

Linkage analysis

Ask: *roughly where on the genome does a risk gene sit?* Track co-inheritance of a disease with genetic markers through pedigrees; a marker that segregates with illness flags a nearby chromosomal region. Quantified by the LOD score. Powerful for rare large-effect Mendelian genes, largely unproductive for polygenic psychiatric disorders (Kaplan & Sadock 2024).

Association and GWAS

Ask: *which common variants are over-represented in cases?* Compare allele frequencies at SNP markers between cases and controls. The genome-wide association study (GWAS) does this at millions of SNPs simultaneously using microarrays, detecting common variants of small effect once samples reach tens to hundreds of thousands (Kaplan & Sadock 2024).

CNV and sequencing methods

Ask: *which rare, large-effect variants are present?* Copy-number variant mapping (via array comparative genomic hybridisation or GWAS-chip intensity) finds sub-microscopic deletions and duplications; whole-exome and whole-genome sequencing find rare point mutations and de novo variants. These uncover the punchy, individually rare risk variants (Kaplan & Sadock 2024).

Polygenic risk scores

Ask: *how much common-variant burden does this one person carry?* Sum the risk alleles across the genome, each weighted by its GWAS effect size, into a single score of genetic liability. The aggregate read-out that turns GWAS summary statistics into an individual-level index (Kaplan & Sadock 2024).

The high-yield structure: the top three designs answer *whether and how much* without touching DNA directly; linkage and association/GWAS answer *where and which*; CNV/sequencing answers *which rare variant*; and the polygenic risk score is the only tool that reports back on a single individual. Modern genome-wide approaches (GWAS, CNV mapping, polygenic analysis, sequencing) have supplanted the older linkage and candidate-gene strategies for complex psychiatric disorders (Kaplan & Sadock 2024).

1.4 The two-architecture picture: common-small versus rare-large

The reason the toolkit splits into GWAS on one side and CNV/sequencing on the other is that the two variant classes have opposite profiles, and examiners test the contrast directly. GWAS is built to catch variants that are *common but weak*; CNV and sequencing are built to catch variants that are *rare but strong*. The full genetic risk for a disorder is the sum of both.

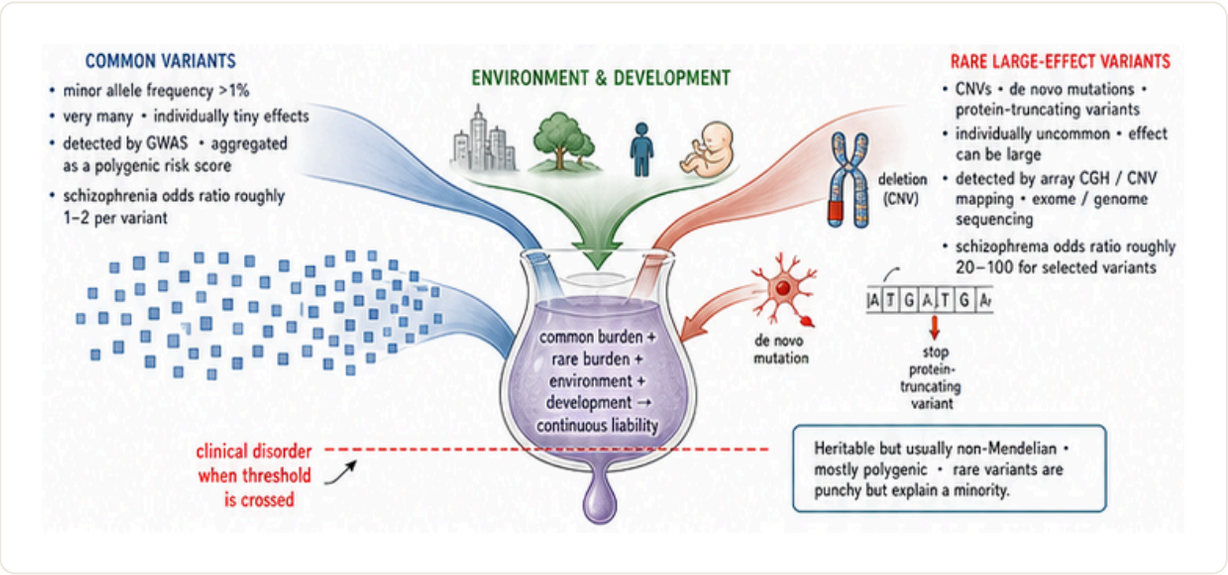


Fig 3.3 The architecture of psychiatric risk.

FEATURE	COMMON VARIANTS (GWAS)	RARE LARGE-EFFECT VARIANTS (CNV / SEQUENCING)
Population frequency	Common (minor allele frequency >1%)	**Rare, often de novo (new, non-inherited)**
Effect size per variant	Tiny: odds ratio roughly 1 to 2 for schizophrenia	**Large: odds ratio roughly 20 to 100 for schizophrenia**
Detecting tool	Genome-wide association study (SNP microarray)	**Array CGH / CNV mapping; whole-exome or whole-genome sequencing**
Sample size needed	Very large (tens to hundreds of thousands) to reach significance	**Large too, but signal is per-variant strong; low signal-to-noise for proving causality**
Aggregated as	**Polygenic risk score**	Total CNV burden; individual pathogenic variant

The classic figure (Singh, Neale & Daly, adapted in Kaplan & Sadock 2024): common variants like complement C4 raise schizophrenia odds one- to two-fold, whereas the 22q11.2 deletion and rare protein-truncating variants raise odds by 20- to 100-fold. Both tails matter, and only summing them captures full genetic risk.

1.5 The toolkit in one ladder, and the master mnemonic seeded

Before the material fans out, bind the whole ladder into one image to redraw from memory. This pearl is the spine of these notes; each later topic pays it back in detail.

THE TOOLKIT IN ONE LADDER

Climb from crude to granular, each rung a sharper question. **Family**: does it run in families? **Twin**: genes or shared environment? (MZ vs DZ concordance gives heritability.) **Adoption**: separate genes from rearing physically. **Linkage**: roughly *where* on the genome? (LOD score; good for rare Mendelian, poor for polygenic.) **Association / GWAS**: *which* common variants? (millions of SNPs, tiny effects, huge samples). **CNV / sequencing**: which rare large-effect variants? (deletions, duplications, de novo mutations, 20- to 100-fold effects). **Polygenic risk score**: how much aggregate common-variant burden does this one person carry? The first three say *whether*, the middle say *where and which*, the last says *how much, for whom*.

MNEMONIC

Families Try Adopting Little Genetic Clues Personally

Walks the ladder in order: **F**amily, **T**win, **A**doption (the classical epidemiological trio) → **L**inkage, **G**WAS/association (localisation and common-variant discovery) → **C**NV and sequencing (rare large-effect) → **P**olygenic risk score (individual aggregate). Seed it now; the consolidation block at the end pays it back as a whole-subject synthesis map.

HOLD THIS

Each method answers exactly one question. The toolkit is a ladder from crudest to most granular: family (does it run in families?), twin (genes or shared environment?), adoption (genes or rearing?), linkage (roughly where?), GWAS (which common variants?), CNV/sequencing (which rare large-effect variants?), polygenic risk score (how much aggregate burden, for whom?).

1.6 Cross-references: what is owned elsewhere

This material is the substantive genetics of psychiatric illness, not the generic machinery of study design or drug metabolism, both of which live in other notes and are only pointed to here.

Study design and biostatistics taxonomy

The general anatomy of study designs (cohort, case-control, cross-sectional), measures of association (odds ratio, relative risk), and the statistics of significance and multiple testing are owned by the Schizophrenia: aetiology, phenomenology, classification & course notes. These notes borrow those tools as applied to genetics (for example why the GWAS significance threshold is set stringently at 5×10^{-8} to correct for a million simultaneous tests) but do not re-teach the biostatistics from scratch. When a genetics topic invokes an odds ratio or a correction for multiple comparisons, point back to the Schizophrenia: aetiology, phenomenology, classification & course notes.

CYP450 and pharmacokinetic metabolism

The cytochrome P450 enzyme system, its isoenzymes and inhibitor/inducer interactions, was established on the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes. The pharmacogenetics and pharmacogenomics topic here builds the *genetic variation* in those enzymes (poor, intermediate, extensive and ultra-rapid metaboliser phenotypes, and the CPIC/DPWG prescribing guidance) on top of that pharmacokinetic foundation rather than re-deriving CYP450 itself.

GOOD TO REMEMBER

- **Schizophrenia twin-study heritability:** approximately 80 percent (New Oxford Textbook of Psychiatry), among the highest in psychiatry.
- **Schizophrenia SNP-based heritability:** roughly 17 to 45 percent of variance captured by common SNPs, illustrating the missing-heritability gap (New Oxford Textbook of Psychiatry).
- **Schizophrenia polygenic risk score:** explains on the order of 7 percent of variance in current data (New Oxford Textbook of Psychiatry).
- **ADHD heritability:** approximately 70 to 80 percent from twin meta-analyses, on a par with autism, bipolar disorder and schizophrenia (New Oxford Textbook of Psychiatry).
- **GWAS genome-wide significance threshold:** $p < 5 \times 10^{-8}$, correcting for roughly a million independent tests (Kaplan & Sadock 2024).
- **Common-variant effect size (schizophrenia):** odds ratio approximately 1 to 2 per risk allele (Kaplan & Sadock 2024).
- **Rare / CNV effect size (schizophrenia):** odds ratio approximately 20 to 100 per variant (Kaplan & Sadock 2024).
- **22q11.2 deletion (velocardiofacial / DiGeorge) syndrome:** raises schizophrenia odds by about 50-fold versus the general population (Kaplan & Sadock 2024).
- **Copy-number variant definition:** structural deletion or duplication typically larger than 1 kilobase; CNVs span about 12 percent of the genome in aggregate (Kaplan & Sadock 2024).
- **Common variant (SNP) definition:** polymorphism with minor allele frequency greater than 1 percent (Kaplan & Sadock 2024).
- **Manolio et al. 2009:** the landmark "Finding the missing heritability of complex diseases" (Nature), the reference for the missing-heritability problem.
- **LOD score:** the logarithm-of-odds statistic quantifying linkage; the metric of the pre-GWAS linkage era.

2 · Modes of inheritance and transmission models

Psychiatric disorders are the paradigm case of **complex inheritance**: they cluster in families but almost never segregate in the tidy ratios that Mendel described for the garden pea. The examinable skill is therefore to hold two frameworks in mind at once, the classical **Mendelian** single-gene patterns that underlie a handful of psychiatrically important syndromes, and the **non-Mendelian** and quantitative models that account for the common disorders. **Why it matters.** Examiners test whether you can say, with confidence, that schizophrenia, bipolar disorder, autism, ADHD and depression are **multifactorial** and **polygenic** rather than Mendelian, and whether you can then deploy the **threshold model** to explain the observations that flow from that: rising recurrence risk with severity, with number of affected relatives, and the sex-specific pattern of the Carter effect.

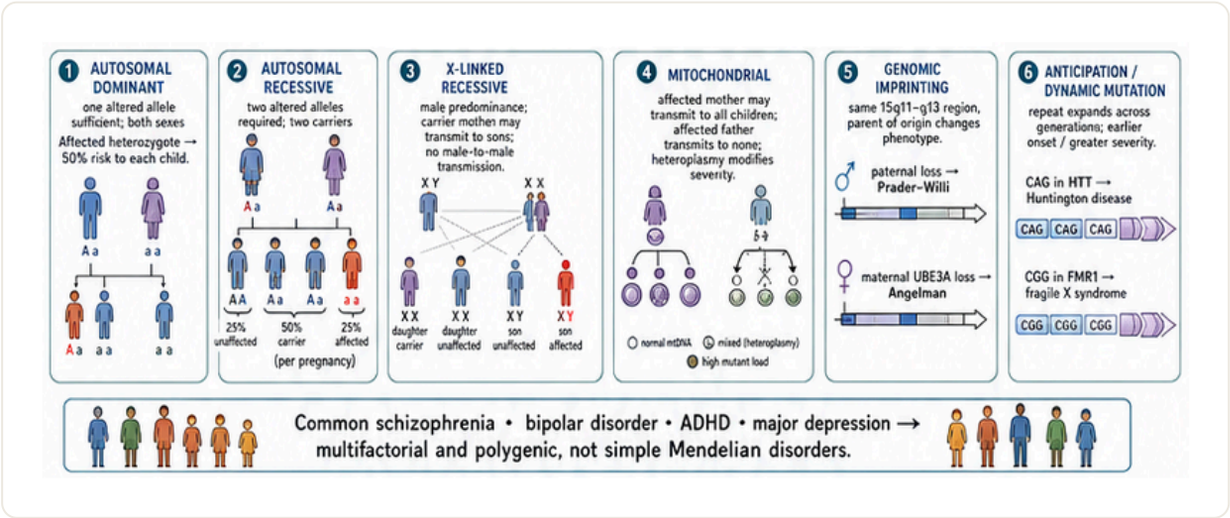


Fig 3.4 Transmission: Mendel and the exceptions.

This topic sets out the full menu of **modes of inheritance**, contrasts single-gene with oligogenic, polygenic and multifactorial architectures, and then develops the **multifactorial-threshold (liability) model** in detail because it is the single most exam-relevant transmission model in psychiatry (Kaplan & Sadock 2024; New Oxford 2020). Pedigree reading is introduced here only briefly, as an orientation; the systematic pedigree-interpretation drill is the discrimination topic.

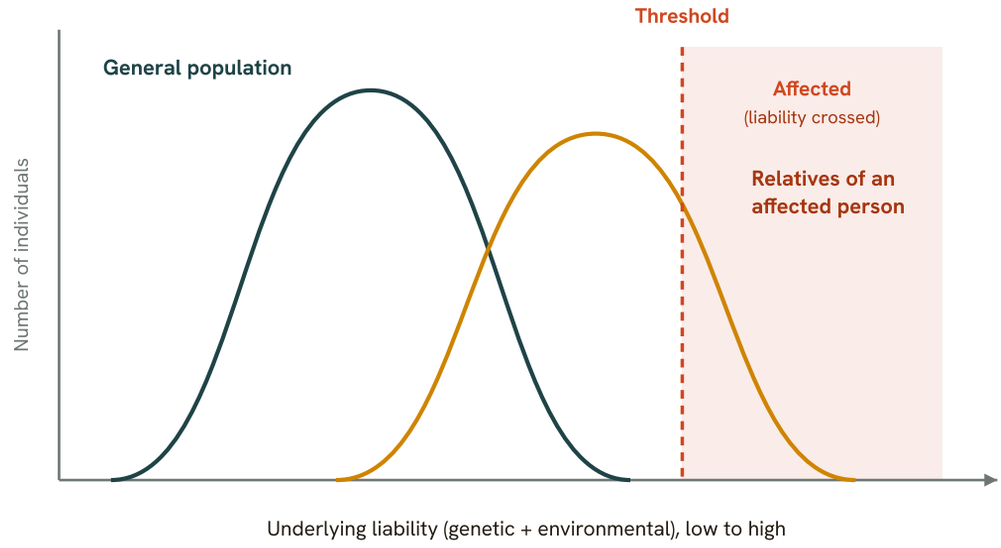


Fig 3.5 The multifactorial-threshold (liability) model. Liability, the summed effect of many genes and the environment, is normally distributed; a person is affected only once their liability crosses a threshold. Relatives of an affected person carry more of the risk alleles, so their whole distribution is shifted right (marigold) and a larger share falls beyond the threshold, which is why recurrence risk is higher in close relatives and rises with the number of affected family members. When one sex is affected less often, its threshold is higher, so its relatives carry higher risk (the basis of the Carter effect).

2.1 Mendel's three laws as the baseline

The rules a complex disorder breaks. Mendel's laws are the reference against which non-Mendelian behaviour is defined. The **Law of Dominance and Uniformity** holds that a dominant

allele masks a recessive one in the heterozygote; the **Law of Segregation** holds that the two alleles at a locus separate during gametogenesis so each parent transmits only one; and the **Law of Independent Assortment** holds that alleles at different loci are transmitted independently (an idealisation that breaks down for linked loci on the same chromosome). A disorder that obeys these laws is **monogenic** or single-gene, shows characteristic pedigree signatures, and gives fixed, high recurrence risks. The point for psychiatry is that the common disorders do exactly the opposite: their familial distributions are, in the words of the standard text, "inconsistent with simple Mendelian modes of inheritance" (Kaplan & Sadock 2024).

2.2 The three Mendelian patterns and their pedigree signatures

Autosomal dominant. One dominant allele on an autosome is sufficient to express the phenotype, so the condition affects both sexes equally, is transmitted vertically through every generation (rarely skips a generation), and confers a 50% risk to each child of an affected heterozygote. Complications examiners exploit are **reduced penetrance** (a carrier who does not express, so the pedigree appears to skip), **variable expressivity**, late age of onset (as in Huntington disease, where the family history may look negative in still-young relatives), and *de novo* mutation, which explains sporadic cases with unaffected parents. **Autosomal recessive.** Two copies are needed, so the phenotype typically appears horizontally in a single sibship of otherwise unaffected, often consanguineous, parents; the recurrence risk to a further child of two carriers is 25%. **X-linked recessive.** The mutant allele lies on the X chromosome, so affected individuals are predominantly male, there is no male-to-male transmission, and transmission runs through unaffected carrier mothers to sons (with knight's-move inheritance across the pedigree).

Penetrance

The proportion of individuals carrying a disease genotype who actually express the phenotype; reduced penetrance makes a dominant pedigree appear to skip generations.

Expressivity

The degree or severity of phenotype among those who do express it; variable expressivity means the same genotype produces different clinical pictures.

de novo mutation

A mutation arising for the first time in the affected individual (or parental germline), producing an isolated case; germline mosaicism can raise sibling recurrence risk above the near-zero expectation.

2.3 Reading a pedigree: an orientation

What the shapes encode. A pedigree is the fastest bedside route to a mode of inheritance. Squares are males, circles females, a filled symbol is affected, a horizontal line joins a mating pair, a vertical line drops to offspring, and a diagonal strike denotes a deceased individual; a double horizontal line marks consanguinity. Reading it, you ask three questions in sequence: are both sexes affected equally (autosomal) or is there a male excess (consider X-linked); is transmission vertical across generations (dominant) or clustered in one sibship (recessive); and is there male-to-male transmission (which excludes X-linkage). The systematic drill, including the

discriminators that separate mitochondrial from X-linked and dominant-with-reduced-penetrance from recessive, is developed in the pedigree-interpretation topic.

2.4 Non-Mendelian mechanism: mitochondrial (maternal) inheritance

Matrilineal, never paternal. Mitochondrial DNA is inherited almost exclusively through the ovum, so a pathogenic mtDNA variant passes from an affected mother to all of her children but is transmitted by none of her affected sons. The pedigree signature is therefore transmission through the maternal line only, with both sexes affected but only females passing the trait on. **Heteroplasmy** (a mixture of mutant and wild-type mitochondria whose ratio must exceed a tissue-specific threshold to cause disease) explains the variable severity within a matriline. Mitochondrial disorders are relevant to psychiatry as a cause of syndromic presentations with neuropsychiatric features and as one of the classic non-Mendelian patterns examiners contrast against X-linkage (New Oxford 2020).

2.5 Non-Mendelian mechanism: genomic imprinting and parent-of-origin effects

Which parent the allele came from matters. Imprinting is the parent-of-origin-specific silencing of an allele by DNA methylation established in the germline, so that the phenotype depends on whether the transmitting parent was the mother or the father (Companion to Psychiatric Studies 2010). The teaching pair is the 15q11-q13 region: loss of the paternally expressed genes produces **Prader-Willi syndrome** (hyperphagia, obesity, intellectual disability, and features overlapping OCD and psychosis), whereas loss of the maternally expressed *UBE3A* gives **Angelman syndrome** (severe intellectual disability, ataxia, and a characteristic happy affect). The same deletion thus yields two entirely different disorders according to parent of origin, which is the defining violation of Mendelian expectation that imprinting demonstrates.

RULE **Same 15q11-q13 deletion, opposite parent: two different syndromes.** Paternal loss gives Prader-Willi; maternal loss (of *UBE3A*) gives Angelman. Parent-of-origin dependence means imprinting.

2.6 Non-Mendelian mechanism: anticipation and dynamic mutation

Earlier and worse each generation. Anticipation describes a disorder that appears at a progressively earlier age and with increasing severity in successive generations. Its molecular basis is **dynamic mutation**, the unstable expansion of a trinucleotide (triplet) repeat during gametogenesis (Companion to Psychiatric Studies 2010). The two archetypes are **Huntington disease** (an expanding CAG repeat in *HTT*, where larger repeats give earlier onset, most markedly with paternal transmission) and **fragile-X syndrome** (a CGG repeat in the 5-prime untranslated region of *FMR1* on the X chromosome; once the repeat expands past the full-mutation range it silences the gene by methylation, the commonest inherited cause of intellectual disability and a recognised association with autism). It is worth noting for the exam that although repeat expansions cause these syndromic and learning-disability phenotypes, no convincing evidence links repeat expansions to the common psychiatric illnesses such as schizophrenia or bipolar disorder (Companion to Psychiatric Studies 2010).

RULE **Earlier and worse each generation means an expanding trinucleotide repeat.** Anticipation flags dynamic mutation: CAG in *HTT* (Huntington), CGG in *FMR1* (fragile-X).

2.7 From single-gene to polygenic: the spectrum of genetic architecture

A continuum, not a dichotomy. Genetic architecture is best pictured as a spectrum of the number of contributing loci and their individual effect sizes. A **single-gene (monogenic)** disorder is driven by one locus of large effect. An **oligogenic** disorder involves a small number of loci of moderate effect. A **polygenic** trait is influenced by very many loci, each of individually tiny effect, whose effects sum; this is **polygenicity**, and it is the genetic architecture now firmly established for schizophrenia, bipolar disorder, ADHD and major depression (Kaplan & Sadock 2024). A **multifactorial** trait is one in which many genes of small effect combine with environmental factors to produce risk; in psychiatry "polygenic" and "multifactorial" are used almost interchangeably because both genetic and environmental contributions are continuously distributed. The empirical signature of polygenicity is the marked inverse relationship between allele effect size and frequency: common variants each carry odds ratios below about 1.3 but, as a group, account for roughly a third of the genetic liability, while rare variants (including copy number variants) can carry large individual effects (Kaplan & Sadock 2024).

ARCHITECTURE	LOCI AND EFFECT	PSYCHIATRIC EXAMPLE	DISTINGUISHING FEATURE
Single-gene (Mendelian)	One locus, large effect	Huntington disease, fragile-X	**Mendelian pedigree; fixed high recurrence risk**
Oligogenic	Few loci, moderate effect	Some syndromic forms	**Non-Mendelian ratios but tractable locus count**
Polygenic	Very many loci, each tiny effect, additive	Schizophrenia, bipolar, ADHD, MDD	**Effect size falls as allele frequency rises**
Multifactorial	Many genes of small effect plus environment	Common psychiatric disorders	**Continuous liability crossing a threshold**

The genetic-architecture spectrum, from the single large-effect locus of Mendelian disease to the many-small-effect-genes-plus-environment model of the common psychiatric disorders.

2.8 The multifactorial-threshold (liability) model in full

A continuous liability with a categorical outcome. The **threshold model**, also called the **liability threshold** or multifactorial-threshold model, reconciles a discontinuous (present or absent) diagnosis with a continuous underlying cause. Its postulate is that every individual carries an underlying **liability**, the summed burden of all genetic and environmental risk and protective factors, which is approximately normally (Gaussian) distributed across the population. The disorder manifests only in those whose liability exceeds a critical **threshold**; below the threshold the person is unaffected, above it they are affected (New Oxford 2020). Because liability is the additive sum of many small contributions, the central-limit theorem makes its population distribution normal, which is precisely what justifies the bell-curve depiction. This model is the workhorse for conceptualising complex disorders such as ADHD, which is described as

"manifestations of an underlying continuously distributed liability, with the diagnosis lying above a certain threshold on this liability curve" (New Oxford 2020).

Why relatives sit further to the right. The crucial move is what the model predicts for relatives of an affected proband. Because relatives share genes (and often environment) with the proband, their liability distribution is shifted rightward, closer to the threshold, than that of the general population. A larger fraction of that shifted distribution therefore lies beyond the threshold, so the recurrence risk in relatives exceeds the population prevalence, and it does so more for closer relatives who share more of the proband's liability. This is exactly the pattern seen for congenital malformations and complex traits, where the first-degree-relative recurrence risk is of the order of 1 to 5% against a population incidence often of 0.1% or less (Kaplan & Sadock 2024).

2.9 Predictions the threshold model makes (and the exam loves)

Recurrence risk rises with severity. A more severe case implies a proband whose liability lies further beyond the threshold, which implies a family carrying a greater liability burden overall, which shifts the relatives' distribution further right and raises their recurrence risk. Hence more severe index cases predict higher risk to relatives. **Recurrence risk rises with the number of affected relatives.** Each additional affected relative is further evidence of a high-liability family, again shifting the relevant distribution rightward and increasing risk for the remaining members; risk is therefore not fixed as in Mendelian disease but conditional on the loading already visible in the pedigree. **Concordance and the heritability gap.** Twin studies quantify the genetic share of liability: schizophrenia has an estimated twin heritability of about 80% (Kaplan & Sadock 2024), yet current schizophrenia polygenic risk scores explain only about 7 to 7.7% of the variance on the liability scale (around 24% on the observed 0-to-1 scale), leaving a substantial "heritability gap" attributed to environmental effects, rare variants, gene-environment interplay and assortative mating (Kaplan & Sadock 2024).

2.10 Sex-specific thresholds and the Carter effect

The less-often-affected sex needs more liability. When a disorder has an unequal sex ratio, the multifactorial model accommodates it by positing **sex-specific thresholds**: the less commonly affected sex has a higher threshold, meaning a member of that sex must carry a greater liability burden to cross into the affected state. The consequence, known as the **Carter effect**, is that affected individuals of the less-often-affected (higher-threshold) sex carry, on average, a heavier liability load, and therefore transmit a higher recurrence risk to their relatives than affected individuals of the more commonly affected sex. The classic non-psychiatric illustration is pyloric stenosis (commoner in males), where the relatives of affected females carry the higher risk. In psychiatry the same logic is invoked for sex-biased conditions such as ADHD and autism, where an affected female, being of the higher-threshold sex, implies greater familial loading. Recognising that the higher-risk-transmitting relatives are those of the rarely affected sex is a frequently tested application of the model (New Oxford 2020).

HOLD THIS

Liability is normally distributed; disease appears above a threshold. Relatives sit shifted rightward, so recurrence risk exceeds prevalence, rises with closeness of relationship, severity of the index case and number affected, and (Carter effect) is higher in relatives of the rarely affected, higher-threshold sex.

COMMON TRAP

Do not call schizophrenia or bipolar disorder "Mendelian" or attribute them to a single gene. Their familial distributions are explicitly incompatible with single-major-locus inheritance and fit a polygenic, multifactorial-threshold model. Equally, do not confuse the shifted-relatives logic: the raised recurrence risk in relatives comes from their liability distribution sitting closer to the threshold, not from any single high-penetrance allele.

PEARL

Anticipation (earlier onset, greater severity each generation) should immediately make you think of an expanding trinucleotide repeat, and parent-of-origin dependence (same deletion, two different syndromes) should immediately make you think of imprinting. These two non-Mendelian mechanisms are the pair most reliably tested against the "why does this not follow Mendel" stem.

MNEMONIC

MITochondria: Mother's line, Inherited by all, Transmitted by none of the affected males.

Use this to lock the maternal-inheritance signature that separates mitochondrial from X-linked recessive: in mitochondrial disease an affected father transmits to no one, whereas in X-linked recessive an affected father transmits carrier status to all daughters.

INDIA

High rates of consanguineous marriage in parts of India raise the population load of autosomal recessive conditions, so a horizontal sibship pattern with related parents should prompt an explicit pedigree enquiry into consanguinity. For the common multifactorial psychiatric disorders, family risk counselling in Indian practice is best framed in threshold-model terms (risk raised above population baseline but not Mendelian) rather than as a fixed inherited certainty, which also keeps the message non-stigmatising.

GOOD TO REMEMBER

- **Schizophrenia twin heritability:** approximately 80% (Kaplan & Sadock 2024).
- **Schizophrenia PRS variance explained:** about 7 to 7.7% on the liability scale, around 24% on the observed 0-to-1 scale (Kaplan & Sadock 2024).
- **Common small-effect alleles in schizophrenia:** account for at least about 25% of total liability and roughly a third of genetic liability; individual odds ratios below about 1.3 (Kaplan & Sadock 2024).
- **ADHD twin heritability:** approximately 70 to 80% (New Oxford 2020).
- **Multifactorial first-degree-relative recurrence risk:** of the order of 1 to 5%, against a population incidence often 0.1% or less (Kaplan & Sadock 2024).
- **HTT (Huntington disease):** expanding CAG trinucleotide repeat; anticipation, earlier onset with larger repeats and paternal transmission.
- **FMR1 (fragile-X syndrome):** CGG repeat in the 5-prime untranslated region on the X chromosome; full-mutation methylation silencing; commonest inherited intellectual disability, autism association.
- **15q11-q13 imprinting pair:** paternal loss gives Prader-Willi syndrome, maternal loss (of *UBE3A*) gives Angelman syndrome.
- **Carter effect:** relatives of an affected individual of the less-often-affected (higher-threshold) sex carry the higher recurrence risk.

3 · Quantitative genetics: family, twin and adoption studies

Before a single risk gene had been identified, the classical epidemiological triad of family, twin and adoption studies had already established that virtually every major psychiatric disorder is substantially heritable. These designs are the historical and conceptual foundation of psychiatric genetics: they partition the observed clustering of a disorder in relatives into genetic and environmental sources, and they generate the heritability estimates that every downstream molecular study (linkage, GWAS, polygenic scores) sets out to explain. **Why it matters.** The examiner expects a candidate to move fluently from the raw observation that a disorder runs in families, through the twin comparison that says *whether* the familial aggregation is genetic, to the adoption design that *separates* genes from the rearing environment, and finally to the biometric machinery (the **ACE model**, path analysis, variance-components modelling) that turns concordance figures into numbers. Knowing the landmark studies, the core assumptions, and the standard critiques is high-yield across MCQs and vivas.

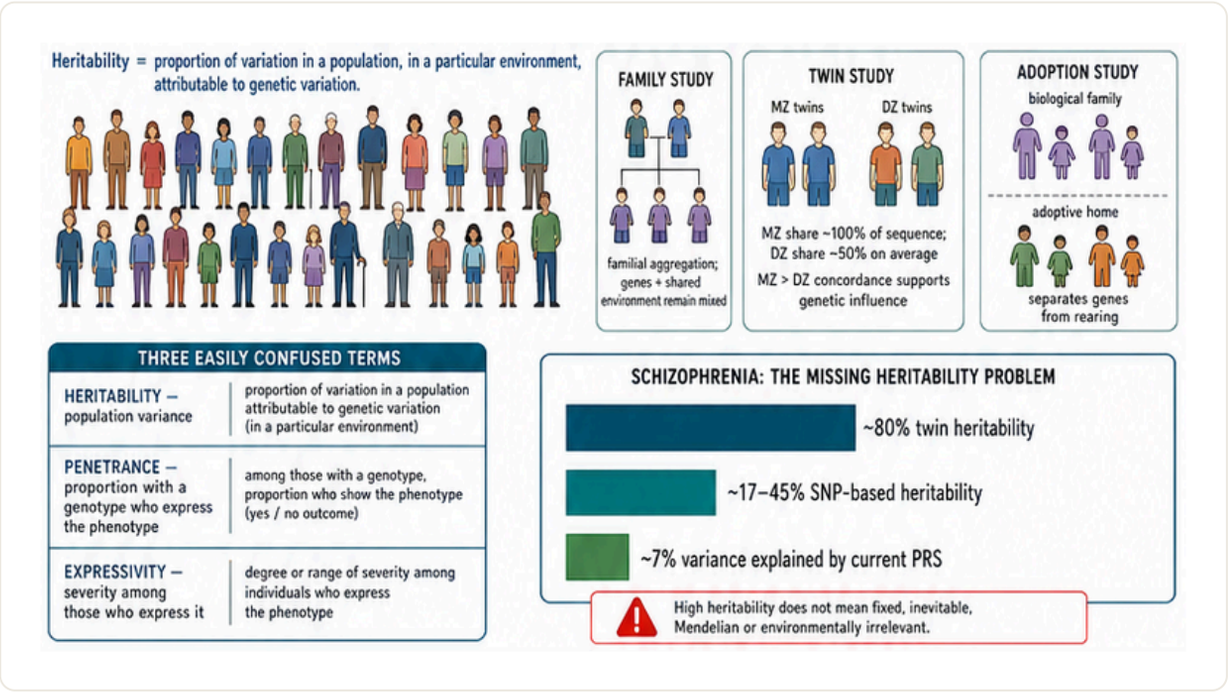


Fig 3.6 Heritability is not destiny.

The logic is sequential and each design answers a question the previous one leaves open. A **family study** establishes that a disorder aggregates in relatives but cannot separate shared genes from shared environment. A **twin study** exploits the difference in genetic sharing between monozygotic and dizygotic pairs to ask whether that aggregation is genetic. An **adoption study** physically separates the genetic parent from the rearing environment and so provides the strongest single test of a genetic contribution in humans (Tasman 2015). Read together, they yielded an unequivocal answer for schizophrenia, mood disorders and most of psychiatry: genes matter, and they matter a great deal.

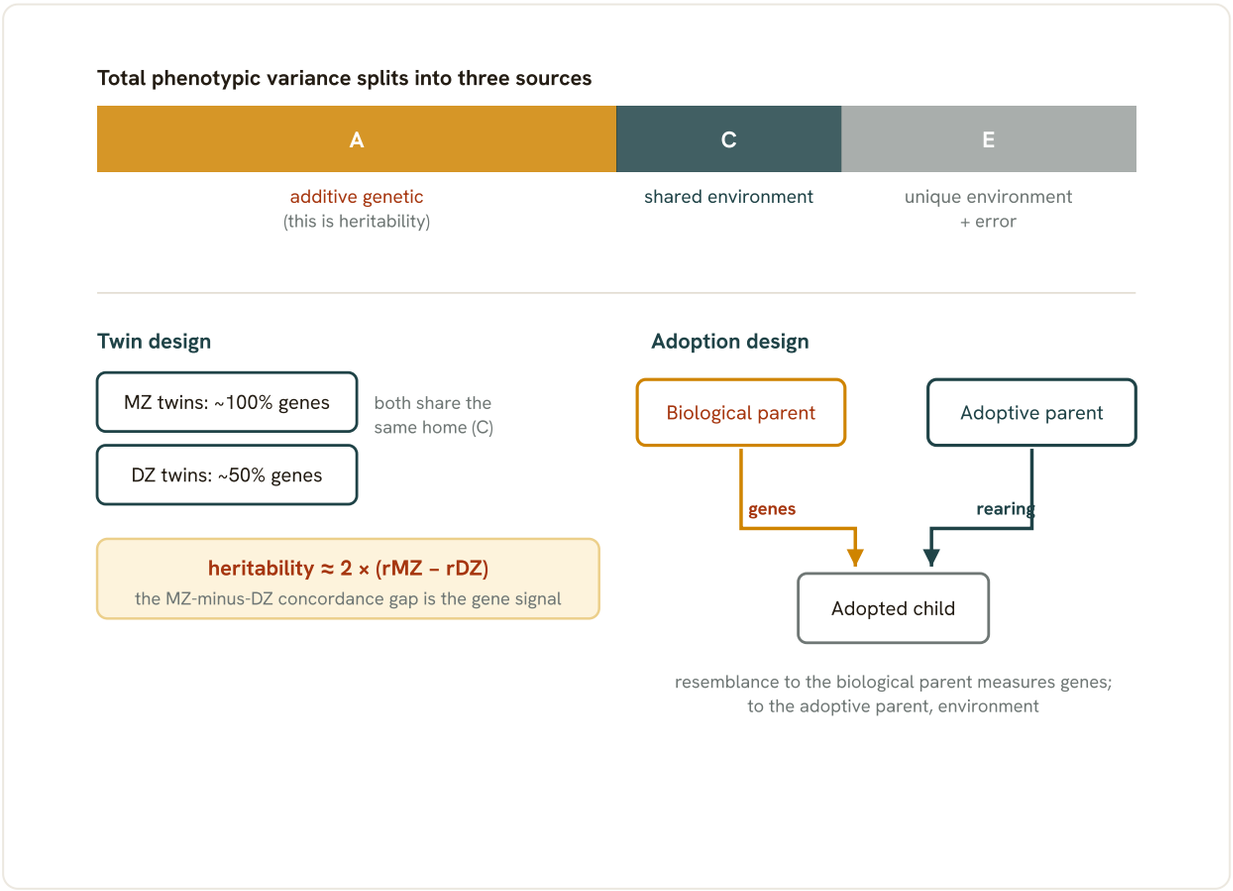


Fig 3.7 The two designs that separate genes from environment. The classical twin study exploits the fact that monozygotic twins share nearly all their genes and dizygotic twins about half, while both share the same home: the extra concordance in MZ over DZ pairs estimates heritability (Falconer's approximation, twice the MZ minus DZ correlation). The adoption study pulls genes and rearing apart in a different way: an adopted child's resemblance to the biological parent indexes genes, and resemblance to the adoptive parent indexes environment. Both feed the ACE model that partitions total variance into additive genetic (A), shared environment (C) and unique environment plus error (E).

3.1 Family studies: recurrence risk and the relative risk ratio

The starting design. A **family study** ascertains probands with the disorder and systematically assesses their relatives, comparing the frequency of the disorder among first-degree relatives (parents, siblings, offspring, who share on average 50% of their genes) with the population base rate. The output is a **recurrence risk** (the morbid risk in relatives) and, more usefully for comparison across disorders, the **relative risk ratio**, conventionally written lambda (the risk in relatives of a proband divided by the population risk). For first-degree relatives this is lambda-one; for siblings, lambda-s. Schizophrenia carries a first-degree-relative recurrence risk of roughly 6 to 10%, about a tenfold increase over the general-population risk of near 1%, so lambda-s for schizophrenia is of the order of 8 to 10 (Kaplan & Sadock 2024). **The interpretive limit.** Aggregation in a family is necessary but not sufficient evidence of genetic causation, because families share their environment as well as their genes. A family study can never, on its own, distinguish nature from nurture; it defines the phenotype's familiality and sets up the twin and adoption designs that follow.

3.2 The classical twin design: MZ versus DZ concordance

The natural experiment. The **twin study** rests on a simple genetic contrast: monozygotic (MZ) twins share essentially 100% of their DNA, whereas dizygotic (DZ) twins share on average 50%, the same as ordinary siblings, yet both twin types are assumed to share their rearing environment to a comparable degree. If a disorder is genetic, MZ pairs should show markedly higher **concordance** (the probability that the co-twin is affected given one twin is affected) than DZ pairs. If MZ and DZ concordance are equal, the familial aggregation is environmental. The greater the excess of MZ over DZ concordance, the greater the inferred heritability (New Oxford 2020).

Probandwise versus pairwise concordance. Two estimators are used and they are not interchangeable. The **pairwise** method divides concordant pairs by all pairs with at least one affected twin. The **probandwise** method counts each independently ascertained affected twin as a proband, so a doubly-ascertained concordant pair is counted twice; it yields a higher figure and is the estimator comparable to a population morbid risk. Probandwise concordance is the modern standard (Torrey 1994). Being aware of which figure a study quotes explains much of the apparent variation in published concordance rates.

3.3 Falconer's formula and heritability

From concordance to a number. **Heritability** (h-squared) is the proportion of the total phenotypic variance in a population attributable to genetic variance; it is a population parameter, not a statement about any individual, and it is specific to the population and environment studied. The classic first approximation from twin correlations is **Falconer's formula**, h-squared is approximately twice the difference between the MZ and DZ correlations, that is 2(rMZ minus rDZ) (Falconer, cited in New Oxford 2020). The doubling reflects the halving of shared genes from MZ to DZ pairs. **A worked intuition.** If rMZ is 0.5 and rDZ is 0.2, the naive estimate is 2(0.5 minus 0.2) equals 0.6, so about 60% of the variance is genetic. The formula is only a rough guide because it assumes purely additive genes and can exceed unity or misbehave when non-additive (dominance) effects or shared environment are present; formal variance-components modelling supersedes it (see 3.6).

RULE **Heritability is roughly twice the MZ-minus-DZ correlation gap.** Falconer: h-squared is about 2(rMZ - rDZ); the doubling reflects the halving of shared genes from MZ to DZ pairs.

COMMON TRAP

Heritability is not a fixed biological constant and does not describe how "genetic" a given person's illness is. A high heritability means that, in the population and environment studied, most of the variation between people is genetic; it says nothing about the modifiability of the trait, nor about the cause in any single patient. A highly heritable disorder can still be entirely prevented or treated environmentally (phenylketonuria is the standard cautionary example). Do not read h-squared of 0.8 as "80% genetic in this patient."

3.4 The ACE model and variance decomposition

Partitioning the phenotypic variance. The workhorse of modern twin analysis is the **ACE model**, which decomposes total phenotypic variance into three latent components: **A**, additive genetic variance; **C**, common (shared) environment, the environmental influences that make co-twins alike regardless of zygosity; and **E**, unique (non-shared) environment, the influences that make co-twins differ, which also absorbs measurement error. Under the model, MZ pairs correlate as A plus C and DZ pairs as one-half A plus C; the divergence between them identifies A, the residual within-MZ difference identifies E, and any residual similarity common to both twin types identifies C (New Oxford 2020). Where non-additive genetic effects are suspected the model is extended to ADE (A, dominance D, and E). Notably the **variance component** E always includes the discordance of MZ pairs, which is why any pair of identical twins discordant for a disorder is direct evidence for non-shared environmental (including stochastic and epigenetic) causation.

3.5 The equal-environments assumption and its critique

The load-bearing assumption. The entire inference from the twin design depends on the **equal-environments assumption** (EEA): that MZ and DZ twins are exposed to trait-relevant environments to an equal degree, so that any excess MZ similarity is genetic rather than environmental. **The critique.** Critics (notably Joseph) argue MZ twins are in fact treated more alike, dress alike, are confused for one another, spend more time together and evoke more similar responses, so that greater MZ concordance could partly reflect a more shared environment, inflating heritability estimates. **The defence.** The mainstream position is that the EEA holds for trait-relevant exposures: studies of twins mistaken about their own zygosity show resemblance tracks true (biological) zygosity rather than perceived zygosity, and greater MZ environmental similarity appears to be largely a consequence of their genetic identity (evoked or selected), not an independent cause of phenotypic similarity (New Oxford 2020). The EEA is the single most examinable methodological criticism of twin studies.

CLASSIC TRAP If asked for the load-bearing weakness of the twin design, name the **equal-environments assumption**: if MZ twins share more trait-relevant environment than DZ twins, heritability is inflated.

3.6 MZ twins reared apart, path analysis and segregation analysis

The strongest twin variant. The **MZ-twins-reared-apart** design studies genetically identical individuals separated early and raised in different families; their phenotypic correlation is a near-direct estimate of heritability because their shared environment (C) is minimised, so rMZ-apart approximates A. The best-known example is the Minnesota Study of Twins Reared Apart, whose reared-apart MZ correlations for many traits were only modestly below reared-together values, supporting substantial heritability (Kaplan & Sadock 2024). The design's weaknesses are selective (non-random) placement, late separation, and small, hard-to-ascertain samples.

The quantitative-methods toolkit. Three named analytic methods recur in the syllabus. **Path analysis** is a structural-equation technique that represents the causal paths from latent A, C and

E factors to the observed phenotype as a diagram, letting the A, C and E variance components be estimated (and their fit compared) simultaneously across MZ and DZ correlations (Tasman 2015). **Variance-components** (biometric) modelling is the general maximum-likelihood framework that fits the ACE or ADE models to raw twin (and family) data and formally tests whether dropping C or D worsens fit, superseding Falconer's arithmetic. **Segregation analysis** works on family (pedigree) data and asks whether the observed pattern of transmission fits a single major gene of Mendelian effect, a polygenic (many-small-genes) model, or a mixed model; for the major psychiatric disorders segregation analyses consistently rejected a single major gene and favoured polygenic or oligogenic inheritance, anticipating the highly polygenic architecture later confirmed by GWAS (New Oxford 2020).

3.7 Adoption designs: separating genes from rearing

Three configurations. The **adoption study** is the most powerful human design for disentangling genetic transmission from the family environment, because the adoptee's genetic parents and rearing parents are different people. Three canonical variants exist. In the *adoptee (adoptees') study* design, the adopted-away offspring of affected biological parents are compared with adopted-away offspring of unaffected biological parents; excess disorder in the former indexes genetic transmission (this is the Heston design). In the *adoptee's-family (parent-as-proband)* design, one starts from affected adoptees and examines rates of the disorder in their biological versus adoptive relatives; a genetic effect predicts higher rates among biological relatives. In the *cross-fostering* design, one compares adoptees with affected biological but healthy adoptive parents against adoptees with healthy biological but affected adoptive parents, directly pitting the genetic against the rearing contribution (Kaplan & Sadock 2024).

3.8 The landmark adoption studies

Heston (1966), the first. Leonard Heston's Oregon study followed 47 offspring born to hospitalised mothers with schizophrenia and adopted away in infancy, against 50 matched control adoptees; roughly 11% (5 of 47) of the index adoptees developed schizophrenia versus none of the controls, with excess sociopathy and neurosis besides. This was the first adoption evidence that the familial risk for schizophrenia is genetically transmitted, since the affected offspring never lived with their ill mothers (Companion 2010; Tasman 2015). **The Danish adoption studies.** Heston's finding was confirmed and greatly extended by the collaborative Danish-American programme of Rosenthal, Wender, Kety and Schulsinger, exploiting Denmark's national adoption and psychiatric registers. Using both the adoptee and the adoptee's-family strategies, they showed a marked excess of schizophrenia and schizophrenia-spectrum disorders among the biological relatives of schizophrenic adoptees, but not among their adoptive relatives, and the cross-fostering arm found that being reared by an ill adoptive parent did not raise risk in genetically low-risk adoptees (Tasman 2015). These studies established the schizophrenia spectrum concept and remain the paradigmatic adoption evidence in psychiatry. **The Finnish Adoptive Family Study.** Tienari's ongoing Finnish study of adopted-away offspring of mothers with schizophrenia added the crucial modern twist: risk in high-genetic-risk adoptees was concentrated in those raised in dysfunctional adoptive families, whereas a healthy adoptive

family environment appeared protective, demonstrating gene-environment interaction rather than genetic determinism (New Oxford 2020). Adoption designs were also decisive for mood disorder (Mendlewicz & Rainer 1977, showing genetic transmission of manic-depressive illness) and for antisocial personality and substance use (Crowe 1974; the Swedish Stockholm adoption studies of Cloninger, Bohman and Sigvardsson).

HOLD THIS

Three nested designs, each removing a confound the last could not. Family study proves aggregation; twin study separates genes from shared environment; adoption study severs genes from rearing. Heston (1966) was the first schizophrenia adoption study; the Danish studies (Kety, Rosenthal, Wender) established the schizophrenia spectrum.

DESIGN	GENETIC SHARING EXPLOITED	WHAT IT CONTROLS FOR	PRINCIPAL LIMITATION
Family study	Graded by relatedness (50% in first-degree)	**Nothing separates genes from shared environment**	Cannot distinguish nature from nurture
Twin study (MZ vs DZ)	MZ 100% vs DZ 50%, environment assumed equal	**Holds shared environment roughly constant across zygosity**	Rests on the equal-environments assumption
MZ reared apart	MZ 100%, shared rearing environment removed	**Removes the common environment (C) directly**	Selective placement, late separation, tiny samples
Adoption study	Biological vs adoptive relatedness dissociated	**Physically separates genes from the rearing family**	Selective placement, prenatal and perinatal confounds, register limits

The three classical designs answer successively harder questions: family studies establish familiality, twin studies test whether it is genetic, and adoption studies (especially the reared-apart and cross-fostering variants) sever genes from rearing altogether. The discriminator for each is what it holds constant or removes.

3.9 Gene-environment interaction and gene-environment correlation

Two distinct phenomena, often confused. **Gene-environment interaction** (GxE) means the effect of an environmental exposure on the phenotype differs according to genotype (or equivalently, genetic risk is expressed only, or more strongly, under a given exposure); the Finnish adoption finding above is a textbook example, and the classic molecular illustration is the moderation of the effect of childhood maltreatment on antisocial outcome by MAOA activity (Caspi 2002, contested in later meta-analyses). **Gene-environment correlation** (rGE) is different: it means exposure to an environment is itself partly under genetic control, so genes and environment are non-randomly associated (Plomin, DeFries & Loehlin 1977).

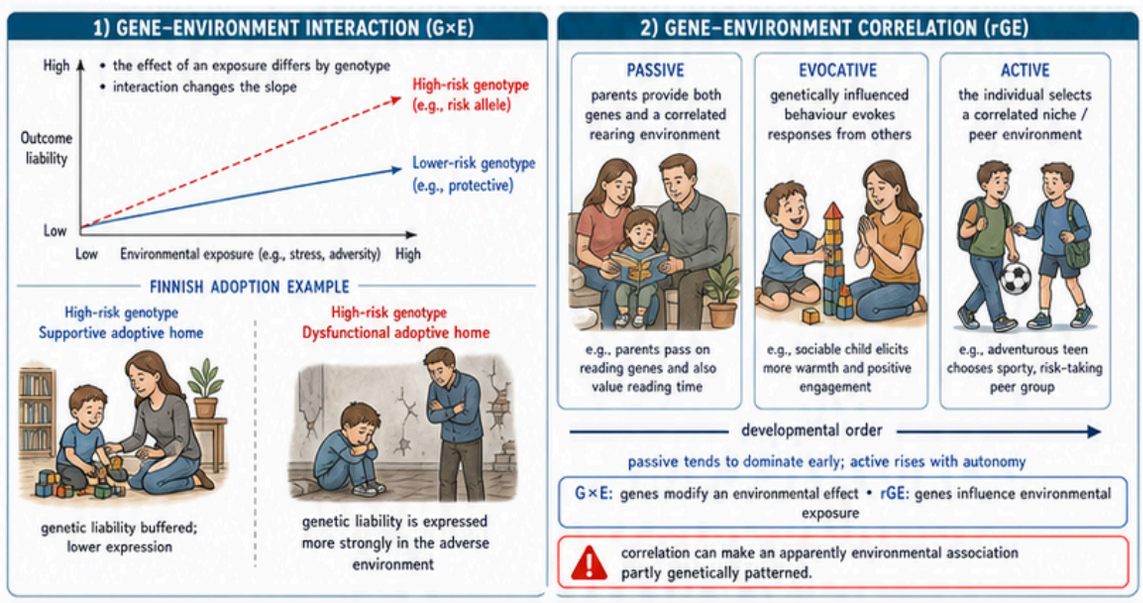


Fig 3.8 Gene and environment: interaction is not correlation.

Three forms of gene-environment correlation. Following Plomin and later Scarr and McCartney (1983), rGE takes three forms. **Passive rGE**: the child passively inherits both risk genes and a correlated rearing environment from the same biological parents (an anxious parent transmits both anxiety-related genes and an anxious home). **Evocative (reactive) rGE**: the child's genetically influenced behaviour evokes correlated responses from others (an irritable, genetically-influenced temperament elicits harsh parenting). **Active (niche-picking) rGE**: the individual actively seeks out environments correlated with their genotype (a sensation-seeking adolescent selects a deviant peer group). The developmental prediction is that passive rGE dominates in early childhood and gives way to active rGE with increasing autonomy (New Oxford 2020). Recognising rGE is essential because it means an apparently "environmental" risk factor identified in a family study may be a marker of genetic risk, one reason adoption and twin designs remain indispensable.

PEARL

A clean one-line discriminator: gene-environment *interaction* is about the environment having a different *effect* depending on the genes (multiplicative moderation); gene-environment *correlation* is about the genes influencing which *environment* a person encounters (non-random exposure). Interaction changes the slope; correlation changes the exposure.

MNEMONIC

ACE decomposes; PEA are the three correlations

The twin variance components are **A**dditive genetic, **C**ommon environment, **E**nvironment (unique). The three gene-environment correlations, in developmental order, are **P**assive (inherited genes plus inherited environment), **E**vocative (behaviour evokes responses), **A**ctive (niche-picking). ACE for the model, PEA for the correlations.

INDIA

Formal twin and adoption registries comparable to the Danish, Swedish and Finnish national registers do not exist at scale in India, so most Indian genetic-epidemiology data derive from family (morbid-risk) studies rather than twin or adoption designs. When counselling Indian families about recurrence risk, the practical figures used are the first-degree-relative risks from these family studies (of the order of 6 to 10% for schizophrenia in a first-degree relative), while remembering that consanguinity, common in parts of India, can inflate familial aggregation for recessive contributions and complicate the interpretation of a family history.

GOOD TO REMEMBER

- **Falconer's formula:** h-squared is approximately 2(rMZ minus rDZ); the doubling reflects the halving of shared genes from MZ to DZ.
- **ACE model:** variance equals A (additive genetic) plus C (common/shared environment) plus E (unique environment plus error); MZ correlate as A+C, DZ as one-half A + C.
- **Schizophrenia twin concordance (probandwise):** Farmer 1987 reported MZ 47.6% vs DZ 9.5%; Onstad 1991 reported MZ 48% vs DZ 4%.
- **Schizophrenia heritability (modern):** Hilker 2018 (Danish twin/psychiatric registers, over 30,000 pairs) found MZ 33% vs DZ 7% probandwise concordance and heritability of 79% (73% for the spectrum).
- **Autism twin data:** Folstein & Rutter reported MZ 36% vs DZ 0% pairwise (higher with broader phenotype); Sandin 2017 (over 37,000 twin pairs) estimated ASD heritability at about 83%.
- **First-degree-relative recurrence risk, schizophrenia:** roughly 6 to 10%, about a tenfold increase over the general-population risk of near 1% (lambda-s of the order of 8 to 10).
- **Heston (1966):** first schizophrenia adoption study (Oregon); about 11%, 5 of 47, of adopted-away offspring of schizophrenic mothers developed schizophrenia vs 0 of 50 controls.
- **Danish adoption studies:** Rosenthal, Wender, Kety & Schulsinger; excess schizophrenia-spectrum disorder in biological (not adoptive) relatives of schizophrenic adoptees; established the schizophrenia spectrum concept.
- **Finnish Adoptive Family Study (Tienari):** genetic risk expressed mainly in dysfunctional adoptive families, demonstrating gene-environment interaction.
- **Mood disorder adoption evidence:** Mendlewicz & Rainer 1977, genetic transmission of manic-depressive illness.
- **Equal-environments assumption:** the critical, load-bearing assumption of the twin design; challenged by Joseph, defended by misassigned-zygosity data.
- **Gene-environment correlation (Plomin 1977; Scarr & McCartney 1983):** passive, evocative, active, shifting from passive to active across development.

Methods: locating the risk

4 · Linkage analysis, LOD score and gene mapping

Before the genome-wide association era, the dominant strategy for finding disease genes was to follow a marker and a putative disease locus *through families* and ask whether they travel together more often than chance allows. This is **linkage analysis**, and its scoring statistic, the **LOD score**, is a recurring viva favourite: examiners want the value of 3, its meaning as 1000:1 odds, and why a method that cracked Huntington disease and cystic fibrosis **largely failed** in schizophrenia and

bipolar disorder. That failure is the whole reason the field pivoted to genome-wide association, so this topic is the conceptual hinge of these notes.

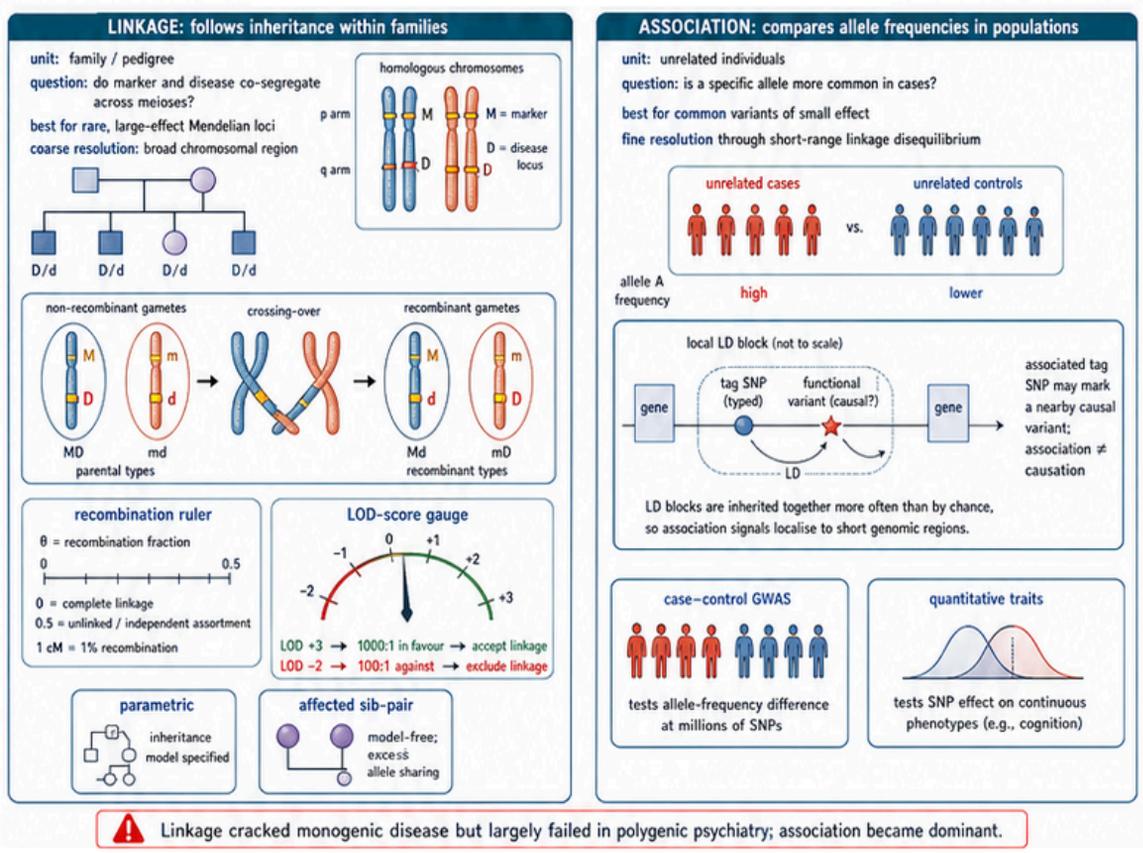


Fig 3.9 Linkage versus association.

The examinable core is a chain of ideas: recombination gives a measurable **genetic distance**; genetic **markers** (RFLP to microsatellite to SNP) let you track chromosomal segments; the recombination fraction feeds a likelihood ratio that becomes the LOD score; parametric linkage needs a specified model, non-parametric (affected sib-pair) does not; and the endpoint is **gene mapping** by positional cloning. Grasp that chain and you can answer any permutation the paper throws at you (Companion to Psychiatric Studies 2010; New Oxford Textbook of Psychiatry 2020).

4.1 Linkage versus association: the fundamental split

Two different questions, two different units. **Linkage** asks whether a marker and a disease locus *co-segregate within families*, tracked across meioses in pedigrees; the unit of analysis is the family. **Association** asks whether a marker allele *co-occurs with disease at the population level*, i.e. is more common in cases than controls; the unit is the unrelated individual. Linkage tolerates any allele at the linked marker (it cares only about recombinant versus non-recombinant transmission), whereas association implicates a specific allele. Linkage detects loci at coarse resolution over tens of centimorgans; association, exploiting the short range of linkage disequilibrium, localises to well under 1 cM (Companion to Psychiatric Studies 2010).

4.2 Recombination fraction theta and genetic distance

Recombination is the ruler. During meiosis, crossing-over between homologous chromosomes reshuffles alleles. The **recombination fraction** (theta) is the probability that a crossover falls between two loci, so it ranges from 0 (the marker is physically inside the gene and never separates) to 0.5 (independent assortment, i.e. unlinked). The nearer two loci sit, the smaller theta and the more often they are inherited together. The Companion likens it to cutting a pack of cards: adjacent cards are least likely to be separated by repeated cuts, distant cards as likely as not. The unit of genetic distance is the **centimorgan (cM)**, defined so that 1 cM corresponds to a 1% recombination frequency; across the human genome 1 cM averages roughly 1 megabase, but the two maps are not interchangeable (see 4.8).

4.3 Genetic markers through history: RFLP to STR to SNP

You cannot track a segment you cannot see. Linkage needs polymorphic markers of known Mendelian inheritance densely spaced along the genome. The marker technology evolved in three generations, and knowing the sequence is a clean exam point (New Oxford Textbook of Psychiatry 2020; genetic-mapping primer, Ott lab).

RFLP (restriction fragment length polymorphism)

First-generation DNA marker (1980s). Sequence variants create or abolish restriction-enzyme cut sites, giving differently sized fragments. Sparse, mostly biallelic, low information content. RFLPs revived family linkage as a genome-wide method.

Microsatellite / STR (short tandem repeat)

Second generation (1990s). Di-, tri- or tetra-nucleotide repeats varying in copy number; highly polymorphic and multi-allelic, so far more informative per locus. Panels of a few hundred microsatellites powered the classic genome-wide linkage scans.

SNP (single-nucleotide polymorphism)

Current standard. Single base-pair variants, usually biallelic but present in millions across the genome and amenable to chip-based genotyping. Individually less informative than an STR but hugely denser; SNPs made genome-wide association feasible.

4.4 Parametric linkage and the LOD score

The scoring statistic examiners want by name. **Parametric** (model-based) linkage specifies the mode of inheritance in advance: penetrance, disease-allele frequency and the recombination fraction. The recombination fraction is estimated by maximum likelihood, and the evidence for linkage is expressed as the **LOD score** (logarithm of the odds; log10 of a likelihood ratio). The numerator is the likelihood of the observed pedigree data assuming linkage at a given theta; the denominator is the likelihood assuming no linkage (theta = 0.5). By convention a **LOD score of +3** is accepted as proof of linkage, corresponding to odds of **1000:1** in favour (10 to the power 3), and a **LOD score of -2** excludes linkage, corresponding to odds of **100:1 against** (Companion to Psychiatric Studies 2010). If good model parameters are known, parametric linkage is very powerful; when the model is uncertain, mis-specification erodes that power.

PEARL

A LOD score is a base-10 logarithm, so it converts multiplicatively: LOD 3 means 10^3 = 1000:1 odds for linkage, LOD -2 means 10^2 = 100:1 odds against. The asymmetric thresholds (+3 to accept, -2 to exclude) reflect the low prior probability that any two random loci are linked, which is why more evidence is demanded to declare linkage than to reject it.

4.5 Non-parametric linkage: the affected sib-pair method

Model-free linkage for complex traits. When the mode of inheritance is unknown (true of every psychiatric disorder), parametric linkage is unsafe because a wrong model destroys power. **Non-parametric** (model-free) linkage sidesteps this by asking only about *allele sharing*. The prototype is the **affected sib-pair** method: two affected siblings share, by chance, 0, 1 or 2 alleles identical-by-descent at any locus, with expected proportions 25%, 50%, 25%. If a locus contributes to the disease, affected sibs share marker alleles at that locus *more often than chance*. The method makes no assumption about penetrance or dominance, relying only on the known Mendelian transmission of the markers. A particular form of affected-sib-pair analysis has a 1:1 correspondence with LOD-score analysis for a fully penetrant recessive disease, and many allele-sharing results are still reported as LOD scores (Ott lab genetic-mapping primer; Companion to Psychiatric Studies 2010).

TRAP Parametric (model-based) linkage needs the mode of inheritance specified in advance, so it is unsafe for psychiatric disorders where the model is unknown; use the model-free affected-sib-pair method instead.

4.6 From linkage to gene: positional cloning

Linkage gives a region, not a gene. **Positional cloning** is the strategy of moving from a mapped chromosomal interval to the actual causal gene using position alone, without prior knowledge of the gene's function (contrast the functional-candidate approach, which starts from a gene of known biology). The pipeline: a genome-wide linkage scan localises the disease to a broad interval; the interval is progressively narrowed by additional markers and by linkage disequilibrium; candidate genes within the region are then sequenced for causal variants. Positional cloning delivered the great single-gene successes (Huntington disease, cystic fibrosis) and, in psychiatry, identified *DISC1* by cloning the breakpoint of a balanced t(1;11) translocation that co-segregated with major psychiatric illness in a large Scottish family (Millar et al 2000; Blackwood et al 2001).

4.7 Fine-mapping with linkage disequilibrium

Sharpening a coarse hit. Once linkage flags an approximate location, **fine-mapping** narrows it using **linkage disequilibrium** (LD), the non-random co-occurrence of alleles at nearby loci in a population. Because a founder mutation stays coupled with neighbouring marker alleles for many generations, disease-associated alleles cluster in a small window around the true gene. In large outbred populations LD decays over very short distances (of the order of 0.3 cM, i.e. a few hundred kilobases), giving far higher mapping resolution than family linkage. Isolated founder populations (the classic example being the Afrikaans-speaking population of South Africa) retain

LD over several centimorgans, which can help or hinder depending on the design (Ott lab genetic-mapping primer 2001). Family-based LD designs use the case-parent *trio* and compare transmitted versus non-transmitted parental alleles, which controls for population stratification.

4.8 Genetic maps versus physical maps

Two rulers for one genome. A **genetic (linkage) map** orders loci by recombination frequency, with distance in centimorgans; it reflects how often crossovers separate loci. A **physical map** orders loci by actual DNA base pairs, with distance in kilobases or megabases, and the ultimate physical map is the reference genome sequence itself. The two do not scale uniformly: recombination is not evenly distributed, so recombination hotspots stretch the genetic map relative to the physical map, while cold regions (for example near centromeres) compress it. Roughly 1 cM averages 1 Mb genome-wide, but this ratio varies severalfold by location, which is why a linkage peak defines a region that must then be resolved on the physical map.

4.9 Why linkage largely failed in psychiatry, and the shift to association

The exam's punchline. Linkage is powerful for rare, highly penetrant, single-gene (Mendelian) disorders where one locus of large effect segregates cleanly in pedigrees. Psychiatric disorders are the opposite: *polygenic*, built from many common variants each of tiny effect, with incomplete penetrance, phenocopies, genetic heterogeneity (different loci in different families) and no clear mode of inheritance. Under these conditions family linkage is badly underpowered, its handful of variants of large effect simply are not there to be found, and the early psychiatric linkage literature became notorious for non-replication (New Oxford Textbook of Psychiatry 2020). Because association (case-control) designs detect common variants of small effect far more efficiently, and dense SNP chips made this genome-wide, the field abandoned linkage for the **genome-wide association study** (GWAS), which is hypothesis-neutral, needs no candidate pre-selection, and permits rigorous ancestry matching. This shift is why modern psychiatric genetics reports polygenic loci and polygenic risk scores rather than single linked genes.

HOLD THIS

Linkage cracks rare Mendelian genes but largely failed in psychiatry. Polygenic architecture, incomplete penetrance, phenocopies and locus heterogeneity leave family linkage underpowered, which is exactly why the field pivoted to genome-wide association.

COMMON TRAP

Do not equate a linkage peak with a gene. Linkage localises a disease to a chromosomal *region* spanning many megabases and dozens of genes; identifying the causal gene requires the further steps of fine-mapping and positional cloning. Similarly, do not confuse the two failure modes of linkage in psychiatry: the problem is not measurement but biology, namely many small-effect variants that no family-based linkage design is powered to catch.

CLINICAL ANCHOR

The clearest psychiatric payoff of positional cloning is *DISC1* (Disrupted-in-Schizophrenia-1), named after the t(1;11) breakpoint it disrupts. The translocation co-segregated with schizophrenia and affective psychosis in a Scottish pedigree at a LOD score of 7.1, far above the threshold of 3, illustrating that when a single large-effect variant genuinely exists in a family, linkage remains decisive. Such variants are the exception, not the rule, in common psychiatric illness.

FEATURE	LINKAGE ANALYSIS	ASSOCIATION STUDY
Unit of analysis	Families / pedigrees (co-segregation across meioses)	**Unrelated individuals (case-control population co-occurrence)**
Effect size detectable	**Rare variants of large effect (Mendelian loci)**	Common variants of small effect (polygenic)
Allele specificity	Allele-agnostic (recombinant vs non-recombinant)	**Implicates a specific allele**
Statistic / threshold	LOD score; +3 proof, -2 exclusion	P value; genome-wide significance $p < 5 \times 10^{-8}$
Mapping resolution	Coarse (tens of cM, many megabases)	**Fine (sub-cM, exploits short-range LD)**
Success in psychiatry	**Largely failed for common disorders; non-replication**	Now dominant; hundreds of polygenic loci, PRS

Linkage versus association across the four axes examiners test: unit of analysis, detectable effect size, resolution, and track record in psychiatric disorders.

MNEMONIC

"LOD 3, odds 1000; minus 2, out the door"

LOD +3 accepts linkage at 1000:1 odds in favour; LOD -2 excludes it at 100:1 against. Pair this with the direction check: positive LOD supports linkage, negative LOD argues against it.

GOOD TO REMEMBER

- **LOD score +3:** conventional threshold for proof of linkage, equals odds of 1000:1 (10^3) in favour (parametric linkage).
- **LOD score -2:** conventional threshold to exclude linkage, equals odds of 100:1 (10^2) against.
- **Recombination fraction (theta):** ranges 0 (never separated, i.e. inside the gene) to 0.5 (unlinked, independent assortment).
- **Centimorgan (cM):** unit of genetic distance, 1 cM = 1% recombination, averaging roughly 1 megabase genome-wide (varies by location).
- **Affected sib-pair sharing:** expected identity-by-descent proportions 25% / 50% / 25% for 0 / 1 / 2 shared alleles under no linkage; excess sharing indicates a disease locus.
- **RFLP, microsatellite/STR, SNP:** three successive marker generations underpinning gene mapping.
- **DISC1 (t(1;11)):** schizophrenia/affective-psychosis candidate cloned from a balanced translocation breakpoint in a Scottish family; linkage LOD 7.1 (Millar et al 2000; Blackwood et al 2001).
- **GWAS genome-wide significance:** conventional threshold p < 5 x 10 to the -8, correcting for roughly one million independent common variants.

5 · Association, GWAS, candidate genes, CNVs and polygenic risk scores

Why this matters. Psychiatric genetics moved in one generation from a graveyard of irreproducible **candidate gene** claims to a robust, sample-size-driven **genome-wide association study** (GWAS) enterprise. The examiner wants you to narrate that arc: why underpowered candidate studies failed, how the **common-disease-common-variant** hypothesis and consortium-scale GWAS finally delivered replicable hits, where rare **copy number variants** sit on the risk spectrum, and why a **polygenic risk score** that captures real biology still cannot predict any individual's diagnosis. The unifying idea is the genetic architecture of complex disorders: many common alleles of tiny effect plus a few rare variants of large effect, with a persistent **missing heritability** gap between them.

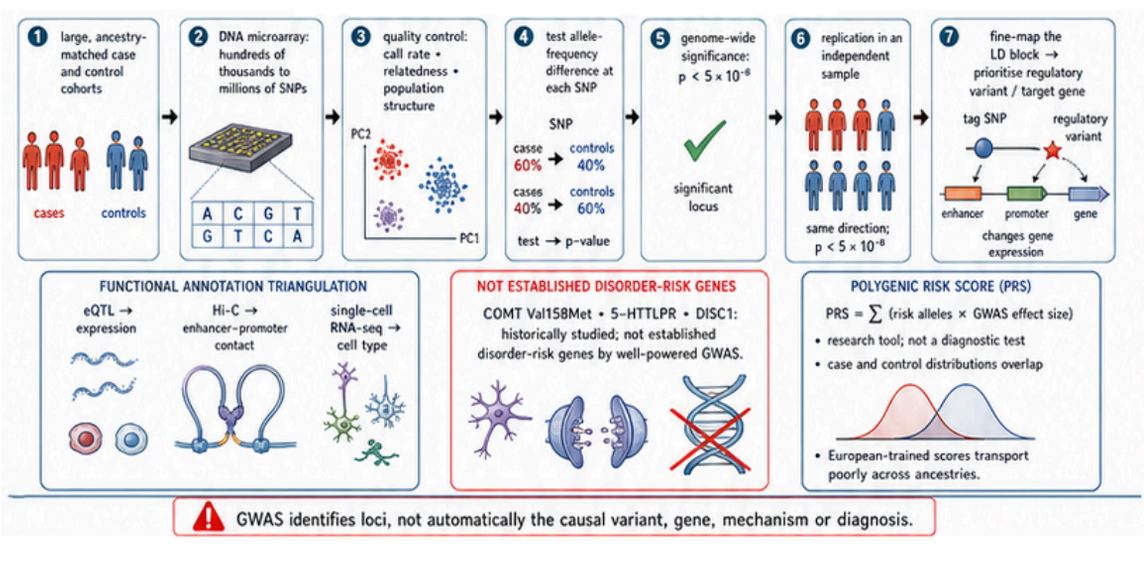


Fig 3.10 How a GWAS finds a locus.

Ground your answer in named findings rather than generalities: the 22q11.2 deletion as the single largest known genetic risk for schizophrenia, the MHC/complement-C4 signal, and the shared loci (e.g. CACNA1C) that blur the schizophrenia to bipolar boundary. These are the load-bearing facts, drawn from Kaplan and Sadock (2024), the New Oxford Textbook, and the Companion to Psychiatric Studies.

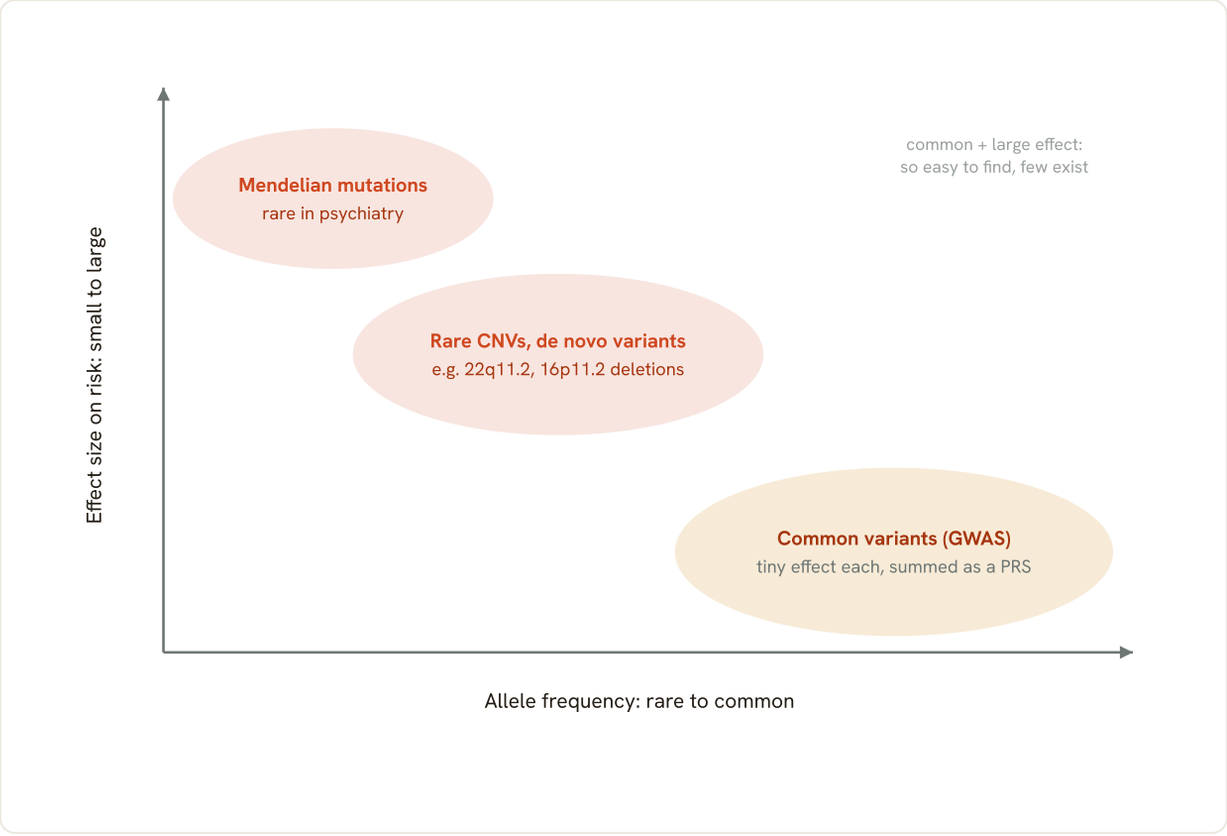
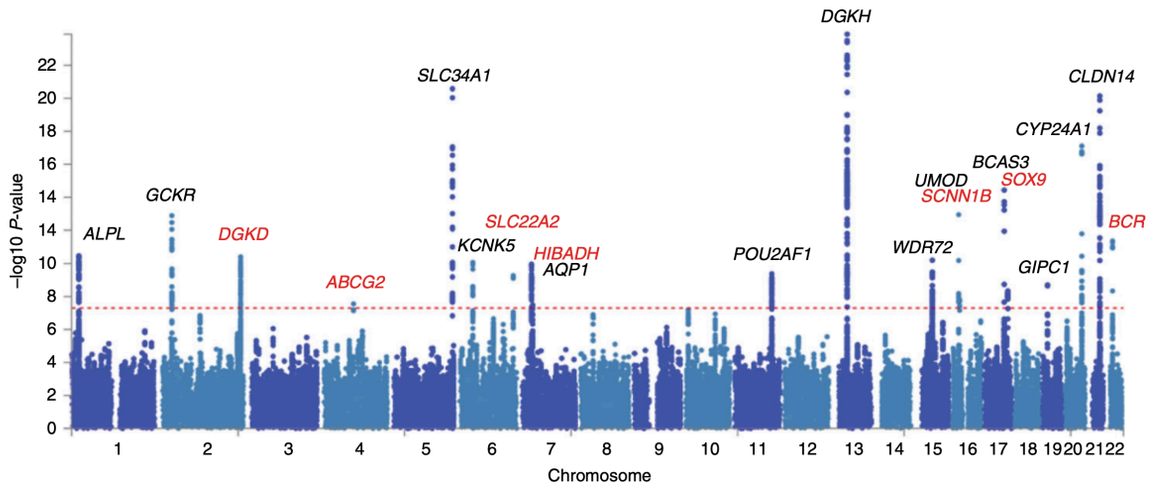


Fig 3.11 The genetic architecture of psychiatric disorders on the allele-frequency by effect-size plane. Risk variants trade off frequency against effect: a very few rare mutations carry large effects (top left, uncommon in psychiatry), rare copy-number and de novo variants sit in the upper band with moderate-to-large effects (the 22q11.2 deletion is the clearest example in schizophrenia), and the bulk of common inherited risk lies bottom right as thousands of common variants each of tiny effect, which genome-wide association detects and a polygenic risk score sums. The empty top-right corner (common and large effect) explains why such variants would already have been found, and the gap between what these methods capture and twin heritability is the missing heritability problem.



Representative GWAS Manhattan plot: S. A. Howles, A. Wiberg, M. Goldsworthy et al., CC BY 4.0, via Wikimedia Commons

Fig 3.12 What a genome-wide association study produces: a Manhattan plot. Each dot is one single-nucleotide polymorphism, placed left to right by its position along the chromosomes, and its height is the strength of association (the negative log base ten of the p-value). The dashed horizontal line marks genome-wide significance (5 x 10 to the minus 8); the peaks rising above it are the associated loci. A psychiatric GWAS looks exactly like this: each significant peak adds only a sliver of risk, which a polygenic risk score later sums across the genome. The plot shown is a representative GWAS used to illustrate the method.

5.1 Association studies: the basic logic and its currencies

The design. An **association study** compares allele frequencies at a genetic marker between unrelated cases and controls: if an allele is over-represented in cases, it (or a variant near it) may raise risk. This is more powerful than linkage for common variants of small effect, which is exactly the architecture complex psychiatric disorders turned out to have (Companion to Psychiatric Studies).

Direct vs indirect association. Because alleles are inherited in blocks, a typed marker need not be causal: **linkage disequilibrium** (LD, the non-random co-inheritance of nearby alleles) means a neutral tag SNP can flag a nearby functional risk allele. GWAS exploits this, so most GWAS hits are markers pointing to a region rather than the causal variant itself (Kaplan and Sadock 2024).

SNP (single-nucleotide polymorphism)

A single base-pair change (e.g. adenine to guanine); occurs roughly once per 1,200 bases; the workhorse marker of GWAS.

Common variant

Minor allele frequency above 1% in the population.

Linkage disequilibrium (LD)

Non-random association of alleles at nearby loci, decaying with recombination distance; lets a tag SNP stand in for an untyped causal allele.

Pleiotropy

One gene affecting multiple traits or disorders; many of the same loci raise risk for schizophrenia, bipolar disorder and ASD.

5.2 The candidate-gene era and its replication failure

The approach. Before genome-wide genotyping, researchers were forced to pre-select a handful of **candidate genes**, chosen either positionally (under a linkage peak) or functionally (a biologically plausible neurotransmitter gene). For schizophrenia alone, more than 1,500 studies examined nearly 800 candidate genes (Tasman 2015).

The cautionary tale. Almost none survived. Farrell and colleagues (2015), reviewing the most-discussed schizophrenia candidates (COMT, DTNBP1/dysbindin, DISC1, DAOA, RGS4, HTR2A, DRD3) against genome-wide data, found the classic candidate literature did not yield clear insight into the genetic basis of schizophrenia: these historical candidates were not supported at genome-wide significance, and the original serotonin-transporter and DISC1 psychiatric associations largely did not replicate (Companion to Psychiatric Studies).

Why they failed. Underpowered samples chasing tiny true effects, publication bias toward positive results, weak priors on which genes to test, and flexible analytic choices produced a literature dominated by false positives (Ioannidis and colleagues). Even where a real effect existed, replication studies were themselves too small to confirm it. The lesson embedded in every modern GWAS is the need for enormous samples and built-in replication.

> **COMMON TRAP**
>
> Do not quote COMT val158met or 5-HTTLPR (the serotonin-transporter length polymorphism, SLC6A4) as established risk genes for a psychiatric disorder. In the exam these are the canonical examples of candidate-gene claims that did not replicate at genome-wide significance. The safe framing: "historically studied candidate, not supported by well-powered GWAS." DISC1 (Disrupted-in-Schizophrenia-1) belongs in the same cautionary basket.

5.3 The common-disease-common-variant hypothesis

The pivot from linkage. Linkage studies, so successful for Mendelian disease, failed to deliver reproducible schizophrenia loci; no Mendelian form of schizophrenia was ever found. This failure was read as evidence against a few genes of major effect, and reframed as the **common-disease-common-variant** (CD/CV) hypothesis: risk is conferred by many common variants, each of small effect, that are old enough to be widespread in the population (Tasman 2015).

Why it justified GWAS. If risk alleles are common, they can be tagged by common SNPs on an array and detected in case-control samples, provided the sample is large enough to see effects with odds ratios near 1.1 to 1.4. CD/CV is the theoretical warrant for genome-wide genotyping; it does not exclude a complementary role for rare, high-penetrance variants (the two-tier architecture in 5.7).

5.4 GWAS methodology: arrays, the Manhattan plot and the 5e-8 threshold

The platform. A GWAS uses a DNA microarray ("gene chip") to assay hundreds of thousands to millions of SNPs across the whole **genome-wide** span simultaneously in tens to hundreds of thousands of people, then tests each SNP for a frequency difference between cases and controls (Kaplan and Sadock 2024).

The Manhattan plot. Results are displayed with chromosomal position on the x-axis and the negative log10 of each SNP's p-value on the y-axis, so the strongest associations rise as skyscraper-like peaks (hence "Manhattan"). A horizontal line marks the significance threshold; peaks crossing it are the reported loci.

Genome-wide significance = 5e-8. Because roughly a million independent tests are performed, the conventional threshold is set at p less than 5 x 10 to the power minus 8 (5e-8), a Bonferroni-style correction for the predicted false positives when a million tests are run (Kaplan and Sadock 2024). Meeting this bar is what separates a credible locus from noise, and is why so many early, small psychiatric GWAS reported nothing.

The QQ plot. A quantile-quantile plot graphs observed against expected p-values under the null. Points hugging the diagonal until an upward tail at the extreme suggest true polygenic signal; an early, uniform lift of the whole line signals confounding (typically population stratification or cryptic relatedness), quantified by the genomic inflation factor lambda. The QQ plot is the standard quality-control read-out for a GWAS.

RULE **Genome-wide significance is $p < 5 \times 10^{-8}$.** It is a Bonferroni-style correction for roughly a million independent common-variant tests, and is the bar that separates a credible locus from noise.

5.5 The Psychiatric Genomics Consortium and sample-size scaling

Size was the missing ingredient. The decisive move was collaborative pooling. The **Psychiatric Genomics Consortium** (PGC) aggregated samples across more than 30 countries, and the schizophrenia signal scaled almost linearly with case number: an early GWAS reporting a handful of loci grew, once tens of thousands of cases were assembled, into the landmark 2014 analysis of about 36,989 cases and 113,075 controls that identified 128 independent associations across 108 distinct genomic loci (Companion to Psychiatric Studies; Kaplan and Sadock 2024).

What the hits mean biologically. At least three-quarters of these loci contained protein-coding genes, enriched for dopamine (DRD2), glutamate (GRIN2A, GRM3) and voltage-gated calcium-channel (CACNA1C) signalling. Most associated variants do not change protein sequence; they most likely alter gene expression, which makes functional interpretation hard (Companion to Psychiatric Studies).

CLINICAL ANCHOR

Named schizophrenia findings worth carrying into a viva. The **MHC/complement-C4 signal** on chromosome 6 is the single most robustly associated locus, though its effect is modest (odds ratio about 1.2); Sekar and colleagues (2016) showed the association is driven by structural variation raising expression of complement component C4A, plausibly linked to excessive synaptic pruning. **DRD2** (the target of every antipsychotic) emerging as a GWAS hit closed a satisfying loop between genetics and pharmacology. **CACNA1C** is a canonical cross-disorder locus shared with bipolar disorder, underlining that genetic boundaries between the two are permeable.

5.6 Copy number variants and named recurrent syndromes

Definition. A **copy number variant** (CNV) is a structural change, a deletion or duplication of a DNA segment larger than 1 kilobase, altering gene dosage. CNVs are common in aggregate (about 12% of the genome is copy-number variable) and mostly benign, but a subset of large, recurrent, gene-rich CNVs carry substantial psychiatric risk (Kaplan and Sadock 2024).

22q11.2 deletion: the flagship. The recurrent hemizygous microdeletion at 22q11.2 was the first de novo CNV described in schizophrenia (Karayiorgou 1995) and, before the GWAS era, the only DNA variant indisputably pathogenic for the disorder (Companion to Psychiatric Studies). It causes velocardiofacial syndrome (DiGeorge syndrome), with cardiac outflow defects, palatal anomalies, hypocalcaemia and learning difficulty, and raises the odds of schizophrenia roughly 50-fold, the single largest known genetic risk (Kaplan and Sadock 2024). Because carriers are recognisable clinically, the psychosis link was demonstrable early.

Other recurrent risk CNVs. A recurring set of loci shows a similar many-to-one, pleiotropic pattern (one CNV, several neurodevelopmental outcomes): 16p11.2 (deletion and duplication, strongly tied to autism and developmental delay), 1q21.1, the 15q11-13 region, 3q29, and deletions disrupting NRXN1 (neurexin-1, a presynaptic cell-adhesion gene). Total CNV burden is elevated in schizophrenia and autism relative to controls, and disease-associated CNVs are larger and more gene-rich than benign ones. Chromosomal microarray is now standard first-line testing in autism and intellectual disability, yielding a molecular diagnosis in over 20% of children tested (Kaplan and Sadock 2024).

~50-fold	~12%	>20%
22Q11.2 RAISES SCHIZOPHRENIA ODDS	OF GENOME IS COPY-NUMBER VARIABLE	CMA MOLECULAR-DIAGNOSIS YIELD IN ASD/ID

LOCUS	CHANGE	SYNDROME / EPONYM	PRINCIPAL PSYCHIATRIC ASSOCIATION
22q11.2	Deletion	**Velocardiofacial / DiGeorge**	**Schizophrenia (about 50-fold; largest known single risk); ADHD, anxiety**
16p11.2	Deletion / duplication	16p11.2 microdeletion/duplication	Autism, developmental delay, intellectual disability
1q21.1	Deletion / duplication	1q21.1 recurrent CNV	Schizophrenia, autism, developmental delay
15q11-13	Duplication	15q duplication (maternal)	Autism; (paternal deletion gives Prader-Willi)
15q11.2	Deletion	15q11.2 (BP1-BP2)	Schizophrenia, epilepsy, developmental delay
NRXN1 (2p16.3)	Deletion	NRXN1 deletion	Schizophrenia, autism, intellectual disability

Recurrent, high-risk copy number variants and their named cytogenetic syndromes; 22q11.2 deletion is the flagship, carrying the single largest known genetic risk for schizophrenia (Kaplan and Sadock 2024; Companion to Psychiatric Studies).

5.7 The genetic architecture plane: allele frequency vs effect size

The core inverse relationship. Plot allele frequency against effect size and a clear gradient appears. Common GWAS SNPs are frequent but tiny in effect (odds ratios about 1.1 to 1.4). Rare CNVs and protein-truncating variants are the opposite: uncommon in the population but with large effect (odds ratios of roughly 20 to 100 for the strongest, e.g. 22q11.2). Mendelian, single-gene disorders sit in the far corner: very rare, near-deterministic effect (Kaplan and Sadock 2024).

Why the corners are empty. There are essentially no common variants of large effect for schizophrenia (a variant that common and that harmful would be culled by natural selection, because affected individuals have markedly reduced fecundity). This is why the disorder is polygenic on the common-variant side and driven by rare, often de novo, variants on the large-effect side. Both tiers must be summed to understand an individual's total genetic liability.

5.8 Polygenic risk scores: construction and limits

Construction. A **polygenic risk score** (PRS, also risk-profile scoring) is built from GWAS summary statistics. In a discovery sample, each SNP is assigned a weight (its estimated effect size); in an independent target individual, you count the risk alleles carried and sum them, weighted, to a single number, an estimate of that person's common-variant genetic liability (Kaplan and Sadock 2024). The method traces to the International Schizophrenia Consortium (ISC), which set a deliberately loose p-value threshold, reasoning that although most such alleles are false, a highly polygenic disorder would still carry a detectable aggregate burden. The ISC confirmed this and estimated the common-variant component is spread across at least 1,000 alleles, contributing roughly one-third of the genetic risk (Companion to Psychiatric Studies).

Variance explained. Even from the largest studies, a schizophrenia **PRS** accounts for only about 7% of the variance in liability; the PGC common-variant signal explains only about 3 to 4% (New Oxford Textbook; Companion to Psychiatric Studies). Across disorders the figures are modest, and for ADHD current PRS explains on the order of 0.1 to 2% of phenotypic variance (New Oxford Textbook).

Why PRS is not yet clinically predictive. Three reasons dominate. First, low variance explained: high PRS shifts population-average risk but the distributions of cases and controls overlap heavily, so an individual score has poor discrimination. Second, portability: GWAS samples are overwhelmingly of European ancestry, and PRS performs worse when applied across ancestries (an equity problem for use in Indian and other non-European populations). Third, PRS captures only the common-variant tier, ignoring the large-effect CNVs and rare variants that matter most for the highest-risk individuals. PRS is a powerful research instrument for genetic architecture, but not a diagnostic test.

HOLD THIS

A PRS sums common-variant burden but cannot diagnose an individual. It explains only about 7% of schizophrenia liability, case and control distributions overlap heavily, and European-derived scores transport poorly to other ancestries.

TRAP Do not quote COMT val158met, 5-HTTLPR (SLC6A4) or DISC1 as established risk genes: they are the canonical candidate-gene claims that did not replicate at genome-wide significance.

INDIA

The Eurocentric ancestry bias of GWAS discovery samples is not an abstraction for Indian practice. A PRS derived in European cohorts loses accuracy in South Asian genomes because LD structure and allele frequencies differ, so any near-term "genetic risk report" marketed for Indian patients should be read with strong caution. Broadening reference panels to non-European ancestries is the stated route to more equitable PRS.

5.9 Missing heritability: where the rest may hide

The gap. Twin studies put schizophrenia heritability high (broadly in the 60 to 80% range for the most heritable psychiatric disorders), yet SNP-heritability (the variance captured by common GWAS variants) and PRS explain only a single-digit-to-modest fraction. The difference is **missing heritability** (Manolio and colleagues 2009).

Candidate hiding places. Several, and probably several at once: (1) rare variants of larger effect, including CNVs and protein-truncating single-nucleotide variants, poorly tagged by common-SNP arrays; (2) many more common variants of effect too small to reach 5e-8 at current sample sizes (still-larger GWAS keep finding them); (3) gene-gene and gene-environment interactions and structural variation not well captured; (4) overestimation of twin heritability itself (shared-environment and equal-environment assumptions). The field's working answer is that no single mechanism accounts for the gap; ever-larger biobank-scale GWAS plus whole-genome and exome sequencing for rare variants are chipping at it from both ends (Companion to Psychiatric Studies; New Oxford Textbook).

MNEMONIC

Common is Small, Rare is Tall

The genetic architecture plane in one line: common variants (GWAS SNPs) are frequent but Small in effect; rare variants (CNVs, protein-truncating variants) are uncommon but Tall in effect. The empty corner (common and tall) is emptied by natural selection.

PEARL

The whole story is a parable about statistical power. Candidate-gene studies failed not because the biology was wrong but because they were underpowered and multiplicity-uncorrected; GWAS succeeded not because it was cleverer but because consortia made it big enough. The genome-wide significance threshold of 5e-8 is the institutional memory of that lesson.

GOOD TO REMEMBER

- **Genome-wide significance threshold:** p less than 5 x 10 to the power minus 8 (5e-8), correcting for about a million tests.
- **22q11.2 deletion:** velocardiofacial / DiGeorge syndrome; single largest known genetic risk for schizophrenia, about 50-fold increased odds; first de novo CNV described in schizophrenia (Karayiorgou 1995).
- **16p11.2 (deletion/duplication):** recurrent CNV, autism and developmental delay.
- **1q21.1:** recurrent deletion/duplication; schizophrenia, autism, developmental delay.
- **15q11-13 (maternal duplication):** autism (paternal deletion of the region gives Prader-Willi).
- **NRXN1 (neurexin-1, 2p16.3) deletion:** schizophrenia, autism, intellectual disability.
- **MHC / complement C4A:** most robustly associated schizophrenia locus (chromosome 6), effect modest (odds ratio about 1.2); C4A implicated in synaptic pruning (Sekar 2016).
- **DRD2:** GWAS-significant schizophrenia locus; antipsychotic target, closing the genetics-pharmacology loop.
- **CACNA1C:** voltage-gated calcium channel; cross-disorder locus shared by schizophrenia and bipolar disorder.
- **COMT (val158met), 5-HTTLPR (SLC6A4), DISC1:** classic candidate genes that largely failed to replicate at genome-wide significance (Farrell 2015); the cautionary examples.
- **PGC schizophrenia GWAS (2014):** about 36,989 cases, 113,075 controls; 128 independent associations at 108 distinct loci.
- **ISC (2009):** common-variant risk spread across at least 1,000 alleles, contributing roughly one-third of genetic risk; origin of polygenic risk scoring.
- **Schizophrenia PRS variance explained:** about 7% of liability (PGC common-variant signal about 3 to 4%); not clinically predictive at the individual level.
- **ADHD PRS variance explained:** about 0.1 to 2% of phenotypic variance.
- **Twin heritability (most heritable psychiatric disorders):** broadly 60 to 80%; the gap to SNP-heritability is the missing heritability (Manolio 2009).

6 · Novel genetic approaches and gene therapy

Array-based **GWAS** gave psychiatric genetics its first robust, replicable common-variant hits, but it is deliberately blind to two things: the rare, large-effect variation that a genotyping chip does not carry, and the biological **mechanism** that turns a statistical association at a locus into a disease. This topic is the Paper-1 delta on everything that has moved beyond the chip: high-throughput **sequencing** to find rare and *de novo* variation, **functional genomics** and stem-cell models to translate a locus into a mechanism, **causal-inference** methods such as Mendelian randomization, **biobank**-scale cohorts, polygenic scores as a research and emerging stratification tool, and finally **gene therapy**, where the honest examination answer is that monogenic neurology has moved but polygenic psychiatry has not (Kaplan & Sadock 2024; New Oxford 2020).

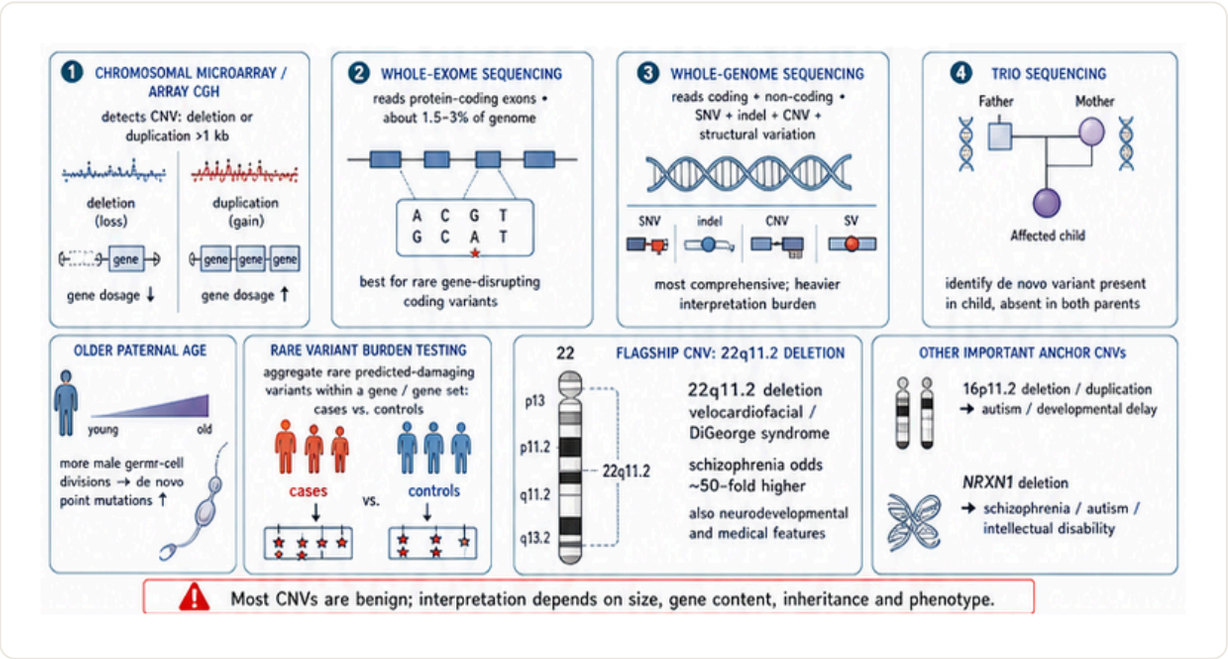


Fig 3.13 Rare variants: which tool finds what?.

Why it matters. Examiners increasingly ask you to place a method against a question: which technology finds rare variants, which infers causality from observational genetic data, why a polygenic disorder is a poor candidate for gene editing. **Framing.** Hold one organising idea throughout: *the architecture dictates the tool*. Rare large-effect variants (autism, intellectual disability, some schizophrenia) are found by sequencing and are conceptually near a targeted therapy; common small-effect variants (the bulk of adult psychiatric liability) are found by GWAS, summarised by polygenic scores, and are nowhere near a molecular cure.

6.1 Sequencing: whole-exome and whole-genome sequencing

What each reads, and why the choice matters. **Whole-exome sequencing** (WES) captures and sequences only the protein-coding portion of the genome, about 1.5 to 3% of the total, which lowers cost and greatly improves interpretability because a coding variant has a readable consequence on protein (Kaplan & Sadock 2024; Wang et al. 2019). It is described in the standard reference as "good for finding gene-disrupting rare variants" (Kaplan & Sadock 2024). **Whole-genome sequencing** (WGS) resequences the entire genome and can in principle detect every class of variation at once, single-nucleotide variants, small insertions and deletions, and structural and copy-number variants, including the regulatory, non-coding variation that WES misses; it is the more comprehensive but more expensive choice. Both have supplanted the older linkage and candidate-gene strategies for gene discovery (Kaplan & Sadock 2024).

■ RULE **The architecture dictates the tool.** Rare large-effect variants are found by sequencing and sit near a targeted therapy; common small-effect variants are found by GWAS, summed as a PRS, and are nowhere near a molecular cure.

6.2 Rare-variant burden testing

Counting damaging variants against chance. Because any single rare variant is, by definition, seen in too few people to reach significance on its own, the analytic trick is the **rare-variant**

burden test: aggregate all rare (minor allele frequency below 1%), predicted-damaging variants within a gene or gene-set and ask whether cases collectively carry a heavier burden than controls. This requires very large samples but has been productive, most famously the finding of an increased burden of ultra-rare protein-altering variants among people with schizophrenia (Genovese et al. 2016, in Wang et al. 2019). A key statistical companion is the **mutation-intolerance** metric: genes can be scored for how strongly they resist loss-of-function variation (the pLI score, probability of loss-of-function intolerance), so that a damaging variant landing in a highly intolerant gene is prioritised as likely pathogenic (Kaplan & Sadock 2024; Wang et al. 2019).

6.3 De novo mutations, autism, and the paternal-age effect

New mutations in the child, absent in the parents. A **de novo mutation** is one present in the affected proband but in neither biological parent, so it is discovered by sequencing parent-child **trios** (two parents plus affected child) or quads (adding an unaffected sibling) and filtering the child's variants against both parents (Wang et al. 2019). De novo variants are individually rare but tend to be more disruptive than inherited variants, which makes them a powerful route into sporadic disease. Their contribution is greatest in the early-onset neurodevelopmental disorders: penetrant de novo mutations are estimated to contribute to autism risk in roughly 11% of trio families, and of de novo loss-of-function variants in autism about 43% are estimated to be pathogenic (against about 13% of de novo missense variants) (Iossifov et al. 2014; Sanders et al. 2015, in Wang et al. 2019). Autism (ICD-11 6A02, DSM-5-TR autism spectrum disorder) and intellectual developmental disorders together dominate the de novo literature. **The paternal-age effect.** Because the male germline keeps dividing across the lifespan, the number of de novo point mutations transmitted rises steadily with paternal age; this is the molecular basis for the epidemiological association of advancing paternal age with schizophrenia and autism in offspring (Malaspina et al. 2001, in Wang et al. 2019). It is the mechanistic pearl that links a demographic risk factor to a class of variant.

6.4 Functional genomics: from a locus to a mechanism

Bridging the association gap. Most GWAS hits sit in non-coding regulatory DNA, so knowing the associated variant does not tell you which gene it acts on or how. Functional genomics is the toolkit that closes that gap. **eQTL** mapping (expression quantitative trait loci) identifies variants that predict the expression level of a gene, so a risk variant that is also an eQTL points to the gene whose dosage it alters (Kaplan & Sadock 2024). **TWAS** (transcriptome-wide association study) formalises this: it imputes genetically-predicted gene expression from eQTL reference data and tests that predicted expression against disease, moving the unit of association from an anonymous SNP to a named gene. **Chromatin conformation** methods, notably **Hi-C** (a chromosome-conformation-capture assay), reveal which physically distant regulatory regions loop into contact with a promoter, so a non-coding variant can be assigned to the gene it actually regulates in three dimensions (Kaplan & Sadock 2024). **Single-cell** RNA sequencing resolves which specific cell type expresses a risk gene, and **MPRA** (massively parallel reporter assay) tests

thousands of candidate regulatory variants at once for their effect on expression. Together these define the mechanistic chain: variant, regulatory element, target gene, cell type, pathway.

6.5 Cellular models: iPSC-derived neurons and brain organoids

Patient biology in a dish. The Nobel-winning discovery that adult somatic cells (skin fibroblasts, hair-follicle cells) can be reprogrammed into **induced pluripotent stem cells** (iPSCs) lets us build neurons that carry an individual patient's exact genetic background, then differentiate them into the neuronal and glial types relevant to the disorder (Yamanaka; New Oxford 2020). iPSC-derived neurons from lithium-responsive bipolar patients show hyperexcitability and dysregulated calcium signalling that lithium itself corrects, tying a clinical phenotype to a cellular one (New Oxford 2020). **Brain organoids** are self-organising three-dimensional cultures that histologically resemble developing human brain and model architecture and connectivity that flat cultures cannot (Kaplan & Sadock 2024; New Oxford 2020). These models are where a genetic finding is functionally validated, and, combined with **CRISPR**/Cas9 editing to introduce or reverse a candidate variant, they let one ask whether a specific mutation is causal for a cellular phenotype (New Oxford 2020).

6.6 Causal inference: Mendelian randomization

Genes as nature's randomised trial. Observational associations cannot distinguish cause from confounding or reverse causation. **Mendelian randomization** (MR) exploits the fact that alleles are randomly allocated at conception, so a genetic variant that raises an exposure (a putative risk factor) acts as an **instrumental variable** that is largely free of the confounding and reverse causation that plague conventional epidemiology (Kaplan & Sadock 2024). If the variant that raises the exposure also raises disease risk, that supports a causal path. The examinable psychiatric applications are instructive precisely because they cut both ways: two-sample MR has supported a causal influence of cannabis use liability on schizophrenia risk, whereas MR has failed to find that genetically-predicted thyroid function causally influences major depression, and has not found that smoking heaviness causally influences anxiety or depression (Kaplan & Sadock 2024; New Oxford 2020). MR is now a standard way to interrogate whether an epidemiological correlate of psychiatric illness is cause or bystander.

6.7 Biobank-scale genetics

Scale as the enabling technology. The recurring lesson of psychiatric genetics is that discovery is sample-size limited, and the modern answer is the population **biobank**: cohorts of hundreds of thousands with linked genotype, deep phenotype, imaging, and health-record data. The **UK Biobank** (about 500,000 participants) has enabled analyses ranging from the medical consequences of pathogenic CNVs in adults to multimodal population brain imaging, and the US **All of Us** programme is explicitly building a more ancestrally diverse resource (Kaplan & Sadock 2024). Biobanks power the large GWAS, provide the replication samples for polygenic scores, and supply the instruments and outcomes for Mendelian randomization; they are the substrate on which the other methods run.

6.8 Polygenic scores as research tool and emerging stratifier

Summing thousands of tiny effects into one number. A **polygenic risk score** (PRS) sums an individual's risk alleles across the genome, each weighted by its GWAS effect size, into a single estimate of genetic liability (Kaplan & Sadock 2024). As a research tool it is well established: PRS quantifies SNP-based heritability, tests genetic overlap between disorders (a schizophrenia PRS also predicts bipolar liability), and positions categorical diagnosis at the tail of a continuous population liability. As a **clinical stratification** tool it remains emerging rather than deployed: current scores explain only a modest fraction of liability, so they shift population-level probabilities rather than diagnose individuals, and, critically, they are derived overwhelmingly from European-ancestry samples and therefore transport poorly to other ancestries, an equity limitation the standard text flags explicitly (Kaplan & Sadock 2024). The honest exam line: a research workhorse and a plausible future stratifier, not yet a clinical test.

6.9 Gene therapy: the monogenic-neurology precedent

Where molecular correction already works. Gene therapy has become real in single-gene neurological disease, which is the precedent examiners want you to cite. In **spinal muscular atrophy** (SMA), an autosomal-recessive motor-neuron disease caused by loss of *SMN1*, two mechanistically distinct approaches are licensed: **nusinersen**, an **antisense oligonucleotide** directed at the *SMN2* gene that modifies its splicing to raise functional SMN protein, given as a repeated intrathecal infusion; and a one-time gene-replacement therapy that uses an **AAV** (adeno-associated virus) vector to deliver a working copy of *SMN1* to motor neurons, raising SMN protein and improving survival (Kaplan & Sadock 2024). In **Huntington disease**, an autosomal-dominant expanded-CAG-repeat disorder, huntingtin-lowering antisense oligonucleotides reached human trials, the proof-of-concept that a defined, single-gene neuropsychiatric disorder is a tractable target even though efficacy results have been mixed. The general toolkit, then, is three-fold: **antisense oligonucleotides** that alter splicing or knock down a transcript, **AAV**-vector gene replacement, and **CRISPR**/Cas9 editing that introduces or reverses a mutation at the DNA level (New Oxford 2020; Kaplan & Sadock 2024).

6.10 Why polygenic psychiatry is not near gene therapy

Architecture forbids a single target. Every gene-therapy success above shares a feature the common psychiatric disorders lack: a single, known, large-effect causal gene. Schizophrenia, bipolar disorder, and major depression are polygenic, driven by thousands of common variants each of tiny effect (individual odds ratios typically below 1.3) plus a scatter of rare variants and heavy environmental contribution, so there is no one locus to edit or replace, and correcting any single variant would move risk negligibly (Kaplan & Sadock 2024). The realistic near-term yield of psychiatric genetics is therefore not a cure but mechanism, drug-target nomination (a GWAS gene as a pharmacological lead), risk stratification, and pharmacogenomics, not germline or somatic editing of a polygenic phenotype.

HOLD THIS

Gene therapy works for single-gene neurology, not polygenic psychiatry. Every precedent (spinal muscular atrophy, Huntington disease) has one large-effect causal gene; schizophrenia, bipolar disorder and depression have no single locus to edit or replace.

6.11 Sequencing versus array-GWAS: choosing the tool

A one-glance comparison. The following table is the examinable summary of which technology answers which question, the point being that no single platform does everything.

METHOD	VARIATION CAPTURED	BEST USE CASE	KEY LIMITATION
Array-GWAS	Common SNPs (chip content)	Common small-effect risk loci, PRS, heritability	**Blind to rare and novel variants; misses de novo**
Whole-exome sequencing	Coding variants (about 1.5 to 3% of genome)	Rare gene-disrupting and de novo coding variants	**Misses non-coding regulatory and most structural variation**
Whole-genome sequencing	All classes (SNV, indel, CNV, structural)	Comprehensive rare and regulatory variant discovery	**Highest cost; heavy interpretation burden for non-coding hits**
Trio de novo design	De novo variants absent in parents	Sporadic autism, intellectual disability, severe cases	**Needs parent samples; small yield outside neurodevelopmental disorders**

Discovery technologies mapped to the variant class each is built to find; the take-home is that architecture, common versus rare versus de novo, dictates the tool.

COMMON TRAP

Do not describe gene therapy as an emerging treatment for schizophrenia, bipolar disorder, or depression. The gene-therapy precedents (SMA, Huntington disease) are all single-gene disorders with a defined causal target; the common psychiatric disorders are polygenic with no such target, which is exactly why they are not near gene therapy. Equally, do not conflate WES and WGS: WES reads only the coding exome and misses non-coding and most structural variation, whereas WGS reads the whole genome.

COMMON TRAP

An eQTL, TWAS, or Mendelian-randomization result is not proof of a mechanism by itself; it is a prioritisation or a causal-inference signal that still needs functional validation (typically iPSC or organoid models plus CRISPR editing). Mendelian randomization in particular is only as good as its instrument: a variant with pleiotropic effects violates the core assumption and can produce a false causal claim.

PEARL

The paternal-age effect is the cleanest link between epidemiology and molecular genetics: the male germline keeps dividing, so older fathers transmit more de novo point mutations, which is the mechanistic explanation for advancing paternal age as a risk factor for schizophrenia and autism. If a stem asks why paternal (not maternal) age matters and why de novo variants are the currency, this is the answer.

MNEMONIC

SEQ-FM-CB-P: SEQuence it, work out the Function and Model it, infer Causality in a Biobank, then score the Polygene.

Walks the modern pipeline in order: sequencing (WES/WGS, de novo, burden) to find variants; functional genomics and cellular models (eQTL, TWAS, Hi-C, iPSC, organoids) to reach mechanism; causal inference (Mendelian randomization) and biobank scale to test and power it; polygenic scores as the summary output. Gene therapy sits outside this loop, reserved for the monogenic disorders.

INDIA

Two practical points for Indian practice. First, the ancestry bias of GWAS and polygenic scores is not abstract: scores trained on European-ancestry biobanks transport poorly to South Asian populations, so a PRS quoted in the literature should not be applied clinically to Indian patients without ancestry-matched validation. Second, the gene-therapies discussed are extremely high-cost, single-gene neurology interventions; when counselling families about the common polygenic psychiatric disorders, the message is that management is pharmacological and psychosocial, framed in liability terms, with no genetic cure on the horizon, which also keeps counselling non-stigmatising.

GOOD TO REMEMBER

- **WES (whole-exome sequencing):** captures protein-coding genome, about 1.5 to 3%; good for rare gene-disrupting variants (Kaplan & Sadock 2024).
- **WGS (whole-genome sequencing):** reads all variant classes (SNV, indel, CNV, structural); more comprehensive, more expensive.
- **De novo mutation yield in autism:** penetrant de novo mutations contribute to about 11% of trio families; about 43% of de novo loss-of-function variants estimated pathogenic (about 13% of missense) (Iossifov et al. 2014; Sanders et al. 2015).
- **Detected DNM rate (predominantly whole-exome):** roughly 1.3 de novo mutations per individual across neuropsychiatric sequencing cohorts in denovo-db, a sequenced-exome yield and not the genome-wide new-mutation rate (Wang et al. 2019).
- **SETD1A:** loss-of-function variants implicated as a schizophrenia susceptibility gene (Takata et al. 2014).
- **Schizophrenia ultra-rare variant burden:** increased burden of ultra-rare protein-altering variants in schizophrenia (Genovese et al. 2016).
- **GWAS genome-wide significance threshold:** P = 5 x 10 to the minus 8 (Kaplan & Sadock 2024).
- **Common psychiatric risk alleles:** individual odds ratios typically below 1.3 (Kaplan & Sadock 2024).
- **UK Biobank:** about 500,000 participants with linked genotype, phenotype, imaging, and records; All of Us builds a more diverse US resource.
- **Nusinersen:** SMN2-directed antisense oligonucleotide (splice modifier) for spinal muscular atrophy, intrathecal (Kaplan & Sadock 2024).
- **SMA AAV gene replacement:** one-time AAV-vector delivery of a working SMN1 copy (Kaplan & Sadock 2024).
- **Huntingtin-lowering ASO:** antisense oligonucleotide against HTT reached human Huntington disease trials; efficacy mixed.
- **CRISPR/Cas9:** genome-editing tool to introduce or reverse disease-associated mutations, used experimentally with iPSC and organoid models (New Oxford 2020).
- **Cannabis and schizophrenia:** two-sample Mendelian randomization supports a causal influence of cannabis use liability on schizophrenia risk (Kaplan & Sadock 2024).

Mechanisms

7 · Epigenetics in psychiatry

The missing half of nature and nurture. Twin studies fix the heritability of schizophrenia near 81 percent and of bipolar disorder near 85 percent (Kaplan & Sadock 2024), yet common variants explain only a fraction of that liability, and monozygotic concordance for schizophrenia sits slightly below 50 percent. **Epigenetics** occupies exactly this gap: it is the molecular layer through which environment writes onto a fixed genome, and it is the single most examinable route by which stress, adversity, and development translate into altered gene expression without touching the DNA sequence.

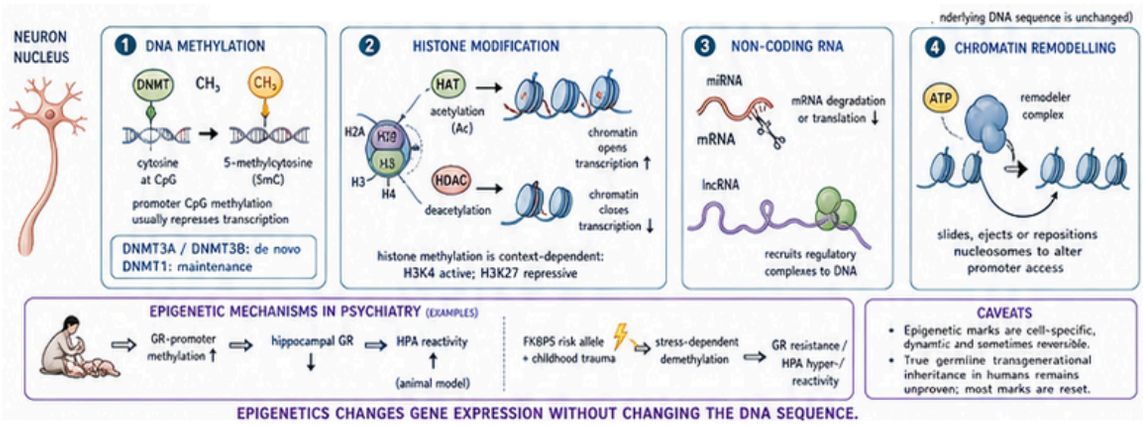
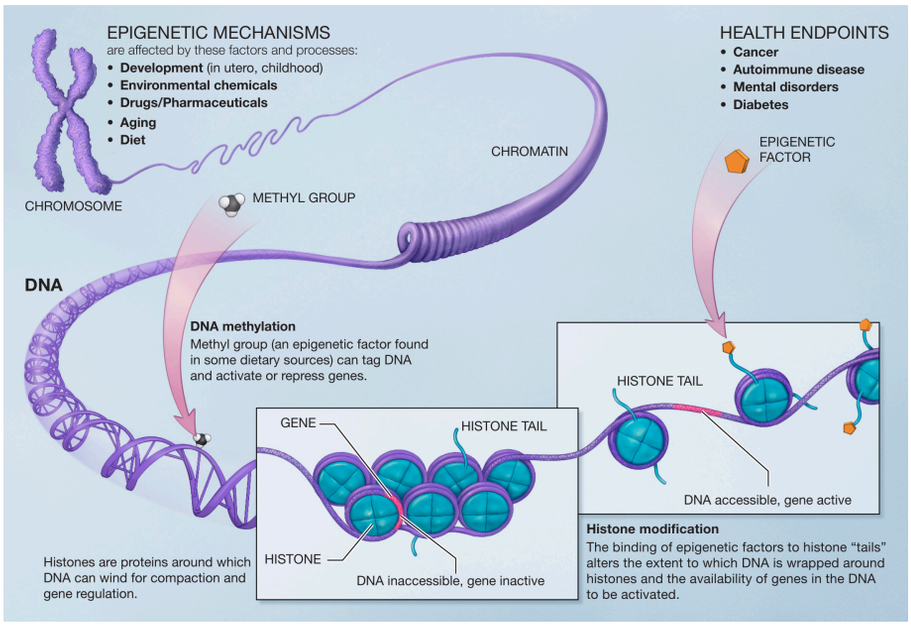


Fig 3.14 Epigenetics: same sequence, different expression.

For the exam, hold three anchors: a clean **definition**, the four **mechanisms** (DNA methylation, histone modification, non-coding RNA, chromatin remodelling), and the flagship human stories (genomic imprinting in Prader-Willi versus Angelman; maternal-care and glucocorticoid-receptor methylation; the FKBP5 gene-by-environment interaction in PTSD). Epigenetics is the substrate that makes gene-environment interaction mechanistic rather than statistical.



Epigenetic mechanisms: National Institutes of Health, public domain, via Wikimedia Commons

Fig 3.15 The two main epigenetic mechanisms, shown from chromosome to DNA. DNA methylation adds a methyl group that tags the sequence and tends to silence transcription without changing the letters of the code. Histone modification alters how tightly DNA is wound around the nucleosome: loosely wound DNA is accessible and its genes active, tightly wound DNA is inaccessible and silent. These marks are laid down by development, early-life environment, drugs, ageing and diet, which is how experience becomes a stable, sometimes heritable, change in gene expression.

7.1 Definition and why it matters

Waddington's term, sharpened. Conrad Waddington fused "genetics" and "epigenesis" in 1942; the working definition today is a stable, potentially heritable change in gene expression that

arises from a modification of the chromosome without any alteration of the underlying DNA sequence (Kaplan & Sadock 2024). The genetic code is one-dimensional, identical in every cell, and unmoved by environment. The epigenetic code is a dynamic three-dimensional layer of proteins and non-coding RNAs, unique to each cell type, and it changes rapidly in response to environmental cues. This is how one genome builds a neuron and a hepatocyte, and how a postmitotic neuron rewrites synaptic-plasticity genes after experience.

~81%	~85%	<50%
SCHIZOPHRENIA HERITABILITY	BIPOLAR DISORDER HERITABILITY	MZ CONCORDANCE, SCHIZOPHRENIA

7.2 DNA methylation and CpG islands

The most examined mechanism. DNA methyltransferases (DNMTs) transfer a methyl group to the 5 position of the cytosine ring at a CpG dinucleotide, generating 5-methylcytosine (Kaplan & Sadock 2024). CpG dinucleotides cluster at high density in **CpG islands** that mark the promoters of active housekeeping genes and are normally unmethylated; aberrant methylation of an island produces a highly repressive, often heritable, chromatin state (X-inactivation and imprinted genes are the classic examples). Methylation silences transcription two ways: it blocks a transcription factor from binding, or it recruits a methyl-binding protein (for example MeCP2) that pulls in HDAC-containing repressive complexes such as NuRD. Three DNMTs matter: DNMT3a and DNMT3b establish methylation de novo, while DNMT1 is the maintenance enzyme that copies the pattern onto the daughter strand at the replication fork, which is why methylation is heritable across mitosis.

7.3 Histone modification: the histone code

Acetylation opens, methylation reads either way. DNA is wound around a histone octamer (H2A, H2B, H3, H4) to form the nucleosome; the protruding N-terminal tails carry reversible marks that set chromatin accessibility (Kaplan & Sadock 2024). **Acetylation** neutralises positively charged lysines, loosens the histone-DNA grip, and activates transcription; histone acetyltransferases (HATs, for example CBP/p300) write it and histone deacetylases (HDACs) erase it. **Histone methylation** is context-dependent: H3K4, H3K36, and H3K79 methylation activate, whereas H3K9, H3K27, and H4K20 methylation repress. This combinatorial logic is the histone code, and it is the direct target of the therapeutic HDAC inhibitors discussed below.

RULE **Methylation silences, acetylation opens.** DNA methylation tends to repress transcription; histone acetylation loosens the histone-DNA grip and activates it, all without changing the base sequence.

7.4 Non-coding RNA and chromatin remodelling

The other two mechanisms. Small and long non-coding RNAs, including microRNAs (miRNAs), silence transcripts and guide chromatin-modifying complexes to specific loci; altered miRNA expression is reported across depression and psychosis, and, critically, miRNA in sperm has been implicated in transmitting the effects of early trauma to offspring (see 7.8). **ATP-dependent chromatin remodellers** (SWI/SNF and related families) hydrolyse ATP to slide, evict, or reposition nucleosomes, maintaining nucleosome-free regions at active promoters. These four

mechanisms do not act in isolation: methylation recruits histone modifiers, which recruit remodellers, forming the self-reinforcing cascades that make epigenetic states stable.

7.5 Genomic imprinting: Prader-Willi versus Angelman

The single best imprinting question in psychiatry. Genomic imprinting is parent-of-origin-specific gene expression established by methylation marks laid down in the germline. Prader-Willi and Angelman syndromes both arise from the same 15q11-q13 locus, and which syndrome results depends entirely on which parental copy is lost (Kaplan & Sadock 2024). Prader-Willi (ICD-11 LD90.3) follows loss of the paternally expressed genes (paternal deletion, or maternal uniparental disomy) and presents with neonatal hypotonia and failure to thrive giving way to hyperphagia, childhood obesity, hypogonadism, and mild intellectual disability. Angelman syndrome follows loss of maternal UBE3A function (maternal deletion, paternal disomy, or a maternal UBE3A mutation) and presents with severe intellectual disability, ataxia, seizures, and a characteristic happy, excitable demeanour.

FEATURE	PRADER-WILLI SYNDROME	ANGELMAN SYNDROME
Locus	15q11-q13	**15q11-q13 (same region)**
Parent-of-origin lesion	**Loss of paternal contribution**	**Loss of maternal UBE3A**
Usual mechanism	Paternal deletion or maternal uniparental disomy	Maternal deletion, paternal disomy, or maternal UBE3A mutation
Key genes	SNRPN, NDN, SNORD116 (paternally expressed)	**UBE3A (maternally expressed)**
Core phenotype	Hypotonia then hyperphagia, obesity, hypogonadism, mild ID	Severe ID, ataxia, seizures, inappropriate laughter
Feeding history	**Failure to thrive, then insatiable appetite**	Not the defining feature

Same 15q11-q13 locus, opposite parental origin: the archetypal demonstration that methylation, not sequence, decides the phenotype.

7.6 Early-life programming: maternal care and the glucocorticoid receptor

The Meaney model. In rodents, high maternal licking-and-grooming during the first postnatal week produces adult offspring with reduced methylation at the hippocampal glucocorticoid-receptor promoter, higher GR expression, and a better-regulated, less reactive stress axis; low-care offspring show the opposite pattern (Meaney and Szyf, summarised in Kaplan & Sadock 2024). The mark is developmentally programmed yet pharmacologically reversible: HDAC inhibitors demethylate and raise GR, while intracerebral methionine (a methyl donor) re-methylates the promoter and increases stress reactivity in adults. This is the paradigm case of behaviour writing a stable epigenetic mark on a stress-axis gene.

7.7 Childhood adversity, FKBP5, and the human translation

From rat brain to human suicide brain. Postmortem hippocampus from suicide decedents with documented childhood abuse shows increased methylation at the GR promoter and reduced GR

expression, mirroring the low-care rat (McGowan and colleagues, in Kaplan & Sadock 2024). The mechanistically richest human example is **FKBP5**, a co-chaperone that restrains the glucocorticoid receptor. The rs1360780 risk allele permits stronger stress-induced FKBP5 induction; in carriers, childhood trauma drives demethylation of a functional glucocorticoid-response element, locking in a GR-resistant, hyper-reactive HPA phenotype and raising PTSD and depression risk in a dose-dependent way (Klengel et al. 2013). This is gene-by-environment interaction made molecular: the genotype sets susceptibility, early trauma supplies the epigenetic hit, and only the combination produces disorder.

HOLD THIS

Methylation is the molecular bridge from environment to gene expression. FKBP5 is the flagship: the rs1360780 risk allele plus childhood trauma demethylates a glucocorticoid-response element, locking in a GR-resistant, hyper-reactive HPA phenotype and raising PTSD and depression risk (Klengel 2013).

7.8 Transgenerational epigenetic inheritance (state the caveat)

Real signals, contested mechanism. Human observational data are suggestive: prenatal exposure during the Dutch Hunger Winter of 1944 to 1945 was associated, six decades later, with reduced methylation of the imprinted IGF2 gene, specific to periconceptional timing (Heijmans et al. 2008); offspring of Holocaust survivors show altered FKBP5 methylation and cortisol (Yehuda et al. 2016). Animal work is stronger: odour fear-conditioning before conception transmits behavioural and sperm-methylation changes across two generations, and injecting sperm RNA from stressed males into naive oocytes reproduces the offspring phenotype (Gapp et al. 2014). The caveat to state explicitly in any answer: true germline transgenerational inheritance in humans remains unproven, because most marks are erased at two global demethylation waves (gametogenesis and post-fertilisation), and confounding by shared environment, in-utero exposure, and maternal effects is very hard to exclude.

TRAP Do not overclaim epigenetic heredity: true germline transgenerational inheritance in humans remains unproven, because marks are largely reset at two demethylation waves.

7.9 Epigenetic clocks and accelerated biological ageing

A quantifiable biomarker. **Epigenetic clocks** estimate chronological age from DNA-methylation levels at a defined panel of CpG sites with high accuracy (Horvath 2013). When methylation age runs ahead of calendar age the excess is termed epigenetic age acceleration, and it is reported in severe mental illness, in trauma exposure, and with adverse environmental exposures such as tobacco smoke. The appeal for psychiatry is practical: methylation is a stable analyte measurable from a very small number of cells, which is exactly the property a field with no validated diagnostic biomarker needs; SKA2 methylation as a candidate predictor of suicidal behaviour is discussed in this same K&S chapter as an example of the biomarker promise.

7.10 Therapeutic angle: HDAC inhibitors and epigenetic editing

Drugs that move the marks. Several established agents act epigenetically. **Valproate** is a class I HDAC inhibitor in addition to its ion-channel and GABAergic actions, which is one proposed

contributor to its mood-stabilising and neuroprotective profile (Stahl 2021); this HDAC-inhibitory activity also underlies its recognised teratogenicity. In schizophrenia models, DNMT inhibitors raise the reduced reelin expression, and chronic clozapine downregulates the mGlu2 receptor via increased HDAC2 binding at its promoter, showing that antipsychotics themselves reshape the histone landscape (Kurita et al., in Kaplan & Sadock 2024). On the horizon, dCas9-based epigenetic editing can add or remove methylation at a chosen locus without cutting DNA, and the Prader-Willi work in which G9A histone-methyltransferase inhibitors (UNC0638, UNC0642) partially reactivated the silenced maternal locus in mice is a proof of concept for locus-specific epigenetic therapy (Kaplan & Sadock 2024).

COMMON TRAP

Do not conflate epigenetic reprogramming with mutation: DNA methylation and histone marks leave the base sequence untouched and Watson-Crick pairing intact. And do not overclaim heredity: acetylation and methylation are reversible and mostly reset in the germline, so "epigenetic inheritance" in humans is far weaker than the popular framing suggests.

PEARL

The one-line integration to give an examiner: methylation is the "molecular bridge" between the genetic code and the environment, converting a statistical gene-by-environment interaction (for example the FKBP5 risk allele plus childhood trauma) into a concrete, measurable, and in principle reversible change in gene expression.

MNEMONIC

MHNC = "My Histones Need Care"

The four epigenetic mechanisms: **M**ethylation of DNA, **H**istone modification, **N**on-coding RNA, **C**hromatin remodelling.

GOOD TO REMEMBER

- **Schizophrenia heritability:** near 81 percent (K&S 2024); MZ concordance slightly below 50 percent.
- **Bipolar disorder heritability:** near 85 percent (K&S 2024).
- **15q11-q13:** shared locus for Prader-Willi (paternal loss) and Angelman (maternal UBE3A loss).
- **Prader-Willi prevalence:** roughly 1 in 15,000 to 30,000; ICD-11 LD90.3.
- **UBE3A:** maternally expressed gene; its loss of function causes Angelman syndrome.
- **SNRPN / SNORD116 / NDN:** paternally expressed 15q11-q13 genes lost in Prader-Willi.
- **MeCP2:** methyl-CpG-binding protein; X-linked mutation causes Rett syndrome.
- **DNMT1:** maintenance methyltransferase (heritability across mitosis); DNMT3a and DNMT3b establish methylation de novo.
- **FKBP5 rs1360780:** risk allele plus childhood trauma leads to GRE demethylation, GR resistance, higher PTSD and depression risk (Klengel et al. 2013).
- **IGF2:** imprinted gene hypomethylated after periconceptional Dutch Hunger Winter exposure (Heijmans et al. 2008).
- **Glucocorticoid-receptor (NR3C1) promoter:** methylation increased by low maternal care in rats (Meaney) and by childhood abuse in human suicide brains (McGowan).
- **Horvath clock (2013):** DNA-methylation estimator of biological age; acceleration reported in severe mental illness.
- **Valproate:** class I HDAC inhibitor (Stahl 2021); links to mood stabilisation and to teratogenicity.
- **Gapp et al. 2014:** sperm-RNA-mediated transgenerational transmission of early-life trauma effects in mice.

8 · Endophenotypes and genetic markers

Why this matters. The heritability of a disorder like schizophrenia is high (60 to 80% from twin studies), yet the road from the genome to the diagnostic checklist is long and noisy. A DSM or ICD label is a **categorical**, subjectively rated, heterogeneous endpoint: two patients carrying the same diagnosis may share almost no symptoms, and unaffected relatives who carry risk alleles score as unaffected. The **endophenotype** strategy was designed to shorten that road, by mapping genes to heritable, quantitative, biologically simpler intermediate traits that sit inside the genotype-to-phenotype pathway rather than at its clinical terminus (Kaplan and Sadock 2024). The examiner wants two things: the Gottesman and Gould (2003) criteria that define a valid endophenotype, and a working list of the named neurophysiological and neurocognitive endophenotypes of schizophrenia with the criteria they satisfy.

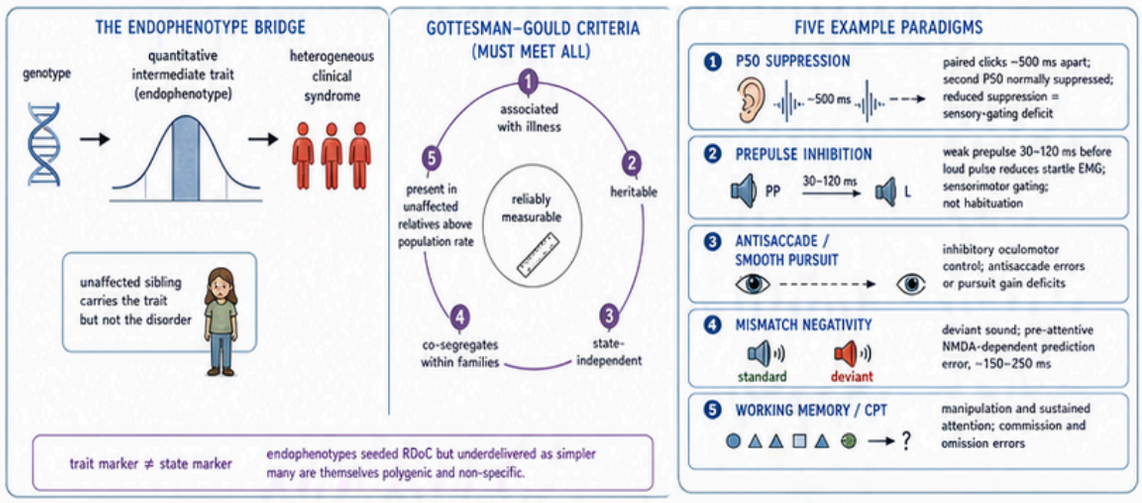


Fig 3.16 Endophenotypes: between gene and syndrome.

The concept also carries a cautionary coda you must deliver: after two decades, endophenotypes have **underdelivered**. A key meta-analysis (Flint and Munafo 2007) concluded that currently identified psychiatric endophenotypes are not superior to conventional phenotypic disease definitions for gene finding, because the endophenotype often turned out to be no simpler genetically, and no more heritable, than the disorder it was meant to decompose (New Oxford Textbook of Psychiatry). Anchor the answer in the named markers (P50, prepulse inhibition, mismatch negativity, antisaccade, working memory) and in the Research Domain Criteria (RDoC) framework that inherited the endophenotype logic.

8.1 The rationale: closing the genotype-to-phenotype gap

The problem. Psychiatric gene mapping relied for decades on categorical diagnoses, and this is argued to be one of the chief obstacles to progress: diagnosis rests on subjective clinical evaluation, and the menu-based classification means two people with the same disorder can display largely non-overlapping symptom sets, likely reflecting distinct underlying causes (Kaplan and Sadock 2024).

The proposed fix. Map **quantitative traits** hypothesised to lie between the genes and the disorder, and that may be simpler to map genetically. Gottesman and Shields imported the term "endophenotype" into schizophrenia research, and Gottesman and Gould (2003) formalised it; the application of these traits to gene finding is now called **deep phenotyping**. Because an endophenotype is "closer to genes" than a diagnostic category, it is expected to carry more power in gene-mapping studies. For a disorder with about 1% prevalence and 60 to 80% heritability, analysing a quantitative endophenotype has been estimated to be roughly 100-fold more efficient than analysing the categorical diagnosis, translating to about a 10-fold increase in statistical power (Greenwood et al. 2019).

8.2 Terminology: endophenotype, intermediate phenotype, biomarker

Endophenotype

A heritable, quantitative trait on the pathway between genotype and clinical phenotype; internal (not visible to the naked eye), measured by biochemical, neurophysiological, neuropsychological or neuroimaging methods (Gottesman and Gould 2003).

Intermediate phenotype

Used interchangeably with endophenotype in Kaplan and Sadock and the New Oxford Textbook; strictly, some authors reserve "intermediate phenotype" for any trait between gene and disease without requiring familial co-segregation.

Biomarker

Any measurable indicator of a biological state; broader than endophenotype, which additionally requires heritability and a specified relation to illness in families. A state marker tracks the active illness; a trait marker (the endophenotype ideal) persists in remission.

Trait vs state

The state-independence criterion is exactly what separates an endophenotype (trait marker, present whether or not the person is currently ill) from a state marker (present only during the episode).

8.2b The Gottesman and Gould (2003) criteria

The five criteria. A candidate must satisfy the following to qualify as a useful endophenotype (Gottesman and Gould 2003; Kaplan and Sadock 2024). These are the load-bearing list for a viva.

MNEMONIC

A HERD Co-segregates

Associated with illness in the population; **HER**itable; state-independent (the "unchanging" trait, here folded under HERD as the stable trait); **D**etectable in unaffected relatives at higher rates than the general population; and it **Co-segregates** with the illness within families. Unpacked as five: (1) associated with the illness in the population, (2) heritable, (3) state-independent (present whether or not the illness is active, with good test-retest stability), (4) co-segregates with the illness within families, (5) found in non-affected family members at a higher rate than in the general population. A practical sixth requirement for gene finding is that it be reliably and objectively measurable.

Why relatives are the crux. Criteria 4 and 5 are what make an endophenotype worth the extra effort: an unaffected relative who carries the risk alleles but has not crossed the clinical threshold still shows the trait, so the trait indexes latent genetic liability rather than the illness or its treatment. This is why endophenotype studies are typically family-based and enriched for genetic loading (Greenwood et al. 2019).

RULE **The family criteria are what make an endophenotype worth the effort.** Beyond heritable and state-independent, it must co-segregate with illness in families and appear in unaffected relatives above the population rate, so it indexes latent liability rather than the illness or its treatment.

8.3 Sensory gating: P50 suppression

The paradigm. P50 is an early positive component of the auditory event-related potential recorded at the vertex about 50 ms after a click. In the paired-click paradigm, two identical clicks are presented about 500 ms apart; in healthy subjects the P50 to the second click is markedly

attenuated relative to the first. This suppression is a measure of **sensory gating**, the brain's ability to suppress its response to repeated, irrelevant stimuli. People with schizophrenia show less P50 suppression, interpreted as a failure of inhibitory gating (Tasman 2015).

TRAP Do not call an endophenotype "just a biomarker" or "an early symptom": a state marker present only in the acute episode is disqualified by the state-independence criterion.

Genetic anchor. A linkage of the sensory-gating deficit to the alpha-7 nicotinic acetylcholine receptor gene (CHRNA7) on chromosome 15q13-14 has been reported, and nicotine transiently normalises the deficit (most antipsychotics, except possibly clozapine, do not). This makes P50 the prototypical schizophrenia endophenotype with a plausible molecular substrate (Tasman 2015). The deficit persists in medicated patients (state-independence) and occurs in unaffected relatives, but it is not specific to schizophrenia, appearing in other psychiatric and neurological conditions.

8.4 Sensorimotor gating: prepulse inhibition (PPI)

The paradigm. Prepulse inhibition is the normal reduction of the acoustic startle reflex (measured as eye-blink electromyography) when a weak prepulse precedes the startling pulse by roughly 30 to 120 ms. It indexes **sensorimotor gating** (it engages both a sensory stimulus and a motor reflex). PPI is reduced in schizophrenia relative to controls, and the deficit is relatively stable across time (Tasman 2015).

Meets the criteria. PPI deficits are present in unaffected relatives and are significantly heritable within schizophrenia families (about 45 to 50%); broad-sense heritability rises to about 47% in families with high genetic vulnerability versus about 29% when family history is not considered, so PPI behaves as a marker of risk rather than a consequence of illness (Greenwood et al. 2019). It is cross-species (measurable in rodents, where dopamine agonists like apomorphine disrupt it), which is why it is a favoured translational endophenotype for RDoC. Distinguish from P50: P50 is EEG-based habituation of an evoked potential; PPI is EMG-based reflex modulation and is not a form of habituation; the two are only weakly correlated.

8.5 Oculomotor markers: smooth pursuit and antisaccade

Smooth-pursuit eye movements. Impaired smooth-pursuit tracking of a moving target (with intrusive saccades) is one of the oldest and most replicated schizophrenia markers, present in patients and in a substantial fraction of their unaffected first-degree relatives, and a classic candidate endophenotype (New Oxford Textbook).

Antisaccade (AS). The subject must fixate a central target and, when a peripheral cue appears, look in the opposite direction; performance is the ratio of correct antisaccades to interpretable saccades. It is an electrophysiological measure of inhibitory failure. Schizophrenia patients show a large deficit (effect size about 1.0), the measure is stable, it is documented in first-degree relatives, and heritability is about 42 to 57% (Greenwood et al. 2019). A B-SNIP consortium GWAS of pursuit initiation and antisaccade error rate implicated genes in nuclear trafficking

(IPO8), axon guidance (PCDH12), nerve-signal transduction (NRSN1) and synaptic glutamate release (SH3GL2).

8.6 Auditory deviance: mismatch negativity (MMN)

The paradigm. Mismatch negativity is the ERP component elicited when an infrequent "deviant" auditory stimulus interrupts a train of "standard" stimuli; it is the difference waveform (deviant minus standard) peaking about 150 to 250 ms after the deviant, and, like PPI, it is preattentive (elicited whether or not the subject attends). Reduced MMN amplitude is one of the most robust findings in schizophrenia, with a large effect size of about 1.0 that is largely unaffected by medication and stable across symptom fluctuations (Greenwood et al. 2019).

Meets the criteria and predicts onset. MMN is about 68% heritable and is present in individuals at genetic risk; reduced MMN has shown promise for predicting transition to psychosis in clinical high-risk cohorts, giving it a prognostic edge over most other markers. It reflects NMDA-receptor-dependent auditory prediction-error, tying it to the glutamate hypothesis (Greenwood et al. 2019).

8.7 Neurocognitive endophenotypes: working memory and attention

Working memory (letter-number sequencing, LNS). A Wechsler Memory Scale subtest requiring the subject to reorder an intermixed string of letters and numbers; it taps verbal working memory with manipulation. Schizophrenia patients and their relatives show persistent deficits; the LNS is highly heritable (about 39% individually) and ranks well for stability and effect size, making working memory a core neurocognitive endophenotype (Greenwood et al. 2019). Working-memory deficits also serve as an endophenotype in ADHD.

Sustained attention (continuous performance test, CPT). Attention deficits date to Bleuler's original descriptions. CPTs (degraded-stimulus DS-CPT, identical-pairs CPT-IP) measure vigilance; patients show large deficits (mean effect size about 1.18), typically unaffected by psychotropics and stable over time. Deficits are reliably present in unaffected relatives, with heritability about 39 to 49% in healthy families and about 38 to 79% in schizophrenia families (Greenwood et al. 2019). General cognitive ability itself is genetically anticorrelated with schizophrenia (COGENT reported a genetic correlation of about minus 0.17).

8.8 Endophenotypes beyond schizophrenia and the imaging tier

Mood and other disorders. In major depression, endophenotypes include heightened processing of negative stimuli, executive and memory deficits, and abnormal prefrontal-amygdala activation on fMRI; the New Oxford Textbook notes their use to reduce the heterogeneity of depression. In bipolar disorder, candidate endophenotypes include cognitive deficits (executive function, attention), altered P300, and structural amygdala and prefrontal changes. In ADHD, response inhibition, working memory and reduced P300 are studied; in ASD, social-cognition and sensory-processing deficits; in OCD, impaired cognitive flexibility and response inhibition with orbitofrontal-striatal hyperactivity (New Oxford Textbook). An impulsivity endophenotype has been proposed as a marker of vulnerability to stimulant addiction (New Oxford Textbook).

Imaging and RDoC. Structural and functional MRI measures (hippocampal volume reduction, prefrontal activation, connectivity) are treated as imaging endophenotypes or "imaging intermediate phenotypes." The endophenotype logic was explicitly adopted by the NIMH **Research Domain Criteria** (RDoC), which takes objectively measurable, dimensional constructs across units of analysis (from genes to circuits to behaviour) as its starting point, on the assumption that specific neural systems underlie specific behavioural dimensions cutting across DSM categories (Tasman 2015).

ENDOPHENOTYPE	DOMAIN / MEASURE	SZ EFFECT (APPROX)	HERITABILITY	IN RELATIVES	STATE-INDEPENDENT
P50 suppression	Sensory gating (auditory ERP, paired click)	Reduced suppression	**Heritable; linked to CHRNA7 (15q13-14)**	**Yes**	Yes (persists on medication)
Prepulse inhibition (PPI)	Sensorimotor gating (startle EMG)	Reduced PPI	**about 45 to 50%**	**Yes**	Yes (stable over time)
Mismatch negativity (MMN)	Preattentive auditory deviance (ERP)	Reduced amplitude, d about 1.0	**about 68%**	**Yes (at-risk carriers)**	Yes (medication-independent)
Antisaccade (AS)	Oculomotor inhibition	Reduced correct ratio, d about 1.0	**about 42 to 57%**	**Yes (first-degree)**	Yes (stable)
Smooth-pursuit	Oculomotor tracking	Impaired pursuit, intrusive saccades	Heritable (classic marker)	**Yes (first-degree)**	Yes
Letter-number sequencing (LNS)	Verbal working memory	Reduced score	**about 39%**	**Yes**	Yes (persistent)
Continuous performance test (CPT)	Sustained attention	Reduced, d about 1.18	**about 39 to 79% (SZ families)**	**Yes**	Yes (psychotropic-independent)

Named schizophrenia endophenotypes mapped against the Gottesman and Gould (2003) criteria: heritable, present in unaffected relatives above population rate, and state-independent. Effect sizes and heritabilities from the PMC review of SZ endophenotypes (Greenwood et al. 2019) and Tasman 2015.

8.9 The genes behind the endophenotypes: a glutamate and neuregulin network

Convergence on a pathway. The Consortium on the Genetics of Schizophrenia (COGS) genotyped candidate genes against these endophenotypes and found 71 SNP-endophenotype associations across 28 genes, with 8 genes showing pleiotropic association across multiple endophenotypes: CTNNA2, ERBB4, GRID2, GRIK3, GRIK4, NOS1AP, NRG1 and RELN (Greenwood et al. 2019). Independent GWAS of schizophrenia diagnosis and of neurocognitive endophenotypes implicated an overlapping set (ATXN7, CSMD1, DRD2, GRIN2A, GRIN3A, GRM3), and rare-variant burden fell on GRIN1, GRIN3A and SLC1A2 (Singh et al. 2022). The

network converges on **glutamatergic neurotransmission and synaptic plasticity**, consistent with the glutamate (NMDA-hypofunction) hypothesis and with NRG1-ErbB4 signalling.

Largest single endophenotype GWAS. The largest GWAS of PPI to date (LOGOS) identified and replicated common variants in NGF and CALN1 at genome-wide significance, and higher schizophrenia polygenic risk was associated with worse PPI, tying the endophenotype back to the polygenic architecture of the disorder (Greenwood et al. 2019).

8.10 Why endophenotypes underdelivered

The core disappointment. The founding promise was that an endophenotype would be genetically simpler than the disorder, controlled by fewer genes of larger effect and therefore easier to map. This largely did not hold: most psychiatric endophenotypes turned out to be about as polygenic and often no more heritable than the disorders themselves, so the expected gain in gene-finding power failed to materialise. A meta-analysis by Flint and Munafo (2007) concluded that identified endophenotypes are not superior to conventional phenotypic disease definitions for this purpose (New Oxford Textbook). The LOGOS PPI result (many small-effect loci) exemplifies the polygenicity even at the endophenotype level (Greenwood et al. 2019).

Other limits. Endophenotypes are effortful and expensive to assess, reducing achievable sample sizes just when large samples turned out to be the decisive ingredient in psychiatric gene finding. Many candidate markers (P50, PPI, MMN) are also non-specific, appearing across schizophrenia, bipolar disorder and other conditions, so a positive marker does not cleanly index one disorder. The field's response has been to fold the endophenotype logic into dimensional frameworks (RDoC) and into biobank-scale studies rather than to expect single traits to crack the genetic architecture alone (New Oxford Textbook; Tasman 2015).

HOLD THIS

The endophenotype bet mostly lost: the intermediate trait was usually just as polygenic as the diagnosis. Flint and Munafo (2007) found identified endophenotypes are not superior to conventional disease definitions for gene finding; the enduring legacies are the five Gottesman-Gould criteria and the dimensional RDoC framework.

CLINICAL ANCHOR

None of these markers is a clinical test. There is no validated blood, ERP or eye-tracking assay that diagnoses schizophrenia or predicts it in an individual patient; they operate at the group level and index latent liability, not diagnosis. Their real clinical relevance is conceptual: they explain why an unaffected sibling of a patient with schizophrenia can carry measurable neurophysiological "soft signs" of the illness without being ill, and they underpin high-risk research (reduced MMN as a candidate psychosis-transition predictor).

COMMON TRAP

Do not describe an endophenotype as merely "a biomarker" or "an early symptom." The distinguishing features an examiner is listening for are heritability and the family criteria: present in unaffected relatives above the population rate, and co-segregating with illness in families. A marker that appears only during the acute episode (a state marker) is explicitly disqualified by the state-independence criterion. Also do not overclaim: the honest examination answer states that endophenotypes have underdelivered as gene-finding shortcuts (Flint and Munafo 2007).

INDIA

Endophenotype paradigms (P50, PPI, MMN, antisaccade, CPT) are relatively low-cost, equipment-based and culture-fair compared with lengthy neuropsychological batteries, which suits high-risk and first-episode research in Indian academic settings where large biobank-scale GWAS infrastructure is limited. The specificity and underdelivery caveats apply identically: these remain research tools, not diagnostic assays for clinical use.

PEARL

The endophenotype was a bet that the trait between gene and diagnosis would be genetically simpler than the diagnosis. The bet mostly lost: the intermediate trait was usually just as polygenic. The enduring legacies are conceptual, not methodological, the five Gottesman and Gould criteria as a rigorous definition of a heritable trait marker, and RDoC as the dimensional framework that absorbed the idea.

GOOD TO REMEMBER

- **Gottesman and Gould (2003):** five endophenotype criteria: associated with illness in the population; heritable; state-independent; co-segregates within families; found in unaffected relatives above the general-population rate (plus reliably measurable).
- **Efficiency claim:** for a disorder with about 1% prevalence and 60 to 80% heritability, a quantitative endophenotype is about 100-fold more efficient than the categorical diagnosis (about 10-fold power gain).
- **P50 suppression:** auditory ERP paired-click sensory gating; deficit linked to CHRNA7 (alpha-7 nicotinic receptor, chromosome 15q13-14); normalised transiently by nicotine, not by most antipsychotics.
- **Prepulse inhibition (PPI):** startle sensorimotor gating; heritability about 45 to 50% (about 47% in high-vulnerability families vs about 29% otherwise); cross-species; largest GWAS (LOGOS) implicated NGF and CALN1.
- **Mismatch negativity (MMN):** preattentive auditory-deviance ERP; effect size about 1.0; heritability about 68%; NMDA-dependent; candidate predictor of psychosis transition.
- **Antisaccade:** oculomotor inhibition; effect size about 1.0; heritability about 42 to 57%; B-SNIP GWAS implicated IPO8, PCDH12, NRSN1, SH3GL2.
- **Smooth-pursuit eye movements:** classic, highly replicated schizophrenia marker; deficits in first-degree relatives.
- **Letter-number sequencing (working memory):** heritability about 39%; deficits in patients and relatives.
- **Continuous performance test (sustained attention):** effect size about 1.18; heritability about 39 to 79% in schizophrenia families.
- **COGS pleiotropic gene set (8 genes across endophenotypes):** CTNNA2, ERBB4, GRID2, GRIK3, GRIK4, NOS1AP, NRG1, RELN; network converges on glutamate and NRG1-ErbB4 signalling.
- **Diagnosis-overlap GWAS genes:** DRD2, GRIN2A, GRIN3A, GRM3, ATXN7, CSMD1; rare-variant burden in GRIN1, GRIN3A, SLC1A2.
- **Underdelivery (Flint and Munafo 2007):** identified psychiatric endophenotypes are not superior to conventional phenotypic disease definitions for gene finding; most are as polygenic as the disorder.
- **RDoC:** NIMH Research Domain Criteria adopted the endophenotype logic as dimensional, cross-diagnostic constructs measurable from genes to circuits to behaviour.

9 · Neurodevelopmental genetics and cross-disorder pleiotropy

This is the topic that reframes everything else in these notes. Heritability and GWAS tell you *how much* of the risk is genetic; this topic tells you *how* that risk is enacted, and the answer is through **neurodevelopment**. Psychiatric risk genes are not scattered at random across the genome or across the lifespan: they cluster in genes that build and prune synapses, remodel chromatin, and regulate transcription, and their protein products are most active in the prenatal and early postnatal brain. Hold that single idea, that genetic liability is a developmental programme gone slightly awry, and both the **neurodevelopmental hypothesis** of schizophrenia and the modern picture of autism as a disorder of fetal cortical wiring fall out of the same logic (Owen et al., New Oxford Textbook 2020).

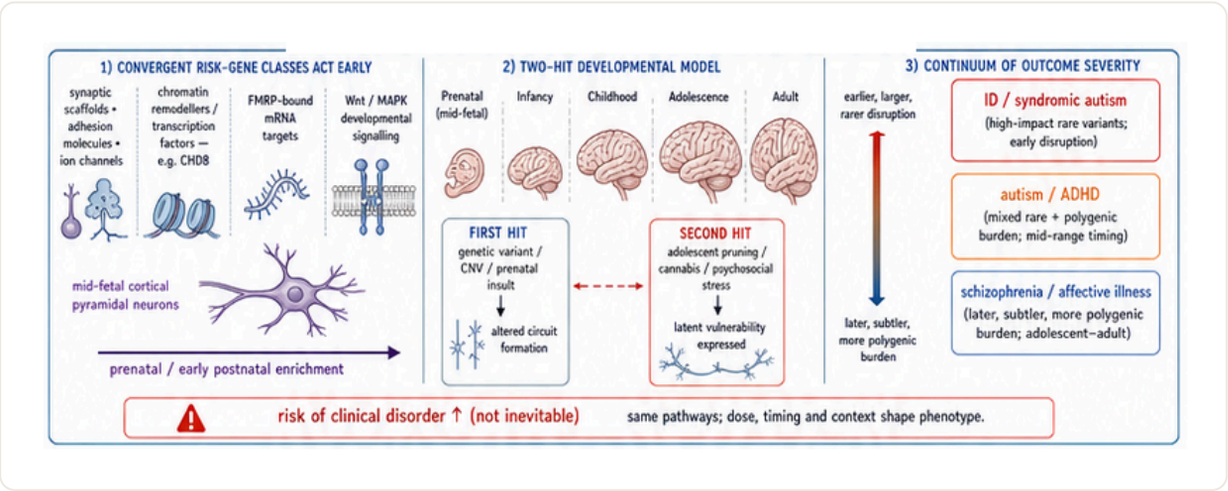


Fig 3.17 Genetic risk builds a developmental brain.

Exam framing. The second half of this topic is where the field has moved fastest and where examiners now probe: **cross-disorder pleiotropy**. Common-variant risk does not respect diagnostic borders. The same alleles push liability across schizophrenia, bipolar disorder, depression, ADHD and autism, producing high **genetic overlap** and a possible **p-factor**, a general dimension of psychopathology. This is the genetic engine behind the categorical-versus-dimensional debate, so learn the two halves, the neurodevelopmental mechanism and the cross-disorder architecture, as one argument: shared developmental genes give shared disorders. Cross-reference the novel-approaches topic for de novo mutation detection and the polygenic risk score material.

9.1 The neurodevelopmental model: genetic risk is a developmental lesion, not an adult one

The **neurodevelopmental hypothesis** holds that the genetic and early-environmental liability to major psychiatric disorders acts on the developing brain long before symptoms appear, leaving a static or slowly evolving vulnerability that is later unmasked by maturation and stress (Kaplan & Sadock 2024). Schizophrenia is the paradigm: the same children who later develop psychosis show, on average, an excess of minor neurodevelopmental abnormalities, delayed milestones, and neurological soft signs years before onset, and the risk-conferring biology is expressed in fetal and perinatal life. The corollary that examiners love is that adult-onset disorders are increasingly reconceptualised as having identifiable prodromal and subclinical childhood manifestations, so the "adult" and "developmental" categories are a continuum in time, not a dichotomy (Kaplan & Sadock 2024).

Two-hit framing. The **two-hit model** gives the mechanism a shape: a first hit (a genetic variant, or an early insult such as a copy number variant, obstetric complication or prenatal infection) primes the developing circuit, and a second hit (adolescent synaptic pruning, cannabis, psychosocial stress) is required to convert latent vulnerability into overt illness. Adolescence matters because it is the period of steep synaptic elimination in association cortex, precisely the process implicated by the risk genes below.

RULE **Genetic risk is enacted through neurodevelopment, not an adult lesion.** Risk genes cluster in synapse, chromatin and transcription and are most active in the prenatal and early postnatal brain; a first hit primes the circuit and a second (pruning, cannabis, stress) unmasks it.

9.2 What the risk genes actually do: synapse, chromatin and FMRP-target enrichment

The single most important empirical fact of modern psychiatric genetics is that risk genes are not random: gene-set enrichment analyses converge on a small number of neurodevelopmental biological processes (Owen et al., New Oxford Textbook 2020). Autism risk genes discovered by whole-exome sequencing illustrate this convergence best, because rare disruptive variants point to individual genes.

Synaptic function

Risk genes encode postsynaptic scaffolding proteins, cell-adhesion molecules and ion channels at excitatory synapses. Convergence on *synapse formation and function* is the dominant theme across autism, schizophrenia and intellectual disability.

Chromatin remodelling and transcriptional regulation

A large fraction of high-confidence autism genes are chromatin remodellers and transcription factors (the prototype is *CHD8*). These are master regulators: disrupting one perturbs the expression of hundreds of downstream neurodevelopmental genes.

FMRP targets

Autism and schizophrenia risk genes are significantly enriched for messenger RNAs bound by the **fragile X mental retardation protein (FMRP)**, the translational repressor lost in fragile X syndrome. This links idiopathic (non-syndromic) disorder back to a monogenic model of synaptic protein dysregulation.

Wnt and MAPK signalling

Additional convergent developmental pathways governing neuronal proliferation, migration and differentiation.

Spatiotemporal signature. Beyond *what* the genes do, *when and where* they act is diagnostic. Autism risk genes are preferentially expressed in **cortical pyramidal (glutamatergic projection) neurons during mid-fetal development** (Owen et al., New Oxford Textbook 2020). This prenatal, cortical, excitatory-neuron signature is the molecular fingerprint of a neurodevelopmental disorder and is exactly why the illness is framed as a wiring problem laid down before birth.

TRAP A low common-variant genetic correlation (schizophrenia-autism 0.16) can coexist with strong overlap at the rare-variant level (shared CNVs and de novo genes): the level of analysis changes the answer.

CLINICAL ANCHOR

The complement gene *C4* is the cleanest schizophrenia example of this developmental logic. C4 tags synapses for elimination by microglia; a common structural allele that raises C4 expression is associated with schizophrenia and is biologically plausible because *excessive synaptic pruning* in adolescence would thin association-cortex connectivity precisely when the disorder declares itself (Kaplan & Sadock 2024). One risk allele, one developmental process, one age of onset.

9.3 De novo mutations and the paternal-age effect

Where a disorder has high heritability yet a very large monozygotic-to-dizygotic concordance gap, **de novo mutations** (new variants present in the child but neither parent) are implicated as a constant source of rare, high-penetrance risk (Tasman 2015). They are the genetic reason a "highly heritable" disorder can appear sporadically in a family with no affected relatives.

The autism de novo story. Three groups simultaneously published exome scans of de novo variation in autism in 2012 (Kaplan & Sadock 2024). Likely-gene-disrupting de novo variants (nonsense, splice-site, frameshift) in brain-expressed genes carry large effects, and recurrent hits on the same gene across unrelated probands is what identifies high-confidence risk genes. Two exam-critical features:

- **Paternal origin, roughly 4:1.** De novo point mutations are overwhelmingly paternal in origin, in about a **4-to-1** ratio, because spermatogonia keep dividing throughout a man's life and accumulate replication errors (Kaplan & Sadock 2024).
- **Paternal-age effect.** De novo mutation load, and consequently offspring risk of autism and schizophrenia, rises with **advanced paternal age** (Tasman 2015). This is the mechanistic bridge between an epidemiological risk factor and molecular genetics, and a favourite single-best-answer link.

De novo CNVs. The recurrent 22q11.2 microdeletion was the first de novo copy number variant described in schizophrenia; genome-wide scans then showed de novo CNVs occur at higher rates in schizophrenia and autism than in controls, and that the genes they hit are enriched for neural and synaptic function (Tasman 2015). Because strong negative selection removes these variants from the population within a few generations, recurrent pathogenic CNVs must keep arising through independent de novo events.

9.4 The neurodevelopmental continuum: a severity gradient from ID to schizophrenia

The same genetic and biological machinery, dosed differently, appears to produce a graded family of conditions rather than discrete diseases. Intellectual disability, autism, ADHD and schizophrenia share risk factors and are increasingly viewed as points along a **neurodevelopmental continuum** or gradient of severity (Owen et al., New Oxford Textbook 2020).

Two lines of evidence anchor the gradient. First, *burden tracks severity*: large, damaging copy number variants and the most disruptive de novo variants are commonest in intellectual disability and syndromic autism, less common in higher-functioning autism, and rarer still in

schizophrenia and ADHD, where common-variant polygenic risk carries relatively more of the load. Second, the ADHD GWAS showed that common-variant risk for the clinical diagnosis is genetically continuous with population-wide cognitive and behavioural traits, supporting the view that a categorical diagnosis sits at the extreme tail of a continuously distributed liability in the general population (Kaplan & Sadock 2024).

PEARL

Read the gradient as a dial on two variables at once: **variant rarity/severity** and **developmental timing**. The earlier and more severe the developmental disruption, the more you see rare high-penetrance variants and the more the phenotype shifts toward intellectual disability and syndromic autism; the later and subtler the disruption, the more it is polygenic common-variant risk and the phenotype shifts toward ADHD, schizophrenia and affective illness. Same genes, different dose and timing.

9.5 Cross-disorder pleiotropy: shared common-variant risk and genetic correlations

Pleiotropy is the property of one gene, or one variant, influencing more than one trait or disorder. It is now regarded as a pervasive, not exceptional, feature of psychiatric genetics: a substantial fraction of the genetic influence on psychopathology transcends diagnostic boundaries (Smoller et al. 2019; Gandal & Geschwind 2021). Pleiotropy is measured at every level, from single loci up to genome-wide **genetic correlation** (the correlation between two disorders of the effect sizes of shared SNPs, estimated by methods such as LD score regression).

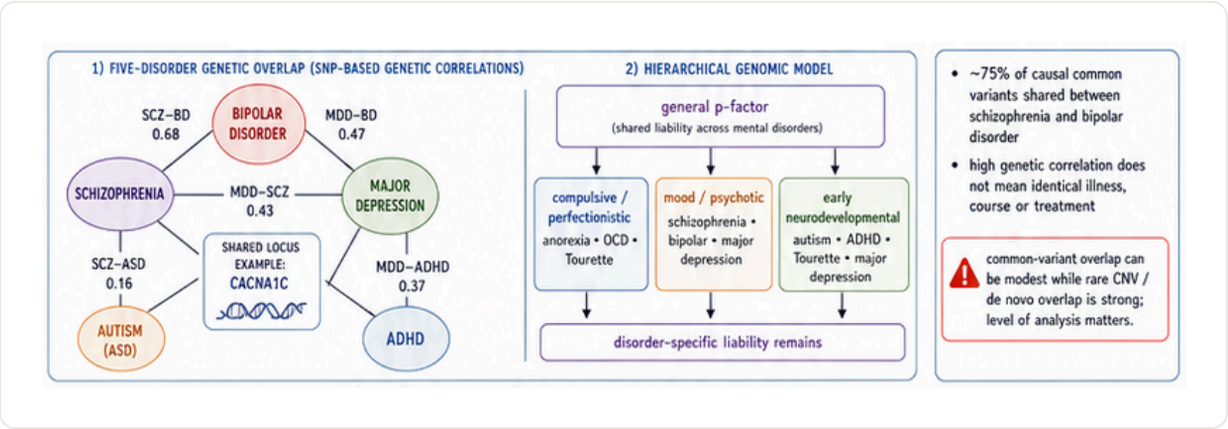


Fig 3.18 Pleiotropy: genetic risk crosses diagnostic borders.

The PGC cross-disorder analyses. The 2013 Cross-Disorder Group of the Psychiatric Genomics Consortium examined five disorders (autism, ADHD, bipolar disorder, major depression, schizophrenia) and found substantial **genetic overlap** (Cross-Disorder Group of the PGC 2013). The correlations were disorder-specific in magnitude, which is why the exact numbers are worth carrying, and they slot neatly onto the continuum from 9.4.

DISORDER PAIR	SNP-BASED GENETIC CORRELATION (RG)	READING
Schizophrenia and bipolar disorder	**0.68**	Highest pair; the two are largely a shared genetic liability
Major depression and bipolar disorder	0.47	Strong mood-axis overlap
Major depression and schizophrenia	0.43	Substantial affective-psychotic overlap
Major depression and ADHD	0.32	Moderate
Schizophrenia and autism	0.16	Modest at the common-variant level

SNP-based genetic correlations from the 2013 PGC cross-disorder analysis. The discriminator is the schizophrenia-bipolar value of 0.68, the exam anchor for the collapse of the Kraepelinian dichotomy at the genetic level.

0.68 SCZ-BD GENETIC CORRELATION (HIGHEST)	**~75%** CAUSAL COMMON VARIANTS SHARED, SCZ-BD	**0.16** SCZ-ASD (MODEST, COMMON-VARIANT)

How much is truly shared. Causal-mixture modelling of the schizophrenia-bipolar overlap estimated that about **75%** of the causal common variants influencing the two disorders are shared (Smoller et al. 2019). Independent evidence converges: post-mortem cortical transcriptomic profiles across these disorders correlate strongly with their pairwise genetic correlations (r about 0.79), and the Brainstorm Consortium, mapping 25 brain disorders, found genetic correlations clustered tightly among the psychiatric disorders (ADHD, depression, bipolar, anxiety, schizophrenia) but little overlap with neurological disorders, showing psychiatric pleiotropy is specific, not an artefact (Smoller et al. 2019). Individual loci show it too: *CACNA1C* is associated with bipolar disorder, schizophrenia and autism (Smoller et al. 2019).

COMMON TRAP

Do not equate a high genetic correlation with genes acting in the same direction, and do not read it as clinical interchangeability. Genetic correlation is a population-level average across thousands of SNPs; two disorders with rg = 0.68 still have distinct clinical courses, treatment responses and disorder-specific variants. Equally, a low rg (schizophrenia-autism at 0.16) at the *common-variant* level coexists with *strong* overlap at the *rare-variant* level (shared CNVs, shared de novo genes). The level of analysis, common versus rare variant, changes the answer, which is exactly the point examiners test.

9.6 The genetic p-factor and the structure of psychopathology

If common-variant risk is so widely shared, does a general dimension of psychopathology exist at the genetic level? Applying **genomic structural equation modelling** to eight disorders, the PGC decomposed the genetic correlation matrix into **three correlated genomic factors** that together accounted for more than half of the genetic variation across these disorders (Smoller et al. 2019):

Factor 1: compulsive/perfectionistic
Anorexia nervosa, obsessive-compulsive disorder, Tourette syndrome.

Factor 2: mood and psychotic
Schizophrenia, bipolar disorder, major depression.

Factor 3: early-onset neurodevelopmental
Autism, ADHD, Tourette syndrome, with major depression also loading here.

The p-factor. That these three factors are themselves correlated is the genetic case for a **p-factor**, a single general dimension of liability to psychopathology sitting above the specific factors, the genomic analogue of the general "p" originally derived from phenotypic covariation. The neurodevelopmental factor is the most genetically integrated, consistent with the theme of this whole topic: shared developmental genes are what generate shared liability.

Where the field is in 2025. The scale has grown. A 2019 PGC analysis of eight disorders found 136 genome-wide loci, of which 109 were pleiotropic (shared across more than one disorder); a 2024 functional follow-up (Won and Sullivan, in *Cell*) showed that pleiotropic variants are active for *longer* across brain development and hit genes more sensitive to disruption than disorder-specific variants, reinforcing the developmental basis of shared risk. A 2025 cross-disorder analysis of 14 disorders in *Nature* identified several hundred loci, a large share of them pleiotropic. The clinical promise, still on the horizon, is that pleiotropic variants may be optimal drug targets because one intervention could act across multiple disorders (Won and Sullivan 2024).

HOLD THIS
Shared developmental genes produce shared disorders. Pervasive pleiotropy and a genetic p-factor mean common-variant risk crosses diagnostic borders; the schizophrenia-bipolar rg of 0.68 is the single strongest genetic argument against the Kraepelinian dichotomy.

9.7 Implications for the categorical-versus-dimensional debate

This is where the genetics feeds directly back into nosology and gives you a ready-made discussion answer. The DSM and ICD categories are, by design, atheoretical and drawn around clinical syndromes; the genetic data are telling us those borders do not map cleanly onto biology (Smoller et al. 2019).

- **Against pure categories.** Pervasive pleiotropy, high genetic correlations, shared CNVs and a genetic p-factor all argue that liability is continuous and trans-diagnostic, not carved at discrete joints. The schizophrenia-bipolar rg of 0.68 is the single strongest genetic argument against the Kraepelinian dichotomy.
- **Not purely dimensional either.** Disorders retain *specific* genetic signal and specific loci alongside the shared component, and clinical course and treatment response still discriminate them. The honest position is *hierarchical*: a general p-factor and a few broad factors on top, with disorder-specific liability underneath.

- **Toward a bottom-up nosology.** Genomic factor structures offer an empirical, biology-first reorganisation of psychopathology, the same impulse behind dimensional frameworks such as RDoC and HiTOP. The likely future is a system that keeps clinically useful categories while formally acknowledging shared, continuously distributed neurodevelopmental liability underneath them (Smoller et al. 2019).

MNEMONIC

"SHARED DEVELOPMENT"

Synaptic, chromatin and FMRP-target enrichment; **H**igh genetic correlations (SCZ-BD 0.68); **A**utism = mid-fetal cortical pyramidal neurons; **R**are de novo variants, paternal 4:1; **E**ight-disorder three-factor structure; **D**imensional p-factor. The common thread is that shared *developmental* genes produce shared *disorders*.

GOOD TO REMEMBER

- **SCZ-BD genetic correlation rg = 0.68:** highest cross-disorder pair (2013 PGC); the genetic collapse of the Kraepelinian dichotomy.
- **MDD-BD rg = 0.47; MDD-SCZ rg = 0.43; MDD-ADHD rg = 0.32; SCZ-ASD rg = 0.16:** the other 2013 PGC five-disorder correlations.
- **~75% shared causal common variants (SCZ-BD):** causal-mixture estimate of the proportion of common causal variants shared between schizophrenia and bipolar disorder.
- **PGC eight-disorder genomic SEM: three factors:** compulsive (AN, OCD, TS); mood-psychotic (SCZ, BD, MDD); early-onset neurodevelopmental (ASD, ADHD, TS, MDD); >50% of genetic variation; genetic basis of the p-factor.
- **2019 PGC: 136 loci, 109 pleiotropic:** eight-disorder cross-disorder GWAS.
- **Won and Sullivan 2024 (Cell): 683 variants:** pleiotropic variants active longer in neurodevelopment and hit more disruption-sensitive genes than disorder-specific ones.
- **2025 Nature, 14 psychiatric disorders:** several hundred loci mapped, a large share pleiotropic; latest cross-disorder landscape.
- **CACNA1C:** classic pleiotropic locus associated with bipolar disorder, schizophrenia and autism.
- **22q11.2 deletion:** first de novo CNV described in schizophrenia; raises schizophrenia odds roughly 50-fold; the paradigm pleiotropic CNV.
- **Complement C4 allele:** higher-expression C4 allele associated with schizophrenia via excessive adolescent synaptic pruning.
- **CHD8:** prototypical high-confidence autism gene; a chromatin remodeller.
- **FMR1 / FMRP targets:** autism and schizophrenia risk genes enriched for FMRP-bound transcripts (link to fragile X syndrome).
- **65 ASD risk genes:** from combined de novo exome and CNV data across >5000 families (Autism Genome Project and Simons Simplex Collection).
- **De novo point mutations ~4:1 paternal bias:** and positively correlated with advanced paternal age, the mechanism behind the paternal-age effect in autism and schizophrenia.
- **Brainstorm Consortium:** genetic correlations cluster among psychiatric disorders with little overlap with neurological disorders (pleiotropy is specific).

Findings in the clinic

10 · Heritability across major disorders

A single comparative table of heritability and twin concordance across the major psychiatric disorders is one of the highest-yield objects in all of psychiatric genetics: it is asked directly in MCQs ("which disorder is most heritable?"), it frames vivas on any single condition, and it anchors the conceptual questions about what heritability actually means. The candidate is expected to reproduce an ordered hierarchy from the highly heritable neurodevelopmental and psychotic disorders at the top, through the moderately heritable substance-use and eating disorders, down to the internalising (depressive and anxiety) disorders at the base, and then to state precisely what a heritability figure does and does not claim. **Why it matters.** The numbers are examinable to the decade, but the deeper marks are won by knowing that heritability is a population variance ratio in a specified environment, not a property of an individual patient and not a statement about immutability (Kaplan & Sadock 2024).

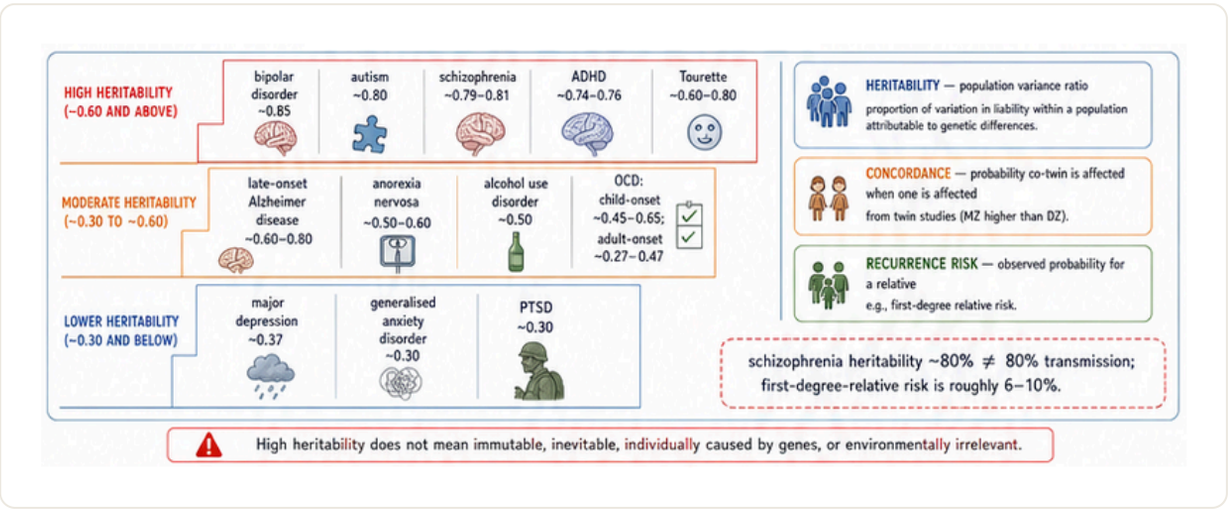


Fig 3.19 Heritability across major disorders.

The hierarchy is remarkably stable across textbooks and across the two great methodologies (classical twin studies and modern population-register sibling studies). Broadly, the neurodevelopmental disorders (autism, ADHD) and the two classic functional psychoses on the psychotic and mood axes (schizophrenia, bipolar disorder) cluster at heritabilities of roughly 0.75 to 0.85; anorexia nervosa, alcohol use disorder and obsessive-compulsive disorder sit in the 0.4 to 0.6 band; and major depression, the generalised anxiety and stress-related disorders occupy the low 0.3s (New Oxford 2020). The same ordering recurs whether one reads concordance rates or variance-decomposition heritabilities, which is itself the strongest internal validation of the twin design.

10.1 Reading the two currencies: concordance and heritability

Concordance is a probability; heritability is a variance ratio. **Concordance** is the probability that the co-twin is affected given that one twin is affected (probandwise is the modern standard, and is the figure comparable to a morbid risk). **Heritability** (narrow-sense h-squared) is the

proportion of the total phenotypic variance in a population that is attributable to additive genetic variance. The bridge between them is the excess of monozygotic (MZ) over dizygotic (DZ) concordance: a large MZ-over-DZ gap implies high heritability (Falconer's first approximation, h-squared is about 2 times the difference in twin correlations). The two currencies carry the same ordering of disorders but are not interchangeable numbers, and mixing them is a common source of error when quoting figures.

10.2 The comparative table across disorders

The core object. The table below collates the standard exam figures. The heritability column gives the twin-study or family-study estimate quoted in the reference texts; the concordance column gives representative probandwise MZ and DZ rates where a canonical figure exists. Ranges reflect genuine between-study variation, not uncertainty about which is "correct"; where a single landmark estimate is conventionally quoted, it is named in the source column.

DISORDER (ICD-11 / DSM-5-TR)	MZ VS DZ CONCORDANCE	HERITABILITY (H-SQUARED)	SOURCE / LANDMARK
Schizophrenia (6A20)	**MZ ~46 to 50% vs DZ ~9 to 14%**	~0.79 to 0.81	Sullivan meta-analysis 2003 (81%); Hilker 2018 Danish registers (79%)
Bipolar disorder (6A60)	**MZ ~40 to 70% (often quoted ~60%) vs DZ ~5 to 20%**	~0.85 (up to ~0.9)	McGuffin 2003; Kieseppa 2004 (0.93 for narrow BP-I); K&S 2024
Autism spectrum disorder (6A02)	MZ high vs DZ low (early studies MZ ~60 to 90%, DZ ~0 to 10%)	~0.80 (range ~0.5 to 0.9)	Sandin 2017 twin meta-analysis (~0.83); New Oxford 2020
ADHD (6A05)	MZ markedly > DZ	~0.74 to 0.76 (twin ~0.70 to 0.80)	Faraone; twin-study consensus (K&S 2024)
Anorexia nervosa (6B80)	MZ > DZ	~0.5 to 0.6 (twin), family ~0.4	Bulik; New Oxford range 0.28 to 0.74
Alcohol use disorder / dependence (6C40)	MZ > DZ	~0.5	K&S 2024; Prescott & Kendler
Obsessive-compulsive disorder (6B20)	MZ > DZ; higher in child-onset	Child-onset ~0.45 to 0.65; adult-onset ~0.27 to 0.47	van Grootheest twin meta-analysis 2005
Major depressive disorder (6A70)	MZ ~40% vs DZ ~20%	~0.37	Sullivan meta-analysis 2000 (0.37); family est. ~0.30 to 0.41
Generalised anxiety disorder (6B00)	MZ > DZ (modest)	~0.30	Hettema meta-analysis 2001 (~0.32); K&S 2024
Post-traumatic stress disorder (6B40)	MZ > DZ	~0.30	True 1993 (Vietnam twin registry); New Oxford 2020

DISORDER (ICD-11 / DSM-5-TR)	MZ VS DZ CONCORDANCE	HERITABILITY (H-SQUARED)	SOURCE / LANDMARK
Tourette syndrome / tic disorder (8A05.0)	**MZ 53% (TS) and 77% (any tic) vs DZ 8% and 23%**	High (~0.6 to 0.8)	Price 1985; twin-study consensus
Alzheimer disease (late-onset) (8A20)	MZ > DZ	High (~0.6 to 0.8); APOE-e4 major locus	Gatz 2006 Swedish twins (~0.58 to 0.79); APOE on chr 19

The heritability hierarchy: neurodevelopmental and psychotic/bipolar disorders at the top (~0.75 to 0.9), eating, substance-use and OCD in the middle (~0.4 to 0.6), depressive and anxiety and stress-related disorders at the base (~0.3). Concordance and heritability carry the same ordering. Several concordance and heritability entries carry genuine between-study spread and are flagged for verification in the metadata.

~0.85	~0.80	~0.37	~0.30
BIPOLAR (MOST HERITABLE)	SCHIZOPHRENIA AND AUTISM	MAJOR DEPRESSION	GAD AND PTSD (BASE)

10.3 The top of the hierarchy: schizophrenia, bipolar, autism, ADHD

The most heritable common psychiatric disorders. The landmark modern figure for schizophrenia is the Sullivan, Kendler and Neale twin meta-analysis of 2003, which gave a heritability of 81% (95% confidence interval roughly 73 to 90%), later corroborated by Hilker's 2018 analysis of the Danish twin and psychiatric registers (over 30,000 pairs) at 79% for narrow schizophrenia and 73% for the spectrum (New Oxford 2020). Bipolar disorder is quoted as the single most heritable major psychiatric disorder, around 0.85 and rising toward 0.9 for narrowly defined bipolar-I, with the MZ co-twin concordance conventionally given as about 60% against a DZ rate an order lower (Kaplan & Sadock 2024; McGuffin 2003). Autism and ADHD are the highly heritable neurodevelopmental disorders, autism around 0.8 (Sandin's 2017 twin meta-analysis gave about 0.83) and ADHD around 0.74 to 0.76, with twin studies clustering at 0.70 to 0.80. **The examinable point.** These four disorders form the "high-heritability" cluster and are the ones for which environmental variance, though real, contributes the smaller share of population variance.

10.4 The base of the hierarchy: depression, anxiety, PTSD

The internalising disorders are the least heritable of the common conditions. Major depressive disorder has a heritability of about 0.37 (Sullivan's 2000 meta-analysis), with MZ concordance around 40% against DZ around 20%; the large Swedish population sibling study gave a family-based estimate of 0.30, the lowest of the eight disorders it examined. Generalised anxiety disorder sits at about 0.30 (Hettema's 2001 meta-analysis of the anxiety disorders gave roughly 0.32), and post-traumatic stress disorder at about 0.30, first established in True's 1993 study of the Vietnam-era twin registry. **The interpretive corollary.** The lower heritabilities do not make these disorders "less biological"; they mean that in the studied populations a larger fraction of the variance between people is environmental (including, for PTSD, the necessary environmental trigger of trauma exposure, which caps the achievable heritability). Depression, anxiety and OCD were precisely the disorders the authors of the Swedish register study singled

out as the ones where environmental aetiological research is most likely to be fruitful (heritability under 0.50).

10.5 The special cases: OCD child-onset, anorexia, alcohol, Tourette, Alzheimer

OCD: an age-of-onset split. The single most examinable nuance in the middle of the table is that obsessive-compulsive disorder is more heritable when it begins in childhood. van Grootheest's twin meta-analysis (2005) reported obsessive-compulsive symptom heritability of roughly 0.45 to 0.65 in children against about 0.27 to 0.47 in adults, consistent with a more strongly genetic early-onset form (New Oxford 2020). **Anorexia nervosa** is moderately-to-highly heritable, twin estimates around 0.5 to 0.6 (the New Oxford range is wide, 0.28 to 0.74), with a family-register estimate of about 0.4. **Alcohol use disorder** is conventionally quoted at a heritability of about 0.5. **Tourette syndrome** is highly heritable with a very high MZ concordance (53% for the full syndrome and 77% for any tic, against 8% and 23% respectively in DZ pairs (Price 1985)), reflecting a strong, largely polygenic genetic contribution. **Alzheimer disease** (late-onset) has a high heritability, around 0.58 to 0.79 in Gatz's 2006 Swedish twin study, with the APOE-e4 allele on chromosome 19 the single largest common-variant risk locus (a heterozygote carries about a two- to three-fold risk, a homozygote considerably more).

HOLD THIS

Psychosis and neurodevelopment high, internalising low. Bipolar, autism, schizophrenia and ADHD cluster at ~0.75 to 0.9; anorexia, alcohol use and OCD in the middle; depression, GAD and PTSD near 0.3. The single richest nuance: OCD is more heritable when it starts in childhood.

CLINICAL ANCHOR

When a family asks "will my child get this too?", the heritability figure is not the answer they need; the recurrence risk is. A heritability of 0.8 for schizophrenia does not mean an 80% chance of transmission, it means that in the studied population most of the variation in liability between people is genetic. The first-degree-relative recurrence risk for schizophrenia is of the order of 6 to 10%, an order of magnitude smaller than the heritability figure, because the disorder is highly polygenic and each relative shares only half the risk alleles. Keeping heritability and recurrence risk separate in your counselling prevents both false reassurance and needless alarm.

10.6 What heritability is, and what it is not

A population parameter, not an individual one. **Heritability** is the ratio of genetic variance to total phenotypic variance in a defined population and environment. It is not the proportion of a given patient's illness that is "genetic", it is not a fixed biological constant, and it says nothing about whether a trait can be changed. The standard cautionary example is phenylketonuria: an essentially fully genetic (single-gene) disorder that is nonetheless completely preventable by an environmental intervention (dietary phenylalanine restriction). A high heritability and full environmental modifiability coexist without contradiction (Kaplan & Sadock 2024).

RULE **Heritability is a population variance ratio, not an individual statement and not immutability.** Phenylketonuria is essentially fully genetic yet fully preventable by diet; a high h-squared says nothing about modifiability or the cause in one patient.

Heritability changes with the environment. Because it is a ratio, heritability rises when environmental variance falls and falls when environmental variance rises. In a population where everyone is exposed to identical environments, the only remaining variance is genetic and heritability approaches unity; in a population with wildly variable environments the same trait can show lower heritability. Heritability is therefore always local to the population and era studied, and figures from Scandinavian registers need not transfer unchanged to other populations. It also tells you nothing about the mean level of a trait, only about the sources of variation around that mean.

10.7 The twin-heritability versus SNP-heritability gap

The missing heritability problem. Twin and family studies estimate **broad or narrow-sense heritability** from the resemblance of relatives; genome-wide association data estimate **SNP-heritability** (h-squared-SNP), the variance captured by common measured single-nucleotide polymorphisms. SNP-heritability is consistently and substantially lower than twin-heritability: in the large Swedish comparison, family-based estimates ran from 0.30 (major depression) to 0.80 (ADHD), whereas the SNP-based estimates from the same diagnoses ran from about 0.10 (alcohol dependence) to 0.28 (OCD). For schizophrenia the case-control SNP-heritability is on the order of 0.23 against a twin-heritability of about 0.81 (New Oxford 2020). **Why the gap.** The shortfall (the "missing heritability") reflects that common SNPs do not tag rare and structural variants (copy-number variants, rare coding variants), incomplete linkage-disequilibrium tagging, non-additive (dominance and epistatic) effects, gene-environment interaction absorbed into the twin estimate, and possible upward bias in twin estimates from violations of the equal-environments assumption. The largest twin-to-SNP gaps in that study were for the neurodevelopmental disorders (ADHD, autism) and schizophrenia, precisely the disorders for which rare and structural variants are known to contribute.

TRAP Do not quote the SNP-heritability of schizophrenia (~0.23) as "the heritability of schizophrenia": the twin-heritability is ~0.81, and the SNP figure is only a lower bound on what common variants capture.

COMMON TRAP

Do not read a heritability of 0.8 as "80% of this patient's illness is genetic" or as "80% chance of passing it on". Heritability is a population-level variance ratio, silent about any individual and silent about transmission risk. Equally, do not treat SNP-heritability and twin-heritability as the same quantity: the SNP figure is a lower bound on what common variants capture, not a correction to the twin figure. Quoting the SNP-heritability of schizophrenia (about 0.23) as "the heritability of schizophrenia" is wrong; the twin-heritability is about 0.81.

PEARL

A clean one-line ordering to carry into the viva: bipolar and autism and schizophrenia and ADHD are the "high" disorders (heritability roughly 0.75 to 0.9); anorexia, alcohol use disorder and OCD are "middle" (0.4 to 0.6); depression, generalised anxiety and PTSD are "low" (about 0.3). The mnemonic hierarchy runs "psychosis and neurodevelopment high, internalising low", and the single richest nuance is that OCD is more heritable when it starts in childhood.

MNEMONIC

Big Brains Are Adaptable, Ordinary Anxious Depressives

Descending the heritability ladder: **B**ipolar (~0.85), **B**rain-development autism (~0.8), **A**utism-and schizophrenia cluster and **A**DHD (~0.75), **O**CD and anorexia and alcohol (~0.4 to 0.6), then the **A**nxiety and **D**epression base (~0.3). The device just fixes the top-to-bottom order; the exact figures still have to be learned.

INDIA

Almost every heritability figure in this table derives from Scandinavian (Swedish, Danish, Finnish) or Anglo-American twin and register cohorts; India has no national twin or adoption register at comparable scale, so Indian genetic-epidemiology data come mainly from family morbid-risk studies. Because heritability is environment-specific, the imported figures should be quoted as the best available estimates rather than as validated Indian values, and consanguinity (common in parts of India) can inflate familial aggregation for any recessive contribution, complicating a family history.

GOOD TO REMEMBER

- **Schizophrenia heritability:** ~0.81 (Sullivan meta-analysis 2003, 95% CI ~73 to 90%); Hilker 2018 Danish registers 0.79 (narrow), 0.73 (spectrum).
- **Bipolar disorder heritability:** ~0.85, the most heritable major psychiatric disorder; MZ concordance often quoted ~60%; Kieseppa 2004 ~0.93 for narrow bipolar-I.
- **Autism heritability:** ~0.80 (Sandin 2017 twin meta-analysis ~0.83); early twin studies MZ concordance far exceeding DZ.
- **ADHD heritability:** ~0.74 to 0.76 (twin studies ~0.70 to 0.80); Faraone consensus.
- **Anorexia nervosa heritability:** ~0.5 to 0.6 twin (New Oxford range 0.28 to 0.74); family estimate ~0.4.
- **Alcohol use disorder heritability:** ~0.5.
- **OCD heritability:** child-onset ~0.45 to 0.65, adult-onset ~0.27 to 0.47 (van Grootheest twin meta-analysis 2005); higher in child-onset is the key nuance.
- **Major depressive disorder heritability:** ~0.37 (Sullivan meta-analysis 2000); family-register estimate ~0.30, the lowest of eight disorders.
- **Generalised anxiety disorder heritability:** ~0.30 (Hettema meta-analysis 2001, ~0.32).
- **PTSD heritability:** ~0.30 (True 1993, Vietnam-era twin registry).
- **Tourette syndrome:** high heritability; MZ concordance 53% for TS and 77% for any tic vs DZ 8% and 23% (Price 1985).
- **Alzheimer disease (late-onset):** heritability ~0.58 to 0.79 (Gatz 2006 Swedish twins); APOE-e4 (chromosome 19) the major common-variant risk allele, heterozygote ~2 to 3 fold risk.
- **SNP-heritability vs twin-heritability gap:** Swedish comparison, family-based 0.30 (MDD) to 0.80 (ADHD) vs SNP-based ~0.10 (alcohol dependence) to 0.28 (OCD); schizophrenia SNP-h-squared ~0.23 vs twin ~0.81.
- **Falconer's formula:** h-squared is approximately 2 times the difference between MZ and DZ twin correlations.

11 · Schizophrenia genetics: the integrative flagship

Why this matters. This is the essay the first paper is built to elicit: take one disorder and let it carry every method taught in these notes. **Schizophrenia** is the ideal vehicle because it is the most intensively genotyped psychiatric phenotype, and its story runs cleanly from classical genetic epidemiology (a heritability near 80% that no candidate gene could explain) through the modern two-tier architecture (a highly polygenic common-variant burden plus rare large-effect structural variants), to a mechanistic hook the examiner loves (the complement C4A signal and synaptic pruning), and finally to the clinical frontier of the polygenic risk score. A strong answer is not a list of genes; it is an argument that schizophrenia is a **neurodevelopmental** disorder of polygenic liability, in which many common alleles of tiny effect and a few rare variants of large effect converge on synaptic and neurodevelopmental biology, with environment tipping vulnerable brains over a threshold.

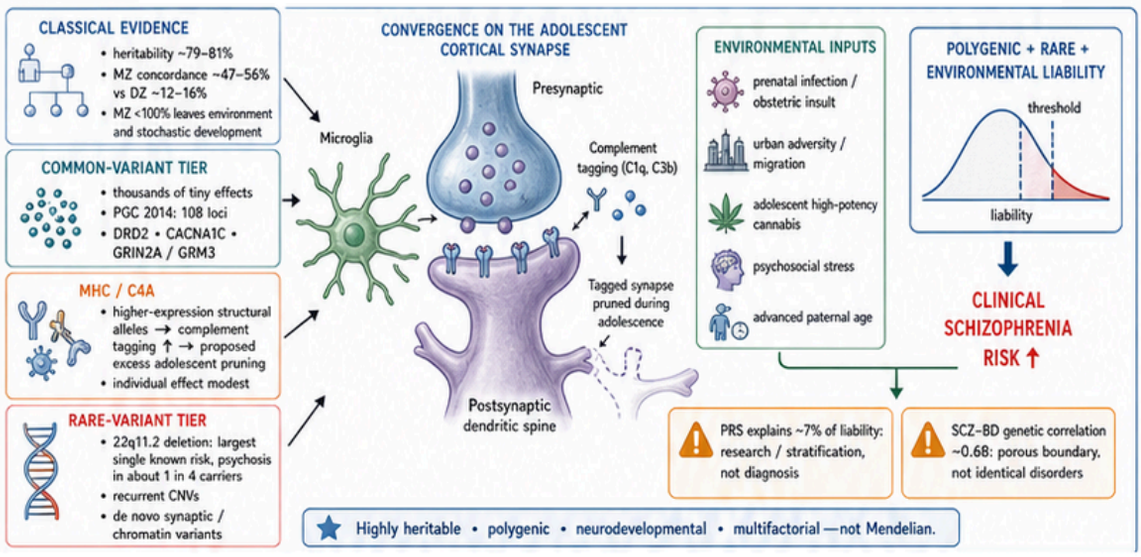


Fig 3.20 Schizophrenia: risk converges on the developing synapse.

Anchor the whole essay on a handful of load-bearing, examinable facts: heritability of the order of 80% with monozygotic concordance far above dizygotic; the 22q11.2 deletion as the single largest known genetic risk; the MHC/C4A complement signal as the most robust common-variant locus; the collapse of the candidate-gene era (COMT, DISC1, NRG1, dysbindin); and a substantial genetic overlap with bipolar disorder that makes the two-disorder boundary permeable. These are grounded in Kaplan and Sadock (2024), the New Oxford Textbook (2020) and Tasman (2015).

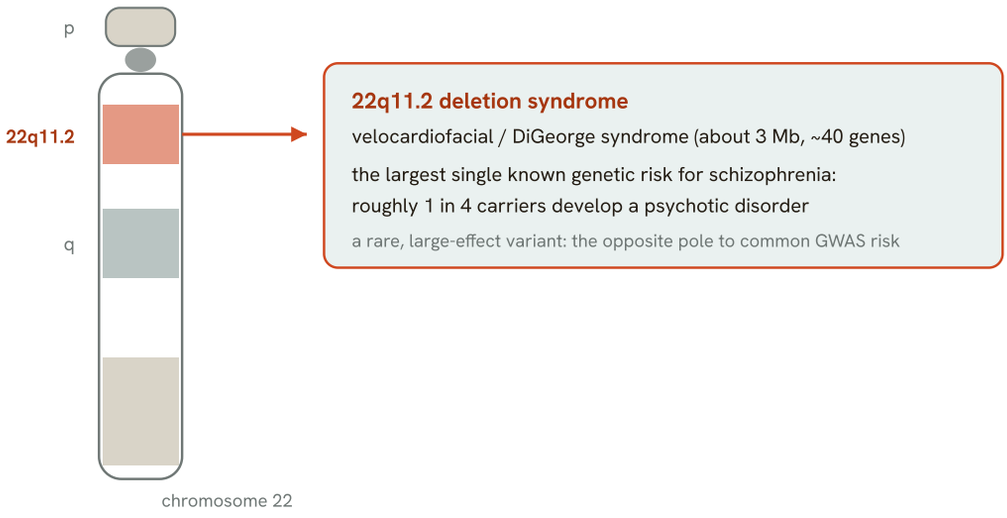


Fig 3.21 The 22q11.2 microdeletion on the long arm of chromosome 22. This roughly 3 megabase deletion of about forty genes causes velocardiofacial (DiGeorge) syndrome and is the single largest known genetic risk factor for schizophrenia: around a quarter of carriers develop a psychotic disorder. It illustrates the rare, large-effect end of the architecture spectrum from Fig 3.11, in contrast to the thousands of common small-effect variants that make up most inherited risk.

11.1 The framing move: state the architecture before the evidence

Open with the thesis. The examiner rewards a candidate who names the target before marshalling data. State it as: schizophrenia has a **complex, polygenic, multifactorial-threshold** architecture, not a Mendelian one. No single-gene form of schizophrenia has ever been found; familial distributions are, in the words of the standard text, inconsistent with simple Mendelian inheritance (Kaplan and Sadock 2024). Everything that follows, twin heritability, GWAS, CNVs, gene-environment interaction, is evidence for and refinement of that one architectural claim.

The two-tier model. Risk is carried at two ends of the frequency-effect spectrum: many **common variants** of individually tiny effect (odds ratios near 1.1, tagged by GWAS), plus rare **copy number variants** and de novo mutations of large effect (odds ratios of several-fold to fifty-fold). Between them sits the **missing heritability** gap: twin heritability near 80% but common-SNP heritability capturing only part of it. Say this once, early, and the rest of the essay slots into it.

RULE **State the architecture before the evidence.** Open the essay by naming schizophrenia as a complex, polygenic, multifactorial-threshold disorder, not a Mendelian one; every finding that follows is refinement of that claim.

11.2 Heritability and the classical evidence: twin and adoption studies

The number to know. Schizophrenia heritability is of the order of 80%, among the highest in psychiatry, with the largest twin meta-analyses placing it near 79 to 81% (Sullivan and colleagues; Hilker and colleagues 2018, the Danish twin registry). Population-register estimates run a little lower (about 64% in Lichtenstein and colleagues 2009), a discrepancy examiners like to probe: twin designs may inflate heritability by capturing gene-environment correlation and non-additive effects (New Oxford 2020).

Twin concordance. Concordance is far higher in monozygotic than dizygotic twins: Kaplan and Sadock (2024) give roughly 47 to 56% for monozygotic and 12 to 16% for dizygotic pairs, rising above 80% in monozygotic pairs with severe, typical illness. The MZ-versus-DZ gap is the core quantitative argument for a genetic contribution; the fact that MZ concordance is well below 100% is the equally important argument that genes are not the whole story (environment and stochastic development matter).

Adoption studies remove shared rearing. The Danish and Finnish adoption studies (Kety, Rosenthal, Tienari) showed that the biological relatives of adopted-away probands, not the adoptive relatives, carry the raised risk, and that offspring of affected biological parents remain at elevated risk even when reared in unaffected adoptive homes. The Finnish Adoptive Family Study (Tienari) added the gene-environment message: the biological high-risk children fared worst specifically when reared in disturbed adoptive families, an early demonstration of interaction rather than pure genetic determinism.

COMMON TRAP

Do not read heritability of 0.8 as "80% genetic in this patient." Heritability is a population variance statistic: it describes how much of the variation between people in a given population and environment is attributable to genetic differences. It says nothing about the cause in any individual, and nothing about modifiability, a highly heritable disorder can still be entirely environmentally treatable (phenylketonuria is the standard cautionary example). Misstating this is a classic viva stumble.

11.3 The candidate-gene era and the lesson it taught

What was done. Before genome-wide genotyping, researchers pre-selected a handful of biologically plausible or positionally implicated **candidate genes**. For schizophrenia, more than 1,500 studies examined nearly 800 candidates (Tasman 2015). The most-cited were COMT (catechol-O-methyltransferase, the val158met functional polymorphism, dopamine catabolism), DISC1 (Disrupted-in-Schizophrenia-1, from a Scottish family with a balanced translocation), NRG1 (neuregulin-1, synaptic and glutamatergic signalling) and DTNBP1 (dysbindin, presynaptic).

What happened. Almost none survived well-powered genome-wide scrutiny. When Farrell and colleagues (2015) tested the classic candidates against GWAS data, the historical candidate literature did not yield clear, genome-wide-significant support. Underpowered samples chasing tiny true effects, publication bias, weak priors and flexible analysis had produced a literature dominated by false positives.

The lesson, and the nuance. The examinable lesson is methodological: complex-trait genetics needs enormous samples and built-in replication, which is exactly what GWAS institutionalised. The nuance worth adding for a top answer: DISC1 illustrates why the target was wrong as much as the method. The original translocation family carried both psychosis and mood disorder, and independent studies later linked DISC1 to schizophrenia, schizoaffective disorder and bipolar disorder (Kaplan and Sadock 2024), so the gene never respected the schizophrenia construct it was named for. The candidates were not testing schizophrenia; they were testing a diagnostic category that does not map cleanly onto biology.

11.4 GWAS and the Psychiatric Genomics Consortium: the common-variant tier

Sample size was the missing ingredient. A **genome-wide association study** (GWAS) assays hundreds of thousands to millions of single-nucleotide polymorphisms across the whole genome and tests each for a case-control frequency difference, at the stringent genome-wide significance threshold of p less than 5 x 10 to the power minus 8 (correcting for about a million tests). Early psychiatric GWAS reported nothing because they were too small. The decisive move was consortium pooling: the **Psychiatric Genomics Consortium** (PGC) aggregated samples across dozens of countries, and the schizophrenia signal scaled almost linearly with case number.

The landmark result. The PGC schizophrenia GWAS (2014) analysed about 36,989 cases and 113,075 controls and identified 108 independent genome-wide-significant loci (Kaplan and Sadock 2024). At least three-quarters contained protein-coding genes, enriched for dopamine

(DRD2, the target of every antipsychotic), glutamate and synaptic plasticity (GRM3, GRIN2A, GRIA1, SRR) and voltage-gated calcium-channel signalling (CACNA1C, CACNB2). Associations were also enriched in immune-related tissue, foreshadowing the complement story. Most associated variants are non-coding, so they most likely act by altering gene expression, which makes functional interpretation the hard part.

The satisfying loop. DRD2 emerging as a GWAS hit closed the circle between unbiased genetics and 60 years of dopamine pharmacology: the receptor blocked by antipsychotics is also a genome-wide-significant risk locus. That single fact is worth a sentence in any answer.

~80%	108	~50-fold
TWIN HERITABILITY	GWAS LOCI (PGC 2014)	22Q11.2 DELETION RISK (LARGEST SINGLE)

11.5 The MHC/C4A complement signal and the synaptic-pruning hypothesis

The most robust locus. The strongest and most replicable common-variant association in schizophrenia lies in the major histocompatibility complex (MHC) on chromosome 6, a gene-dense region of extensive linkage disequilibrium. Fine-mapping this signal is the standout mechanistic success of psychiatric GWAS (Sekar and colleagues 2016).

What Sekar and colleagues showed. Human complement component 4 is encoded by two genes, C4A and C4B, which vary in structure (a HERV insertion giving long or short forms) and copy number. Sekar and colleagues genotyped these structural alleles and found that alleles raising C4A expression in brain raised schizophrenia risk in proportion to their effect on expression, with relative risks for the common structural alleles ranging from about 1.0 to 1.27. Post-mortem brain confirmed higher C4A RNA in patients than controls.

The pruning hypothesis. Complement tags synapses for elimination by microglia (C4 promotes C3 activation; C3 marks synapses for removal). In a C4-knockout mouse, C3 deposition and synaptic refinement in the visual pathway were disrupted. The inference: excess C4A drives excessive **synaptic pruning** during adolescence, plausibly the molecular basis of the long-observed grey-matter loss and reduced synaptic density in schizophrenia. This is the mechanism that links a GWAS peak to the neurodevelopmental model and to the adolescent onset of illness, the single most quotable convergence in the field.

HOLD THIS

MHC/C4A is the most robust locus, and the only one with a worked-out mechanism. Structural alleles raising C4A expression raise risk (relative risk up to about 1.27) by driving excess synaptic pruning in adolescence, tying a GWAS peak to the neurodevelopmental model and the age of onset (Sekar 2016).

CLINICAL ANCHOR

Three named common-variant findings to carry into a viva. The **MHC/C4A** signal is the most robust schizophrenia locus, effect modest (relative risk up to about 1.27), and the only one with a worked-out mechanism (excess pruning). **DRD2** as a GWAS hit unites genetics with antipsychotic pharmacology. **CACNA1C** is a canonical cross-disorder calcium-channel locus shared with bipolar disorder, the clearest single illustration that the schizophrenia-bipolar genetic boundary is porous.

11.6 The rare-variant tier: 22q11.2 deletion, recurrent CNVs and de novo mutation

22q11.2: the largest single risk. The recurrent hemizygous microdeletion at **22q11.2** was the first de novo CNV described in schizophrenia (Karayiorgou 1995) and, before the GWAS era, the only DNA variant indisputably pathogenic for the disorder. It causes velocardiofacial (DiGeorge) syndrome, cardiac outflow defects, palatal anomalies, hypocalcaemia and learning difficulty, and raises the odds of schizophrenia roughly 25 to 30-fold (often quoted as up to fiftyfold), the single largest known genetic risk (Kaplan and Sadock 2024). About one in four carriers develops a psychotic illness, so 22q11.2 deletion syndrome is a naturally occurring genetic model of schizophrenia.

A shared, pleiotropic set. A recurring group of large CNVs shows a many-to-one pattern (one CNV, several neurodevelopmental outcomes): 16p11.2 (deletion and duplication, autism and developmental delay), 1q21.1, 15q11.2, 15q13.3 (which spans CHRNA7, the alpha-7 nicotinic receptor gene tied to the P50 gating deficit) and NRXN1 (neurexin-1) deletions. Total CNV burden is elevated in schizophrenia relative to controls, and risk CNVs are larger and more gene-rich than benign ones.

De novo mutation and the paternal-age link. An excess of de novo point mutations and CNVs, disrupting synaptic and chromatin genes, is found particularly in sporadic cases. This dovetails with the epidemiological association of advanced paternal age with schizophrenia risk, since de novo mutations accumulate in the paternal germline with age, a neat gene-to-epidemiology bridge.

LOCUS / CLASS	FREQUENCY	EFFECT SIZE	DETECTION METHOD	EXAMPLE
Common SNP	Minor allele >1%	**Tiny (OR about 1.05 to 1.2)**	GWAS	MHC/C4A, DRD2, CACNA1C
Recurrent CNV	Rare	**Large (OR several-fold to about 30 to 50-fold)**	Chromosomal microarray	**22q11.2 deletion (largest single risk)**
De novo mutation	Very rare, sporadic	Large; often severe phenotype	Exome/genome sequencing	Synaptic and chromatin genes; paternal-age effect

The two-tier architecture of schizophrenia: an inverse frequency-effect relationship, common variants abundant but weak, rare structural variants scarce but powerful, with de novo mutation a sporadic third source.

11.7 Endophenotypes: neurophysiological markers of latent liability

The rationale. An **endophenotype** is a heritable, state-independent, familial trait that co-segregates with illness and is present in unaffected relatives above the population rate (the Gottesman and Gould 2003 criteria). The bet was that a trait between gene and diagnosis would be genetically simpler than the diagnosis itself, and so easier to map. Three markers recur in schizophrenia.

P50 sensory gating

Auditory evoked potential about 50 ms after a click; in the paired-click paradigm the response to the second click is normally suppressed. Reduced suppression in schizophrenia indexes failed inhibitory gating, linked to CHRNA7 (alpha-7 nicotinic receptor, 15q13-14) and transiently normalised by nicotine (Tasman 2015).

Prepulse inhibition (PPI)

Normal reduction of the acoustic startle blink when a weak prepulse precedes the pulse; indexes sensorimotor gating. Reduced in schizophrenia, heritable (about 45 to 50% within families), cross-species and dopamine-sensitive, hence a favoured translational marker.

Eye-tracking

Smooth-pursuit eye-movement dysfunction and antisaccade errors are among the oldest and best-replicated schizophrenia trait markers, present in unaffected first-degree relatives, indexing frontal-executive oculomotor control.

The verdict. Endophenotypes underdelivered as gene-finding shortcuts, the intermediate trait usually proved just as polygenic as the diagnosis (Flint and Munafo 2007). Their enduring value is conceptual: they explain how an unaffected sibling can carry measurable neurophysiological soft signs of the illness without being ill, and they seeded the dimensional RDoC framework.

11.8 Gene-environment interaction: environment tips vulnerable brains over threshold

The principle. High heritability leaves real room for environment (MZ concordance is well below 100%), and the modern model is interactional: environmental exposures raise risk chiefly in genetically vulnerable individuals, tipping latent liability over the disease threshold. The examinable exposures cluster around early neurodevelopment and adolescence.

Cannabis

Adolescent, heavy, high-potency cannabis use is associated with roughly doubled odds of later psychosis, dose-dependently; Mendelian randomisation supports a causal effect of cannabis-use liability on schizophrenia risk (Kaplan and Sadock 2024). Interaction with COMT and other risk variants has been proposed.

Urbanicity

Being born and raised in an urban environment raises schizophrenia risk in a dose-dependent way; the effect is not explained by drift and interacts with familial liability.

Migration

First- and second-generation migrant status raises risk, most markedly where the migrant group is a visible minority, implicating social defeat and chronic adversity rather than genetics of the migrating population.

Obstetric complications

Prenatal infection and maternal immune activation, hypoxia and obstetric complications, and winter-spring birth are replicated early risk factors, consistent with a prenatal neurodevelopmental insult.

Advanced paternal age

Raises risk, mechanistically tied to the accumulation of de novo mutations in the ageing paternal germline (link to 11.6).

11.9 The neurodevelopmental synthesis

The unifying model. Pull the threads together with the **neurodevelopmental** hypothesis (Weinberger, Murray): schizophrenia is the late clinical expression of an early, largely genetic disturbance of brain development, unmasked by the normal maturational events of adolescence and young adulthood. Its strongest empirical support is convergent: gene-set enrichment analyses show that schizophrenia risk genes are not random but cluster in neurodevelopmental and synaptic processes (Owen and colleagues, New Oxford 2020).

Why adolescence. The C4A pruning story gives the model a molecular clock: adolescence is the period of steep synaptic elimination in association cortex, precisely the process the complement signal implicates. Excess pruning of an already atypically wired brain plausibly explains why a disorder of neurodevelopmental origin declares itself in the late teens and twenties. Common variants set the baseline liability, rare variants and de novo mutations add large hits in a minority, and environmental exposures (cannabis, obstetric insult, urban adversity) tip the vulnerable brain over threshold, the "multiple-hit" reading of the multifactorial-threshold model.

11.10 Polygenic risk scores and the clinical horizon

Construction. A **polygenic risk score** (PRS) sums an individual's risk alleles across the genome, each weighted by its GWAS effect size, into a single number capturing common-variant liability. The schizophrenia PRS is derived directly from the PGC common-variant signal.

The honest limits. The schizophrenia PRS explains roughly 7% of liability on the liability scale (the common-variant signal itself about 3 to 4% of variance), enough to shift population risk between deciles but nowhere near enough to predict any individual's diagnosis. PRS is a research and stratification tool, not a diagnostic test; it cannot yet counsel a specific patient. Say this plainly, examiners test whether candidates over-claim.

The frontier (currency). The useful clinical horizon is cross-disorder and pharmacogenomic rather than diagnostic: PRS as one axis of transdiagnostic risk stratification, integration with rare-variant and CNV screening in early-onset or syndromic presentations, and the wider pharmacogenomic move (CPIC and DPWG CYP2D6/CYP2C19 guidance) that is already actionable for drug dosing while diagnostic PRS is not.

TRAP Do not over-claim the schizophrenia PRS: it explains only about 7% of liability, enough to shift population risk but nowhere near enough to predict any individual's diagnosis.

11.11 Genetic overlap with bipolar disorder: the permeable boundary

The evidence. Schizophrenia and bipolar disorder share substantial genetic liability. Family and twin data show cross-transmission (a schizophrenia diagnosis in one twin raises the co-twin's risk of both schizophrenia and affective psychosis), and the PGC cross-disorder analysis gives a schizophrenia-bipolar genetic correlation of about 0.6 to 0.68, the highest between any two major psychiatric disorders (Kaplan and Sadock 2024). Shared specific loci (CACNA1C, and historically DISC1, NRG1, dysbindin, G72/DAOA) sit at the interface, and 22q11.2 and other CNVs raise risk across the psychosis spectrum.

The correct reading. A genetic correlation of 0.6 does not mean the disorders are the same: two disorders with high rg still have distinct courses, treatment responses and disorder-specific variants (New Oxford 2020). The examinable conclusion is that genetic liability to psychosis is continuous and partly transdiagnostic, evidence that the Kraepelinian dichotomy is a clinical convention that genetics only partly respects, not a natural biological joint.

MNEMONIC

"HANDS on Cannabis, Urban, Migrant Paths"

Architecture in one breath: **H**eritability ~80%, **A**rchitecture two-tier (common + rare), **N**eurodevelopmental model, **D**eletion 22q11.2 (largest single risk), **S**ynaptic pruning via C4A. Then the environmental quintet: **C**annabis, **U**rbanicity, **M**igration, **P**aternal age, obstetric insult (prenatal).

PEARL

The single most integrative sentence you can write: schizophrenia is a highly heritable, polygenic neurodevelopmental disorder in which common variants of tiny effect (converging via C4A on excess synaptic pruning) set baseline liability, rare large-effect CNVs such as 22q11.2 add powerful hits in a minority, and environmental exposures tip the vulnerable adolescent brain over a multifactorial threshold, with a genetic architecture that overlaps substantially with bipolar disorder rather than respecting the diagnostic boundary between them.

INDIA

Formal twin and adoption registers on the Danish, Swedish or Finnish scale do not exist in India, so most Indian genetic-epidemiology data come from family (morbid-risk) studies rather than twin or adoption designs. When counselling an Indian family about recurrence, the practical figures are the first-degree-relative risks (of the order of 6 to 10% for schizophrenia in a first-degree relative), framed against a population risk near 1%. Two culturally specific cautions: consanguinity, common in parts of India, can inflate familial aggregation for recessive contributions and complicate a family history; and strong family expectation around marriage and childbearing means recurrence-risk counselling must be handled with care, giving population-level probabilities without implying determinism, and without naming a diagnosis to the family in a way that stigmatises the proband or unaffected relatives.

GOOD TO REMEMBER

- **Heritability:** of the order of 80% (twin meta-analyses about 79 to 81%; population registers lower, about 64% in Lichtenstein 2009).
- **Twin concordance:** monozygotic about 47 to 56% versus dizygotic about 12 to 16% (Kaplan and Sadock 2024); above 80% in severe typical illness.
- **First-degree-relative recurrence risk:** of the order of 6 to 10% against a population risk near 1%.
- **Genome-wide significance threshold:** p less than 5 x 10 to the power minus 8 (about a million tests).
- **PGC schizophrenia GWAS (2014):** about 36,989 cases and 113,075 controls; 108 genome-wide-significant loci (Kaplan and Sadock 2024).
- **MHC / complement C4A:** most robust common-variant locus (chromosome 6); structural alleles raise C4A expression and risk (relative risk up to about 1.27); excess synaptic pruning mechanism (Sekar 2016).
- **DRD2:** genome-wide-significant locus and antipsychotic target; unites genetics and pharmacology.
- **CACNA1C:** voltage-gated calcium channel; cross-disorder locus shared with bipolar disorder.
- **22q11.2 deletion:** velocardiofacial / DiGeorge syndrome; single largest known genetic risk for schizophrenia (about 25 to 30-fold, quoted up to 50-fold); roughly one in four carriers develops psychosis; first de novo CNV described (Karayiorgou 1995).
- **Other recurrent CNVs:** 16p11.2, 1q21.1, 15q11.2, 15q13.3 (spans CHRNA7), NRXN1 deletion; pleiotropic across the neurodevelopmental spectrum.
- **Candidate genes (failed to replicate at genome-wide significance):** COMT (val158met), DISC1, NRG1 (neuregulin-1), DTNBP1 (dysbindin); the cautionary examples (Farrell 2015).
- **Endophenotypes:** P50 sensory gating (CHRNA7, 15q13-14), prepulse inhibition (heritability about 45 to 50%), smooth-pursuit / antisaccade eye-tracking; Gottesman and Gould (2003) criteria.
- **Schizophrenia PRS:** explains about 7% of liability (common-variant signal about 3 to 4% of variance); not individually predictive.
- **Schizophrenia-bipolar genetic correlation:** rg about 0.6 to 0.68 (PGC cross-disorder), the highest between two major psychiatric disorders.
- **Environmental risk factors:** cannabis (about doubled odds, MR-supported causal), urbanicity, migration, obstetric complications / prenatal infection, advanced paternal age.

12 · Pharmacogenetics and pharmacogenomics

Interindividual variation in drug response is one of the oldest observations in clinical psychiatry: two patients on the same molecule at the same dose may show remission, no effect, or a serious adverse reaction. **Pharmacogenetics** is the study of how variation in *single genes* (classically drug-metabolising enzymes) shapes drug response, while **pharmacogenomics** is the broader, genome-wide study of drug response, including polygenic architecture and treatment-response polygenic risk scores (Kaplan & Sadock 2024, Licinio & Wong). Both terms are used interchangeably in much of the literature, but the distinction matters for the exam: single-gene, actionable, guideline-backed (pharmacogenetic) versus multi-gene, exploratory, precision-medicine frontier (pharmacogenomic).

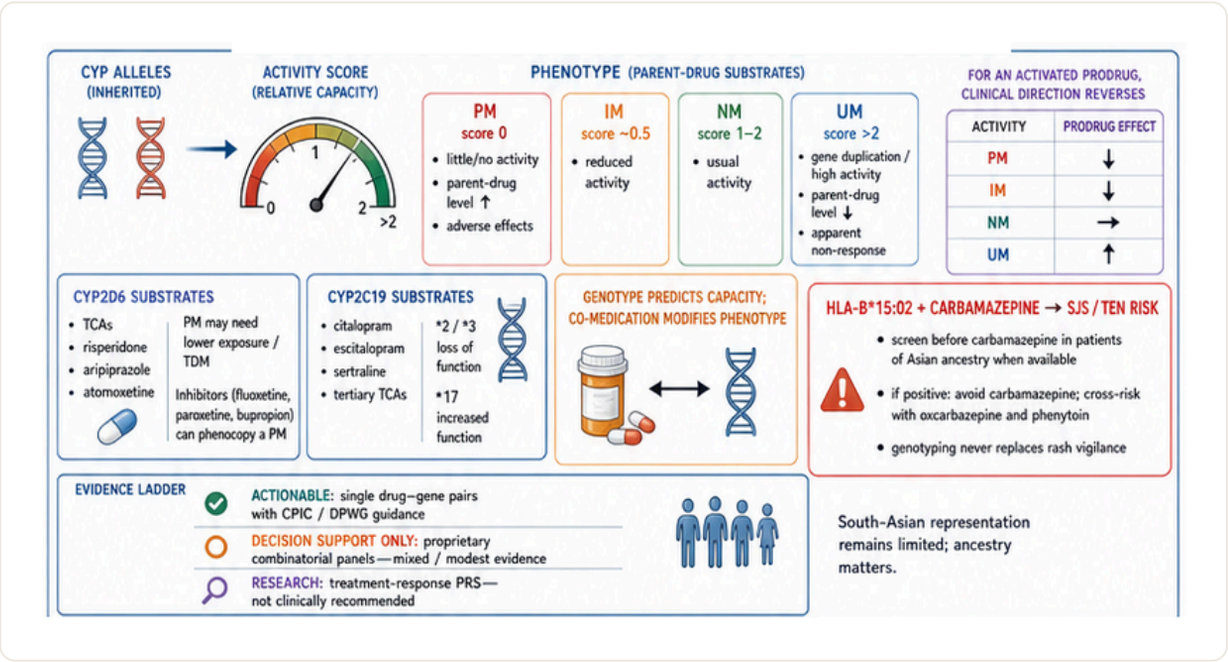


Fig 3.22 Pharmacogenetics: actionable core, hype at the edges.

Why it matters. Only a handful of drug-gene pairs are genuinely actionable, and one of them, **HLA-B*15:02** before carbamazepine, is a life-saving screen that is mandated in patients of Asian ancestry, which makes it a high-yield item for an Indian exam. The rest of the topic is a controlled deflation of hype: combinatorial commercial panels (GeneSight and similar) have weak and mixed randomised-trial support, and treatment-response polygenic scores are not yet clinical. Examiners reward candidates who can separate the evidence-based actionable core from the marketing. Cross-reference the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes for the underlying CYP450 induction and inhibition mechanics.

12.1 Two overlapping definitions

Pharmacogenetics. The study of how variation in a *single gene*, most often a drug-metabolising enzyme or an immune-response gene, alters the efficacy or toxicity of a drug (Kaplan & Sadock 2024). It is the older, narrower term, and its wins are concrete single drug-gene pairs with dosing guidance.

Pharmacogenomics

The genome-wide study of how the whole genetic profile, interacting with diet, microbiome, age and lifestyle, determines drug response. It is a multi-omic, exploratory approach that includes treatment-response polygenic risk scores and pathway analysis (psychscenehub 2023; New Oxford Textbook of Psychiatry).

Pharmacokinetic (PK) genes

Genes affecting drug absorption, distribution, metabolism and elimination, i.e. what the body does to the drug. In psychiatry, the cytochrome P450 enzymes, above all **CYP2D6** and **CYP2C19**.

Pharmacodynamic (PD) genes

Genes affecting the drug target or the tissue response, i.e. what the drug does to the body. Includes receptor and transporter variants (HTR2A, HTR2C, SLC6A4) and immune/HLA alleles that drive idiosyncratic hypersensitivity.

12.2 Metaboliser phenotypes and the activity score

Star-allele nomenclature. CYP alleles are named with the star (asterisk) system, e.g. CYP2D6*1 (reference, fully functional), *4 (null), *10 (decreased function). The combination of two inherited alleles is translated into a **metaboliser** phenotype (Kaplan & Sadock 2024).

The four phenotypes. *Poor metaboliser* (PM): two nonfunctional alleles, little or no enzyme activity, drug accumulates. *Intermediate metaboliser* (IM): reduced-function alleles, activity between poor and normal. *Normal (extensive) metaboliser* (NM/EM): standard activity, the reference phenotype. *Ultrarapid metaboliser* (UM): gene duplication or multiplication, greater than normal activity, drug cleared too fast.

The clinical trap. A UM on a standard dose looks like a non-responder (subtherapeutic levels) and a PM on a standard dose looks intolerant (accumulation and adverse effects); both are often mislabelled as treatment-refractory when the real problem is a dose mismatched to their metabolic capacity (Kaplan & Sadock 2024). For prodrugs the logic inverts: a codeine UM overproduces morphine and risks respiratory depression, while a codeine PM gets no analgesia.

Activity score (AS). Because two alleles combine and function varies continuously, CPIC assigns each allele a value (0 for null, 0.25 or 0.5 for decreased, 1 for normal) and sums them: an activity score of 0 predicts PM, 0.5 predicts IM, 1 to 2 predicts NM, and above 2 predicts UM (Gaedigk, cited in Kaplan & Sadock 2024). The score is more granular than the four discrete labels and can be substrate-dependent.

RULE **Activity score sets the phenotype: 0 is poor, 0.5 intermediate, 1 to 2 normal, above 2 ultrarapid.** A poor metaboliser on a standard dose looks intolerant; an ultrarapid one looks like a non-responder.

12.3 CYP2D6: the antipsychotic and TCA enzyme

Scope. CYP2D6 (chromosome 22) metabolises roughly **25 percent** of clinically used drugs and is arguably the single most important PK gene in psychiatry: it handles all tricyclic antidepressants, several SSRIs (fluoxetine, paroxetine, fluvoxamine), venlafaxine and duloxetine, and the antipsychotics haloperidol, risperidone, aripiprazole and perphenazine (Kaplan & Sadock 2024; Tasman). Key actionable pairs are risperidone and aripiprazole (PM: higher levels, adverse effects; UM: possible loss of effect), tricyclics (PM: reduce starting dose by roughly 50 percent and use therapeutic drug monitoring), and atomoxetine.

Atomoxetine worked example. Atomoxetine levels peak about **10-fold** higher in CYP2D6 poor metabolisers, which is why a normally rare sedation signal is over-represented in PMs and why the FDA label carries CYP2D6 dosing guidance ().

Phenocopying. A CYP2D6 inhibitor (e.g. paroxetine, bupropion, fluoxetine) can convert a genotypic normal metaboliser into a functional PM, a phenomenon called phenocopying; a drug that inhibits its own metabolism at steady state produces autophenocopying (Kaplan & Sadock 2024). Genotype therefore predicts, but co-medication modifies, the observed phenotype. See the

Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes for the CYP inhibition and induction mechanics behind this.

12.4 CYP2C19: the SSRI and clozapine enzyme

Scope. CYP2C19 (chromosome 10q24) metabolises citalopram, escitalopram and sertraline, the tertiary-amine TCAs (imipramine, amitriptyline, clomipramine), and contributes to clozapine metabolism (Kaplan & Sadock 2024; Maudsley Prescribing Guidelines). Loss-of-function alleles *2 and *3 reduce activity (PM), while the gain-of-function *17 allele increases it (UM); all three belong on a minimal PK testing panel.

Escitalopram and citalopram. CYP2C19 poor metabolisers accumulate (es)citalopram and, because these drugs are dose-dependently QT-prolonging, a maximum dose of **20 mg** citalopram is advised in PMs; CYP2C19 ultrarapid metabolisers may under-respond, and CPIC suggests choosing an alternative not primarily metabolised by CYP2C19 (CPIC). Note the *17 allele adds only about 20 percent enzyme capacity, tempering the clinical size of the UM effect.

Sertraline and clozapine. CYP2C19 PMs have higher dose-adjusted sertraline concentrations; for clozapine, genotype-informed metabolic classification (PM, IM, NM) helps interpret plasma levels, though CYP1A2 is the dominant clozapine enzyme and CYP2D6 plays almost no role (Maudsley).

12.5 HLA alleles: idiosyncratic immune reactions

HLA-B*15:02 and carbamazepine. This is the flagship pharmacodynamic (immune) pharmacogenetic association. Carriers of HLA-B*15:02 are markedly more likely to develop carbamazepine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN); the allele is common in Han-Chinese and several South-East and South-Asian groups and rare in Europeans (Kaplan & Sadock 2024). CPIC and the FDA recommend genotyping before starting carbamazepine in patients of Asian ancestry; the allele also flags cross-risk with oxcarbazepine and phenytoin. Genotyping never replaces clinical vigilance.

HLA-A*31:01. A separate allele associated with carbamazepine hypersensitivity, including SJS/TEN, DRESS and maculopapular exanthema, across a broader range of ancestries than HLA-B*15:02 (Kaplan & Sadock 2024).

TPMT and azathioprine. Outside psychiatry but a classic exemplar: thiopurine S-methyltransferase (TPMT) poor-metaboliser variants cause severe, potentially fatal myelosuppression with standard-dose azathioprine, so TPMT (and NUDT15) status guides thiopurine dosing (Kaplan & Sadock 2024, PharmGKB). It is the textbook example of a PK-driven toxicity screen.

RULE **Screen HLA-B*15:02 before carbamazepine in patients of Asian ancestry.** If positive, avoid carbamazepine (and the cross-risk agents oxcarbazepine and phenytoin); it is the one mandated, life-saving pre-prescription test in psychiatry.

12.6 Pharmacodynamic response signals: HTR2A and ANK3

HTR2A. The serotonin 2A receptor gene, a candidate pharmacodynamic marker included on several commercial panels (GeneSight, Genecept), studied for antidepressant response and tolerability; its independent clinical validity remains modest (Kaplan & Sadock 2024).

ANK3. Ankyrin-3, a robust GWAS-implicated bipolar susceptibility gene, has also been examined as a pharmacogenetic signal for lithium and mood-stabiliser response; the pharmacogenomic response evidence is preliminary rather than actionable. These loci illustrate the shift from single-gene PK certainties to multi-gene PD probabilities.

12.7 Guidelines, databases and resources

CPIC

Clinical Pharmacogenetics Implementation Consortium: NIH-funded, publishes gene-drug dosing guidelines (which drug to avoid or how to adjust for a given phenotype). The dominant clinical resource.

DPWG

Dutch Pharmacogenetics Working Group: the European equivalent, issues therapeutic recommendations for actionable variants; CPIC and DPWG broadly agree but differ on some thresholds.

PharmGKB

Pharmacogenomics Knowledgebase: curated repository of variant-drug annotations, allele-frequency data and clinical-annotation levels of evidence.

PharmVar

Pharmacogene Variation Consortium: the reference catalogue of CYP star alleles (for example, more than 170 CYP2D6 alleles).

12.8 Combinatorial commercial testing and the weak evidence base

What they are. Combinatorial pharmacogenomic panels (Myriad's GeneSight, Genomind's Genecept, Invitae's panel) genotype a bundle of PK and PD genes and return a proprietary weighted, colour-coded prescribing report. GeneSight, for instance, covers eight genes (PK: CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4; PD: HTR2A and SLC6A4) (Kaplan & Sadock 2024).

The evidence. Meta-analyses of randomised controlled trials comparing genetically guided to unguided prescribing (e.g. Bousman et al. 2018) suggest a modest improvement in depression remission, but the trials are heterogeneous, several are industry-sponsored and often unblinded, and large independent studies have been more equivocal, so professional bodies frame these panels as decision-support tools, not mandates (psychscenehub 2023; International Society of Psychiatric Genetics 2019). The single-drug CYP and HLA pairs, not the combinatorial algorithms, carry the real actionable weight.

12.9 The pharmacogenomic frontier: PRS for treatment response

Beyond single genes. The genuinely pharmacogenomic (as opposed to pharmacogenetic) horizon is the treatment-response polygenic risk score: aggregating thousands of common variants to

predict antidepressant, antipsychotic or lithium response. Current PRS explain little variance and are not clinically recommended (International Society of Psychiatric Genetics 2019; New Oxford Textbook of Psychiatry). Biobank-scale samples and cross-ancestry GWAS, including work on lithium response, are the active research direction; a recurring caveat for Indian practice is that South-Asian populations remain under-represented in the discovery cohorts, limiting portability of European-derived scores.

HOLD THIS

The actionable core is single drug-gene pairs, not the combinatorial panels. HLA-B*15:02 before carbamazepine and CYP-based dosing of tricyclics and citalopram carry guideline weight; GeneSight-type panels and treatment-response PRS have weak, mixed evidence and are not clinically ready.

INDIA

HLA-B*15:02 is the highest-yield actionable pharmacogenetic screen for Indian practice. The allele is common across South and South-East Asian populations, and Indian cohorts show a strong association between HLA-B*15:02 and carbamazepine-induced SJS/TEN, mirroring the Han-Chinese and Thai data (Kaplan & Sadock 2024; Lim, Kwan & Tan 2008). CPIC and FDA guidance to genotype before starting carbamazepine in patients of Asian ancestry therefore applies directly to Indian patients; where testing is unavailable, heightened clinical vigilance for early rash in the first weeks and a low threshold to stop the drug are essential. India is genetically stratified (North, South and East Indian populations are distinct), so pooling all Indians as one Asian group in dosing algorithms is a recognised limitation.

CLINICAL ANCHOR

Before starting carbamazepine in a patient of Asian ancestry, screen for HLA-B*15:02 if available; if positive, avoid carbamazepine (and oxcarbazepine and phenytoin, which share cross-risk) and select an alternative mood stabiliser. For the common antidepressants and antipsychotics, order CYP2D6 or CYP2C19 genotyping reactively, when a patient reports unusually severe adverse effects or unexplained non-response on an actionable drug (a TCA, citalopram, risperidone, aripiprazole, atomoxetine), rather than as a routine pre-prescription panel.

COMMON TRAP

Do not conflate the evidence tiers. HLA-B*15:02 to carbamazepine and CYP-based dosing of tricyclics and citalopram are actionable single-gene pairs with guideline backing. Combinatorial commercial panels and treatment-response polygenic scores are not: their randomised-trial evidence is weak, mixed and often industry-linked, and PRS for response is explicitly not recommended for clinical use. Calling GeneSight "proven" or PRS "clinically ready" is a marked-down answer.

GENE	VARIANT / PHENOTYPE	DRUG	CLINICAL ACTION
CYP2D6	Poor metaboliser (e.g. *4/*4)	Tricyclics, risperidone, aripiprazole, perphenazine	**Reduce starting dose (roughly 50 percent for TCAs), use TDM, or choose a non-CYP2D6 drug**
CYP2D6	Poor metaboliser	Atomoxetine	**Levels peak about 10-fold higher; adjust dose per FDA label, watch for sedation**
CYP2D6	Ultrarapid metaboliser	Codeine, tramadol (prodrugs)	**Avoid: overproduction of active metabolite risks respiratory depression**
CYP2C19	Poor metaboliser	Citalopram, escitalopram	**Accumulation and QT risk; cap citalopram at 20 mg or use an alternative**
CYP2C19	Ultrarapid metaboliser (*17)	Escitalopram, tertiary-amine TCAs	**Possible under-response; consider a non-CYP2C19 alternative**
CYP2C19	Poor metaboliser	Sertraline, clozapine	**Higher dose-adjusted levels; interpret plasma concentrations accordingly**
HLA-B	*15:02 positive	Carbamazepine (also oxcarbazepine, phenytoin)	**Avoid: high SJS/TEN risk; screen before starting in Asian-ancestry patients**
HLA-A	*31:01 positive	Carbamazepine	**Increased hypersensitivity (SJS/TEN, DRESS) across ancestries; caution**
TPMT	Poor metaboliser	Azathioprine (thiopurines)	**Reduce dose sharply or avoid: risk of severe myelosuppression**

Actionable psychiatric drug-gene pairs: pharmacokinetic CYP and TPMT pairs (dose adjustment) versus pharmacodynamic HLA pairs (avoidance for idiosyncratic toxicity).

MNEMONIC

"2D6 = Doses; 2C19 = Citalopram; HLA = Halt"

CYP2D6 problems are dose problems (tricyclics, risperidone, aripiprazole, atomoxetine, all metabolic, all fixed by dose adjustment or drug switch). CYP2C19 keys to Citalopram and escitalopram (the QT and 20 mg cap). HLA-B*15:02 means Halt the carbamazepine, the one immune, life-threatening, screen-before-you-start pair.

PEARL

The single most examinable distinction: pharmacogenetic PK pairs (CYP2D6, CYP2C19) tell you *how much* drug to give, whereas the pharmacodynamic HLA pairs tell you *whether* to give the drug at all. Only HLA-B*15:02 before carbamazepine in Asian-ancestry patients is a genuinely mandated, life-saving pre-prescription test in psychiatry; everything else is dose-tuning or research.

GOOD TO REMEMBER

- **CYP2D6 (chr 22):** metabolises about 25 percent of drugs; all TCAs, some SSRIs, risperidone, aripiprazole, atomoxetine; PM accumulates, UM under-responds.
- **CYP2D6*4:** commonest null allele driving the poor-metaboliser phenotype (about 75 percent of PMs are *4 homozygotes).
- **CYP2D6*10:** decreased-function allele, high frequency in East and South Asian populations.
- **CYP2C19 (chr 10q24):** citalopram, escitalopram, sertraline, tertiary-amine TCAs; *2 and *3 = loss of function (PM), *17 = gain of function (UM).
- **CYP2C19 PM + citalopram:** accumulation and QT prolongation; cap citalopram at 20 mg.
- **Activity score:** 0 = PM, 0.5 = IM, 1 to 2 = NM, above 2 = UM (CPIC/Gaedigk).
- **HLA-B*15:02:** carbamazepine-induced SJS/TEN; common in Han-Chinese and South/South-East Asians; screen before starting; cross-risk with oxcarbazepine and phenytoin.
- **HLA-A*31:01:** carbamazepine hypersensitivity (SJS/TEN, DRESS) across broader ancestries.
- **TPMT (and NUDT15):** poor-metaboliser variants cause severe azathioprine myelosuppression; screen before thiopurines.
- **HTR2A, ANK3:** candidate pharmacodynamic response signals; ANK3 is a robust bipolar GWAS locus; response evidence preliminary, not actionable.
- **Atomoxetine in CYP2D6 PM:** levels peak about 10-fold higher (FDA-labelled).
- **Resources:** CPIC and DPWG (dosing guidelines), PharmGKB (variant-drug annotations), PharmVar (CYP star-allele catalogue).
- **GeneSight:** 8-gene combinatorial panel (PK: CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP3A4, CYP2D6; PD: HTR2A, SLC6A4); weak, mixed RCT evidence, decision-support only.
- **PRS for treatment response:** the pharmacogenomic frontier; explains little variance, not clinically recommended; South-Asian under-representation limits portability.

Discriminate

13 · Discriminate: match the finding to the right design and read a pedigree

These notes have walked through every genetic method one at a time. The examinable skill, and the reason this topic exists, is the opposite move: given a clinical or research *question*, name the **study design** that answers it, and given a family drawn on paper, read the **pedigree** correctly. Vivas and single-best-answer stems rarely ask "define a twin study"; they ask "which design would tell you whether the aggregation is genetic or environmental?" and expect you to say twin study without hesitation. This is a discrimination drill, not a definitions list.

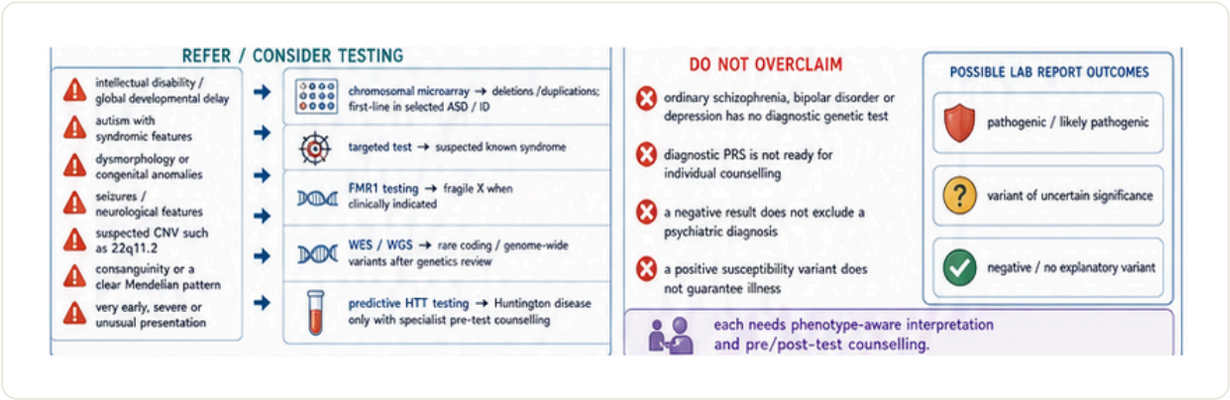


Fig 3.23 When genetic testing helps, and when it does not.

The whole set of notes collapses into one decision tree that Kaplan and Sadock frame as a logical progression of five questions (Kaplan & Sadock 2024): does it run in families, how much is genes versus environment, how is it transmitted, roughly where is the gene, and which specific variants. Bolt on to that the modern clinical add-ons (rare-variant testing, aggregate risk prediction, drug-response prediction) and the classic reading errors that trap the unwary, and you can answer any permutation the paper throws at the material. Then the second half: the standard **pedigree** and **genogram** symbols, recognising an inheritance pattern from them, and turning a family drawing into a recurrence-risk estimate.

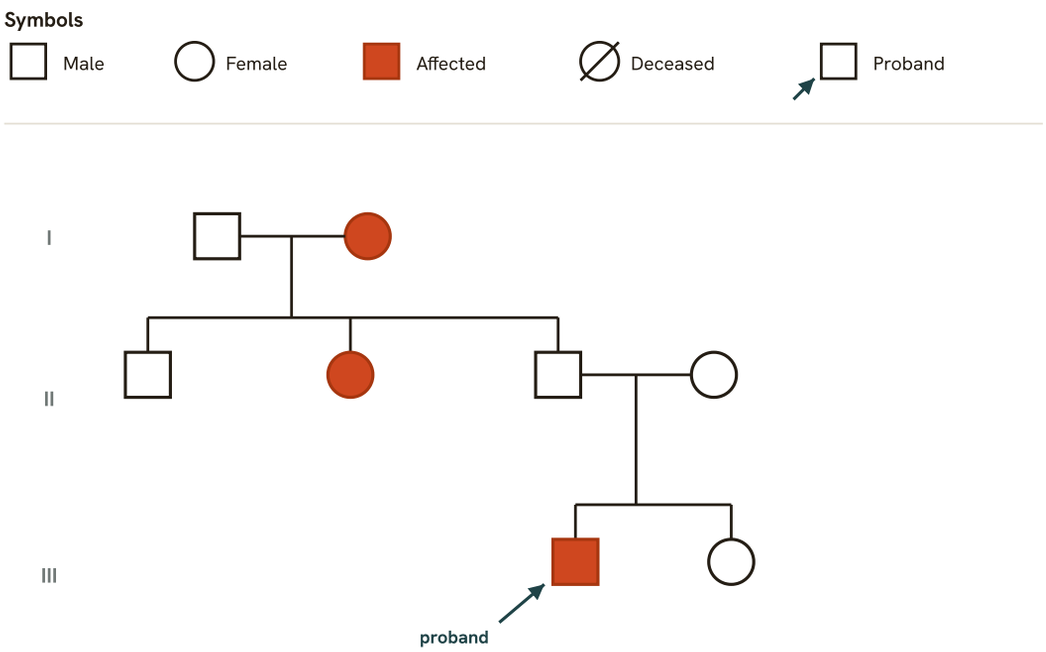


Fig 3.24 Reading a pedigree. The legend gives the standard symbols: squares are male, circles female, a filled symbol is affected, a slash marks deceased, and the arrow marks the proband, the person through whom the family came to attention. In the worked three-generation pedigree, affected members appear in each generation and in both sexes with no clean skipping, which reads as familial aggregation on a multifactorial background rather than a single-gene Mendelian pattern. Recognising the pattern is the first step in choosing the right study design and estimating recurrence risk in counselling.

13.1 The question drives the design: the five-question spine

Answer the question with the cheapest sufficient tool. Genetic epidemiology proceeds as an ordered sequence, and each rung has exactly one design that answers it (Kaplan & Sadock 2024). "Does the phenotype run in families?" is answered by a **family study** (compare disorder rates in relatives of affected probands versus relatives of controls; if genetic, risk rises with closeness of relationship). Familial aggregation alone cannot separate genes from a shared household, so the next question, "how much is genes versus shared environment?", needs a **twin study** (monozygotic versus dizygotic concordance yields heritability). To strip out the confound that families share both genes and rearing, the **adoption study** separates genetic parents from rearing parents. "How is it transmitted?" is a **segregation analysis** (fit Mendelian and non-Mendelian models to pedigree data). "Roughly where is the gene?" is **linkage analysis**, reported as a LOD score. "Which specific variants?" is an **association study**, at genome-wide scale a GWAS. The trick in choosing which design is to read what the stem asks you to *rule out*.

RULE **Answer the question with the cheapest sufficient tool, and read what the stem asks you to rule out.** "Genes or environment?" is a twin study; add "controlling for rearing" and it becomes an adoption study.

13.2 The discrimination table: research question to correct design

This is the memory anchor for the whole set of notes. Read the question in the left column, commit the design in the middle, and note the single word in the right column that discriminates it from its neighbours. The three classic epidemiological designs (family, twin, adoption) form a nested logic: each is introduced to remove a confound the previous one cannot (New Oxford Textbook of Psychiatry 2020; Kaplan & Sadock 2024).

RESEARCH QUESTION (AS THE STEM PHRASES IT)	CORRECT DESIGN	WHAT ONLY THIS DESIGN SETTLES
Does the disorder run in families?	Family study	**Familial aggregation; risk scales with degree of relationship**
Is the aggregation genes or shared environment?	Twin study (MZ vs DZ concordance)	**Separates genes from environment; yields heritability**
Is it genes or the rearing environment specifically?	Adoption study	**Splits genetic parents from rearing parents**
How is the trait transmitted through generations?	Segregation analysis	Tests goodness-of-fit of Mendelian vs complex models
Roughly where on the chromosomes is the locus?	Linkage analysis (LOD score)	**Coarse chromosomal region via co-segregation in families**
Which common variants raise risk across the population?	Association study / GWAS	**Specific common alleles; unit is the unrelated individual**
Is there a specific rare cause in this one patient?	Chromosomal microarray (CMA) for CNVs; sequencing (WES/WGS)	**Individual molecular diagnosis, not population inference**
What is this patient's aggregate inherited liability?	Polygenic risk score (PRS)	Sums weighted effects of many common SNPs into one score
Will this drug work or harm this patient?	Pharmacogenetic test (e.g. CYP metaboliser status, HLA risk allele)	**Predicts drug response or toxicity, not disease risk**

The decision tree in one grid: match the phrasing of the stem to the design, then check the discriminator that separates it from its nearest rival.

13.3 The two commonest confusions: which design, and which level

Family versus twin, and population versus individual. Two axes trip candidates. First, **which design** along the family-to-molecular axis: a family study proves aggregation but can never separate genes from a shared household, so any stem that says "distinguish genetic from environmental transmission" demands a twin study, and one that adds "controlling for the rearing environment" demands an adoption study. Second, the *level* of inference: family, twin, adoption, linkage and association all make *population-level* statements about a disorder, whereas CMA, sequencing, PRS and pharmacogenetic testing make statements about *this individual patient in front of you*. When a stem is framed clinically ("a 6-year-old boy with autism and dysmorphism", "an antidepressant non-responder"), the answer is almost always an individual-level test

(microarray, sequencing, or a pharmacogenetic panel), not a research design (Kaplan & Sadock 2024).

HOLD THIS

Population design or individual test? A clinical stem means an individual-level test. Family, twin, adoption, linkage and association make population statements; CMA, sequencing, PRS and pharmacogenetic testing speak to the one patient in front of you.

COMMON TRAP

Do not answer "twin study" when the stem asks to separate genetic transmission from the *rearing* environment specifically: that is the adoption study's job, because twins reared together share both genes and household. And do not answer "GWAS" for a single patient's diagnostic workup: GWAS is a population design that discovers common risk alleles, whereas a chromosomal microarray or sequencing panel is what yields a molecular diagnosis in one child.

13.4 Reading a pedigree: the standard symbols

You cannot interpret a family you cannot decode. A pedigree (the clinical drawing is a **genogram** when it also carries relationship and social detail) uses a fixed symbol set that examiners expect you to read on sight. Learn the core glyphs cold; a mislabelled proband or a missed consanguinity line changes the whole interpretation.

Square
Male.

Circle
Female.

Diamond
Sex unknown or unspecified.

Filled (shaded) symbol
Affected individual. A half-filled or dotted symbol conventionally marks a carrier or a milder/subthreshold phenotype.

Open (unfilled) symbol
Unaffected.

Diagonal line (slash) through a symbol
Deceased.

Arrow (with "P")
The proband, i.e. the index case through whom the family was ascertained.

Horizontal line joining two symbols
A mating (partnership).

Double horizontal line
Consanguineous mating (partners are blood relatives): a major clue to autosomal recessive inheritance.

Vertical line down to a horizontal sibship line
Offspring of the mating; siblings hang off the sibship line left to right by birth order.

Roman numerals (I, II, III) down the left margin

Generations, oldest at the top. Individuals within a generation are numbered left to right in Arabic numerals, so "II-3" is a specific person.

13.5 Recognising the inheritance pattern from the drawing

The pattern is in the geometry. Once decoded, the shape of shading across generations suggests the mode of transmission, and this is a favourite viva move. Autosomal dominant: affected individuals in every generation (vertical transmission), roughly half of offspring affected, and male-to-male transmission is possible. Autosomal recessive: affected individuals cluster in a single sibship with unaffected parents (horizontal pattern), and consanguinity (the double line) raises the odds; both sexes affected equally. X-linked recessive: mostly affected males, transmitted through unaffected carrier females, with *no* male-to-male transmission (a father cannot pass his X to a son). X-linked dominant: affected in every generation, but affected fathers transmit to all daughters and no sons. Mitochondrial: transmitted only through the maternal line, all children of an affected mother at risk, no transmission through affected fathers. Psychiatric disorders fit *none* of these cleanly, which is itself the exam point: they are polygenic and multifactorial, so a pedigree shows aggregation without a recognisable Mendelian signature (New Oxford Textbook of Psychiatry 2020).

TRAP Do not force a psychiatric pedigree into a Mendelian pattern: familial aggregation without a clean dominant, recessive or X-linked signature is the expected picture for a polygenic, multifactorial disorder.

13.6 Estimating recurrence risk from the genogram

From drawing to a number for counselling. For a clear single-gene pattern, recurrence risk follows Mendelian arithmetic: autosomal dominant gives about 50% to each child of an affected parent, autosomal recessive about 25% to the next child of two carrier parents (one in four), X-linked recessive gives 50% of sons of a carrier mother affected and 50% of daughters carriers. For the multifactorial psychiatric disorders you actually counsel on, there is no Mendelian fraction; you fall back on **empirical recurrence risks** derived from family studies. For schizophrenia these are the numbers to carry: roughly 5 to 15% for a first-degree relative against a population baseline near 1%, rising steeply with the number of affected relatives and with closeness of relationship (Kaplan & Sadock 2024). Recurrence risk in multifactorial disease also rises with severity of the index case and with the number already affected in the family, and it falls off faster than the Mendelian halving as you move to more distant relatives.

CLINICAL ANCHOR

A CMA (chromosomal microarray) finding of a 22q11.2 deletion in a child reframes the whole pedigree: this single CNV carries an associated risk of roughly 25 to 30% of developing a psychotic disorder (Kaplan & Sadock 2024), a far larger per-carrier effect than any common SNP. It is the standard worked example of why, for an individual patient with intellectual disability or syndromic features, you order a microarray (an individual-level rare-variant test) rather than reasoning from population heritability.

13.7 The classic false conclusions when reading families

Aggregation is not proof of a shared gene. The reason twin and adoption designs exist is that a pedigree can mislead in half a dozen stereotyped ways, and naming these is a reliable viva question. Each is a way a family can look genetic when it is not, or look non-genetic when it is (Kaplan & Sadock 2024; New Oxford Textbook of Psychiatry 2020).

Assortative mating

Affected individuals partner non-randomly with similarly affected partners, concentrating risk alleles in a lineage and inflating apparent aggregation beyond simple transmission.

Phenocopy

An environmentally produced case clinically identical to the genetic form; an affected person in the pedigree who carries none of the family's risk variants, blurring co-segregation.

Incomplete (reduced) penetrance

A gene carrier who never manifests the disorder appears as an unaffected symbol, so the gene seems to "skip" and dominant inheritance is missed.

Variable expressivity

The same variant produces different or milder phenotypes across relatives (a hallmark of many CNVs, e.g. 16p11.2), so the "same" gene looks like different conditions in one family.

Genetic (locus) heterogeneity

Different genes cause the same phenotype in different families; pooling pedigrees dilutes any single linkage signal, a core reason linkage failed in psychiatry.

Shared environment mistaken for shared genes

A common household exposure (diet, toxin, trauma, infection) aggregates in relatives and mimics genetic transmission; only twin and adoption designs can distinguish it.

PEARL

Every one of these six is a reason a pedigree alone cannot prove a genetic cause, which is exactly why the field built twin and adoption designs on top of the family study. Turn the list around at exam time: if asked "why is familial aggregation not sufficient evidence of a genetic cause?", these six confounders (led by shared environment) are your answer.

MNEMONIC

FAMILY - TWIN - ADOPT - SEGREGATE - LINK - ASSOCIATE

Runs it? FAMILY study. Genes or environment? TWIN. Genes or rearing? ADOPT. How transmitted? SEGREGATE. Where is it? LINK (LOD). Which variant? ASSOCIATE (GWAS). The order is also the historical and logical order in which each question can only be asked once the previous is answered.

GOOD TO REMEMBER

- **Family study:** answers "does it run in families?"; proband and relatives vs control relatives; risk scales with degree of relationship (first-degree share ~50% of genes).
- **Twin study:** answers "genes vs environment?"; MZ vs DZ concordance yields heritability.
- **Adoption study:** answers "genes vs rearing environment?"; separates genetic from rearing parents.
- **Linkage analysis:** answers "roughly where?"; LOD +3 = proof (1000:1 odds for), LOD -2 = exclusion.
- **Association / GWAS:** answers "which common variant?"; genome-wide significance threshold p < 5 x 10 to the -8.
- **Schizophrenia empirical recurrence risk:** first-degree relative ~5 to 15% vs population ~1% (Kaplan & Sadock 2024).
- **Schizophrenia twin concordance:** MZ ~40 to 60%, DZ ~10 to 16%; heritability ~80% (Kaplan & Sadock 2024).
- **22q11.2 deletion syndrome:** CNV detectable on CMA; associated psychosis risk ~25 to 30% per carrier (Kaplan & Sadock 2024).
- **16p11.2 CNV:** variable expressivity, linked across ASD, schizophrenia and bipolar disorder (Tasman 2015).
- **PRS for schizophrenia:** best current score explains ~11% of liability; theoretical ceiling ~25% (Kaplan & Sadock 2024).
- **Pedigree symbols:** square male, circle female, filled affected, diagonal deceased, arrow proband, double line consanguinity, generations in Roman numerals.

Apply and consolidate

14 · Genetic counselling in psychiatry

Genetic counselling in psychiatry is the clinical process of helping a patient and family understand the genetic and environmental contributions to a psychiatric disorder, appreciate the chance of recurrence in relatives, and reach their own decisions about reproduction, testing and life planning (Kaplan & Sadock 2024; Austin 2020). It is deliberately distinct from the Mendelian counselling of single-gene disease: psychiatric disorders are complex and polygenic, so recurrence chances are quoted as **empirical risks** derived from family, twin and adoption studies, not from Mendelian ratios. The modern model, well developed in the psychiatric genetic-counselling outcomes literature, treats the encounter as more existential than arithmetical, centred on the question "Why me?" and on relieving guilt, blame and fear rather than on delivering a number (Inglis et al. 2015; Austin 2020).

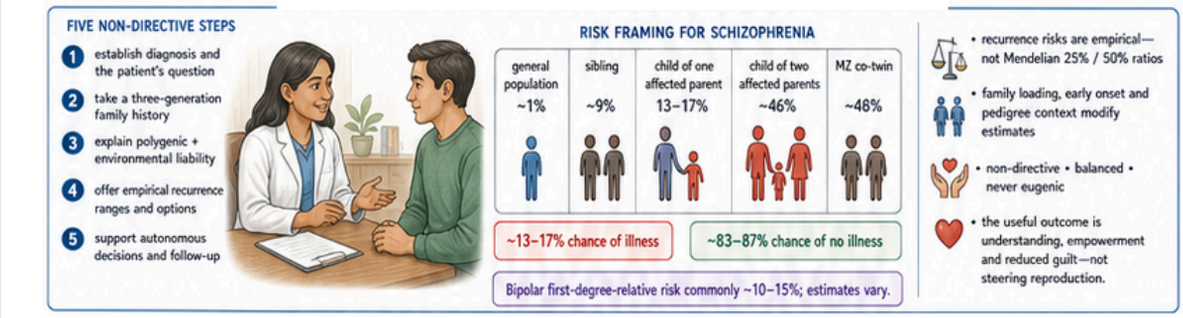


Fig 3.25 Genetic counselling: numbers without destiny.

Why it matters. This is a high-yield exam topic that sits at the junction of genetics, ethics and Indian practice. Examiners reward candidates who can state the standard empirical figures for schizophrenia and bipolar disorder, articulate the **non-directive** stance, know when to refer to clinical genetics, and place the whole discussion inside a consent and capacity framework. The India layer, consanguinity, arranged-marriage disclosure pressure and family-level decision-making, is what turns a textbook answer into a distinction answer. For the underlying consent, capacity and ethics scaffolding, cross-reference paper iii.

14.1 What genetic counselling is, and is not

A communication process, not a verdict. The classic definition frames genetic counselling as a communication process dealing with the human problems associated with the occurrence, or risk of occurrence, of a genetic disorder in a family: helping the individual comprehend the medical facts, appreciate how heredity contributes, understand the options for dealing with recurrence, choose the course of action congruent with their goals and values, and make the best adjustment to the disorder (Resta et al. 2006, adapting Fraser). Every clause is about supported autonomous decision-making, not about reducing the incidence of illness.

Not eugenics. A goal of reducing the birth rate of a condition is explicitly eugenic and is not an acceptable aim of counselling; the counsellor must not present any reproductive decision as correct or advantageous for the patient or for society (National Academies consensus). This principle is load-bearing for the ethics viva.

Delivered increasingly by specialists. Reproductive genetic counselling is now largely the province of medical geneticists and certified genetic counsellors rather than psychiatrists, given the pace of testing technology; but the psychiatrist must recognise the situations in which counselling is indicated and make the referral (Harrison et al., Shorter Oxford Textbook of Psychiatry 2018). Dedicated psychiatric genetic-counselling clinics (for example the Adapt clinic, British Columbia) accept both physician referrals and self-referrals (Inglis et al. 2015).

14.2 Non-directiveness: the governing stance

Definition. **Non-directive counselling** means the counsellor provides balanced, accurate information and emotional support but does not steer the patient toward any particular reproductive or testing decision; the choice, and the values that drive it, belong to the patient

(Kaplan & Sadock 2024). It is the declared standard of care for reproductive planning and for counselling around untreatable disorders.

Why psychiatry stresses it. People weigh reproductive risk by their felt ability to cope with an affected child far more than by precise numerical probabilities, and risk perception is shaped by control, treatability, visibility and whether they know an affected person (Lippman-Hand & Fraser). A directive stance overrides exactly the personal calculus that counselling exists to protect.

The realistic caveat. Pure non-directiveness is an ideal; skilled counsellors still shape the frame through which information is presented, so the safeguard is transparency and reflection rather than a pretence of value-neutrality.

RULE **Non-directive, and never eugenic.** Supply balanced information and support, leave the reproductive decision to the patient, and never frame reducing the birth rate of a condition as a goal of counselling.

14.3 Step one: establish the diagnosis and build the pedigree

Diagnosis first. No risk figure is meaningful until the proband's diagnosis is secure, because empirical risks are disorder-specific and the schizophrenia figures differ from the mood-disorder figures. A misassigned diagnosis propagates a wrong risk estimate to the whole family.

The three-generation pedigree. Best-practice psychiatric genetic counselling bases chances on a detailed, systematically taken three-generation family history, then applies empirical data to that specific pedigree rather than quoting a generic textbook number (Austin et al. 2008; Austin 2020). Family loading (number and closeness of affected relatives, early onset) shifts the individualised estimate above or below the population figure.

Contracting. Fewer than half of patients presenting for psychiatric genetic counselling actually want a recurrence number at referral; the counsellor contracts explicitly, discusses aetiology and recovery first, then checks again whether the patient wants specific figures. After that discussion only around 40 percent opt to hear specific chances, and interest often falls once the emotional driver behind the question is addressed (Borle et al. 2018).

14.4 Step two: communicate empirical recurrence risks

Empirical, not Mendelian. Because liability is polygenic and multifactorial, recurrence chances come from observed rates in relatives of probands (corrected for the age of risk, so-called expectancy rates or **morbid risks**), not from Mendelian segregation ratios (Shorter Oxford Textbook of Psychiatry 2018). Figures are best given as absolute risks and frequencies with broad ranges, always anchored against the roughly 1 percent population baseline for schizophrenia (Austin et al. 2008; Borle et al. 2018).

Schizophrenia. Using the pooled lifetime-risk figures (Gottesman, reproduced in Shorter Oxford Textbook of Psychiatry 2018): a sibling of a proband carries about 9 percent, a child of one affected parent about 13 to 17 percent, a child of two affected parents about 46 percent, and the monozygotic co-twin about 48 percent (with twin studies converging on 40 to 50 percent).

Bipolar disorder: the first-degree-relative risk is of the order of 10 to 15 percent in the narrower estimates commonly quoted in counselling, with older broad-liability family studies giving figures as high as 25 to 27 percent for offspring of one affected parent; the monozygotic co-twin concordance is around 60 percent (Shorter Oxford Textbook of Psychiatry 2018). The spread itself is the teaching point: quote a range, name the source, and never imply false precision.

How to frame the number. Present risk in the context of the population rate, avoid framing that inflates dread ("a 13 percent chance of illness" also means an 87 percent chance of no illness), and pair every figure with the reminder that genes set liability while environment and chance decide expression.

RELATIONSHIP TO PROBAND	SCHIZOPHRENIA LIFETIME RISK	BIPOLAR DISORDER RISK
General population (baseline)	~1%	**~1%**
Sibling	~9%	**~5 to 10%**
Child, one affected parent	~13 to 17%	**~10 to 15% (up to ~25 to 27% in broad-liability studies)**
Child, both parents affected	~46%	**markedly higher (broad studies quote up to ~74%)**
Dizygotic co-twin	~17%	**~20%**
Monozygotic co-twin	~48% (range 40 to 50%)	**~60%**

Empirical recurrence risks by relationship: schizophrenia figures from the Gottesman pooled data (Shorter Oxford 2018); bipolar figures span narrow counselling estimates and older broad-liability family studies, hence the ranges.



14.5 When to refer to clinical genetics

The referral triggers. The psychiatrist should refer to a medical geneticist or genetic-counselling service when features suggest a discrete, testable cause rather than ordinary polygenic liability: *dysmorphology* (an unusual facial gestalt or congenital anomalies), *intellectual disability* or global developmental delay accompanying the psychiatric presentation, a *suspected syndromic or copy-number cause* (for example 22q11.2 deletion presenting with psychosis, or fragile X in ID with autism features), and *consanguinity*, which raises the yield of autosomal-recessive and homozygous-variant conditions.

Why it matters clinically. These situations may carry a much larger, sometimes near-Mendelian, individual risk than the polygenic average: an individual with a 3q29 deletion has been estimated to have roughly a one-in-three chance of developing schizophrenia, and chromosomal microarray is now a routine test in selected patients (Shorter Oxford Textbook of Psychiatry 2018; Baker et al. 2014). A syndromic diagnosis also reframes counselling, prognosis and, occasionally, targeted management.

Practical rule. Ordinary schizophrenia or bipolar disorder without dysmorphology, ID or a suggestive family pattern is counselled with empirical risks; add-red-flag features earn a genetics referral and possible cytogenetic or microarray testing.

HOLD THIS

Counsel with empirical, not Mendelian, risks; refer the red flags. Polygenic liability means recurrence comes from family-study rates against the ~1% baseline; dysmorphology, intellectual disability, a suspected CNV or consanguinity earn a clinical-genetics referral.

14.6 Predictive and prenatal testing, and their ethical weight

No clinical predictive test exists for common psychiatric disorders. For schizophrenia and bipolar disorder there is no validated genetic test that predicts who will fall ill; the honest answer to "will it happen again?" is that we cannot predict with certainty (Austin & Peay). Predictive testing in the true sense applies to the rare high-penetrance neuropsychiatric conditions, above all Huntington's disease, where presymptomatic DNA testing is possible and mandates pre-test counselling by a clinical geneticist (Companion to Psychiatric Studies; MacLeod et al. 2013).

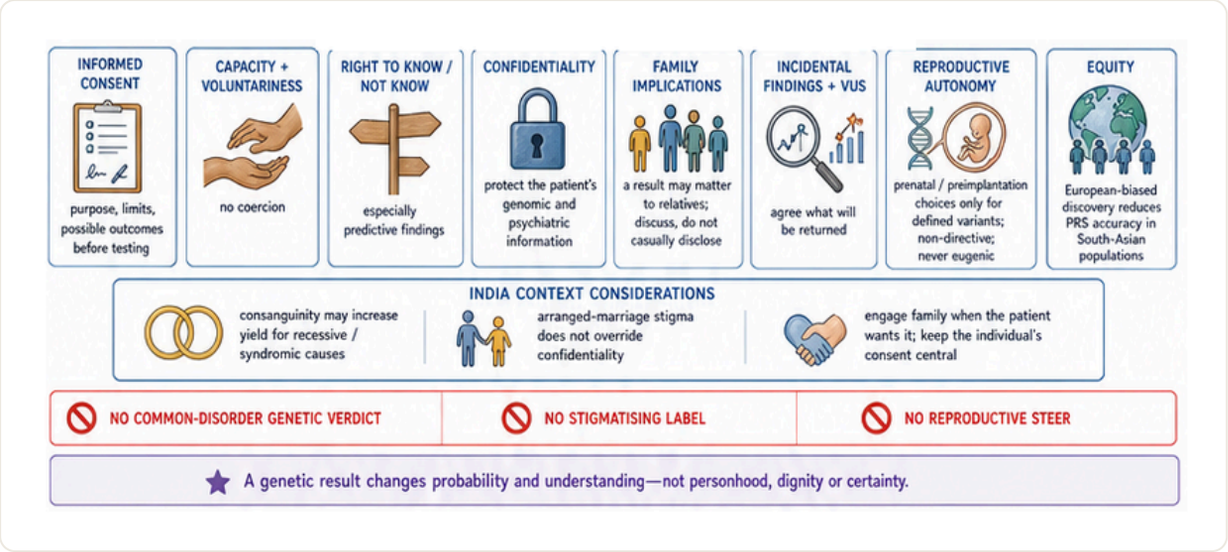


Fig 3.26 Ethics, equity and genomic humility.

The weight of a presymptomatic result. Learning one's status for an untreatable condition carries risks to mood, self-image, reproductive and career decisions and insurability; a positive result has implications for other family members who may not wish to know theirs (New Oxford Textbook of Psychiatry; Kaplan & Sadock 2024). Protocols therefore insist on informed consent, a cooling-off structure, and support before and after disclosure.

Prenatal testing. Prenatal or preimplantation testing is meaningful only for the rare identifiable single-gene or chromosomal causes, not for polygenic psychiatric liability; where offered, non-directiveness and full pre- and post-test counselling are the standard, and the decision to test or to continue a pregnancy is left to the couple (National Academies consensus).

14.7 Incidental findings and the meaning of a "negative"

Incidental (secondary) findings. Broad testing such as chromosomal microarray or exome sequencing can reveal variants unrelated to the presenting complaint, including variants of

uncertain significance and medically actionable secondary findings; consent must cover in advance what will be returned and what the patient wishes to know (Kaplan & Sadock 2024).

The two-sided interpretation trap. Because these are susceptibility not diagnostic tests, many people with a clear psychiatric diagnosis carry no identified variant, and many carriers never fall ill. A "negative" result may wrongly make a patient doubt the validity of their diagnosis or reduce treatment adherence, and may paradoxically increase parental guilt by removing a biological explanation; a positive susceptibility result labels risk without certainty (Kaplan & Sadock 2024). Pre-test counselling must rehearse the meaning of both outcomes.

14.8 Polygenic risk scores: not yet clinical

What a PRS is. A **polygenic risk score** sums the effects of many common risk alleles weighted by GWAS data to estimate an individual's genetic liability to a disorder (Kaplan & Sadock 2024). It captures the en-masse effect of variants that are not individually genome-wide significant.

Why it is not used in counselling. Current PRS modify a family-history-based estimate only marginally, are not definitively predictive, and are far less informative outside populations of European ancestry because the discovery datasets are predominantly European, an equity problem acute for Indian patients (Kaplan & Sadock 2024; Murray et al. 2021; Wray et al. 2021). The consensus through 2026 is that PRS remain a research tool, not a clinical counselling instrument, and should not be quoted as an individual risk to a patient. Communicating a non-definitive score risks being read as higher than warranted or being discounted, in ways that vary with the patient's coping style (Kaplan & Sadock 2024).

INDIA

Consanguinity. Consanguineous marriage is common in parts of India and raises the yield of autosomal-recessive and syndromic causes of intellectual disability, autism and epilepsy that can present with psychiatric features; a consanguineous pedigree is itself a trigger to consider a clinical-genetics referral rather than to quote polygenic empirical risks alone. **Disclosure pressure.** In the arranged-marriage context a family history of mental illness carries heavy stigma, and families may face pressure either to conceal a psychiatric diagnosis during matchmaking or to demand disclosure from the other party. The counsellor's duty is to the patient's confidentiality and autonomy: information about a proband is shared only with the patient and, where relevant, guardians of a dependent child, never volunteered to grandparents or prospective in-laws (Borle et al. 2018). Framing risk to reduce stigma, and resisting any eugenic or "don't marry / don't have children" steer, matters more here than anywhere. **Family-level decisions.** Reproductive and marital choices are frequently made at the level of the extended family rather than the individual, so non-directive counselling in India often means engaging the family unit while still protecting the individual patient's consent and confidentiality. See paper iii for the consent, capacity and confidentiality framework these tensions sit within.

COMMON TRAP

Quoting Mendelian ratios (25 percent, 50 percent) for schizophrenia or bipolar disorder. These are polygenic conditions; recurrence is given as *empirical* risk from family and twin studies, corrected for age of risk. A "25 percent" answer for a first-degree relative may coincidentally resemble a broad-liability figure for bipolar disorder, but the reasoning (autosomal-dominant segregation) is wrong and loses marks.

PEARL

The best-evidenced *outcome* of psychiatric genetic counselling is increased patient empowerment and reduced guilt, not changed reproductive decisions, and the largest gains occur in people who initially wanted a recurrence number but changed their mind after discussing aetiology and recovery (Borle et al. 2018; Inglis et al. 2015). The number is often the ticket in, not the therapeutic ingredient.

CLINICAL ANCHOR

A 28-year-old woman with schizophrenia (ICD-11 6A20; DSM-5-TR schizophrenia) asks what chance her future child has of the illness. You secure the diagnosis, take a three-generation pedigree (no other affected relatives), and, after contracting, offer an empirical figure of roughly 13 percent for a child of one affected parent against a population baseline near 1 percent, framed non-directively and alongside the 87 percent chance of no illness. No PRS is quoted. Because there is no dysmorphology, intellectual disability or consanguinity, no clinical-genetics referral is needed.

MNEMONIC

DR PACE

Diagnosis confirmed, **R**ecords and three-generation pedigree, **P**opulation-anchored empirical risk (not Mendelian), **A**utonomy and non-directiveness, **C**onsent for predictive or prenatal testing (and paper iii capacity/ethics), **E**motional support and follow-up. The steady pace of psychiatric genetic counselling: diagnosis before numbers, support around the numbers.

GOOD TO REMEMBER

- **Schizophrenia, sibling of proband:** ~9% lifetime risk (Gottesman, Shorter Oxford 2018).
- **Schizophrenia, child of one affected parent:** ~13 to 17% (classic Gottesman figure ~13%; Shorter Oxford table lists 17%).
- **Schizophrenia, child of two affected parents:** ~46%.
- **Schizophrenia, monozygotic co-twin:** ~48% (twin-study range 40 to 50%); dizygotic co-twin ~17%.
- **Schizophrenia population baseline:** ~1%.
- **Bipolar disorder, first-degree relative / child of one parent:** ~10 to 15% in narrow counselling estimates; older broad-liability family studies give up to ~25 to 27%.
- **Bipolar disorder, monozygotic co-twin concordance:** ~60%; dizygotic ~20%.
- **3q29 deletion:** ~1-in-3 (~33%) chance of developing schizophrenia, an example of a high-risk CNV warranting clinical-genetics referral.
- **22q11.2 deletion:** syndromic cause of psychosis; a referral trigger when psychosis co-occurs with dysmorphology or developmental features.
- **Huntington's disease:** the exemplar of true presymptomatic (predictive) DNA testing, mandating pre-test genetic counselling.
- **Polygenic risk score (PRS):** sums many common GWAS alleles; NOT clinically actionable in counselling as of 2026, and less valid in non-European (including Indian) populations.

15 · Apply: four genetics vignettes

The whole set of notes converges here. Psychiatric genetics earns its exam marks only when a family history, an ancestry, a dysmorphic phenotype or a metaboliser report is made to *predict* a clinical consequence and then force a first move. These four vignettes are deliberately drawn from four corners of the discipline, so the discriminator in each is a different genetic tool: an **empirical recurrence risk** read off polygenic familial data, a **pharmacogenomic HLA test** that averts a fatal skin reaction, a **copy-number variant** hunted with a cytogenetic assay, and a **pedigree read alongside a CYP genotype**. Each runs to the three-beat rhythm the examiners reward: the **presentation**, then the **genetic reasoning** that alone explains it, then the **counselling, testing or dosing action** the genetics forces.

Read each as a reasoning drill, not a fact to memorise. If you can name the tool the moment the stem lands, whether the answer is a probability given non-directively, an allele screened before a drug, an assay ordered before a referral, or a study design chosen to match a transmission pattern, the response is already written. Numbers that carry weight are given only where a canonical source verifies them, and any figure to confirm against a current guideline or formulary before quoting is flagged (Kaplan & Sadock 2024; New Oxford 2020; Maudsley 2021). A hard rule threaded through all four: give population-level probabilities without implying determinism, and never name a diagnosis to a family in a way that stigmatises the proband or an unaffected relative.

15.1 Vignette 1: a couple ask about their child's risk when one partner has bipolar disorder, the empirical-risk counselling drill

CLINICAL ANCHOR

Case: a couple attend for pre-conception advice. The husband has an established diagnosis of bipolar type I disorder (ICD-11 6A60; DSM-5-TR bipolar I disorder), well controlled on lithium. The wife has no psychiatric history and no affected relatives. They ask, directly, what the chance is that a future child will develop the same illness, and whether they should have children at all.

Reasoning. Bipolar disorder is the single most heritable major psychiatric disorder (heritability around 0.85, rising toward 0.9 for narrowly defined bipolar-I; MZ co-twin concordance conventionally around 60 percent against a DZ rate an order lower), yet its inheritance is *polygenic and non-Mendelian*: it does not segregate in simple ratios, so there is no single-gene calculation to offer (Kaplan & Sadock 2024; McGuffin 2003). What counselling uses instead is the **empirical recurrence risk**, the observed rate of illness in relatives of probands read straight off family-study data. For a child with one affected parent the empirical risk of bipolar disorder is of the order of 10 to 15 percent, several-fold above the roughly 1 to 2 percent population baseline; the risk of any mood disorder (including unipolar depression) in that child is higher still, and the figure climbs further, toward 40 to 50 percent, if both parents are affected (verify the exact figures against a current text before quoting). Recurrence risk in this model rises with the severity of the index case and with the number of affected relatives, the same liability-threshold logic that governs all the common disorders.

Counselling action (non-directive). The mechanism dictates the manner. Genetic counselling here is **non-directive**: you supply the empirical probability as a probability, frame it against the population baseline so it is neither minimised nor catastrophised, and explicitly leave the reproductive decision to the couple rather than advising for or against childbearing. Add the constructive counterweight that most children of an affected parent do *not* develop bipolar disorder, that no prenatal or predictive genetic test exists for a polygenic condition of this kind, and that early recognition and treatment of any future illness improves outcome. Where relevant, fold in the separate, drug-specific reproductive-safety discussion (lithium and first-trimester exposure) as its own strand, and route the detailed peri-conception medication protocol to the clinical psychiatry chapters (Paper II).

COMMON TRAP

Do not quote a Mendelian fraction (a "one in four" or "one in two") for a polygenic psychiatric disorder: that arithmetic belongs to single-gene conditions and misrepresents the biology. And do not drift into directive advice ("you shouldn't have children") or false reassurance ("it won't be passed on"). The examinable failure modes are the Mendelian-ratio error and the loss of non-directiveness; the correct answer is an empirical percentage, delivered neutrally, with the decision left to the couple.

15.2 Vignette 2: carbamazepine in a patient of Han-Chinese or South-Asian ancestry, the HLA-B*15:02 screen before starting

CLINICAL ANCHOR

Case: a 30-year-old man of Han-Chinese ancestry (the same caution applies across South-East and South Asian populations, including Thai and many Indian groups) is to be started on carbamazepine, whether for a mood-stabilising indication in bipolar disorder or for trigeminal neuralgia or epilepsy. He is treatment-naive to the drug. Before writing the prescription, the question is what to check.

Reasoning. Carbamazepine can precipitate the life-threatening severe cutaneous adverse reactions **Stevens-Johnson syndrome** and **toxic epidermal necrolysis (SJS/TEN)**. The susceptibility is pharmacogenomic and strongly ancestry-linked: the class I HLA allele **HLA-B*15:02** is the established risk marker for carbamazepine-induced SJS/TEN, and its carrier frequency is substantial in Han-Chinese, Thai and many South and South-East Asian populations while being rare in Europeans (Kaplan & Sadock 2024). The mechanism is immunogenetic, not metabolic: the risk allele shapes the HLA-restricted T-cell response to the drug, so this is a pharmacodynamic pharmacogenetic marker of a hypersensitivity reaction rather than a dose-handling problem. Because the reaction is idiosyncratic and severe, the genetic test is deployed *pre-emptively*, before the first dose, in the at-risk ancestry groups.

Testing action. Screen for **HLA-B*15:02** before initiating carbamazepine in patients of the relevant ancestry, and if the patient is positive, *avoid carbamazepine* and choose an alternative agent unless the benefit clearly outweighs the risk. Two examinable refinements: HLA-B*15:02 positivity also flags cross-risk with other aromatic antiepileptics that cause SJS/TEN, notably phenytoin and oxcarbazepine, so phenytoin is *not* a safe substitute in a positive patient; and a distinct allele, HLA-A*31:01, is linked to a broader spectrum of carbamazepine hypersensitivity (including DRESS and maculopapular eruption) across other ancestries including Europeans. Genotyping does not replace clinical vigilance: counsel every starter about the early rash and mucosal warning signs and the instruction to stop and present immediately (verify current screening thresholds and the exact at-risk populations against a live guideline; Kaplan & Sadock 2024; Maudsley 2021).

INDIA

This vignette is squarely an Indian-practice issue: HLA-B*15:02 carriage is appreciable across several South Asian groups, so ancestry-based pre-carbamazepine screening is directly relevant to prescribing here, not a Western-only footnote. Where testing is not readily available or affordable, the pragmatic and defensible move is to favour an alternative mood stabiliser or antiepileptic in a patient from a high-frequency background, and to document an explicit informed discussion of the SJS/TEN risk and the early warning signs.

15.3 Vignette 3: developmental delay, dysmorphism and later psychosis, recognising 22q11.2 and ordering the right assay

CLINICAL ANCHOR

Case: a young person carries a history of developmental delay and learning difficulty from childhood, with subtle dysmorphic features, a history of a congenital cardiac anomaly and recurrent infections, and a characteristically nasal quality to the speech. In late adolescence he now presents with a first episode of psychosis (ICD-11 6A20 schizophrenia; DSM-5-TR schizophrenia). The task is to recognise the pattern and act on it.

Reasoning. The constellation of developmental delay, dysmorphism, a conotruncal cardiac lesion, immune and palatal features, and a markedly elevated risk of psychosis is the signature of the **22q11.2 deletion syndrome** (velocardiofacial syndrome / DiGeorge syndrome), a microdeletion on the long arm of chromosome 22. It is the single best-characterised and highest-yield copy-number variant in psychiatric genetics: it is a large recurrent deletion that confers one of the strongest known monogenic-scale risks of schizophrenia, with a substantial minority of 22q11.2-deletion carriers developing a schizophrenia-spectrum psychosis, which is why the deletion has focused attention on genes in that region as predisposing to psychosis in general (New Oxford 2020; Shorter Oxford 2018). Unlike a single-nucleotide polymorphism, a CNV of this size behaves like a miniature chromosomal abnormality of high penetrance, so recognising the somatic phenotype behind the psychosis is what converts a routine first-episode presentation into a specific genetic diagnosis.

Testing and referral action. Order a genetic test that can detect a submicroscopic deletion: **chromosomal microarray (CMA)** is the first-line genome-wide assay for copy-number variants and is the appropriate broad test when the differential is open, while a *targeted* assay, fluorescence in-situ hybridisation (FISH) for the 22q11.2 locus (or MLPA), confirms the deletion quickly when 22q11.2 is specifically suspected on the phenotype. A standard karyotype will typically *miss* a microdeletion of this size and is the wrong test. Refer to **clinical genetics** for confirmation, cascade family testing and formal genetic counselling, because the deletion is often de novo but can be inherited, and coordinate the multisystem workup (cardiac, immune, endocrine including calcium). The psychiatric management of the psychosis itself follows standard first-episode lines and belongs to the clinical psychiatry chapters (Paper II).

COMMON TRAP

Do not order a conventional karyotype expecting it to find 22q11.2: it resolves whole-chromosome and large structural changes, not a microdeletion of this scale, so a normal karyotype is falsely reassuring. The correct first-line for CNV detection across an undifferentiated developmental-delay-plus-dysmorphism-plus-psychosis picture is chromosomal microarray; FISH (or MLPA) is the fast targeted confirmatory step when the phenotype points specifically at 22q11.2.

15.4 Vignette 4: a three-generation pedigree plus a CYP2D6 poor-metaboliser report, reading the pattern and adjusting the drug

CLINICAL ANCHOR

Case: you are handed a three-generation pedigree of a family with recurrent depressive illness and a laboratory report on the index patient stating she is a **CYP2D6 poor metaboliser** (for example homozygous for a null allele such as CYP2D6*4). She has developed marked adverse effects on a standard dose of a CYP2D6-dependent antidepressant. Two separate questions are embedded: what does the pedigree tell you about study design, and what does the genotype tell you about her drug.

Reasoning, part one: reading the pedigree for a study design. A pedigree with illness appearing across successive generations but *not* segregating in clean Mendelian ratios, affecting both sexes, with variable expression and incomplete penetrance, is the familiar picture of a common, polygenic psychiatric disorder rather than a single-gene trait. The genetic-epidemiology tool matched to that pattern is *not* classical parametric linkage, which assumes a specified single-locus model and a known mode of inheritance and is powerful only for rare monogenic traits; it is the family-based and population approaches suited to complex inheritance: non-parametric linkage or affected-sib-pair methods, and above all association designs (genome-wide association studies) that detect the many small-effect common variants. The reading skill is to let the transmission pattern pick the design: male-to-male transmission excludes X-linkage, a clean vertical dominant or clustered recessive pattern would invite a Mendelian linkage approach, whereas this "familial but not Mendelian" pedigree signals a polygenic architecture and an association or non-parametric strategy (Kaplan & Sadock 2024; New Oxford 2020).

Reasoning, part two, and the dosing action. The **CYP2D6** report is a pharmacokinetic pharmacogenetic result about a hepatic drug-metabolising enzyme. A **poor metaboliser** (two non-functional alleles, activity score 0) clears CYP2D6-dependent drugs slowly, so at a standard dose plasma concentrations run high and dose-related adverse effects and toxicity follow, exactly her picture. The action the genotype forces is to *reduce the dose* of the CYP2D6-substrate antidepressant, or switch to an agent not dependent on CYP2D6, guided by the genotype and by therapeutic drug monitoring where available; the mirror-image caution is the *ultrarapid* metaboliser (gene duplication) who under-responds at standard doses because the drug is cleared too fast. This is the corner of pharmacogenetics closest to immediate clinical translation, with the important honesty that the evidence base for single-gene dose adjustment is stronger than that for combinatorial multi-gene "which drug" panels (Kaplan & Sadock 2024; Maudsley 2021).

PEARL

Keep the two halves of this vignette in separate drawers, because the exam fuses them to test whether you can. The *pedigree* answers a genetic-epidemiology question (which study design fits which inheritance pattern: linkage for Mendelian, association/GWAS for polygenic). The *CYP2D6 report* answers a pharmacology question (poor metaboliser means lower dose; ultrarapid means higher dose or switch). One family, two tools: one reads transmission to choose a design, the other reads an enzyme genotype to choose a dose.

15.5 The four vignettes at a glance: tool, discriminator, first move

The consolidating grid. Read the discriminator column first: in each stem it is the single feature that names the genetic tool and therefore writes the answer.

VIGNETTE	GENETIC TOOL	DISCRIMINATOR IN THE STEM	FIRST MOVE
1. Couple with one bipolar partner ask about a child's risk	Empirical recurrence risk (polygenic, non-Mendelian)	**Bipolar I in one parent, no Mendelian pattern; a probability is requested**	Counsel the empirical offspring risk (~10 to 15% for BD) non-directively; decision left to the couple
2. Carbamazepine in a Han-Chinese or South-Asian patient	Pharmacogenomic HLA screening (immunogenetic)	**At-risk ancestry plus a planned carbamazepine start; SJS/TEN risk**	Screen HLA-B*15:02 before the first dose; if positive, avoid carbamazepine (and phenytoin)
3. Developmental delay, dysmorphism, cardiac anomaly, later psychosis	Copy-number variant detection (cytogenetic)	**Multisystem developmental phenotype behind the psychosis, pointing at 22q11.2**	Chromosomal microarray (or targeted FISH/MLPA for 22q11.2); refer to clinical genetics
4. Three-generation pedigree plus CYP2D6 poor-metaboliser report	Pedigree analysis + pharmacokinetic pharmacogenetics	**Familial-but-not-Mendelian pattern; genotype-confirmed poor metaboliser with toxicity**	Choose association/GWAS for the polygenic pattern; reduce dose or switch off the CYP2D6 substrate

Four tools, four discriminators: an empirical recurrence risk, a pharmacogenomic HLA screen, a copy-number-variant assay, and a pedigree read alongside a CYP genotype. In every row the discriminator names the tool and the tool forces the first move.

HOLD THIS

Name the tool the moment the stem lands and the answer is already written. The discriminator in the stem (a probability requested, an at-risk ancestry, a dysmorphic phenotype, a metaboliser report) names the genetic tool, and the tool forces the first move.

GOOD TO REMEMBER

- **Bipolar disorder (ICD-11 6A60):** most heritable major psychiatric disorder, heritability ~0.85 (up to ~0.9 for narrow BP-I); MZ concordance conventionally ~60%; empirical offspring recurrence risk ~10 to 15% with one affected parent (verify), higher for any mood disorder and ~40 to 50% if both parents affected.
- **HLA-B*15:02:** risk allele for carbamazepine-induced Stevens-Johnson syndrome / toxic epidermal necrolysis; frequent in Han-Chinese, Thai and South/South-East Asian populations, rare in Europeans; screen before starting carbamazepine, avoid if positive; cross-risk with phenytoin and oxcarbazepine.
- **HLA-A*31:01:** linked to a broader carbamazepine hypersensitivity spectrum (DRESS, maculopapular rash) across other ancestries including Europeans.
- **22q11.2 deletion syndrome:** velocardiofacial / DiGeorge syndrome; recurrent microdeletion on chromosome 22q; one of the strongest CNV risks for schizophrenia (a substantial minority of carriers develop psychosis); developmental delay, dysmorphism, conotruncal cardiac lesion, immune and palatal features.
- **Detection assay:** chromosomal microarray (CMA) is first-line for genome-wide CNV detection; FISH or MLPA is the targeted confirmatory test for 22q11.2; a standard karyotype misses microdeletions of this size.
- **CYP2D6 poor metaboliser:** two non-functional alleles (activity score 0, e.g. CYP2D6*4 homozygote); high plasma levels and toxicity at standard dose of CYP2D6-dependent drugs, so reduce dose or switch; ultrarapid metaboliser (gene duplication) under-responds and needs a higher dose or a switch.
- **Counselling principle:** genetic counselling is non-directive, gives population-level empirical probabilities without implying determinism, and never names a diagnosis to a family in a stigmatising way.
- **Study-design rule:** classical (parametric) linkage suits rare Mendelian traits with a known model; association / genome-wide association studies (and non-parametric or affected-sib-pair linkage) suit the common, polygenic, non-Mendelian psychiatric disorders.

16 · Consolidate: mnemonic total, retrieval and synthesis

This closing block is not new material; it is a **consolidation device** for the whole of these notes. The material has run one long circuit through psychiatric genetics: the methods ladder from twins to biobanks, the inheritance models and the liability-threshold idea, the twin and adoption designs, parametric linkage and the LOD score, the GWAS and CNV and polygenic-risk era, the newer sequencing and gene-therapy approaches, epigenetics and imprinting, endophenotypes, the neurodevelopmental and pleiotropy picture that dissolves the Kraepelinian line, the heritability league table across disorders, the worked example of schizophrenia genetics, pharmacogenetics, and finally the counselling clinic where all of it becomes a recurrence-risk figure spoken to a family. **Study by producing, not by re-reading.** Durable learning comes from spaced *active recall* (self-testing from memory) rather than repeated passive review, the testing effect that Roediger and Karpicke (2006) demonstrated directly. The three subtopics below give you the loop to run it: one master mnemonic that chains the smaller mnemonics into a single spine, a set of answer-free retrieval prompts, and a one-page synthesis map to redraw from memory.

Use them in that order. Recite the mnemonic spine to confirm the scaffold is intact, close the notes and work the retrieval prompts aloud, then take a blank sheet and rebuild the whole-day

circuit from method through architecture to the disorders arrayed on it. Where a limb of the map will not come, that gap is the prediction error naming the exact topic to reopen, which is the entire point of the exercise.

HOLD THIS

One architecture of common and rare variation, differing in dose and neurodevelopmental timing, generates the whole spectrum. Recite the mnemonic spine, work the retrieval prompts aloud, then redraw the architecture plane from memory; the gaps name the topics to reopen.

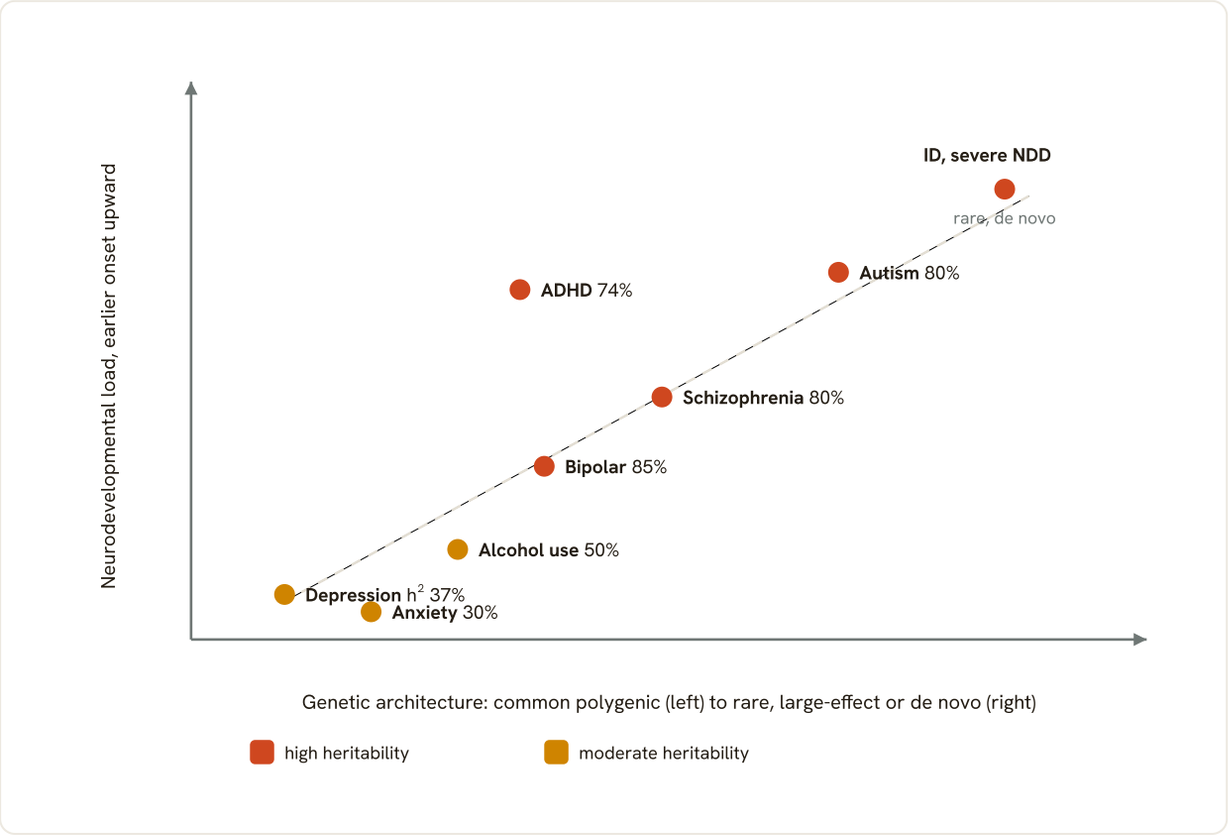


Fig 3.27 The whole subject on one map: major disorders placed by genetic architecture and neurodevelopmental load. Reading left to right, risk shifts from common-variant polygenic (depression, anxiety, much of bipolar and schizophrenia) toward an increasing contribution of rare, large-effect and de novo variants (autism and severe intellectual disability). Reading bottom to top, disorders carry more neurodevelopmental load and earlier onset. Colour marks heritability tier. Redraw this from memory as the synthesis of these notes: for any disorder, you should be able to place it and name the methods that would find its risk.

16.1 Master mnemonic total: chaining the whole subject into one spine

Every topic here already carries its own mnemonic. The problem at revision is not recalling any single one but retrieving the correct one under time pressure and in the right order. The device below is a *mnemonic of mnemonics*: a spine that indexes the methods ladder, the inheritance and threshold logic, the twin and adoption designs, the linkage-to-GWAS mapping tools, the polygenic and copy-number architecture, the newer approaches, epigenetics, endophenotypes, the pleiotropy story, the heritability league, the schizophrenia worked example, pharmacogenetics and counselling, so that recalling the spine pulls each sub-mnemonic up with it. Walk it in the order the material ran, from how we look, through what the architecture is, to what we do with it in clinic.

MNEMONIC

"TWINS LADDER Climb the Threshold, LOD Maps the GWAS-CNV-PRS Triangle, New Genomes Cut and Splice, Marks Above the Genes, Endophenotypes Bridge, Pleiotropy Breaks the Dichotomy, Rank the Heritable, SZ is the Case, CYP-HLA Dose, and Counsel the Family"

TWINS LADDER Climb the Threshold fixes the opening two limbs. The methods ladder runs "Family, Twin, Adoption, Linkage, Association, biobank" as a rising sequence of resolution, each rung answering a sharper question than the last, from is-it-familial to which-variant-and-in-whom. The inheritance limb runs "Mendel is Simple, Psychiatry is Multifactorial: Liability crosses a Threshold": single-gene Mendelian rules give clean segregation ratios, but the common disorders are polygenic and multifactorial, modelled as a normally distributed underlying liability with an abrupt threshold above which the phenotype appears (Falconer). Two threshold corollaries carry exam weight: the more-often-affected sex sits at the lower threshold, so relatives of an affected member of the rarer, higher-threshold sex carry the higher recurrence risk (the Carter effect); and rising recurrence risk with more affected relatives or a more severe proband is the signature of multifactorial, not Mendelian, transmission.

LOD Maps the GWAS-CNV-PRS Triangle chains the mapping and architecture core. Parametric linkage runs on "Three to prove, minus Two to exclude": a LOD (logarithm of odds) of plus 3 (odds of 1000 to 1) proves linkage and minus 2 (odds of 100 to 1 against) excludes it, with the recombination fraction theta running from 0 (never separated, inside the gene) to 0.5 (unlinked). Association then runs on the GWAS threshold "Five times ten to the minus eight" (correcting for about a million independent common variants), and the architecture resolves into a triangle: common SNPs of tiny effect (odds ratios about 1 to 1.2), rare CNVs of large effect (odds ratios about 20 to 100), and the polygenic risk score (PRS) that sums the common alleles into one liability index. The single most useful discriminator for the whole field: "Common is small and many; Rare is large and few", the inverse relationship between allele frequency and effect size.

New Genomes Cut and Splice encodes the novel-approaches limb. Sequencing runs on "Exome for the coding 2 percent, Genome for everything", with trio designs catching de novo mutations that carry large effect (prominent in autism). Therapy runs on "Cut, Splice or Replace": genome editing (CRISPR) cuts, antisense oligonucleotides (ASOs) modify splicing or lower transcript, and viral (AAV) vectors replace a gene, the three exemplified by the spinal muscular atrophy precedents (the SMN2-splice-modifying ASO nusinersen and the AAV SMN1 replacement) and the huntingtin-lowering ASO trials in psychiatry-adjacent neurology.

Marks Above the Genes is the epigenetics line, "Methylation Silences, Acetylation Opens; Imprinting is Parent-of-origin": DNA methylation (laid by the DNMT enzymes) generally silences, histone acetylation generally opens chromatin, and imprinting means expression depends on the parent of origin, the exemplar being the single 15q11-q13 locus that yields Prader-Willi from paternal loss and Angelman from maternal loss (of UBE3A). The gene-by-environment epigenetic mediator to remember is FKBP5, where a risk allele plus childhood trauma demethylates a regulatory element and yields glucocorticoid-receptor resistance (Klengel 2013).

Endophenotypes Bridge, Pleiotropy Breaks the Dichotomy chains two conceptual limbs. Endophenotypes run on the Gottesman and Gould (2003) criteria "Heritable, State-independent,

Co-segregates, seen in unaffected Relatives, and disease-Associated", the measurable intermediate markers (P50 gating, prepulse inhibition, mismatch negativity, antisaccade, smooth pursuit) meant to sit closer to the genes than the diagnosis. Pleiotropy then runs on "One variant, Many disorders": the high cross-disorder genetic correlations (schizophrenia to bipolar rg about 0.68, the highest pair) and shared loci such as CACNA1C and the 22q11.2 deletion collapse the categorical boundaries into a shared cross-disorder architecture, the genetic basis of the p-factor.

Rank the Heritable, SZ is the Case is the quantitative payload. The heritability league runs top to bottom on "Bipolar and Autism High, Schizophrenia and ADHD Next, Depression and Anxiety Low": bipolar about 0.85 and autism about 0.80 at the top, schizophrenia about 0.80 and ADHD about 0.75 next, major depression about 0.37 and the anxiety and stress disorders about 0.30 at the floor. Schizophrenia is then the worked case that ties it all together: high heritability but a polygenic architecture (108 loci in the 2014 PGC GWAS), the MHC / complement C4A signal driving excess synaptic pruning, DRD2 closing the genetics-to-pharmacology loop, and the 22q11.2 deletion as the single largest known genetic risk.

CYP-HLA Dose, and Counsel the Family closes on the two clinical limbs. Pharmacogenetics runs on "CYP for the Dose, HLA for the Danger": the CYP2D6 and CYP2C19 metaboliser phenotypes (poor to ultrarapid, captured as an activity score) set drug exposure and dose, while the HLA alleles flag life-threatening reactions, HLA-B*15:02 for carbamazepine-induced Stevens-Johnson syndrome (screen in Han-Chinese and South and South-East Asian ancestry) and HLA-A*31:01 across broader ancestries. Counselling then runs on "Empiric risk, Non-directive, Genetics-clinic referral for the syndromic and the predictive": most psychiatric counselling gives empiric recurrence figures non-directively, reserving formal clinical-genetics referral for syndromic CNVs (22q11.2, 3q29) and true presymptomatic testing (the Huntington disease model), with PRS explicitly not yet clinically actionable and less valid in non-European (including Indian) populations.

The table restates the spine so you can quiz yourself on any single link. Cover the right two columns and recall the sub-mnemonic and its content from the cue phrase alone.

SPINE LINK	SUB-MNEMONIC	WHAT IT UNLOCKS
Methods ladder	Family, Twin, Adoption, Linkage, Association, Biobank	**Rising resolution: is-it-familial to which-variant-in-whom; twins give heritability, adoption separates genes from rearing**
Inheritance / threshold	Mendel Simple, Psychiatry Multifactorial; Liability crosses a Threshold	Polygenic liability model; Carter effect (rarer-sex relatives higher risk); rising risk with load signals multifactorial
Linkage / LOD	Three to prove, minus Two to exclude; theta 0 to 0.5	**LOD +3 = 1000:1 for linkage, -2 = 100:1 against; recombination fraction; DISC1 from a translocation breakpoint**

SPINE LINK	SUB-MNEMONIC	WHAT IT UNLOCKS
GWAS / CNV / PRS	Five times ten to the minus eight; Common small, Rare large	Genome-wide significance; the frequency-effect-size triangle; PRS sums common alleles into one liability index
Novel approaches	Exome coding 2 percent, Genome everything; Cut, Splice, Replace	**WES vs WGS; de novo trios; CRISPR / ASO / AAV therapy, exemplified by the SMA and Huntington precedents**
Epigenetics	Methylation Silences, Acetylation Opens; Imprinting parent-of-origin	DNMTs and histone marks; 15q11-q13 gives Prader-Willi vs Angelman; FKBP5 gene-by-trauma mediator
Endophenotypes	Heritable, State-independent, Co-segregates, in Relatives, Associated	**Gottesman-Gould criteria; P50, prepulse inhibition, mismatch negativity, antisaccade, smooth pursuit**
Pleiotropy / cross-disorder	One variant, Many disorders	SCZ-BD rg about 0.68; CACNA1C and 22q11.2 shared; p-factor and the collapse of the Kraepelinian dichotomy
Heritability league	Bipolar and Autism High, SZ and ADHD Next, Depression and Anxiety Low	**BD about 0.85, ASD about 0.80, SCZ about 0.80, ADHD about 0.75, MDD about 0.37, anxiety about 0.30**
Schizophrenia case	High heritability, polygenic; C4A prunes, DRD2 loops, 22q11.2 biggest	108 PGC loci; complement-driven pruning; genetics-pharmacology loop; largest single CNV risk
Pharmacogenetics	CYP for the Dose, HLA for the Danger	**CYP2D6 / CYP2C19 metaboliser phenotype and activity score; HLA-B*15:02 and HLA-A*31:01 for carbamazepine reactions**
Counselling	Empiric risk, Non-directive, Genetics-clinic referral	Empiric recurrence figures given non-directively; syndromic-CNV and predictive-testing referral; PRS not yet actionable

The twelve-link master spine for this chapter, each row a cue phrase pointing to a topic mnemonic; recall the middle and right columns from the left cue alone.

16.2 Active-recall prompts: cover the page and answer aloud

These are retrieval questions, not a summary. They are deliberately answer-free, so that they force you to generate the answer from memory, which is where the testing effect does its work; printing a model answer here would defeat the device. This is the *retrieval practice* set for these notes: cover everything below the label, answer each aloud in a full sentence, then reopen the relevant topic only for the prompts you could not complete.

RETRIEVAL PRACTICE, COVER THE ANSWERS

1. State the six rungs of the genetic methods ladder in ascending order of resolution, and say precisely what question the twin design and the adoption design each answer that a family study cannot.
2. Define the liability-threshold model, explain the Carter effect in one sentence, and give the two features of a recurrence-risk pattern that point to multifactorial rather than Mendelian inheritance.
3. Write Falconer's formula for heritability from twin correlations and the ACE model, and explain the equal-environments assumption and why it is the design's load-bearing weakness.
4. Give the LOD score thresholds for proving and for excluding linkage with the odds each represents, and define the recombination fraction theta with its two limiting values.
5. State the GWAS genome-wide significance threshold and what it corrects for, then contrast the effect sizes of common SNPs against rare CNVs and state the general frequency-to-effect-size rule.
6. Explain what a polygenic risk score is, roughly how much schizophrenia liability it currently captures, and two reasons it is not yet used in clinical counselling.
7. Distinguish whole-exome from whole-genome sequencing, and explain why the trio design is the efficient way to detect the de novo mutations that matter in autism.
8. Name the three gene-therapy modalities (edit, splice-modify, replace) with one clinical exemplar each, and say which spinal muscular atrophy agent represents which modality.
9. Contrast the effects of DNA methylation and histone acetylation on transcription, then explain how a single imprinted 15q11-q13 locus produces two different syndromes.
10. State the five Gottesman and Gould criteria for an endophenotype, and name one candidate endophenotype together with the gene or receptor most associated with it.
11. Give the schizophrenia-to-bipolar genetic correlation and explain what such high cross-disorder correlations imply for the Kraepelinian dichotomy and the p-factor.
12. Rank bipolar disorder, autism, schizophrenia, ADHD, major depression and generalised anxiety by twin heritability from highest to lowest with an approximate figure for each.
13. For schizophrenia, name the most robust common-variant locus and its proposed synaptic mechanism, the locus that closes the genetics-pharmacology loop, and the single largest known genetic risk factor.
14. Distinguish the poor, intermediate, normal and ultrarapid metaboliser phenotypes, name the two CYP enzymes most relevant in psychiatry, and give one dosing consequence of each extreme.
15. Name the HLA allele that must be screened before carbamazepine and the ancestry group it is common in, and state what reaction it predicts.
16. Outline the principles of non-directive psychiatric genetic counselling, name two situations that warrant clinical-genetics referral, and state why polygenic risk scores are not yet part of counselling.

If more than a third of these will not come cleanly, do not push through the list a second time the same day; space the next attempt, because retrieval spaced across days is what builds durable

memory (Roediger and Karpicke 2006).

16.3 Synthesis map: the one page to redraw from memory

The final consolidation step is to build a single **synthesis map** and *redraw from memory* the whole of psychiatric genetics as one two-axis plane. Draw the **genetic-architecture plane**: the horizontal axis running from common-polygenic (many small-effect common variants) on the left to rare-large-effect (single CNVs and de novo mutations) on the right, and the vertical axis carrying neurodevelopmental load from low at the bottom to high at the top. Then place the major disorders onto it from memory: autism and intellectual disability high and toward the rare-large-effect right (de novo and CNV enriched, high neurodevelopmental load); schizophrenia high on neurodevelopmental load but sitting across the middle of the horizontal axis, with both a dense common-polygenic component (108 loci) and a rare tail (22q11.2, NRXN1); bipolar disorder mid-height, mostly common-polygenic and sharing much of its architecture with schizophrenia; ADHD toward the neurodevelopmental top but common-polygenic; and major depression and the anxiety and stress disorders low on both axes, common-polygenic with modest heritability. Annotate the plane with the frequency-to-effect-size gradient along the bottom (common small, rare large), the pleiotropy links drawn as arcs between the disorders that share loci (the schizophrenia-bipolar arc the thickest), and the clinical endpoints in the margin (PRS for the common-polygenic pole, clinical-genetics referral for the rare-large-effect pole, pharmacogenetic CYP and HLA testing as the treatment overlay). Redraw it once from memory, then check it against the figures above and fill only the gaps; the act of reconstructing the plane, not admiring a finished one, is what fixes the central claim, that a single architecture of common and rare variation, differing in dose and in neurodevelopmental timing, generates the whole spectrum of psychiatric disorder. The figure to rebuild is that two-axis plane, common-polygenic to rare-large-effect against neurodevelopmental load, with the disorders placed as points and the shared-locus pleiotropy drawn as connecting arcs. [FLAG concept_svg CF6]

Previously asked

Real long-essay (25-mark) and short-note (10-mark) questions from the genetics territory.

? LONG ESSAYS (25 MARKS)

- **Q** Describe the role of genetics, biological and psychological factors in the development of personality. MUHS 2018

? SHORT NOTES (10 MARKS)

- **Q** Role of psychopharmacogenetics in psychiatry. MUHS 2013
- **Q** Gene mapping. MUHS 2012
- **Q** Neurogenetics. MUHS 2011

Genetics is a compact but recurring examiner favourite: pharmacogenetics, gene mapping and the broad "neurogenetics" note all appear, and genetics features inside integrative essays on personality and on individual disorders (schizophrenia genetics is the most examinable long answer). Prepare the methods well enough to define any one in three lines and to name the key findings.

Quick review

The whole picture in one table	
THE GENETICS TOOLKIT	An evidence hierarchy, each method one question: family (does it run in families?), twin (genes vs shared environment?), adoption (genes vs rearing?), linkage (roughly where?), GWAS (which common variants?), CNV and sequencing (rare large-effect variants?), polygenic risk score (aggregate burden?). Risk is mostly common-variant polygenic plus a minority of rare large-effect variants; much heritability is still missing; risk is read out through neurodevelopment.
MODES OF INHERITANCE	Mendelian (autosomal dominant, autosomal recessive, X-linked) vs non-Mendelian (mitochondrial, genomic imprinting, anticipation via trinucleotide repeats). Psychiatric disorders are polygenic and multifactorial. The multifactorial-threshold (liability) model: liability is normally distributed, disease appears above a threshold; relatives are shifted right, so recurrence exceeds prevalence. Sex-specific thresholds give the Carter effect.
TWIN, FAMILY AND ADOPTION STUDIES	MZ vs DZ concordance; heritability approximately 2 times (rMZ minus rDZ); the ACE model splits variance into additive genetic, common environment and unique environment; the equal-environments assumption is the main critique. Adoption designs (adoptee, adoptee's-family, cross-fostering; Heston 1966; the Danish studies). Quantitative methods: segregation analysis, path analysis, variance-components. Gene-environment interaction and correlation.
LINKAGE, LOD SCORE, GENE MAPPING	Linkage tracks co-segregation within families; markers ran RFLP to microsatellite to SNP. LOD (logarithm of the odds) of 3 or more is significant, minus 2 excludes; affected sib-pair is the model-free version. Positional cloning, genetic vs physical maps, fine-mapping. Linkage largely failed for polygenic psychiatric traits (Lander and Kruglyak thresholds), which drove the move to genome-wide association.
GWAS, CANDIDATE GENES, CNVS, PRS	Candidate-gene studies (COMT, 5-HTTLPR, DISC1) mostly did not replicate. GWAS: genome-wide significance 5 x 10 to the minus 8, the Psychiatric Genomics Consortium, sample size the key. Schizophrenia: the complement C4 / MHC signal (Sekar 2016), 108 then 287 loci (Trubetskoy 2022). CNV syndromes: 22q11.2 (largest single risk), 16p11.2, 1q21.1, NRXN1. Polygenic risk scores sum common variants but are not yet individually predictive. Missing heritability.
NOVEL APPROACHES AND GENE THERAPY	Whole-exome and whole-genome sequencing; rare-variant burden; de novo mutations (paternal-age effect, large in autism). SCHEMA named ten genes (SETD1A, GRIN2A, others; Singh 2022). Functional genomics (eQTL, TWAS), iPSC neurons and organoids, Mendelian randomization, biobanks. Gene therapy (antisense oligonucleotides, AAV,

The whole picture in one table	
	CRISPR) is real in monogenic neurological disease but not in polygenic psychiatric disorders.
EPIGENETICS	Stable change in expression without a sequence change: DNA methylation, histone modification, non-coding RNA. Genomic imprinting (Prader-Willi vs Angelman, 15q11-13). Early-life programming: FKBP5 demethylation with childhood trauma (Klengel 2013), Dutch-famine methylation (Heijmans 2008). Epigenetic clock (Horvath 2013) and accelerated ageing. Valproate is a histone-deacetylase inhibitor.
ENDOPHENOTYPES	Heritable intermediate traits closer to gene action. Gottesman and Gould (2003) criteria: associated with illness, heritable, state-independent, co-segregates in families, present in unaffected relatives. Examples: P50 sensory-gating deficit, prepulse inhibition deficit, smooth-pursuit and antisaccade abnormalities, mismatch negativity, working memory. They often proved no simpler genetically than the disorder (Flint and Munafo).
NEURODEVELOPMENTAL GENETICS AND PLEIOTROPY	Risk genes are enriched for synaptic, chromatin and FMRP-target functions and for early expression: risk acts through neurodevelopment. A continuum runs from intellectual disability through autism and ADHD to schizophrenia. De novo mutations and the paternal-age effect. Cross-disorder pleiotropy and the genetic p-factor: shared common-variant risk across disorders (Cross-Disorder PGC).
HERITABILITY ACROSS DISORDERS	Twin-based heritability (population variance ratio, not an individual statement, not immutable): schizophrenia about 80%, bipolar about 85%, autism about 80%, ADHD about 74%, major depression about 37%, generalised anxiety about 30%, alcohol use about 50%, OCD higher in child-onset. SNP-based heritability is lower than twin heritability (part of missing heritability).
SCHIZOPHRENIA GENETICS (FLAGSHIP)	Heritability about 80%; architecture is highly polygenic plus rare CNVs and de novo variants. GWAS and the C4 / synaptic-pruning story; 22q11.2 deletion the largest single risk; candidate-gene history (COMT, DISC1, NRG1, DTNBP1); endophenotypes (P50, PPI); gene-environment interaction (cannabis, urbanicity, migration, obstetric complications, paternal age); neurodevelopmental model; polygenic risk scores; genetic overlap with bipolar.
PHARMACOGENETICS AND PHARMACOGENOMICS	Pharmacogenetics is single-gene, pharmacogenomics is genome-wide drug response. CYP2D6 and CYP2C19 metaboliser phenotypes (poor, intermediate, normal, ultrarapid): CYP2D6 for risperidone, aripiprazole, tricyclics; CYP2C19 for escitalopram, clozapine. Immune-mediated: HLA-B*15:02 and carbamazepine Stevens-Johnson syndrome (screen first; frequent in South-East Asian and some Indian groups), HLA-A*31:01. Guidelines: CPIC, DPWG.

The whole picture in one table	
DISCRIMINATE: DESIGN AND PEDIGREE	Match the question to the design: familial? family study; genes vs shared environment? twin; genes vs rearing? adoption; roughly where? linkage; which common variants? GWAS; a rare cause in this patient? chromosomal microarray or sequencing; predict aggregate risk? polygenic score; drug response? pharmacogenetic test. Read a pedigree (squares male, circles female, filled affected, arrow proband). Pitfalls: assortative mating, phenocopy, incomplete penetrance, genetic heterogeneity.
GENETIC COUNSELLING	Non-directive; use empirical recurrence risks, not Mendelian ratios: offspring of one parent with schizophrenia about 10 to 13%, both parents about 40 to 46%, sibling about 9%; bipolar offspring about 10 to 15%. Refer to clinical genetics for dysmorphism, intellectual disability or a suspected CNV. Predictive and prenatal testing carry ethical weight; polygenic scores are not yet clinical. India: consanguinity, disclosure pressure, stigma.
APPLIED VIGNETTES	Counsel a couple (one parent with bipolar) with the empirical offspring risk, non-directively. Screen HLA-B*15:02 before carbamazepine in a patient of South or East Asian ancestry. A child with developmental delay, dysmorphism and later psychosis: order chromosomal microarray, consider 22q11.2, refer. Read a pedigree plus a CYP2D6 poor-metaboliser report and adjust.
CONSOLIDATE	The master mnemonic chains it all together. The retrieval prompts are answer-free (cover and recall). The synthesis map places each disorder on the genetic-architecture plane: common-polygenic to rare-large-effect on one axis, neurodevelopmental load on the other. For any disorder you should be able to place it and name the methods that would find its risk.

References

These notes are grounded in the standard texts (the source hierarchy below); landmark, contested and numeric claims carry a PubMed-verified journal citation. Every PMID here was checked against PubMed this build, and citations whose identifier did not resolve to the cited paper were corrected or dropped.

SOURCE HIERARCHY (TEXTBOOKS)

1. Boland R, Verduin ML, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 11th ed. Philadelphia: Wolters Kluwer; 2024. [primary depth bar; genetics chapter: architecture, GWAS, CNVs, heritability]
2. Geddes JR, Andreasen NC, Goodwin GM, eds. New Oxford Textbook of Psychiatry. 3rd ed. Oxford: Oxford University Press; 2020. [genetic epidemiology, linkage, GWAS, endophenotypes, counselling]
3. Tasman A, Kay J, Lieberman JA, First MB, Riba MB, eds. Psychiatry. 4th ed. Chichester: Wiley-Blackwell; 2015. [quantitative genetics, endophenotype markers]
4. Stahl SM. Stahl's Essential Psychopharmacology. 5th ed. Cambridge: Cambridge University Press; 2021. [pharmacogenetics, HDAC and valproate]

5. Taylor DM, Barnes TRE, Young AH. The Maudsley Prescribing Guidelines in Psychiatry. 14th ed. Oxford: Wiley Blackwell; 2021. [pharmacogenetic prescribing, HLA-B*15:02 and carbamazepine]
6. Johnstone EC, Owens DGC, Lawrie SM, et al, eds. Companion to Psychiatric Studies. 8th ed. Edinburgh: Churchill Livingstone/Elsevier; 2010. [linkage and LOD, DISC1, quantitative methods]
7. Cowen P, Harrison P, Burns T. Shorter Oxford Textbook of Psychiatry. 7th ed. Oxford: Oxford University Press; 2018. [recurrence risks, named CNV syndromes]

JOURNAL REFERENCES (PUBMED-VERIFIED, 58)

1. Heston LL. Psychiatric disorders in foster home reared children of schizophrenic mothers. Br J Psychiatry. 1966;112:819-25. PMID: 5966555.
2. Plomin R, DeFries JC, Loehlin JC. Genotype-environment interaction and correlation in the analysis of human behavior. Psychol Bull. 1977;84:309-22. PMID: 557211.
3. Scarr S, McCartney K. How people make their own environments: a theory of genotype greater than environment effects. Child Dev. 1983;54:424-35. PMID: 6683622.
4. True WR, Rice J, Eisen SA, et al. A twin study of genetic and environmental contributions to liability for posttraumatic stress symptoms. Arch Gen Psychiatry. 1993;50:257-64. PMID: 8466386.
5. Lander E, Kruglyak L. Genetic dissection of complex traits: guidelines for interpreting and reporting linkage results. Nat Genet. 1995;11:241-7. PMID: 7581446.
6. Karayiorgou M, Morris MA, Morrow B, et al. Schizophrenia susceptibility associated with interstitial deletions of chromosome 22q11. Proc Natl Acad Sci U S A. 1995;92:7612-6. PMID: 7644464.
7. Cardno AG, Marshall EJ, Coid B, et al. Heritability estimates for psychotic disorders: the Maudsley twin psychosis series. Arch Gen Psychiatry. 1999;56:162-8. PMID: 10025441.
8. Millar JK, Wilson-Annan JC, Anderson S, et al. Disruption of two novel genes by a translocation co-segregating with schizophrenia. Hum Mol Genet. 2000;9:1415-23. PMID: 10814723.
9. Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. Am J Psychiatry. 2000;157:1552-62. PMID: 11007705.
10. Malaspina D, Harlap S, Fennig S, et al. Advancing paternal age and the risk of schizophrenia. Arch Gen Psychiatry. 2001;58:361-7. PMID: 11296097.
11. Blackwood DH, Fordyce A, Walker MT, et al. Schizophrenia and affective disorders--cosegregation with a translocation at chromosome 1q42 that directly disrupts brain-expressed genes: clinical and P300 findings in a family. Am J Hum Genet. 2001;69:428-33. PMID: 11443544.
12. Hettema JM, Neale MC, Kendler KS. A review and meta-analysis of the genetic epidemiology of anxiety disorders. Am J Psychiatry. 2001;158:1568-78. PMID: 11578982.
13. Gottesman II, Gould TD. The endophenotype concept in psychiatry: etymology and strategic intentions. Am J Psychiatry. 2003;160:636-45. PMID: 12668349.
14. McGuffin P, Rijsdijk F, Andrew M, et al. The heritability of bipolar affective disorder and the genetic relationship to unipolar depression. Arch Gen Psychiatry. 2003;60:497-502. PMID: 12742871.
15. Sullivan PF, Kendler KS, Neale MC. Schizophrenia as a complex trait: evidence from a meta-analysis of twin studies. Arch Gen Psychiatry. 2003;60:1187-92. PMID: 14662550.
16. Tienari P, Wynne LC, Sorri A, et al. Genotype-environment interaction in schizophrenia-spectrum disorder. Long-term follow-up study of Finnish adoptees. Br J Psychiatry. 2004;184:216-22. PMID: 14990519.
17. van Grootheest DS, Cath DC, Beekman AT, et al. Twin studies on obsessive-compulsive disorder: a review. Twin Res Hum Genet. 2005;8:450-8. PMID: 16212834.
18. Gatz M, Reynolds CA, Fratiglioni L, et al. Role of genes and environments for explaining Alzheimer disease. Arch Gen Psychiatry. 2006;63:168-74. PMID: 16461860.
19. Roediger HL, Karpicke JD. Test-enhanced learning: taking memory tests improves long-term retention. Psychol Sci. 2006;17:249-55. PMID: 16507066.
20. Resta R, Biesecker BB, Bennett RL, et al. A new definition of Genetic Counseling: National Society of Genetic Counselors' Task Force report. J Genet Couns. 2006;15:77-83. PMID: 16761103.
21. Flint J, Munafò MR. The endophenotype concept in psychiatric genetics. Psychol Med. 2007;37:163-80. PMID: 16978446.
22. Braff DL, Freedman R, Schork NJ, et al. Deconstructing schizophrenia: an overview of the use of endophenotypes in order to understand a complex disorder. Schizophr Bull. 2007;33:21-32. PMID: 17088422.

23. Austin JC, Palmer CG, Rosen-Sheidley B, et al. Psychiatric disorders in clinical genetics II: Individualizing recurrence risks. J Genet Couns. 2008;17:18-29. PMID: 18071888.
24. Heijmans BT, Tobi EW, Stein AD, et al. Persistent epigenetic differences associated with prenatal exposure to famine in humans. Proc Natl Acad Sci U S A. 2008;105:17046-9. PMID: 18955703.
25. Lichtenstein P, Yip BH, Björk C, et al. Common genetic determinants of schizophrenia and bipolar disorder in Swedish families: a population-based study. Lancet. 2009;373:234-9. PMID: 19150704.
26. Purcell SM, Wray NR, Stone JL, et al. Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. Nature. 2009;460:748-52. PMID: 19571811.
27. Manolio TA, Collins FS, Cox NJ, et al. Finding the missing heritability of complex diseases. Nature. 2009;461:747-53. PMID: 19812666.
28. Light GA, Swerdlow NR, Rissling AJ, et al. Characterization of neurophysiologic and neurocognitive biomarkers for use in genomic and clinical outcome studies of schizophrenia. PLoS One. 2012;7:e39434. PMID: 22802938.
29. Sullivan PF, Daly MJ, O'Donovan M. Genetic architectures of psychiatric disorders: the emerging picture and its implications. Nat Rev Genet. 2012;13:537-51. PMID: 22777127.
30. Kurita M, Holloway T, García-Bea A, et al. HDAC2 regulates atypical antipsychotic responses through the modulation of mGlu2 promoter activity. Nat Neurosci. 2012;15:1245-54. PMID: 22864611.
31. Klengel T, Mehta D, Anacker C, et al. Allele-specific FKBP5 DNA demethylation mediates gene-childhood trauma interactions. Nat Neurosci. 2013;16:33-41. PMID: 23201972.
32. Lee SH, Ripke S, Neale BM, et al. Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. Nat Genet. 2013;45:984-94. PMID: 23933821.
33. Horvath S. DNA methylation age of human tissues and cell types. Genome Biol. 2013;14:R115. PMID: 24138928.
34. Gapp K, Jawaid A, Sarkies P, et al. Implication of sperm RNAs in transgenerational inheritance of the effects of early trauma in mice. Nat Neurosci. 2014;17:667-9. PMID: 24728267.
35. Takata A, Xu B, Ionita-Laza I, et al. Loss-of-function variants in schizophrenia risk and SETD1A as a candidate susceptibility gene. Neuron. 2014;82:773-80. PMID: 24853937.
36. Schizophrenia Working Group of the Psychiatric Genomics Consortium. Biological insights from 108 schizophrenia-associated genetic loci. Nature. 2014;511:421-7. PMID: 25056061.
37. Iossifov I, O'Roak BJ, Sanders SJ, et al. The contribution of de novo coding mutations to autism spectrum disorder. Nature. 2014;515:216-21. PMID: 25363768.
38. Baker K, Costain G, Fung WL, et al. Chromosomal microarray analysis-a routine clinical genetic test for patients with schizophrenia. Lancet Psychiatry. 2014;1:329-31. PMID: 26360988.
39. Sanders SJ, He X, Willsey AJ, et al. Insights into Autism Spectrum Disorder Genomic Architecture and Biology from 71 Risk Loci. Neuron. 2015;87:1215-1233. PMID: 26402605.
40. Inglis A, Koehn D, McGillivray B, et al. Evaluating a unique, specialist psychiatric genetic counseling clinic: uptake and impact. Clin Genet. 2015;87:218-24. PMID: 24773225.
41. Zeng T, Long YS, Min FL, et al. Association of HLA-B*1502 allele with lamotrigine-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in Han Chinese subjects: a meta-analysis. Int J Dermatol. 2015;54:488-93. PMID: 25428396.
42. Farrell MS, Werge T, Sklar P, et al. Evaluating historical candidate genes for schizophrenia. Mol Psychiatry. 2015;20:555-62. PMID: 25754081.
43. Hicks JK, Bishop JR, Sangkuhl K, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clin Pharmacol Ther. 2015;98:127-34. PMID: 25974703.
44. Genovese G, Fromer M, Stahl EA, et al. Increased burden of ultra-rare protein-altering variants among 4,877 individuals with schizophrenia. Nat Neurosci. 2016;19:1433-1441. PMID: 27694994.
45. Yehuda R, Daskalakis NP, Bierer LM, et al. Holocaust Exposure Induced Intergenerational Effects on FKBP5 Methylation. Biol Psychiatry. 2016;80:372-80. PMID: 26410355.
46. Sekar A, Bialas AR, de Rivera H, et al. Schizophrenia risk from complex variation of complement component 4. Nature. 2016;530:177-83. PMID: 26814963.
47. Sandin S, Lichtenstein P, Kuja-Halkola R, et al. The Heritability of Autism Spectrum Disorder. JAMA. 2017;318:1182-1184. PMID: 28973605.
48. Hilker R, Helenius D, Fagerlund B, et al. Heritability of Schizophrenia and Schizophrenia Spectrum Based on the Nationwide Danish Twin Register. Biol Psychiatry. 2018;83:492-498. PMID: 28987712.

49. Borle K, Morris E, Inglis A, et al. Risk communication in genetic counseling: Exploring uptake and perception of recurrence numbers, and their impact on patient outcomes. Clin Genet. 2018;94:239-245. PMID: 29766486.

50. Smoller JW, Andreassen OA, Edenberg HJ, et al. Psychiatric genetics and the structure of psychopathology. Mol Psychiatry. 2019;24:409-420. PMID: 29317742.

51. Greenwood TA, Shutes-David A, Tsuang DW. Endophenotypes in Schizophrenia: Digging Deeper to Identify Genetic Mechanisms. J Psychiatr Brain Sci. 2019;4:e190005. PMID: 31245629.

52. Wang W, Corominas R, Lin GN. De novo Mutations From Whole Exome Sequencing in Neurodevelopmental and Psychiatric Disorders: From Discovery to Application. Front Genet. 2019;10:258. PMID: 31001316.

53. Cross-Disorder Group of the Psychiatric Genomics Consortium. Cross-Disorder Group of the Psychiatric Genomics Consortium. Genomic Relationships, Novel Loci, and Pleiotropic Mechanisms across Eight Psychiatric Disorders. Cell. 2019;179:1469-1482.e11. PMID: 31835028.

54. Stevens B. Impact of Emerging Technologies in Prenatal Genetic Counseling. Cold Spring Harb Perspect Med. 2020;10. PMID: 31570384.

55. Wray NR, Lin T, Austin J, et al. From Basic Science to Clinical Application of Polygenic Risk Scores: A Primer. JAMA Psychiatry. 2021;78:101-109. PMID: 32997097.

56. Murray GK, Lin T, Austin J, et al. Could Polygenic Risk Scores Be Useful in Psychiatry?: A Review. JAMA Psychiatry. 2021;78:210-219. PMID: 33052393.

57. Singh T, Poterba T, Curtis D, et al. Rare coding variants in ten genes confer substantial risk for schizophrenia. Nature. 2022;604:509-516. PMID: 35396579.

58. Trubetskoy V, Pardiñas AF, Qi T, et al. Mapping genomic loci implicates genes and synaptic biology in schizophrenia. Nature. 2022;604:502-508. PMID: 35396580.

PART IV

IV

General & Developmental Psychology

The mind studied as theory: perception, memory, thought and motivation, and how children become who they are.

01 Foundations

02 General psychology

03 The three depth-psychology schools

04 Developmental psychology

05 Discriminate

06 Apply and consolidate

General & Developmental Psychology

Six sections · 23 topics · one complete notes document

Psychology is a Paper-1 staple because examiners test the *logic of the theories*, not just their conclusions. These notes are built to make each theory tell its own story: for every cognitive and affective topic you get the same shape, so the structure itself becomes a memory aid.

Learn how the idea evolved, not just where it landed. First the schools of thought as a map, then the general-psychology functions (perception, memory, thinking and intelligence, motivation, emotion, consciousness, creativity, emotional intelligence, the mind-body question), each told as a history: the early theory, what the next theory fixed and what it still argued about, the mechanism now accepted, its neural correlate and a worked example. Then the three great depth-psychology schools (Freud, Adler, Jung) and the developmental theorists (Erikson, Piaget, Kohlberg, attachment, temperament, Mahler, milestones), and finally the payoff figure that lays the stage theories side by side down one shared age axis. The examinable skill throughout is discrimination: telling James-Lange from Cannon-Bard, Piaget from Vygotsky, Freud from Jung, and reading a child by stage.

HOW TO USE THESE NOTES

Every general-psychology topic follows one fixed flow: the idea in brief, then the **theories in the order they appeared** (what each fixed, what stayed debated), then the **currently accepted mechanism**, then its **neural correlate**, then a worked example. Figures declare one axis and code it in colour and shape: **petrol** marks structure and the neutral relay, **coral** marks conflict, pathology or the point of debate, and **marigold** highlights the accepted answer. Watch for the boxes marked **Good to remember**: they gather every named theorist, stage, age and hard classification in one place so the reference facts sit apart from the reasoning.

Foundations

1 · Orientation: the schools of psychology as a map

General and developmental psychology begins with a single most useful thing to fix before any of the detail, the **map**: psychology is not one theory of the mind but a small set of competing **lenses,** each of which explains behaviour by looking at a different **unit of analysis**. A biologist looks at the brain, a cognitivist at information flow, a behaviourist at the observable response, a psychodynamicist at the unconscious, a humanist at the striving self. The paper does not usually ask you to pick which school is *correct*; it asks you to recognise which lens a given claim, therapy, or experiment belongs to, and to know whose name sits under it. Almost every later topic on these notes (perception, memory, thinking, motivation, emotion, then the developmental theorists) is a special case of one or more of these lenses (Kaplan & Sadock 2024).

The second orienting idea, and the spine that recurs across these notes, is that the schools appeared in a **historical sequence** in which each usually fixed a gap the last one left open. Introspection could not be verified, so behaviourism banished the inner world and studied only

stimulus and response; behaviourism could not explain language or memory, so the cognitive revolution reopened the mind as information processing; none of the laboratory schools spoke to meaning or suffering, which is where the psychodynamic and humanistic traditions had always lived. Hold that as an *evolution of theories*, because most functions on these notes are best learned as the theory that came first, what it fixed, what it left debated, then the currently accepted account and its neural correlate. This orientation topic lays out the five lenses and previews the developmental theorists; the topics that follow pay them off.

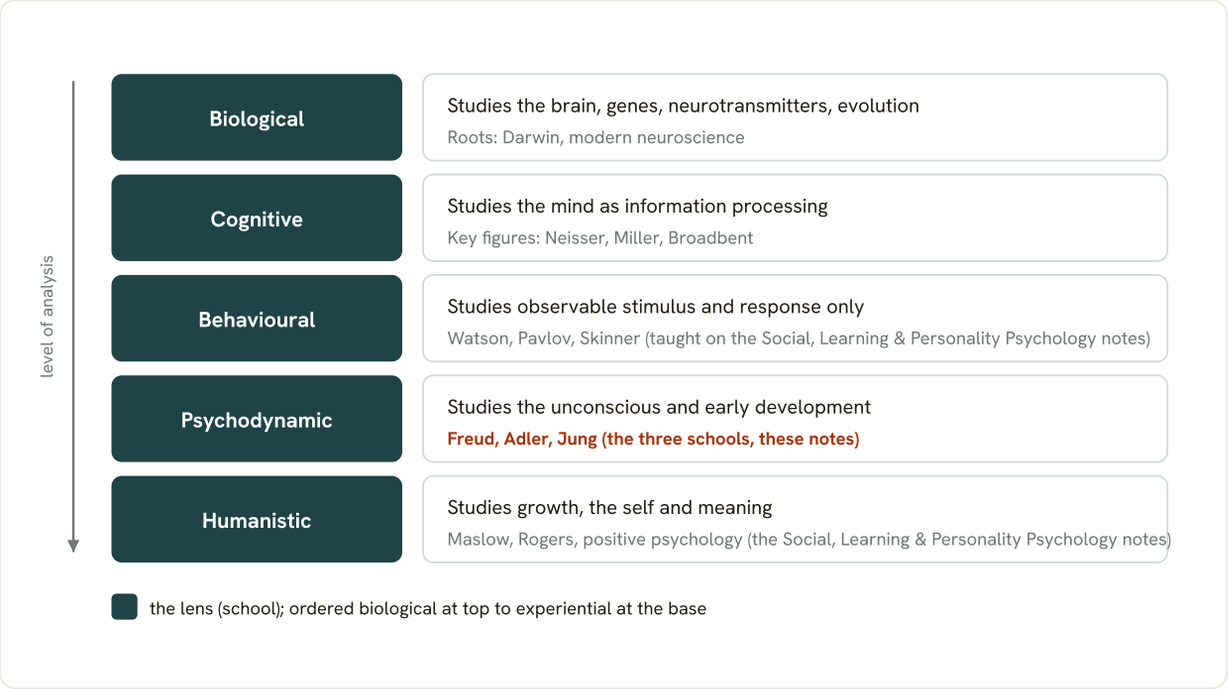


Fig 4.1 The five schools of psychology as one map. Each lens defines its own unit of analysis and answers a different question about the same mind, and each historically arose partly to fix what the previous lens left out: behaviourism against introspection, the cognitive revolution against radical behaviourism, humanistic psychology against both. These notes teach the three depth-psychology schools (Freud, Adler, Jung) in full and the developmental theorists; behaviourism, social psychology and the rest of personality theory are the Social, Learning & Personality Psychology notes.

1.1 Why a map, not a list: the mind through competing lenses

Each school is defined by its unit of analysis. The reason five schools coexist rather than one replacing all others is that they answer different questions about the same behaviour, and each is strongest exactly where the others are silent. A useful discipline for the viva is to ask, of any statement about the mind, "at what level is this explanation pitched?": molecules and circuits (biological), representations and computations (cognitive), observable contingencies (behavioural), unconscious conflict and early development (psychodynamic), or growth, agency and meaning (humanistic). The same clinical fact, say a patient's low mood, is a serotonergic and limbic-circuit story to the biological lens, a negative cognitive schema to the cognitive lens, a loss of reinforcement to the behavioural lens, an unresolved loss turned inward to the psychodynamic lens, and a blocked need for self-actualisation to the humanistic lens. None is wholly wrong; the exam skill is naming the lens (Kaplan & Sadock 2024; Companion to Psychiatric Studies 2010).

1.2 The five lenses as a map

Bind each school to its unit of analysis and its key figures. This is the schema for the whole set of notes: read the school, hold its unit of analysis (what it counts as data), and attach the names examiners expect. Behaviourism gets its full treatment on the Social, Learning & Personality Psychology notes (learning theory, social and personality psychology); the humanistic school and its modern descendant, positive psychology, are also opened deeper on the Social, Learning & Personality Psychology notes.

Biological (biopsychology)

Unit of analysis: the mind *as brain*. Behaviour is explained by genes, neurotransmitters, hormones, neural circuits, and evolutionary pressures. Data are physiological. This lens underwrites the whole of the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes and the Psychiatric Genetics notes (neuroanatomy, neurochemistry, genetics) and the neural-correlate step of every function. Key roots: Darwin (evolution), Sherrington and the neurophysiologists; in psychiatry it is the dominant explanatory frame.

Cognitive

Unit of analysis: the mind *as information processing*. The mind takes input, encodes, stores, retrieves and transforms it, and produces output, on the deliberate analogy of a computer (the **computer metaphor**). Key figure: Ulric Neisser, whose *Cognitive Psychology* (1967) named and consolidated the field. Underwrites perception, attention, memory, thinking and language, and the cognitive model of therapy.

Behavioural

Unit of analysis: *only observable stimulus and response*. The inner mind is treated as a black box; learning is the lawful change in behaviour produced by conditioning. Key figures: John B. Watson (who launched behaviourism in 1913 and demanded psychology study only observable behaviour) and B. F. Skinner (operant conditioning). Fuller treatment on the Social, Learning & Personality Psychology notes.

Psychodynamic

Unit of analysis: *unconscious drives and early development*. Behaviour is driven by conflict among unconscious forces laid down in childhood. Key figures: Sigmund Freud (psychoanalysis, the structural and psychosexual models), Alfred Adler (individual psychology, inferiority and striving), Carl Jung (analytical psychology, the collective unconscious and archetypes). Underwrites psychodynamic formulation and defence mechanisms.

Humanistic

Unit of analysis: *growth, meaning and the self*. The person is an agent striving toward self-actualisation, studied from the inside (phenomenology) rather than reduced to reflexes or drives. Key figures: Abraham Maslow (hierarchy of needs, self-actualisation) and Carl Rogers (client-centred therapy, unconditional positive regard). Its modern scientific descendant is **positive psychology** (Martin Seligman), which studies well-being, strengths and flourishing. Deeper on the Social, Learning & Personality Psychology notes.

RULE **Name the lens, not the verdict.** The paper rarely asks which school is correct; it asks which unit of analysis a given claim, therapy or experiment belongs to, and whose name sits under it.

HOLD THIS

Five lenses, five units of analysis, five images. Biological = brain, cognitive = computer, behavioural = black box, psychodynamic = iceberg, humanistic = growing self. Attach the right image and lead name and you have placed the school.

PEARL

The five lenses in one line: the biological lens sees a *brain*, the cognitive lens sees a *computer*, the behavioural lens sees a *black box*, the psychodynamic lens sees an *iceberg*, and the humanistic lens sees a *growing self*. If you can attach the right image and the right lead name to a claim, you have placed the school.

1.3 The schools appeared in order, each fixing the last one's gap

Read the schools as an evolution, not a menu. The historical arc is itself examinable and it explains why the field looks as it does. The earliest scientific psychology (Wundt's 1879 Leipzig laboratory, and the introspectionism and structuralism of Wundt and Titchener) tried to catalogue conscious experience by trained self-report; it foundered because introspection could not be independently verified. Behaviourism (Watson 1913, then Skinner) fixed that by refusing to talk about the unobservable mind at all and studying only stimulus and response, which bought rigour at the cost of ignoring meaning, memory and language. The **cognitive revolution** of the 1950s to 1960s (crystallised by Neisser 1967) reopened the black box, arguing that the mind can be studied scientifically *as* information processing without abandoning rigour. Running alongside the laboratory tradition, the psychodynamic school (Freud, from the 1890s) had always addressed the unconscious and development, and the humanistic school (Maslow and Rogers, mid-twentieth century) arose as an explicit "third force" reacting against both behaviourism's mechanism and psychoanalysis's pessimism, insisting on agency and growth. Positive psychology (Seligman, from 1998) is the humanistic impulse rebuilt on empirical method (Kaplan & Sadock 2024).

1.4 The developmental theorists, previewed side by side

Four stage theorists run down one age axis. The second half of this material is developmental psychology, and its core is a small set of theorists who each carved the lifespan into stages, but along *different dimensions*. Previewing them together now prevents the commonest error, which is blurring one theorist's stage into another's at the same age. Freud staged **psychosexual** development by the body zone of libidinal focus; Erikson restaged the whole lifespan as **psychosocial** crises, each a tension to be resolved; Piaget staged **cognitive** development by how the child constructs knowledge; Kohlberg extended Piaget into **moral** reasoning. They share an age scaffold but measure different things, and the discriminate topic later on makes you place a described behaviour with the correct theorist. Attachment (Bowlby and Ainsworth), temperament (Thomas and Chess), and separation-individuation (Mahler) sit alongside them as the relational and constitutional strands.

ROUGH AGE	FREUD (PSYCHOSEXUAL)	ERIKSON (PSYCHOSOCIAL)	PIAGET (COGNITIVE)	KOHLBERG (MORAL)
Infancy (0 to ~1.5 yr)	**Oral**	Trust vs mistrust	**Sensorimotor**	(pre-moral)
Toddler (~1.5 to 3 yr)	**Anal**	Autonomy vs shame and doubt	Sensorimotor into preoperational	Preconventional
Preschool (~3 to 6 yr)	**Phallic (Oedipal)**	Initiative vs guilt	**Preoperational**	Preconventional
School age (~6 to 11 yr)	Latency	Industry vs inferiority	**Concrete operational**	Conventional
Adolescence (~12 yr on)	Genital	**Identity vs role confusion**	**Formal operational**	Postconventional
Adulthood	Genital (mature sexuality)	**Intimacy, then generativity, then integrity**	(formal operational persists)	Postconventional

The developmental theorists on one age axis: same scaffold, different dimensions (body zone, social crisis, cognition, moral reasoning). Exact stage boundaries and full descriptions are paid off in the developmental topics; here, hold the parallelism.

1.5 How these notes is wired to the rest of the paper

Know where each thread is finished. This orientation deliberately opens more than it closes, so keep the cross-references straight. Behaviourism (classical and operant conditioning, learning theory), social psychology and personality theory are given full treatment on the Social, Learning & Personality Psychology notes; the humanistic school and positive psychology also go deeper there. Psychological testing, intelligence measurement and the psychometric properties of scales are the Psychometry, Assessment and Descriptive Psychopathology notes. In these notes, the general-psychology functions (perception, memory, thinking and intelligence, motivation, emotion) each run as an evolution of theories ending in the currently accepted mechanism and its neural correlate, and the developmental theorists each run as a stage model ending in a good-to-remember box. Treat this topic as the index page you flip back to whenever a later claim needs placing on the map.

MNEMONIC

Big Cats Bite Prey Hungrily

The five lenses in appearance-and-argument order: **B**iological, **C**ognitive, **B**ehavioural, **P**sychodynamic, **H**umanistic. Big (Biological, the brain) Cats (Cognitive, the computer) Bite (Behavioural, the black box) Prey (Psychodynamic, the iceberg) Hungrily (Humanistic, the growing self). This is the master mnemonic for these notes: every general-psychology function can be interrogated through these five, in this order, and the letters also seed the structure of the material.

GOOD TO REMEMBER

- **Biological lens:** unit = the brain (genes, neurotransmitters, circuits, evolution); roots in Darwin and neurophysiology; the dominant frame in psychiatry.
- **Cognitive lens:** unit = information processing; the computer metaphor; Ulric Neisser, *Cognitive Psychology* (1967).
- **Behavioural lens:** unit = observable stimulus and response; John B. Watson (behaviourism launched 1913) and B. F. Skinner (operant conditioning); full treatment the Social, Learning & Personality Psychology notes.
- **Psychodynamic lens:** unit = unconscious drives and early development; Sigmund Freud (psychoanalysis), Alfred Adler (individual psychology, inferiority), Carl Jung (analytical psychology, archetypes).
- **Humanistic lens:** unit = growth, meaning and the self; Abraham Maslow (hierarchy of needs) and Carl Rogers (client-centred therapy); modern descendant = positive psychology (Martin Seligman); deeper the Social, Learning & Personality Psychology notes.
- **Positive psychology:** Seligman, from 1998; empirical study of well-being, strengths and flourishing.
- **Historical arc:** Wundt's first psychology laboratory, Leipzig 1879; introspection to behaviourism (Watson 1913) to the cognitive revolution (Neisser 1967); humanistic school as the "third force".
- **Freud (psychosexual):** oral, anal, phallic, latency, genital; staged by body zone of libidinal focus.
- **Erikson (psychosocial):** eight stages of paired crises across the whole lifespan (e.g. trust vs mistrust in infancy, identity vs role confusion in adolescence).
- **Piaget (cognitive, 1896 to 1980):** sensorimotor, preoperational, concrete operational, formal operational.
- **Kohlberg (moral):** preconventional, conventional, postconventional; an extension of Piaget into moral reasoning.
- **Relational and constitutional strands:** attachment (Bowlby and Ainsworth), temperament (Thomas and Chess), separation-individuation (Mahler).

General psychology

2 · Perception and attention

Perception is the exam's most philosophically loaded psychological function, and the one whose theory maps most directly onto psychopathology. The theme of the whole topic is a single argument that runs across a century: whether what we perceive is *read off* the world (data-driven, **bottom-up**) or *constructed* by the brain from expectation (concept-driven, **top-down**), a debate that resolves, in the currently accepted view, into perception as a prediction. That resolution is not academic trivia; it is the mechanistic spine of the modern account of the **hallucination**, which is why this topic carries a dedicated theories-of-hallucinations block at its close. **Learn the debate, and the hallucination theories fall out of it.**

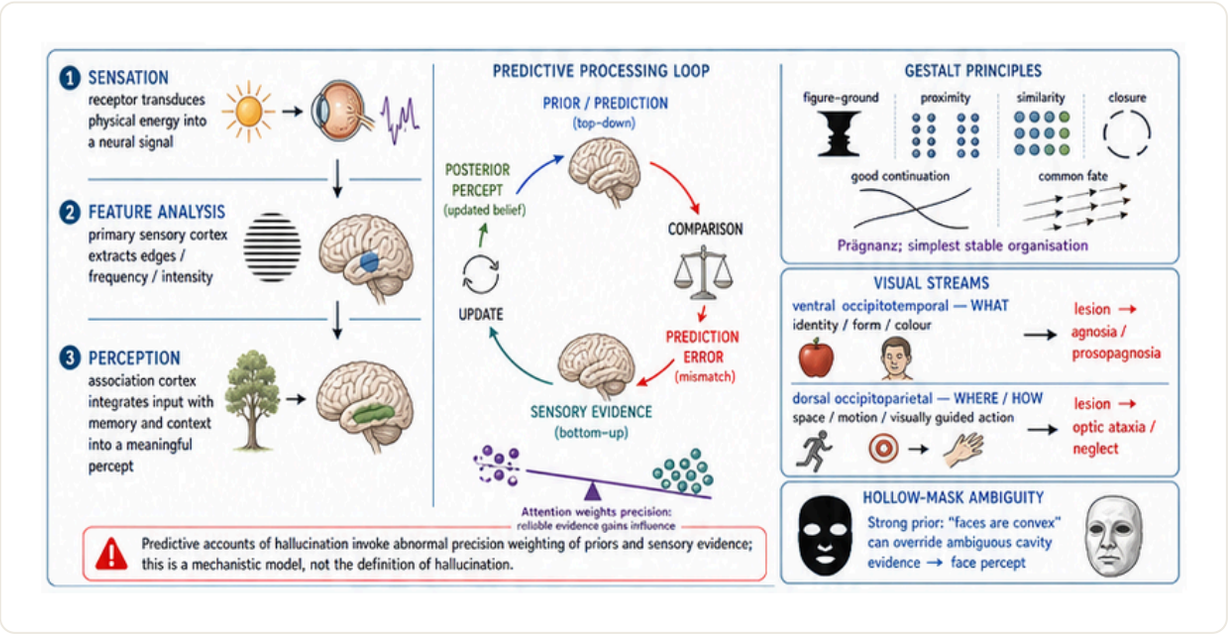


Fig 4.2 Perception: the brain's best constrained guess.

The topic follows the standard evolution-of-theories flow: first the psychophysics that quantified sensation, then the perceptual theories in the order they appeared, each fixing a flaw in the last, then the currently accepted predictive account, its neural correlate in the sensory-association cortex and the two visual streams, a worked example, and finally the parallel evolution of hallucination theory. Attention is folded in as its own theory-sequence, because in the modern view attention is precisely the mechanism that weights bottom-up against top-down. Ground text is Kaplan and Sadock (2024) and the New Oxford Textbook of Psychiatry for the descriptive scaffold.

2.1 Sensation versus perception: the two-stage definition

Sensation. Sensation is the transduction of physical energy at a receptor into a neural signal: light on the retina, pressure on the skin, molecules at the olfactory epithelium. It is bottom-up by definition and largely passive. **Perception** is the active organisation and interpretation of those raw sensations into a meaningful representation of objects and events. The classic exam line is that *sensation is what the sense organ registers, perception is what the mind makes of it*. The distinction matters clinically because the disorders divide along it: a sensory deficit (deafness) sits at the sensation stage, whereas an illusion or hallucination is a disorder of the perceptual stage with the sensory apparatus often intact (Kaplan and Sadock 2024).

Sensation

Receptor-level transduction of a physical stimulus into a neural signal; passive, bottom-up, modality-specific.

Perception

Active organisation and interpretation of sensory data into meaningful percepts; combines bottom-up input with top-down knowledge.

Percept

The finished mental representation of an object or event, the output of perception.

2.2 Psychophysics I: absolute and difference thresholds, Weber-Fechner

Psychophysics, founded by Gustav Fechner in 1860, is the quantitative study of the relation between physical stimulus magnitude and perceived sensation. Two thresholds anchor it. The **absolute threshold** is the smallest stimulus intensity detectable 50 per cent of the time (the criterion of half the trials is the examinable detail, since detection is probabilistic, not all-or-none). The **difference threshold**, or just-noticeable difference (JND), is the smallest change in a stimulus that can be detected 50 per cent of the time.

Weber's law (1834). Ernst Weber found the JND to be a constant fraction of the baseline stimulus, not a fixed absolute amount: the ratio of the change to the baseline (delta-I over I) equals a constant k, the Weber fraction, specific to each sensory dimension. Adding 50 grams to a 1 kg weight is just noticeable; on a 100 gram weight the same 50 grams is glaring, because the fraction, not the absolute amount, governs detection. **Fechner's law** then integrated Weber's law to state that sensation grows as the logarithm of stimulus intensity, so equal ratios of stimulus produce equal steps of sensation. The examinable refinement is **Stevens's power law (1957)**, which replaced the logarithm with a power function that fits a wider range of modalities, expanding for pain and contracting for brightness. What Weber-Fechner fixed was the naive assumption of a linear stimulus-to-sensation map; what it left debated was whether a fixed threshold even exists, a question signal detection theory answered next.

2.3 Psychophysics II: signal detection theory, d-prime and criterion

Signal detection theory (Green and Swets 1966) is the single most important quantitative idea in this topic and a recurring exam favourite, because it dissolves the notion of a fixed threshold. Its claim is that every detection is a decision made against a noisy background, so performance factors into two independent components: *sensitivity* and *bias*. On each trial the observer's internal signal falls somewhere on a continuum; the observer sets a decision **criterion** and says "signal present" whenever the internal evidence exceeds it. This yields the four-cell outcome that must be reproducible on demand: a *hit* (signal present, said yes), a *miss* (present, said no), a *false alarm* (absent, said yes), and a *correct rejection* (absent, said no).

MEASURE	WHAT IT CAPTURES	MOVED BY
d-prime (d')	**Sensitivity: the separation between the signal and noise distributions, a pure measure of the perceptual system's discriminability**	Stimulus strength, acuity, attention, fatigue; NOT by motivation
Criterion (beta or c)	**Response bias: where the observer places the yes/no cut-off, independent of sensitivity**	Payoffs, expectations, base rates; a liberal criterion raises hits and false alarms together, a conservative one lowers both

The two orthogonal parameters of signal detection theory: d-prime is what the system can discriminate, criterion is how willing the observer is to say yes.

The clinical payoff is large. A patient who reports faint voices may have a genuine perceptual change (raised d-prime for that content) or merely a lowered criterion (a bias to say "yes, I hear

it"), and the two demand different formulations. Signal detection theory fixed the fixed-threshold error of classical psychophysics and, crucially, was the first framework to make the perceiver's *expectation and bias* a formal, measurable part of perception, prefiguring the top-down and predictive theories that follow.

TRAP d-prime is **sensitivity** (moved by stimulus strength, acuity, attention, not motivation); criterion is **response bias** (moved by payoffs, expectations, base rates). Do not let a lowered criterion be mistaken for a genuine perceptual change.

2.4 Theory era 1: Wundt, structuralism and introspection

Scientific perception research begins with Wilhelm Wundt's Leipzig laboratory (1879) and the school of **structuralism** (formalised by his student Titchener). Its method was *introspection*: trained observers reported the elementary sensations, images and feelings composing a conscious experience, on the assumption that perception could be decomposed into atomic sensory elements, much as chemistry decomposes compounds. What structuralism fixed was the pre-scientific vagueness of the mind, giving psychology a laboratory method. What it left fatally debated was reliability and reductionism: introspective reports could not be verified between observers, and, more damagingly, perception plainly showed properties that were not present in any of the parts, an objection the Gestalt school turned into a whole movement.

2.5 Theory era 2: Gestalt organisation, the whole over the parts

Gestalt psychology (Wertheimer, Kohler and Koffka, from 1912) is the highest-yield perception theory for the exam and must be reproducible with its laws. Its founding claim, against structuralism, is that *the whole is different from the sum of its parts*: a percept is an emergent, integrated configuration (a Gestalt) that the brain organises spontaneously by self-organising field forces. The master principle is the **law of Prägnanz** (the minimum principle): the perceptual system settles into the simplest, most stable, most regular organisation the stimulus allows. From it descend the grouping laws.

Figure-ground

The visual field is split into a bounded figure and a receding ground; the reversible Rubin vase shows the split is perceptual, not in the stimulus.

Proximity

Elements near one another are grouped together.

Similarity

Elements alike in colour, shape or size are grouped together.

Closure

The system completes incomplete contours into whole, closed figures.

Good continuation

Elements arranged along a smooth line or curve are grouped as a continuous form.

Common fate

Elements moving together in the same direction are grouped together.

What Gestalt fixed was structuralism's atomism, establishing that perception is actively organised and that organisation follows lawful rules. What it left debated was mechanism: the "global field forces" were never specified and the minimum principle could not be quantified or made to yield testable predictions, so the school declined through the 1950s and 1960s. The unresolved question, then, was the source of the organising rules, and it split into two opposed answers: are they built into the incoming stimulation (Gibson) or imposed by the brain's knowledge (Gregory)? That is the bottom-up versus top-down fork, and it is the heart of the topic.

2.6 Theory era 3a: Gibson's direct, bottom-up perception (affordances)

James Gibson's **ecological theory of direct perception** (1966, 1979) is the purest **bottom-up**, data-driven position. Gibson argued that the optic array reaching the eye is already so rich in structure (texture gradients, optic flow, invariants that stay constant as the observer moves) that perception needs no inference, no hypothesis and no stored knowledge: the information is *directly picked up* from the environment. His signature concept is the **affordance**, the action possibility an object offers an organism directly and without deliberation: a chair affords sitting, a handle affords grasping, a cliff-edge affords falling. What Gibson fixed was the poverty-of-the-stimulus assumption that had made perception seem to require guesswork; he showed the ambient array is information-rich and that behaviour in the natural world is often immediate. What he left debated was the equally obvious fact that perception is frequently wrong, ambiguous or illusory, that we can see two things in one figure, and that expectation demonstrably shapes what we see, all of which a purely direct theory struggles to explain.

2.7 Theory era 3b: Gregory's constructivist, top-down perception (perception as hypothesis)

Richard Gregory's **constructivist theory** (1970, 1980) takes the opposite, **top-down**, concept-driven view, reviving Helmholtz's nineteenth-century idea of perception as *unconscious inference*. Gregory's claim is that the retinal image is impoverished and ambiguous, so perception must be an active construction: the brain forms a *perceptual hypothesis*, its best guess about the distal cause, using prior knowledge and expectation, and the percept is that hypothesis, not the raw data. His strongest evidence is precisely the phenomena Gibson could not handle: visual illusions (the Müller-Lyer, the Ponzo, the hollow-mask illusion where a concave face is seen as convex because faces are always convex in experience), and the way a percept flips when the hypothesis changes. What Gregory fixed was the inability of direct perception to explain error, ambiguity and the manifest influence of knowledge on seeing. What he left debated was the reverse problem: if perception is all hypothesis, why is it so fast, so accurate and so stable in the ordinary rich world where Gibson is clearly right? The enduring debate, bottom-up data versus top-down concept, is not resolved by choosing a side but by combining them, which is the modern answer.

2.8 Attention: the theories in time, from early filter to capacity

Attention is the selection and prioritisation of some information for deeper processing at the expense of the rest, and its theory ran a parallel evolution over exactly where in the processing stream selection happens. The exam wants the four models in order with their author and their locus of selection.

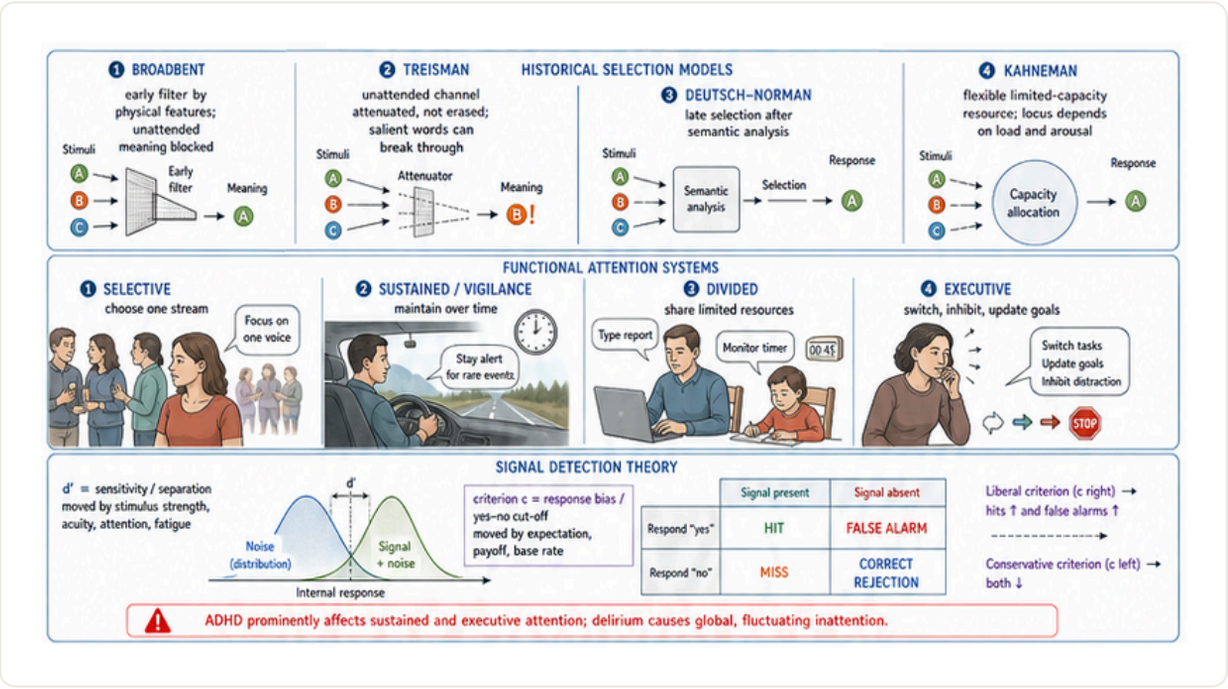


Fig 4.3 Attention: filter, resource and decision.

MODEL (AUTHOR, YEAR)	LOCUS OF SELECTION	WHAT IT FIXED / LEFT OPEN
Broadbent early-filter (1958)	**Early, before meaning: a bottleneck filters by physical features (ear, pitch) and unattended input is blocked before semantic analysis**	Explained selective listening; could not explain why your own name breaks through from the unattended channel (the cocktail-party effect)
Treisman attenuation (1964)	**Early but graded: the filter attenuates rather than blocks the unattended channel; high-salience words with low thresholds still get through**	Fixed Broadbent's leak; left unclear how much late semantic processing really occurs
Deutsch and Norman late-selection (1963, 1968)	**Late, after meaning: all input is analysed for meaning, and selection happens only at the response/memory stage**	Accounted for semantic breakthrough; criticised as metabolically wasteful and hard to reconcile with clear early limits
Kahneman capacity/resource (1973)	**Not a fixed locus at all: attention is a limited pool of mental effort flexibly allocated; selection is early or late depending on load and arousal**	Dissolved the early-late war into a resource question; foreshadowed load theory (Lavie)

The attention sequence: the debate migrated from where the filter sits (Broadbent to Deutsch-Norman) to how much resource is available (Kahneman), the modern framing.

The clinical taxonomy of attention layered on top: *selective* attention (focusing on one stream and ignoring distractors, the cocktail party), *divided* attention (splitting resources across tasks, degraded by load), and *sustained* attention or vigilance (holding focus over time, the deficit probed by the Continuous Performance Test and impaired in ADHD and delirium). In the predictive framework below, attention is reconceived as the mechanism that sets the *weight* given

to incoming sensory evidence relative to prior expectation, which ties the attention story directly into perception.

2.9 Currently accepted: perception as prediction (predictive processing)

The **currently accepted** account, predictive processing or the Bayesian-brain framework (Friston 2010; Clark 2013), synthesises the whole century of debate. The brain is a hierarchical prediction machine: higher levels continuously generate *top-down predictions* (priors) about the causes of sensory input, these predictions are compared against the actual *bottom-up sensory signal*, and only the mismatch, the **prediction error**, is passed up to revise the model. Perception is the brain's best hypothesis (Gregory) constrained by the rich sensory array (Gibson), settling on the interpretation that best explains the data with the least error (a formalisation of Gestalt's Prägnanz as maximising the Bayesian posterior). The relative influence of prior and evidence is set by their *precision* (reliability), and precision-weighting is exactly what attention does: attending to a stimulus raises the precision, and therefore the gain, of its sensory prediction error. This single framework absorbs signal detection theory (criterion is the prior, d-prime is precision-weighted evidence), the bottom-up/top-down fork (both, hierarchically combined), and the attention models (precision allocation), which is why it has become consensus.

RULE **Perception is precision-weighted prediction.** The brain balances bottom-up evidence against top-down priors, and attention is exactly the precision-weighting that sets which one wins.

2.10 Neural correlate: primary versus association cortex, the two streams

The **neural correlate** of the sensation-to-perception pipeline maps cleanly onto the cortical hierarchy. *Primary sensory cortex* (striate cortex V1 for vision, Heschl's gyrus A1 for hearing, postcentral gyrus S1 for touch) performs the first, feature-level, bottom-up analysis: orientation, edges, frequency. *Association (secondary and higher) cortex* integrates these features across modalities and with memory into meaningful percepts; a lesion here produces an *agnosia*, a failure to recognise with intact primary sensation. Above V1 the visual pathway splits into the two anatomically and functionally distinct streams first described by Ungerleider and Mishkin (1982):

Ventral "what" stream

Occipitotemporal, V1 to inferotemporal cortex: object identity, recognition, form and colour. Its damage yields visual agnosia and prosopagnosia.

Dorsal "where/how" stream

Occipitoparietal, V1 to posterior parietal cortex: spatial location, motion, and the visual guidance of action. Its damage yields optic ataxia and, with wider parietal injury, hemispatial neglect.

In the predictive scheme, feedforward connections up the hierarchy carry prediction error while feedback connections carry top-down predictions, and the salience network (anterior insula and dorsal anterior cingulate) with striatal dopamine sets the precision or salience assigned to signals, the node that fails in psychosis (Kaplan and Sadock 2024).

2.11 Worked example: the hollow-mask and a footstep on the stairs

Two everyday demonstrations make the predictive account concrete. **The hollow-mask illusion.** Look at the concave (hollow) back of a face mask and you see it as a normal convex face bulging toward you. The bottom-up sensory data (shading, disparity) correctly specify a hollow surface, but the lifelong prior that "faces are convex" is so strong and high-precision that it overrides the evidence: perception goes with the hypothesis, a direct visualisation of top-down priors winning. The examinable clinical hook is that people with schizophrenia are notably *less* susceptible to this illusion, seeing the true hollow shape, consistent with weakened perceptual priors, which is the mechanism the hallucination theories exploit. **The footstep at night.** Home alone, expecting no one, a creak on the stairs is heard as footsteps and a heart-pounding percept of an intruder; the same creak by day is nothing. Identical sensory input, different prior (and a lowered criterion under fear, in signal detection terms), yielding a different percept, which is perception as prediction in one sentence.

2.12 Theories of hallucinations and their evolution

A **hallucination** is a percept arising without a corresponding external stimulus, experienced with the full force and clarity of a true perception and located in external (objective) space. The full descriptive taxonomy of the disorders of perception (illusions, the pseudohallucination, functional, reflex, extracampine and autoscopic phenomena, and the modality-specific patterns) belongs to the Psychometry, Assessment and Descriptive Psychopathology notes and is treated there in detail (cross-ref: Descriptive Psychopathology, Disorders of Perception). What belongs *here*, as the culmination of the perception theories above, is the mechanism and how the explanation of the hallucination evolved, each theory fixing a defect in the last, ending in the same predictive framework that closed the perception debate.

1. Perceptual-release theory (Hughlings Jackson 1889; West 1962). The oldest neurological account. John Hughlings Jackson proposed a hierarchy in which higher centres normally inhibit lower ones; when higher control is lost (release), lower-level activity is disinhibited and emerges into consciousness. Louis JWest (1962) developed this into the perceptual-release hypothesis: normally, a steady stream of sensory input suppresses stored perceptual traces (memories, images) from reaching awareness; when either sensory input falls (sensory deprivation, eye disease, deafness) or arousal-gating fails, these stored images are *released* and experienced as hallucinations. It elegantly explains the Charles Bonnet hallucinations of the blind, hypnagogic imagery, sensory-deprivation and peduncular hallucinations. What it fixed was the naive idea that a hallucination needs an abnormal stimulus. What it left debated was the specifically psychotic hallucination, where sensory input is intact, and the question of *why* a released image is misattributed to the outside world.

2. Source-monitoring failure (Frith 1992). The cognitive account for psychosis. Christopher Frith proposed that the auditory verbal hallucination is inner speech (subvocal self-talk) that the patient fails to recognise as self-generated. The failure is one of *source monitoring*: a breakdown of the efference-copy or corollary-discharge signal by which the brain normally tags its own motor and cognitive acts as self-produced, so that self-generated inner speech is misattributed to an

external agent. This is why the classic hallucinated voice is in the second or third person and often commenting: it is the patient's own thought, disowned. What it fixed was perceptual release's silence on intact-input psychosis, giving a specific self-versus-other mechanism. What it left debated was the emotional charge and the compelling reality of the voice, and it fit awkwardly with non-verbal and visual hallucinations.

3. Dopaminergic aberrant salience (Kapur 2003). The neurochemical bridge from biology to phenomenology. Building on the finding that midbrain dopamine neurons code reward prediction error and thereby assign *incentive salience* to stimuli (Schultz 1997), Shitij Kapur proposed that in psychosis dysregulated striatal dopamine fires chaotically and assigns **aberrant salience** to internal and external stimuli that do not merit it. Neutral events, thoughts and percepts become urgently, inexplicably significant; hallucinations are the direct experience of aberrant salience attached to a percept, and delusions are the cognitive effort to explain that unbidden significance. It powerfully unifies the pharmacology (antipsychotics are D2 blockers), the prodromal "delusional mood," and the salience of psychotic symptoms. What it fixed was the mechanistic gap between the dopamine hypothesis and lived experience. What it left debated was the finer computational question of *why* salience becomes aberrant, answered by the next account.

4. Predictive-coding / predictive-processing account (Fletcher and Frith 2009; Corlett, Powers, Sterzer, and colleagues, 2010s). The **currently accepted**, integrative mechanism, and the one to lead with. Within the Bayesian-brain framework of 2.9, a hallucination is a percept dominated by an *over-weighted prior*: when top-down predictions are given excessive precision relative to bottom-up sensory evidence, the brain "hears" or "sees" what it expects even in the absence of, or against, the sensory data. Powers and Corlett's conditioned-hallucination experiments demonstrate this directly, showing that people prone to hallucinations over-rely on priors. This single account subsumes its predecessors: perceptual release is the special case where *weak* sensory input lets priors dominate; source-monitoring failure is a miscomputed prediction about the agency of self-generated signals (a failed forward model); and aberrant salience is aberrant precision-weighting of prediction errors driven by dopamine. The hollow-mask finding (2.11), reduced illusion susceptibility in schizophrenia, is the same story seen from the perceptual side. Perception is prediction; the hallucination is prediction unmoored from evidence.

- **Perceptual release** - Hughlings Jackson 1889, West 1962; reduced input plus lost gating releases stored images.
- **Source-monitoring failure** - Frith 1992; inner speech misattributed as external via failed efference copy.
- **Aberrant salience** - Kapur 2003; dysregulated dopamine assigns undue salience; antipsychotics are D2 blockers.
- **Predictive coding** - Fletcher and Frith 2009; over-weighted priors override evidence; the currently accepted account that unifies the earlier three.

HOLD THIS

The hallucination is an over-weighted prior overriding sensory evidence. The four theories are a historical progression (perceptual release, source-monitoring failure, aberrant salience, predictive coding), not rivals, and predictive coding unifies them.

COMMON TRAP

Do not conflate the four hallucination theories as rivals to be chosen between; the exam rewards showing they are a *historical progression* that the predictive-coding account finally unifies. Also keep the two "Friths" straight in your head: the source-monitoring model is Christopher Frith's cognitive theory; the predictive-coding synthesis is Fletcher and Frith (2009), same Chris Frith, later work. And note perceptual release predicts hallucinations from *reduced* input (blindness, deafness), the opposite of what a naive "overstimulation" guess would say.

PEARL

The whole topic is one idea told twice. In normal perception the brain balances bottom-up evidence against top-down priors, weighted by precision (attention). In hallucination that balance tips toward the prior. Every theory on the page, from signal detection's criterion to Kapur's aberrant salience, is a statement about where that balance sits and what moves it. If you can say "perception is precision-weighted prediction, and psychosis is a precision failure," you can reconstruct the rest.

GOOD TO REMEMBER

- **Fechner (1860):** founded psychophysics; absolute threshold = detected 50% of the time.
- **Weber (1834):** JND is a constant fraction of the baseline stimulus (delta-I / I = k, the Weber fraction).
- **Fechner's law:** sensation grows as the logarithm of stimulus intensity; Stevens (1957) refined it to a power law.
- **Signal detection theory (Green and Swets 1966):** d-prime = sensitivity; criterion = response bias; hit / miss / false alarm / correct rejection.
- **Wundt (1879), Titchener:** structuralism, introspection, elementary sensations; failed on reliability and reductionism.
- **Gestalt (Wertheimer, Kohler, Koffka, 1912):** whole differs from the sum of parts; law of Prägnanz; figure-ground, proximity, similarity, closure, good continuation, common fate.
- **Gibson (1966/1979):** direct, bottom-up perception; affordances; optic array is information-rich.
- **Gregory (1970):** constructivist, top-down perception; perception as unconscious inference and hypothesis; explains illusions.
- **Broadbent (1958):** early-filter attention (physical features, before meaning).
- **Treisman (1964):** attenuation (unattended channel dampened, not blocked).
- **Deutsch and Norman (1963/1968):** late selection (all input analysed for meaning, selection at response).
- **Kahneman (1973):** capacity/resource model of attention (limited effort, flexibly allocated).
- **Attention types:** selective (cocktail party), divided (load-limited), sustained (vigilance, CPT, ADHD/delirium).
- **Predictive processing (Friston 2010; Clark 2013):** currently accepted; hierarchical priors vs prediction error, precision-weighting = attention.
- **Neural correlate:** primary sensory cortex (V1/A1/S1) = features; association cortex = meaning (lesion = agnosia); ventral "what" (occipitotemporal) vs dorsal "where/how" (occipitoparietal), Ungerleider and Mishkin (1982).
- **Perceptual release (Hughlings Jackson 1889; West 1962):** lost higher inhibition + reduced sensory input releases stored images (Charles Bonnet, sensory deprivation).
- **Source-monitoring failure (Frith 1992):** inner speech misattributed as external via failed efference copy.
- **Aberrant salience (Kapur 2003):** dysregulated dopamine assigns undue salience; delusion explains it; antipsychotics = D2 block.
- **Predictive-coding hallucination (Fletcher and Frith 2009; Corlett, Powers, Sterzer):** over-weighted priors override sensory evidence; unifies the earlier three.

3 · Memory: types, processes and forgetting

Memory is the set of processes by which experience is **encoded**, held over time (**storage**), and later brought back into use (**retrieval**). It is not one faculty but a family of dissociable systems, and the history of the field is the story of that family being progressively subdivided: from Ebbinghaus measuring one homogeneous "memory" as a decaying trace, to the boxes-and-arrows stores of the multi-store model, to the componential working memory that replaced the single short-term box, to Tulving's taxonomy of long-term systems that a single amnesic brain can double-dissociate. **Read the topic as an evolution, not a list.** Each model is best understood by what it fixed in its predecessor and what it left unsettled for the next, and the whole argument is anchored in one patient whose surgery in 1953 proved the divisions are real in tissue.

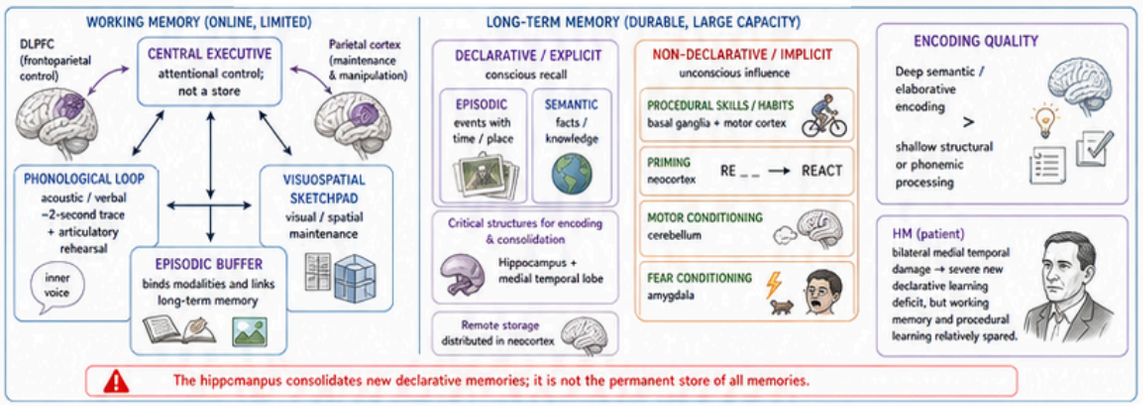


Fig 4.4 Memory is plural: workspace, systems and brain.

For the exam, the payload is fourfold: the ordered theories with their named authors and the specific findings that forced each revision; the taxonomy of long-term memory (episodic, semantic, procedural; declarative versus non-declarative; explicit versus implicit); the four mechanisms of forgetting plus the modern twist that retrieval itself destabilises a memory (reconsolidation, the misinformation effect); and the neural correlate that maps each memory system onto a distinct structure. The functions cross-refer directly to the Functional Neuroanatomy & Neurophysiology notes synaptic plasticity: the cellular basis of the encoding described here is long-term potentiation in the hippocampus.

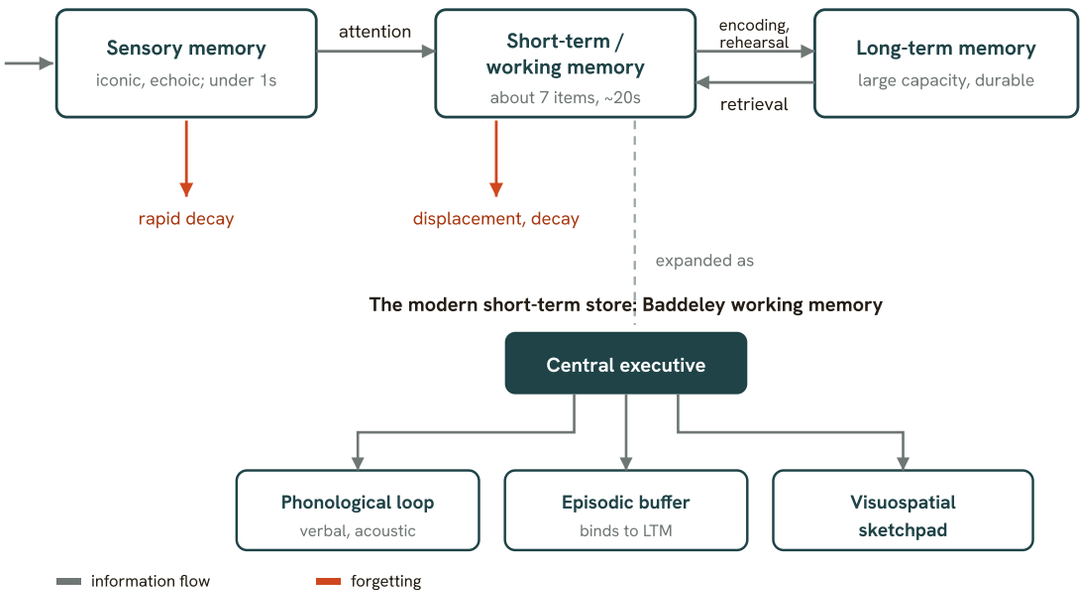


Fig 4.5 The memory system: the Atkinson-Shiffrin multi-store model (top) reads left to right, with attention passing sensory traces into a limited short-term store and rehearsal encoding them into a durable long-term store, from which material is retrieved back. Information is lost by rapid decay from sensory memory and by displacement or decay from the short-term store (coral). Baddeley and Hitch reconceived the short-term store as working memory (below): a central executive directing a phonological loop, a visuospatial sketchpad and an episodic buffer that binds information and links to long-term memory.

3.1 Ebbinghaus: forgetting as a measurable curve, and the savings method

The first quantitative theory. Hermann Ebbinghaus (1885), experimenting on himself with lists of meaningless three-letter *nonsense syllables* (chosen to strip out prior meaning), turned memory into a measurable quantity for the first time. His two enduring contributions are the **forgetting curve**, showing that retention falls steeply in the first hours after learning and then flattens into a long slow tail, and the **savings method**, his index of retention: even when a list can no longer be recalled, relearning it to the original standard takes fewer trials than learning it fresh, and that saving in trials quantifies the memory that survives below the threshold of conscious recall. He also first described the *spacing effect* (learning distributed over time beats massed cramming) and the *serial position* advantage. **What it fixed.** It replaced philosophical introspection about memory with a reproducible curve. **What it left debated.** It treated memory as one undifferentiated store decaying with time, so it could describe the rate of forgetting but said nothing about its architecture or its cause, the very questions the next century answered (Kaplan and Sadock 2024).

3.2 Atkinson and Shiffrin: the multi-store (modal) model and its three stores

The boxes-and-arrows model. Atkinson and Shiffrin (1968) proposed the **multi-store** model (the "modal model") in which information flows sequentially through three structurally separate stores, gated by attention and rehearsal. Incoming stimulation first enters **sensory memory**, a modality-specific register of very large capacity and sub-second duration (iconic for vision, echoic for hearing); whatever is *attended* passes into **short-term** store; and material that is *rehearsed* is transferred into **long-term** store. The stores differ on three axes: encoding, capacity, and duration. Short-term store holds roughly seven items (Miller's 7 plus or minus 2, 1956) for about 15 to 30 seconds and codes mainly acoustically; long-term store is effectively unlimited in capacity and duration and codes mainly semantically. Crucially, Atkinson and Shiffrin distinguished the fixed *structural* stores from flexible *control processes* (rehearsal, coding, retrieval strategies) that the person deploys within them.

What it fixed. It gave forgetting an architecture, explaining why a phone number vanishes in seconds yet a childhood address lasts decades, and it accounted for the serial-position curve: the primacy effect reflects rehearsed items already in long-term store, the recency effect reflects the last items still sitting in short-term store (Glanzer and Cunitz 1966 abolished only the recency limb with a filled delay). **What it left debated.** Two weaknesses forced the next models. First, it treated short-term store as a single passive holding box, yet neuropsychological patients showed the box had parts. Second, it made rehearsal the sole route into long-term memory, which is empirically false: depth of meaning matters more than repetition, the gap that levels-of-processing filled (Kaplan and Sadock 2024).

<2 s	7 ± 2	15 to 30 s
SENSORY MEMORY	SHORT-TERM ITEMS (MILLER)	SHORT-TERM DURATION

3.3 Baddeley and Hitch: working memory replaces the single short-term box

From passive store to active workspace. Baddeley and Hitch (1974) showed that the unitary short-term box could not be right: participants could hold a string of digits *and* simultaneously reason or comprehend prose, which is impossible if a single limited store does both. They replaced it with **working memory**, a multi-component system for the temporary holding *and manipulation* of information. In the model, a limited-capacity *central executive* (an attentional controller, not a store) supervises two modality-specific slave systems: the *phonological loop* for speech-based and acoustic material (a store that decays in about two seconds unless refreshed by articulatory rehearsal) and the *visuospatial sketchpad* for visual and spatial material. Baddeley (2000) later added a fourth component, the *episodic buffer*, a general store that binds information across the two slave systems and links it to long-term memory, explaining how we integrate what we see and hear into a single remembered scene.

What it fixed. It explained dual-task performance (two tasks in the same code interfere, two in different codes do not) and made rehearsal optional rather than the only mechanism, and it mapped cleanly onto brain lesions in a way the single box never did. **What it left debated.** The central executive stayed a poorly specified "homunculus," and the number and independence of the components remained contested, so rival accounts followed (Cowan's embedded-processes model treats working memory as the activated portion of long-term memory plus a focus of attention). This is where the field currently sits (Kaplan and Sadock 2024).

3.4 Craik and Lockhart: levels of processing, from structure to depth

Not where you store it, how deeply you process it. Craik and Lockhart (1972) attacked the multi-store assumption that retention depends on *how long* an item sits in a store. They argued instead that durability depends on the *depth* of processing at encoding along a shallow-to-deep continuum: *shallow* structural processing (the word's typeface) and phonemic processing (its sound) leave weak traces, whereas *deep* semantic processing (its meaning, its links to what you already know) leaves durable ones. This reframed Atkinson and Shiffrin's rehearsal: mere *maintenance rehearsal* (rote repetition) keeps material available briefly but transfers little to long-term memory, whereas *elaborative rehearsal* (giving it meaning and associations) is what actually encodes it. **What it fixed.** It explained the store-model's key failure, why meaningful material is remembered far better than repeated-but-meaningless material, and it grounds every effective study technique. **What it left debated.** "Depth" was circular (we call processing deep because it is well remembered), and the framework describes encoding without specifying the storage systems themselves, which Tulving supplied (Kaplan and Sadock 2024).

RULE **Depth of meaning beats duration in a store.** Elaborative (semantic) rehearsal encodes; maintenance (rote) rehearsal only holds material briefly and transfers little to long-term memory.

3.5 Tulving: the taxonomy of long-term memory

Long-term memory is plural. Tulving (1972, 1985) subdivided long-term store into dissociable systems, the taxonomy the exam tests most heavily. The master division is **declarative** (explicit) memory, available to conscious recollection and expressible in words, versus **non-declarative**

(implicit) memory, expressed through performance without conscious access. Declarative memory splits into *episodic* memory (personally experienced events tagged with time and place, "remembering") and *semantic* memory (context-free general facts and knowledge, "knowing"). Non-declarative memory is a heterogeneous family: *procedural* memory (motor and cognitive skills and habits, riding a bicycle), *priming* (facilitated processing of a recently encountered stimulus), simple *classical conditioning*, and *non-associative* learning (habituation, sensitisation). The defining claim is that these are separable in the brain, not merely conceptual labels.

CLINICAL ANCHOR

The declarative/non-declarative line is the single most useful memory distinction in clinical work. Amnesia (from medial temporal or diencephalic damage) devastates declarative memory while leaving non-declarative memory intact, which is why an amnesic patient can learn a mirror-drawing skill perfectly across days yet swear each morning they have never done it. The mirror image is Alzheimer disease, where declarative (especially episodic) memory fails first because the pathology begins in the medial temporal lobe.

3.6 The four mechanisms of forgetting

Why memories fail. Four classical mechanisms are distinguished, and they are not mutually exclusive.

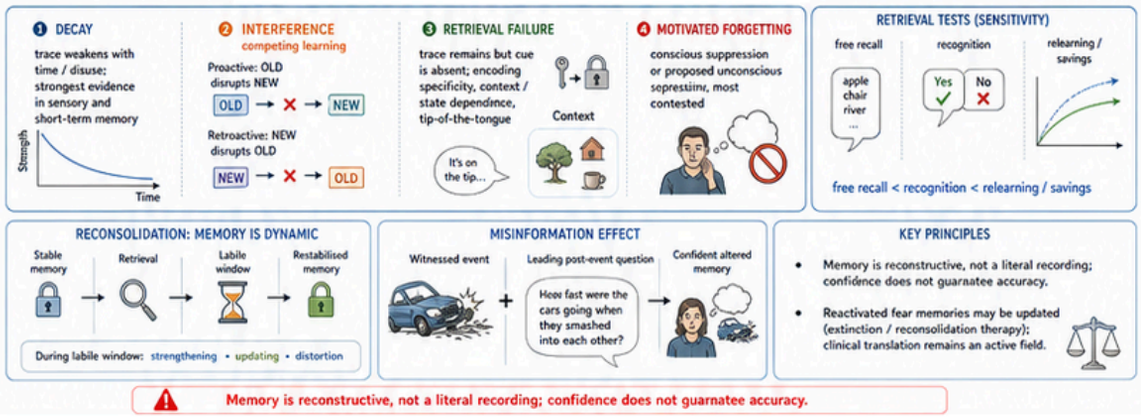


Fig 4.6 Why we forget, and why recall can change memory.

Decay (trace decay)

The memory trace fades with the mere passage of time if not used (Thorndike's law of disuse). Best supported for sensory and short-term stores; heavily disputed for long-term memory, where critics (McGeoch; Nairne 2002) argue it is the intervening events, not time itself, that cause the loss.

Interference

Other learning competes with the target memory. *Proactive* interference: older learning disrupts newer (your old phone number intrudes on the new one). *Retroactive* interference: newer learning disrupts older (learning Spanish erodes your French). The single commonest cause of everyday long-term forgetting.

Retrieval failure (cue-dependent forgetting)

The trace is intact but inaccessible because the right retrieval cue is absent; the memory returns when the cue is restored. The tip-of-the-tongue state is the everyday case; encoding-specificity and context-dependent and state-dependent recall are its corollaries. Recall (cue-free) is the most sensitive retrieval test, recognition easier, relearning (savings) the most sensitive of all.

Motivated forgetting

Emotionally threatening material is kept out of awareness, whether by active suppression or by unconscious repression (the psychodynamic account). Invoked for the amnesia of trauma; the most theoretically contested of the four.

TRAP **Pro**active interference = **old** learning disrupts new (old phone number intrudes); **retro**active interference = **new** learning disrupts old (Spanish erodes French). The prefix names what is disrupted, not what does the disrupting.

3.7 Reconsolidation and the misinformation effect: memory as reconstruction

Retrieval changes the memory. The modern correction to every box model is that a stored memory is not a fixed recording played back unchanged. On retrieval a consolidated memory returns to a labile state and must be restabilised, a process called *reconsolidation*, during which it can be updated, strengthened, or corrupted before it is re-fixed. This makes memory reconstructive rather than reproductive, and it is the mechanism behind Loftus's **misinformation effect**: post-event information, especially a subtly leading question, is incorporated into the original memory so that eyewitnesses confidently report details they never saw (Loftus and Palmer 1974 showed the verb in "how fast were the cars going when they smashed / hit each other" shifted both speed estimates and later false memories of broken glass).

Why it matters. It undermines the reliability of confident eyewitness testimony and recovered memories, and reconsolidation is now an active treatment target, using the reactivation window to weaken maladaptive fear memories in PTSD (Kaplan and Sadock 2024).

3.8 The currently accepted synthesis

A componential working memory feeding a distributed, systems-organised long-term memory. The *currently accepted* account is not any single historical model but their integration. A limited-capacity working memory (a componential attentional workspace, whether framed as Baddeley's components or as the activated portion of long-term memory in Cowan's embedded-processes model) selects and manipulates incoming information; material processed deeply and elaboratively is *consolidated* into long-term memory, a hippocampus-dependent process that gradually transfers the memory to distributed neocortical stores where it becomes independent of the hippocampus (systems consolidation). Long-term memory is not one store but the parallel taxonomy of dissociable systems (declarative and non-declarative), and forgetting is chiefly cue-dependent retrieval failure and interference rather than passive decay, with retrieval itself capable of updating the trace through reconsolidation (Kaplan and Sadock 2024).

3.9 The neural correlate: one structure per memory system

The systems map onto tissue. The strongest evidence that Tulving's taxonomy is biologically real is that each system has a distinct **neural correlate** and can be lost in isolation.

MEMORY SYSTEM	CRITICAL STRUCTURE(S)	EVIDENCE / NOTE
Declarative encoding and consolidation	**Hippocampus and the wider medial temporal lobe (entorhinal, perirhinal, parahippocampal cortex); medial diencephalon (mammillary bodies, dorsomedial thalamus)**	Bilateral MTL damage causes anterograde amnesia (HM, EP); CA1-restricted lesions give milder amnesia (RB); diencephalic version is Korsakoff. Cellular basis is hippocampal LTP (cross-ref the Functional Neuroanatomy & Neurophysiology notes).
Working memory	**Prefrontal cortex (dorsolateral PFC for manipulation, ventrolateral for maintenance), with parietal cortex**	Frontal lesions impair manipulation, monitoring and retrieval strategy; fMRI shows PFC engagement scaling with memory load.
Procedural / skill and habit learning	**Basal ganglia (striatum), with cerebellum and motor cortex**	Preserved in MTL amnesia; degraded in Parkinson and Huntington disease.
Classical conditioning of motor responses	**Cerebellum (deep nuclei and cortex)**	Cerebellar lesions abolish the conditioned eyeblink response while sparing the reflex.
Emotional (fear) conditioning	**Amygdala (with hippocampus for context)**	Amygdala attaches affect to stimuli; model for anxiety disorders. PFC drives extinction.
Remote consolidated memory	**Distributed neocortex**	Old memories survive hippocampal loss (temporally graded retrograde amnesia); slow-wave sleep aids declarative consolidation via hippocampal replay.

The double dissociation across these rows, declarative lost while procedural is spared, is the anatomical proof that "memory" is plural.

COMMON TRAP

Do not equate "short-term memory" with "working memory," and do not call the hippocampus the store of memories. The hippocampus is required to *encode and consolidate* new declarative memories, not to store old ones: consolidated remote memories live in distributed neocortex, which is why HM kept childhood memories while forming no new ones. Working memory (an active PFC workspace) is a superset of the older passive short-term store.

3.10 Worked example: patient HM and the amnesic dissociation

The case that founded the field. Henry Molaison (patient HM) underwent bilateral medial temporal lobectomy by William Scoville in 1953 for intractable epilepsy, removing much of both hippocampi and adjacent cortex. The result, documented over decades by Brenda Milner, was a clean dissociation that no single-store model could accommodate. HM had a dense *anterograde amnesia*: he could not form new declarative memories, failing to learn new facts or events and never recognising his caregivers or learning that his parents had died. Yet three functions were

preserved, and each proves a separate system. His *short-term / working memory was intact* (he could hold a number in mind and converse normally), proving short-term and long-term stores are separate. His *remote memories from before surgery were largely spared*, proving the hippocampus is needed to *form* declarative memories, not to *store* consolidated ones. And most strikingly, he could *learn new motor skills* (mirror-drawing improved across sessions) while insisting each time he had never attempted the task, proving non-declarative (procedural) memory is independent of the medial temporal lobe. **One patient, three dissociations.** HM is the empirical bridge from the abstract boxes of Atkinson and Shiffrin to the tissue-level taxonomy of Tulving, and Atkinson and Shiffrin themselves cited his profile to justify the short-term versus long-term split (Kaplan and Sadock 2024).

HOLD THIS

HM proves memory is plural: one patient, three dissociations. Intact short-term memory (STM separate from LTM), spared remote memory (hippocampus forms but does not store declarative memory), and preserved mirror-drawing (procedural memory is independent of the medial temporal lobe).

GOOD TO REMEMBER

- **Ebbinghaus (1885):** forgetting curve (steep early loss then a tail) and the savings method (relearning is faster); used nonsense syllables; also the spacing effect.
- **Atkinson and Shiffrin (1968):** multi-store / modal model, three stores: sensory, short-term, long-term; attention gates the first transfer, rehearsal the second; structural stores versus control processes.
- **Sensory memory:** modality-specific, huge capacity, under about 2 seconds; iconic (visual) and echoic (auditory).
- **Short-term store:** about 7 plus or minus 2 items (Miller 1956), about 15 to 30 seconds, mainly acoustic coding.
- **Long-term store:** effectively unlimited capacity and duration, mainly semantic coding.
- **Baddeley and Hitch (1974) working memory:** central executive (attentional controller) plus phonological loop and visuospatial sketchpad; episodic buffer added by Baddeley (2000).
- **Craik and Lockhart (1972):** levels of processing; depth (semantic) beats shallow (structural/phonemic); elaborative rehearsal beats maintenance rehearsal.
- **Tulving (1972, 1985):** declarative (explicit) = episodic + semantic; non-declarative (implicit) = procedural, priming, conditioning, non-associative.
- **Serial position:** primacy (long-term store, rehearsed) plus recency (short-term store); recency abolished by a filled delay (Glanzer and Cunitz 1966).
- **Four types of forgetting:** decay, interference (proactive = old disrupts new; retroactive = new disrupts old), retrieval failure / cue-dependent, motivated forgetting (suppression/repression).
- **Loftus (misinformation effect):** post-event leading information corrupts the memory; basis of unreliable eyewitness testimony; mechanism is reconsolidation of a labile trace on retrieval.
- **Neural correlates:** hippocampus and medial temporal lobe = declarative encoding (LTP, the Functional Neuroanatomy & Neurophysiology notes cross-ref); prefrontal cortex = working memory; basal ganglia and cerebellum = procedural; cerebellum = conditioned motor responses; amygdala = fear conditioning; distributed neocortex = remote consolidated memory.
- **Patient HM (Henry Molaison):** bilateral medial temporal lobectomy, Scoville 1953, studied by Milner; dense anterograde amnesia with intact short-term memory, spared remote memory, and preserved procedural (mirror-drawing) learning.

4 · Thinking, problem-solving and intelligence theories

This topic pairs the two ends of higher cognition the exam most reliably tests together: the *process* of thinking (how the mind forms concepts, reasons, and solves problems, and how that process fails through bias) and the *capacity* for it (intelligence, and the century-long fight over whether it is one thing or many). The first half is a toolkit of named effects (heuristics, biases, mental set, insight) that recur in cognitive psychology, in cognitive-behavioural therapy, and in the psychopathology of thought. The second half is a clean evolution-of-theories story, from Spearman's single **g** to the modern **CHC** consensus, that rewards the candidate who can lay the models out in time and say what each one fixed. **One process, one capacity, one debate: is intelligence unitary or plural?**

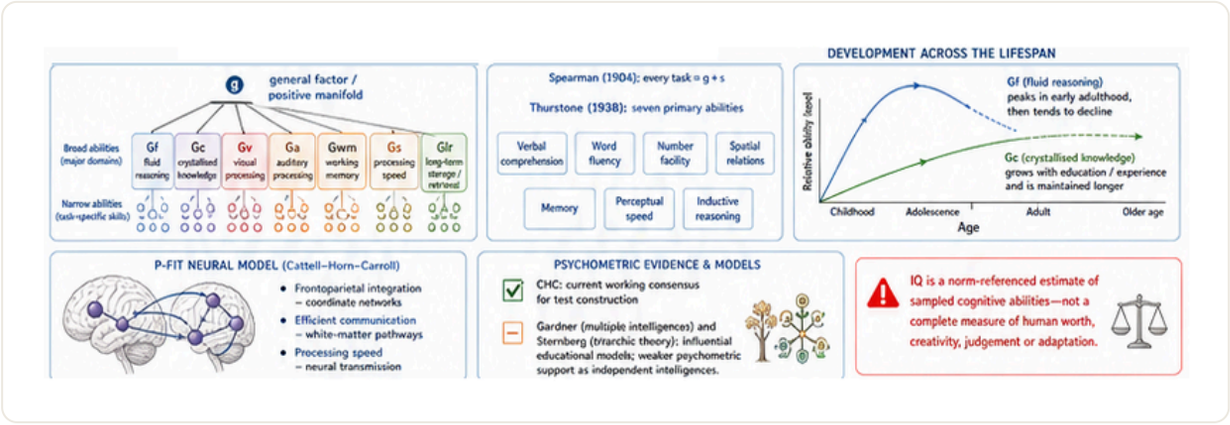


Fig 4.7 Intelligence: one general factor, many broad abilities.

The intelligence half follows the standard evolution-of-theories flow: a definition, then the theories in the order they appeared, each fixing a flaw in the last, then the currently accepted model (CHC), its neural correlate (the parieto-frontal integration theory and processing speed), and a worked example. Note the deliberate split from the Psychometry, Assessment and Descriptive Psychopathology notes: the theories of intelligence are taught here, but the instruments that operationalise them (Binet-Simon, the Wechsler scales, deviation IQ, the diagnostic bands) are taught on the Psychometry, Assessment and Descriptive Psychopathology notes (cross-ref: Psychometry and assessment, IQ testing). Ground text is Kaplan and Sadock (2024) and the New Oxford Textbook of Psychiatry, with the historical chronology cross-checked against the standard intelligence literature (Carroll 1993; Warne 2023).

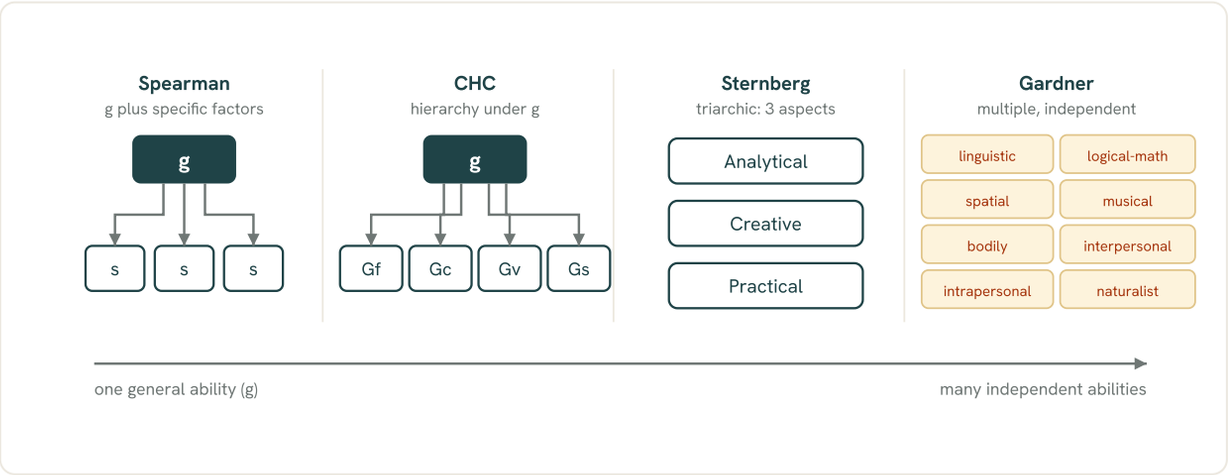


Fig 4.8 The theories of intelligence read as one argument: is intelligence a single thing or many? Spearman's positive manifold pointed to a general factor g with task-specific factors; the Cattell-Horn-Carroll model keeps g but organises the broad abilities (fluid Gf, crystallised Gc, visual Gv, processing speed Gs and more) beneath it, and is the modern working consensus. Sternberg's triarchic model and Gardner's multiple intelligences push toward the plural end, valuing abilities that classic IQ tests miss. Intelligence testing itself is taught on the Psychometry, Assessment and Descriptive Psychopathology notes.

4.1 Thinking and concept formation: the units of thought

Thinking is goal-directed mental manipulation of internal representations (images, words, concepts, propositions) to reach a conclusion, form a judgement, or solve a problem. Its basic unit is the **concept**, a mental category that groups objects, events, or ideas by shared features, letting the mind treat many particulars as one kind and so economise on cognitive effort. **Concept formation** proceeds in two classic ways. On the *classical* view a concept is defined by a set of necessary and sufficient features (a bachelor is unmarried and male and adult). On the more psychologically accurate *prototype* view (Rosch 1975), a concept is organised around a best example or prototype, and membership is graded by family resemblance: a robin is a more prototypical bird than a penguin, and the mind classifies faster the closer an instance sits to the prototype. Clinically, the breakdown of concept formation, the loss of the capacity to abstract and a slide into concrete, over-inclusive, or literal categorisation, is a core sign in schizophrenia and in the frontal and organic states, and is probed by proverb interpretation and card-sorting.

4.2 Reasoning: deductive and inductive

Reasoning is thinking directed at drawing a conclusion from premises, and it comes in two forms the exam contrasts. **Deductive reasoning** moves from general premises to a specific, logically certain conclusion: if all premises are true and the form is valid, the conclusion *must* be true (all humans are mortal; Socrates is human; therefore Socrates is mortal). It is truth-preserving but adds no new content. **Inductive reasoning** moves the other way, from specific observations to a general, probable conclusion: every swan I have seen is white, so swans are probably white. It is content-expanding but not certain, since a single black swan refutes it, and it is the engine of hypothesis-generation and everyday learning. Human reasoning departs systematically from formal logic, as the Wason selection task shows (people fail abstract logical versions but succeed on concrete social ones), which sets up the study of the biases that follow.

4.3 Problem-solving: algorithms versus heuristics

Problem-solving is the sequence of operations that moves a start state to a goal state, and it runs on two contrasting strategies. An **algorithm** is an exhaustive, step-by-step procedure that is *guaranteed* to find the solution if one exists (checking every permutation of a lock, following long division): it is reliable but often slow and effortful, sometimes computationally impossible for large problems. A **heuristic** is a mental shortcut or rule of thumb that reduces a hard problem to a manageable one and usually delivers a good-enough answer fast, at the cost of no guarantee and a systematic vulnerability to error (working backward from the goal, means-ends analysis, hill-climbing). The trade-off is the whole point: algorithms buy certainty with effort, heuristics buy speed with the risk of bias. The specific heuristics Tversky and Kahneman identified are the bridge to the next subtopic.

Algorithm

Exhaustive rule-based procedure guaranteeing a solution; reliable but slow and effortful.

Heuristic

Shortcut or rule of thumb; fast and low-effort but not guaranteed and prone to systematic bias.

Means-ends analysis

A heuristic that repeatedly reduces the difference between the current state and the goal by setting subgoals.

4.4 The Tversky and Kahneman heuristics and biases

The **heuristics-and-biases programme** (Tversky and Kahneman 1974) is the single most examinable block in this half of the topic, because the same biases reappear as cognitive distortions in CBT and as reasoning errors in delusion and depression. The claim is that judgement under uncertainty is governed by a few economical heuristics that are usually useful but produce predictable, replicable errors. Three are core.

HEURISTIC	THE SHORTCUT	THE BIAS IT PRODUCES
Availability	**Judge probability by how easily instances come to mind**	Vivid, recent, or emotionally charged events are over-estimated (fear of plane crashes over car crashes; a doctor over-diagnoses the condition last seen)
Representativeness	**Judge probability by resemblance to a prototype, ignoring base rates**	The base-rate fallacy and the conjunction fallacy (the "Linda problem"); a shy tidy man judged more likely a librarian than a farmer despite farmers being far more numerous
Anchoring and adjustment	**Start from an initial value (the anchor) and adjust insufficiently**	Estimates stay pulled toward an arbitrary starting number, even a plainly irrelevant one; the basis of negotiation and pricing effects

The three core Tversky and Kahneman heuristics: each is a serviceable shortcut whose failure mode is a named, reproducible bias.

Two allied effects round out the block and are worth naming. **Framing**: the same option is chosen or rejected depending on whether it is described in terms of gains or losses (the surgery "90 per cent survive" versus "10 per cent die"), a violation of the invariance that rational choice requires and a cornerstone of prospect theory (Kahneman and Tversky 1979). **Confirmation bias**: the tendency to seek, weight, and recall evidence that supports a prior belief and to discount evidence against it, the reasoning engine behind the maintenance of delusions and the negative schemas of depression.

TRAP **Availability** judges by ease of recall (vivid/recent events over-estimated); **representativeness** judges by resemblance to a prototype and ignores base rates (the Linda / base-rate fallacy). Do not swap them.

4.5 Dual-process theory: System 1 and System 2

The heuristics-and-biases findings are organised by **dual-process theory** (Stanovich and West 2000; popularised as *Thinking, Fast and Slow*, Kahneman 2011), the currently dominant framework for reasoning. It holds that two systems generate judgements. **System 1** is fast, automatic, effortless, parallel, emotional, and unconscious: it runs the heuristics and produces intuitions and snap judgements. **System 2** is slow, deliberate, effortful, serial, logical, and conscious: it can monitor and override System 1 but is lazy and capacity-limited, so it often endorses System 1's output unchecked. Most biases are System 1 intuitions that System 2 failed to catch. The clinical resonance is direct: CBT can be read as training System 2 to interrupt and re-appraise the automatic, System 1 negative thoughts that drive emotional disorder.

4.6 Barriers to problem-solving: mental set, functional fixedness, insight

Three classic obstacles and their resolution are high-yield, drawn from the Gestalt tradition of problem-solving. **Mental set** (Einstellung) is the tendency to persist with a strategy that worked before even when a simpler or better one is available, demonstrated by Luchins's water-jar problems, where subjects keep using a laborious learned formula after a one-step solution appears. **Functional fixedness** is a special case: the inability to see that an object can be used for a function other than its usual one, shown in Duncker's candle problem, where subjects fail to use the tack-box as a candle-holder because they fix on its role as a container. The escape from both is **insight**, the Gestalt phenomenon of a sudden, complete restructuring of the problem, the "aha" experience described by Kohler in his chimpanzees (Sultan stacking boxes to reach a banana): the solution appears abruptly and whole rather than by gradual trial and error, marked by a felt click of comprehension. Insight problems are solved all-at-once; incremental problems are solved by heuristic search.

Mental set (Einstellung)

Persisting with a previously successful strategy when a better one exists (Luchins's water-jar task).

Functional fixedness

Failing to use an object in a novel function because its usual function dominates (Duncker's candle problem).

Insight

Sudden, complete perceptual restructuring of a problem; the Gestalt "aha" (Kohler's apes).

4.7 Intelligence defined, and the one-versus-many debate

Intelligence is the global capacity to think rationally, act purposefully, and deal effectively with the environment (Wechsler's classic definition), or more operationally the aggregate ability to learn from experience, reason abstractly, and adapt to novel and complex situations (Kaplan and Sadock 2024). Every theory below is an answer to one question that has run for over a century and is *still* formally open: is intelligence a single general capacity, or a set of separate abilities? Kaplan and Sadock (2024) state it plainly, that whether intelligence is best regarded as a single general capacity, the **g** proposed by Spearman in 1904, or a range of modular capabilities as first proposed by Thurstone in 1938, remains an open question with no consensus. Hold that debate as the spine: each theorist moves the count of "how many intelligences" and each is judged against one stubborn empirical fact, the *positive manifold*, that scores on almost all cognitive tests are positively correlated.

4.8 Spearman's two-factor theory: g and s, the positive manifold

Charles **spearman** (1904, 1927), inventing factor analysis to do it, made the founding observation: performance on any one mental test correlates positively with performance on almost every other, a pattern he named the **positive manifold**. To explain it he proposed the **two-factor theory**: every cognitive performance draws on a single *general* factor, **g**, common to all tasks and representing overall mental energy or power, plus a *specific* factor, *s*, unique to that particular task. A person high in g tends to do well across the board; the s factors explain why they are nonetheless better at some tasks than others. What Spearman *fixed* was the pre-scientific vagueness of "intelligence," giving it a measurable, statistically derived core (g) and the tool (factor analysis) that all successors would use. What he *left debated* was whether one general factor could really account for the full diversity of human ability, and whether g was a real entity or a statistical artefact of how tests are built.

4.9 Thurstone's primary mental abilities: the plural challenge

Louis L. **thurstone** (1938), using a more advanced (multiple-factor) form of factor analysis, rejected a single dominant g and argued instead for several independent **primary mental abilities**, identifying seven: verbal comprehension, word fluency, number facility, spatial visualisation, perceptual speed, associative memory, and inductive reasoning. On his account an overall IQ score misleads, because a person is a profile of distinct strengths, not one number. What Thurstone *fixed* was Spearman's reductionism, insisting that ability is multidimensional and that the profile matters. What he *left debated*, and eventually conceded, was that his seven abilities were themselves positively intercorrelated and, when factored again, yielded a higher-order g. The debate thus did not resolve so much as move up a level: both a general factor and specific abilities seemed to be real, which is exactly what the hierarchical models would later formalise.

4.10 Cattell and Horn: fluid versus crystallised intelligence

Raymond **cattell** and John Horn (1960s) split g itself into two broad, empirically separable intelligences, the distinction the exam wants most from this era. **Fluid intelligence (Gf)** is the capacity to reason, see relationships, and solve novel problems independent of acquired knowledge, largely biological and content-free (matrix reasoning, novel puzzles). **Crystallised intelligence (Gc)** is the store of acquired knowledge, vocabulary, and skills built up through education and culture (general knowledge, word meanings). Their evidence came from outside factor analysis, in the aging data: the two follow different lifespan trajectories, with **fluid** intelligence peaking in early adulthood and declining from around the third to fourth decade, while **crystallised** intelligence rises through life and is maintained into old age. This dissociation is clinically vital, because it is the basis of "hold" versus "no-hold" tests in dementia assessment: preserved vocabulary (Gc) against declining novel problem-solving (Gf) estimates premorbid ability and flags decline. What Cattell and Horn *fixed* was the monolithic g, showing it fractionates into meaningfully different, differently-ageing components. What they *left debated* was, again, that Gf and Gc are themselves correlated and combine into a general factor, so the one-versus-many question persisted.

RULE **Fluid falls, crystallised holds.** Fluid intelligence (Gf, novel reasoning) peaks in early adulthood and declines from the third to fourth decade; crystallised intelligence (Gc, acquired knowledge) is preserved into old age, which is the basis of "hold" tests in dementia.

4.11 The Cattell-Horn-Carroll (CHC) three-stratum model: the synthesis

John Carroll's survey of over 460 factor-analytic datasets (1993) resolved the century-old dichotomy by making it a hierarchy, and merging with the Cattell-Horn work gave the **chc** (Cattell-Horn-Carroll) theory, the great synthesis. It is a **three-stratum model**: at the top (Stratum III) sits general intelligence, g; the middle (Stratum II) holds around eight to ten *broad abilities* (fluid reasoning Gf, crystallised knowledge Gc, short-term/working memory, long-term retrieval, visual processing, auditory processing, processing speed, and others); the bottom (Stratum I) holds many *narrow abilities* (Thurstone's primary factors sit here). What CHC *fixed* was the false either-or of Spearman versus Thurstone: g and multiple abilities are not rivals but different levels of one nested structure, so the positive manifold (a real g) and profile diversity (real broad and narrow abilities) are both accommodated. It is the model that underlies most modern intelligence tests, which is why they report both a global IQ and index scores. The debate it *leaves* is now a matter of detail (the exact number and boundaries of the broad abilities), not of principle.

4.12 Gardner's multiple intelligences: the outward expansion

Howard **gardner** (1983, *Frames of Mind*) pushed hardest against g, proposing that intelligence is not one or a few abilities but a set of largely *independent* intelligences, each with its own developmental course and neural substrate, and each capable of dissociating (as in savant syndrome or focal brain injury). He named seven, later expanded to eight, with a ninth proposed: linguistic, logical-mathematical, spatial, musical, bodily-kinaesthetic, interpersonal, intrapersonal, and naturalistic (with existential intelligence suggested). What Gardner *fixed*, or tried to, was the

narrowness of the "book-smart" tradition, giving academic status to musical, bodily, and social talents that IQ tests ignore, which is why his theory is so popular in education. What he *left* deeply *debated*, and where the exam expects the critique, is the evidence: his core claim that the intelligences are independent contradicts the single most robust finding in the field, the positive manifold, since these abilities are in fact positively correlated. The "learning styles" industry that grew from his theory is likewise unsupported by research. Gardner is best remembered as the boldest pluralist whose reach exceeded the data.

4.13 Sternberg's triarchic theory: intelligence for real-world success

Robert **sternberg** (1985, *Beyond IQ*) offered a smaller, more defensible pluralism aimed at what predicts success in life, not just in school. His **triarchic theory** names three intelligences. **Analytical** intelligence is the academic, problem-solving ability that traditional IQ tests measure (close to g). **Creative** (experiential) intelligence is the ability to deal with novelty and generate new ideas, the capacity IQ tests neglect. **Practical** (contextual) intelligence is "street smarts," the tacit, unspoken know-how for adapting to, shaping, and selecting real-world environments. What Sternberg *fixed* was the exclusion of creativity and practical adaptation from the concept of intelligence, and he was the first to bring creativity formally inside the tent. What he *left debated* is that practical intelligence has not been shown to be a single unified ability transferring across domains, and traditional IQ (which he cast as merely academic) in fact predicts a wide range of real-world outcomes well, undercutting the sharp separation his theory draws.

4.14 Currently accepted: CHC as the working consensus

The **currently accepted** position in intelligence research is the **chc** (Cattell-Horn-Carroll) model (4.11). It is the mainstream because it is the one framework that honours both halves of the century-old debate: a genuine general factor g at the apex (vindicating Spearman and explaining the positive manifold) sitting above a rich layer of broad and narrow abilities (vindicating Thurstone, Cattell, and Horn and explaining ability profiles). Gardner's and Sternberg's pluralist theories, though influential in education and useful for widening what we value, are held to sit outside the empirical mainstream precisely because they deny or minimise g, which the data will not allow. The practical upshot is that modern tests are built on CHC: they yield a full-scale IQ (the g estimate) alongside index scores that map onto the broad abilities.

> HOLD THIS
>
> **Every intelligence theory lives or dies on the positive manifold.** Because cognitive scores all correlate positively, the pluralist theories that deny g (Gardner, Sternberg) cannot be the consensus, and CHC can, by nesting g over broad over narrow abilities.

4.15 Neural correlate: the P-FIT model and processing speed

The **neural correlate** of general intelligence is captured by the **parieto-frontal integration theory (P-FIT)** (Jung and Haier 2007), the leading neurobiological account and the current consensus on the biology of g. Its claim is that intelligence is not localised to one region but reflects the *efficiency of a distributed network*, chiefly the dorsolateral prefrontal cortex, the inferior and superior parietal lobules, the anterior cingulate, and the white-matter tracts (notably

the arcuate fasciculus) that connect frontal to parietal cortex. On this model, sensory information is elaborated in temporal and occipital cortex, integrated and abstracted in the parietal lobe, evaluated and problem-solved in the prefrontal cortex, with the parieto-frontal loop generating the solution, and the integrity and speed of the connecting white matter set the ceiling on performance. Two robust biological correlates support it: **processing speed** (faster, more efficient neural conduction, indexed behaviourally by reaction time and biologically by white-matter integrity, correlates with higher g) and the *neural efficiency hypothesis* (higher-ability brains recruit *less*, not more, activation for a given task, working more economically). Overall brain volume correlates modestly with IQ (roughly r = 0.3 to 0.4), but network efficiency, not size, is the operative variable (Kaplan and Sadock 2024).

4.16 Worked example: reading the debate in one candidate

Consider a medical student who reasons brilliantly through an unseen clinical problem, has an encyclopaedic command of facts, plays the sitar beautifully, and is socially adept on the ward. Each theory reads her differently, and seeing the same person through each lens fixes the models. **Spearman**: her across-the-board excellence is high g, one general capacity lifting every performance (the positive manifold in a person). **Thurstone**: she is a profile, strong verbal, numerical, and spatial primary abilities. **Cattell and Horn**: her novel problem-solving is fluid intelligence (Gf), her stored medical knowledge is crystallised intelligence (Gc), and if we tested her at seventy the Gc would still be intact while the Gf had slipped. **Gardner**: her sitar is musical intelligence and her ward manner interpersonal intelligence, talents an IQ test would miss, though the critic notes these still correlate with her academic ability. **Sternberg**: her exam ability is analytical, her novel formulations creative, her ward-management practical intelligence. **CHC**: all of it nests, a high g at the apex expressed through strong broad abilities (Gf, Gc, and others). **P-FIT**: the shared substrate is an efficient, fast, well-connected fronto-parietal network. The one candidate, six readings, one nested truth.

COMMON TRAP

Do not present Gardner and Sternberg as the "modern, correct" theories because they feel inclusive and appealing: the exam rewards the opposite, that both sit outside the empirical mainstream because they deny or minimise g, and the currently accepted model is CHC. Equally, do not put IQ testing here: Binet-Simon, the Wechsler scales, deviation IQ, and the diagnostic bands are assessment-day material (cross-ref: Psychometry and assessment). And keep the pairing straight, fluid intelligence *declines* with age while crystallised intelligence is *preserved*, which is the direction that grounds "hold" tests in dementia.

PEARL

The entire intelligence half is one axis: how many intelligences are there, and what does the positive manifold allow? Spearman said one (g), Thurstone said seven, Cattell and Horn said two (Gf and Gc), Gardner said eight or nine, Sternberg said three, and Carroll's CHC said all of them at once by stacking g over broad over narrow abilities. Every theory lives or dies on the positive manifold, the fact that cognitive scores intercorrelate, which is why the pluralist theories that deny g cannot be the consensus and the hierarchical CHC can.

GOOD TO REMEMBER

- **Concept:** mental category grouping particulars; classical (necessary/sufficient features) vs prototype (Rosch 1975, best example).
- **Deductive reasoning:** general to specific, logically certain, truth-preserving. **Inductive:** specific to general, probable, content-expanding.
- **Algorithm:** exhaustive, guaranteed, slow. **Heuristic:** shortcut, fast, not guaranteed, bias-prone.
- **Tversky and Kahneman (1974):** availability (ease of recall), representativeness (resemblance, ignores base rates), anchoring and adjustment (pulled to a starting value).
- **Framing (prospect theory, Kahneman and Tversky 1979):** gain vs loss wording flips choice. **Confirmation bias:** seeking belief-consistent evidence.
- **Dual-process (Stanovich and West 2000; Kahneman 2011):** System 1 fast/automatic/intuitive vs System 2 slow/deliberate/logical.
- **Mental set (Einstellung):** Luchins's water-jars. **Functional fixedness:** Duncker's candle. **Insight:** Gestalt "aha," Kohler's apes.
- **Spearman (1904/1927):** two-factor theory, g (general) + s (specific); positive manifold; invented factor analysis.
- **Thurstone (1938):** seven primary mental abilities (verbal comprehension, word fluency, number, spatial, perceptual speed, memory, reasoning); the plural challenge.
- **Cattell and Horn (1960s):** fluid (Gf, novel reasoning, declines with age) vs crystallised (Gc, acquired knowledge, preserved with age).
- **Carroll / CHC (1993):** three-stratum hierarchy, Stratum III = g, Stratum II = broad abilities, Stratum I = narrow abilities; the synthesis, currently accepted.
- **Gardner (1983):** multiple intelligences, seven then eight (linguistic, logical-mathematical, spatial, musical, bodily-kinaesthetic, interpersonal, intrapersonal, naturalistic); critique: contradicts positive manifold.
- **Sternberg (1985):** triarchic, analytical + creative + practical; brought creativity into intelligence.
- **Currently accepted:** CHC (Cattell-Horn-Carroll), g over broad over narrow.
- **Neural correlate:** P-FIT (Jung and Haier 2007), efficient fronto-parietal network (DLPFC, parietal, anterior cingulate, arcuate fasciculus); processing speed and neural efficiency; brain volume r approx 0.3 to 0.4.

5 · Motivation theories

Motivation is the internal process that *energises*, *directs* and *sustains* goal-directed behaviour: it answers not what an organism can do but why it does it now, in this direction, with this persistence. For the exam the topic is best read as a single argument that runs across the twentieth century, from a purely biological push (behaviour as the discharge of a bodily deficit) to a psychological pull (behaviour as the pursuit of value and meaning), and finally to the

recognition that neither alone suffices and the mind runs several motivational systems in parallel. **Learn the sequence and you can place any scenario stem.**

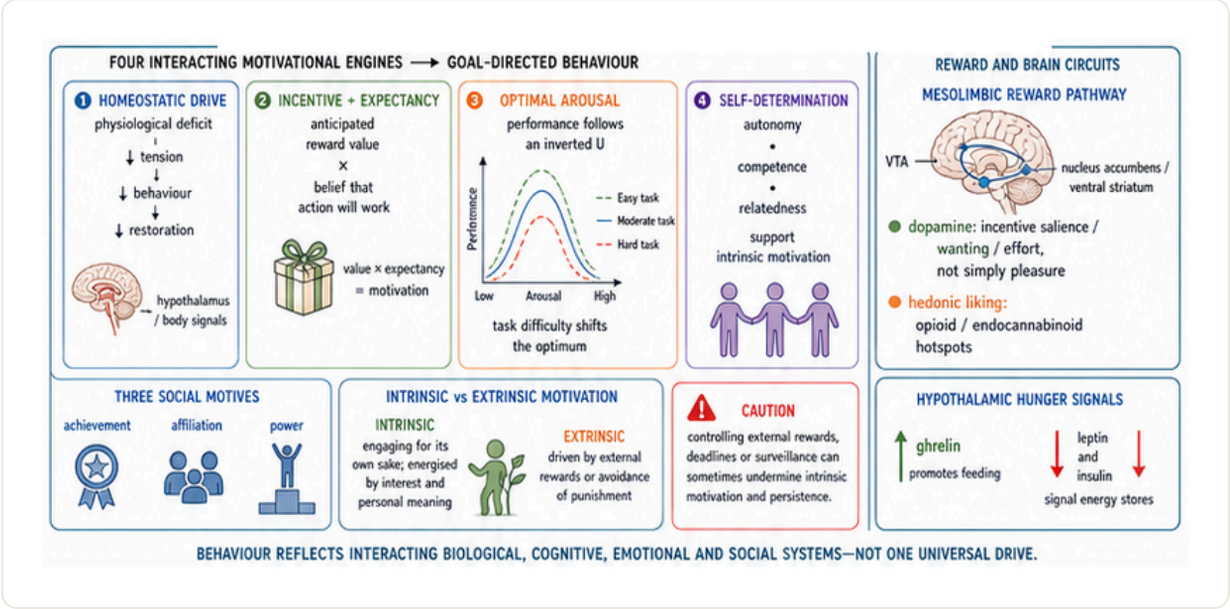


Fig 4.9 Motivation: need, value, control and reward.

The topic follows the standard evolution-of-theories flow: the theories in the order they appeared, each fixing a flaw in the last, from instinct through **drive**-reduction, arousal and **incentive** to the humanistic and cognitive-need theories, then the currently accepted multi-system view, its **neural correlate** in the mesolimbic dopamine reward pathway and the hypothalamic feeding centres, and a worked example. The single organising question is the one drive-reduction could not answer: if all behaviour serves homeostasis, why does a well-fed, safe, warm person still read, explore, climb and strive? Ground text is Kaplan and Sadock (2024), the New Oxford Textbook of Psychiatry, and Tasman (2015) for the developmental placement of Maslow.

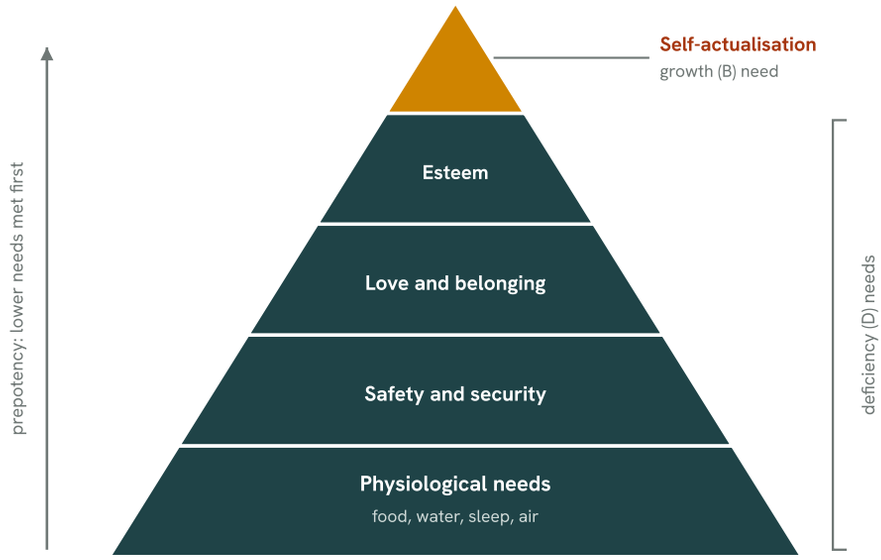


Fig 4.10 Maslow's hierarchy of needs. Needs are arranged by prepotency: the lower, deficiency (D) needs (physiological, safety, belonging, esteem) generally press for satisfaction before the higher growth (B) need of self-actualisation becomes the person's motive. The model captures why homeostatic drive-reduction cannot be the whole story of motivation, since a fed and safe person still strives; later revisions loosen the strict ordering and add cognitive, aesthetic and self-transcendence needs.

5.1 Definition and the three questions motivation must answer

What a motivation theory must deliver. A complete account of motivation must specify three things about a behaviour: its *activation* (what initiates it and how much energy it commands), its *direction* (why this goal and not another), and its *persistence* (why it continues against obstacles). The classic distinction is between the *push* of internal states (a need or drive that shoves behaviour out) and the *pull* of external goals (an incentive that draws behaviour toward it). The whole history below is the field discovering that human behaviour needs both, plus a layer of higher goals that neither push nor pull can capture (Kaplan and Sadock 2024).

Need

A physiological or psychological deficit or requirement (food, safety, belonging).

Drive

The aroused, tension-like internal state that a need produces and that energises behaviour to reduce it; the engine of the "push" theories.

Incentive

An external stimulus or goal whose anticipated value pulls behaviour toward it, independent of any internal deficit.

Motive

A relatively stable, often learned, disposition that gives behaviour a characteristic direction (achievement, affiliation, power).

5.2 Instinct theory: McDougall and the innate-programme account

The first theory. The earliest scientific account, from William James and above all **William McDougall (1908)**, held that behaviour, like animal behaviour, is driven by **instincts**: innate, biologically fixed, purposive dispositions inherited by every member of a species and triggered by specific stimuli. McDougall catalogued human instincts (flight, curiosity, pugnacity, gregariousness, parental care) and argued each carried its own emotion. In the animal literature the same idea became the ethologists' *fixed action pattern* (Lorenz, Tinbergen): a stereotyped, unlearned behavioural sequence released by a sign stimulus, such as the greylag goose rolling any round object back to the nest or the stickleback attacking any red-bellied shape. **What it fixed.** It rooted motivation in biology and made it heritable and species-general, a genuine advance on faculty psychology. **What it left debated.** The list exploded: within two decades psychologists had named thousands of contradictory "instincts" with no unifying principle and no way to falsify any of them, and the theory could not explain the sheer flexibility of human behaviour. Naming an instinct merely re-described the behaviour rather than explaining it, and the school collapsed, though its evolutionary logic survives in modern evolutionary psychology.

5.3 Drive-reduction theory: Hull, homeostasis and the tension model

The homeostatic engine. Clark Hull (1943) replaced the unfalsifiable instinct list with a mechanistic learning theory built on **homeostasis**, the body's tendency to hold its internal milieu at a stable set point (a concept from Cannon and Bernard). A biological need (food deprivation) creates an aversive internal tension, the **drive**; behaviour that reduces the drive is reinforced and learned; once the need is met and homeostasis restored, the drive falls and motivation subsides until the next deficit. Hull distinguished *primary drives*, unlearned and biological (hunger, thirst, sex, sleep, temperature, pain-avoidance), from *secondary drives*, acquired by conditioned association with primary ones (money, status, achievement become motivating because they predict primary reinforcement). His formula made behaviour a multiplicative product of drive and learned habit strength. **What it fixed.** It grounded motivation in measurable physiological need and tied it rigorously to learning and reinforcement, giving the field a testable engine. **What it left debated.** The fatal gap, and the pivot of the whole topic, is that drive-reduction explains only *deficit*-driven behaviour and cannot explain behaviour that *raises* arousal or serves no homeostatic deficit at all: curiosity, exploration, play, sensation-seeking, and the pursuit of achievement. A monkey solves puzzles for no food reward; a sated, safe person reads a novel or rides a rollercoaster, deliberately increasing tension. Homeostasis has no account of this, and its failure spawned the arousal and incentive theories (Kaplan and Sadock 2024).

RULE **The curiosity problem is the pivot of the whole topic.** Drive-reduction explains only deficit-driven behaviour; that a sated, safe person still explores, plays and strives is what forces arousal, incentive and higher-need theories.

5.4 Arousal and optimal-level theory: the Yerkes-Dodson inverted-U

Fixing the curiosity problem. Arousal (optimal-level) theory answered drive-reduction's central failure by proposing that organisms are motivated not to *minimise* arousal but to maintain an *optimal level* of it: too little arousal is aversive (boredom drives us to seek stimulation, which is

why curiosity and exploration exist), and too much is also aversive (we withdraw to calm down). The quantitative core is the **Yerkes-Dodson law (1908)**: performance relates to arousal as an inverted U, rising with arousal to a peak then falling as high arousal degrades performance. The examinable refinement is that the optimum *shifts with task difficulty*: simple, well-learned tasks have a high optimal arousal, whereas complex or novel tasks have a low optimum, so anxiety wrecks a hard exam but barely dents a routine drill. **What it fixed.** It explained the exploratory and stimulation-seeking behaviours that homeostasis could not, and it linked motivation directly to emotion and performance. **What it left debated.** It described the level of arousal sought but said little about the *direction* of behaviour or why a specific goal is chosen, which the pull theories addressed next.

5.5 Incentive and expectancy theory: the pull of anticipated reward

From push to pull. Incentive theory shifted the locus of motivation from an internal deficit to the external goal itself: behaviour is drawn by the anticipated *value* of a reward (or the threat of a punishment), so that a stimulus can motivate even with no bodily need, which is why we eat an appealing dessert when already full. This is the conceptual home of *extrinsic motivation*.

Expectancy theories then made the pull cognitive: what motivates is not the reward alone but the product of how much the person *values* the outcome and how strongly they *expect* their effort to attain it. Tolman's early work on purposive behaviour and cognitive maps, Vroom's *expectancy-value* model in organisational psychology, and Atkinson's expectancy-value theory of achievement all share this form: motivation equals value multiplied by expectancy, so a prize you cannot realistically win, or a trivial prize you easily could, both fail to motivate. **What it fixed.** It accounted for goal-directedness, choice between goals, and the power of external rewards, and it introduced the person's beliefs and expectations as motivational variables. **What it left debated.** It still treated the person as reactive to external payoffs and said little about the higher, self-generated needs that dominate a secure human life, which the humanistic theory placed at the summit.

5.6 Maslow's hierarchy of needs: deficiency versus growth motivation

The humanistic summit. Abraham Maslow (1943, 1970) interpreted the whole person in motivational terms and arranged human needs in an ascending **hierarchy of needs**, usually drawn as a pyramid, in which lower needs must be reasonably satisfied before higher ones become the salient motivators. The five classic levels, bottom to top, are *physiological* (food, water, sleep, sex), *safety* (security, protection, order), *love and belonging* (affection, intimacy, group membership), *esteem* (self-respect and the respect of others, competence, recognition), and *self-actualisation* (the realisation of one's unique potential) at the apex. The master distinction is between the lower four as **deficiency needs** (D-needs), which are driven by lack and quieten once met, and self-actualisation as a **growth need** (B-need, being-need), which is never sated and grows with fulfilment. Maslow later placed the fleeting, transcendent *peak experience* at the top and argued psychology had been too fixated on pathology, calling for a focus on positive mental health, a direct ancestor of positive psychology. **What it fixed.** It captured the higher, self-generated strivings that push and pull theories miss, and it explained the ordering of human

concerns (the starving man risks danger and ostracism for food, but the well-fed man is dominated by esteem and meaning). Its exam-relevant caveats are that the strict order is not rigidly followed (Maslow himself noted creators who skip lower levels straight to self-actualisation, and in late life the hierarchy can invert per Tasman 2015), and the theory resists tidy empirical test. **What it left debated.** It is a taxonomy of *what* we want, not a mechanism of *how* a need moves behaviour, and its needs are broad classes rather than testable processes, gaps the next two theories addressed.

5.7 Murray's needs and McClelland: achievement, affiliation and power

Making needs measurable. Henry Murray (1938) proposed a long list of *psychogenic needs* and the method to measure them, the *Thematic Apperception Test* (TAT), in which the stories a person tells to ambiguous pictures reveal their dominant motives. **David McClelland (1961)** distilled Murray's list into three learned social motives that account for most individual differences in striving, assessed projectively and each with a characteristic behavioural signature.

Need for achievement (nAch)

The drive to meet standards of excellence and master challenges; high-nAch people prefer tasks of moderate, calculated difficulty (where effort, not luck, decides the outcome) and seek concrete performance feedback.

Need for affiliation (nAff)

The drive for warm, close interpersonal relationships and social acceptance; high-nAff people prioritise harmony and belonging over competition.

Need for power (nPow)

The drive to influence, control or have impact on others; splits into personalised power (dominance for self) and socialised power (influence for collective ends), the latter linked to effective leadership.

What it fixed. It turned Maslow's abstract higher needs into specific, measurable, individually varying motives and showed that these motives are learned and predict real-world behaviour (entrepreneurship, leadership). **What it left debated.** It described the *content* of human motives but not the underlying process that makes any activity feel self-driven versus coerced, the question self-determination theory finally formalised.

5.8 Self-determination theory: Deci and Ryan, intrinsic versus extrinsic

The process of autonomous motivation. **Self-determination** theory (SDT), developed by Edward Deci and Richard Ryan (1985, 2000), is the dominant contemporary framework and the most exam-relevant of the modern theories. Its central claim is that the *quality* of motivation matters more than its quantity, and quality depends on how self-endorsed the behaviour is. SDT distinguishes *intrinsic motivation* (acting for the inherent interest, enjoyment and satisfaction of the activity itself, the "loves the activity for its own sake" pole) from *extrinsic motivation* (acting for a separable outcome such as a reward, grade, or the avoidance of punishment). Crucially, extrinsic motivation lies on a continuum of *internalisation*, from purely external regulation, through introjected and identified regulation, to fully integrated regulation that feels autonomous even though the goal is instrumental. SDT roots all of this in three innate, universal *basic psychological needs*: **autonomy** (a sense of volition and self-authorship), **competence** (feeling

effective and masterful), and **relatedness** (feeling connected to and cared for by others). Contexts that satisfy the three needs foster intrinsic motivation, well-being, persistence and creativity; contexts that thwart them breed control, ill-being and, in the extreme, forms of psychopathology. The signature empirical finding is the *overjustification effect*: paying people to do something they already enjoy can *undermine* their intrinsic motivation, because an external reward shifts the perceived locus of causality from inside to outside. **What it fixed.** It supplied the missing mechanism, why the same behaviour can be vitalising or draining depending on need satisfaction, and it reconciled the earlier incentive theories (extrinsic pull) with the humanistic emphasis on growth (autonomy and self-actualisation), unifying the field's push, pull and higher-need strands.

5.9 Currently accepted: a multi-system view of motivation

The **currently accepted** position is not a single winning theory but an explicitly *multi-system* account, because the century of debate showed each theory captures a genuine and partly separable component. Contemporary affective neuroscience holds that motivation is generated by several interacting systems: *homeostatic drives* that defend biological set points (the truth in Hull), a *reward and incentive-salience* system that assigns motivational pull to cues and goals (the truth in incentive theory, now with a precise neural substrate), and *higher cognitive goal systems* in the prefrontal cortex that pursue self-generated, value-laden aims and can override the lower systems (the truth in Maslow, McClelland and SDT). The modern refinement, from Berridge's work, is the dissociation of *wanting* (the dopaminergic motivational pull toward a reward, incentive salience) from *liking* (the opioid-mediated hedonic pleasure of consuming it), which explains why addicts intensely want a drug they no longer like. Motivation, on this view, is the moment-to-moment arbitration between competing systems, which is why a dieter genuinely wants both the cake (incentive plus homeostatic hunger) and the goal weight (a higher cognitive value), and either can win.

5.10 Neural correlate: mesolimbic dopamine and the hypothalamic centres

The neural correlate of motivation maps onto two levels that mirror the push-versus-pull divide of the theories. The *homeostatic drives* are governed by the **hypothalamus**, and the feeding example is the exam classic: the **lateral hypothalamus** is the "hunger" or feeding-on centre, so its stimulation elicits eating and its lesion produces *aphagia* (the lateral hypothalamic syndrome, animal stops eating and starves), whereas the *ventromedial hypothalamus* is the "satiety" or feeding-off centre, so its lesion produces *hyperphagia* and obesity (the ventromedial hypothalamic syndrome). This dual-centre feeding model is cross-referenced to the hypothalamus and drive states covered on the biological-bases days (cross-ref: the Functional Neuroanatomy & Neurophysiology notes, Neuroanatomy of the hypothalamus; the Neurochemistry, Neuroendocrinology, Neuroimaging & Basic Psychopharmacology notes, Homeostasis and drive states). The *incentive and reward* system, the neural home of "wanting", is the **mesolimbic dopamine pathway**, projecting from the *ventral tegmental area* to the *nucleus accumbens* (ventral striatum), with input to and from the prefrontal cortex and amygdala. Schultz (1997) showed these midbrain dopamine neurons fire in proportion to *reward prediction error* (better-than-

expected outcomes), the teaching signal that assigns **incentive salience** to cues, and Berridge showed this dopaminergic signal codes wanting rather than the pleasure (liking) of reward. This is the same aberrant-salience system implicated in psychosis and the common final pathway hijacked by every drug of addiction, tying motivation directly to psychopathology (Kaplan and Sadock 2024).

HOLD THIS

Lateral hypothalamus = hunger-on (lesion causes aphagia); ventromedial = satiety (lesion causes hyperphagia and obesity). On the reward side, mesolimbic dopamine codes *wanting* (incentive salience), not *liking* (opioid pleasure).

5.11 Worked example: the medical student before the exit exam

A single scenario shows every theory operating at once, and shows how a scenario stem is decoded. A resident revising for the exit exam skips lunch (a **drive-reduction** and homeostatic hunger signal builds, driven by the lateral hypothalamus, and eventually pulls attention off the books). The looming pass or fail is an **incentive** whose motivational force is the product of how much the resident values passing and how much they expect their effort to secure it (**expectancy-value**): a certain pass or a hopeless one both demotivate, moderate odds motivate most. Exam-day anxiety illustrates the **Yerkes-Dodson inverted-U**: a little arousal sharpens recall, but panic past the optimum (low, because the task is complex) collapses performance. In **Maslow's** terms the resident cannot focus on the esteem-level goal of qualifying if safety or belonging needs are unmet, and the drive to master the material is an **achievement** motive (nAch) in McClelland's sense, best sustained on challenges of moderate difficulty. Finally, whether the studying feels vitalising or grinding turns on **self-determination**: a resident who studies because medicine genuinely fascinates them (intrinsic, autonomous, competence-satisfying) persists and performs better than one grinding only to avoid the shame of failure (controlled extrinsic regulation), the practical payoff of the whole topic.

MNEMONIC

"I Drove A Incentive to Maslow's Mountain, Met McClelland, and Self-Determined."

The theories in historical order: **I**nstinct (McDougall), **D**rive-reduction (Hull), **A**rousal (Yerkes-Dodson), **Incentive** and expectancy, **Maslow's** hierarchy, **McClelland** (Murray's needs), and **Self-Determination** (Deci and Ryan). Read the list as push, then pull, then higher needs, then the modern process account.

COMMON TRAP

Do not confuse **drive-reduction** with **arousal** theory: drive-reduction is about *lowering* tension to restore homeostasis after a deficit, so it cannot explain curiosity; arousal theory is about seeking an *optimal* level, which is precisely why it can. Second trap: intrinsic motivation is not always stronger than extrinsic. The *overjustification effect* shows adding a reward to an already-enjoyed activity can *reduce* intrinsic motivation. Third: on the neural correlate, dopamine codes *wanting* (incentive salience), not *liking* (hedonic pleasure), a Berridge dissociation examiners favour.

GOOD TO REMEMBER

- **Instinct theory (McDougall 1908):** behaviour driven by innate, fixed, purposive instincts; animal parallel is the fixed action pattern.
- **Drive-reduction (Hull 1943):** a biological need creates a drive; behaviour reduces it to restore homeostasis; primary vs secondary drives. Cannot explain curiosity.
- **Arousal / optimal-level (Yerkes-Dodson 1908):** organisms seek an optimal arousal; inverted-U of arousal versus performance; optimum is lower for complex tasks.
- **Incentive and expectancy (Tolman; Vroom; Atkinson):** behaviour pulled by anticipated reward value; motivation equals value multiplied by expectancy.
- **Maslow's hierarchy of needs (1943, 1970):** physiological, safety, love/belonging, esteem, self-actualisation; deficiency needs vs the growth need at the apex; peak experience.
- **Murray (1938):** psychogenic needs, measured by the Thematic Apperception Test (TAT).
- **McClelland (1961):** three learned motives, need for achievement (nAch, prefers moderate-difficulty tasks), affiliation (nAff), and power (nPow).
- **Self-determination theory (Deci and Ryan 1985, 2000):** intrinsic vs extrinsic motivation on an internalisation continuum; three basic needs, autonomy, competence, relatedness; overjustification effect.
- **Currently accepted:** a multi-system view, homeostatic drives plus incentive salience plus higher cognitive goals; wanting (dopamine) dissociated from liking (opioid).
- **Neural correlate:** mesolimbic dopamine (ventral tegmental area to nucleus accumbens) for incentive salience and reward prediction error; lateral hypothalamus = hunger/feeding-on centre (lesion causes aphagia); ventromedial hypothalamus = satiety centre (lesion causes hyperphagia and obesity).

6 · Emotion theories and neural circuits

An **emotion** is a brief, intense, object-directed affective response with three coupled components: a felt subjective experience, a physiological (autonomic and endocrine) change, and an expressive-behavioural output, all triggered by an appraised event. It is distinguished from **mood**, which is a more prolonged, less intense, and often objectless affective background. The whole topic is best read as one long argument about *sequence*: given a bear on the path, which comes first, the pounding heart or the fear? **Body-first or cognition-first.** Every named theory is a different answer to that single question, and each one fixed a specific hole in the theory before it.

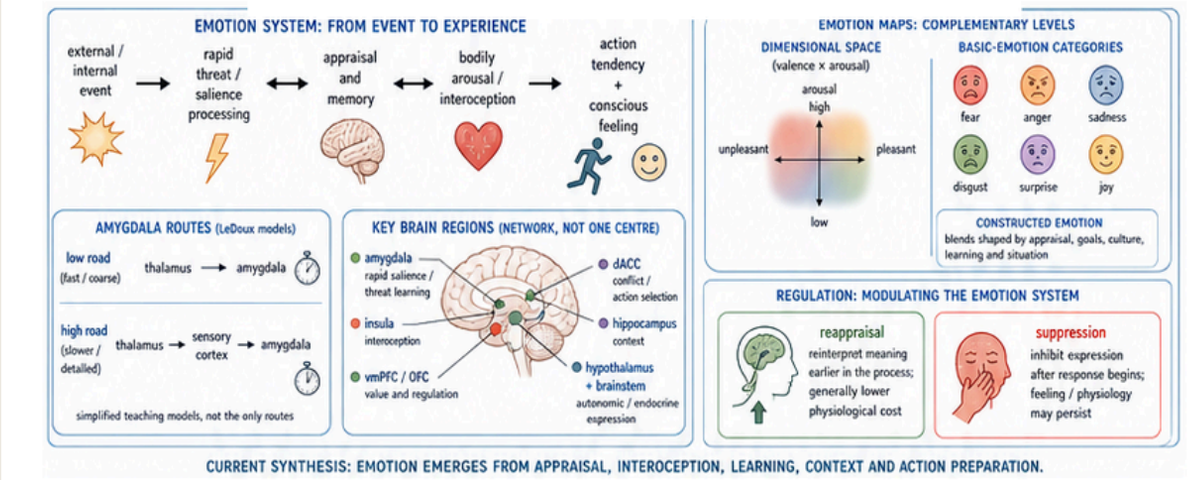


Fig 4.11 Emotion: appraisal, body, action and construction.

For the exam the payload is fourfold: the ordered theories with their authors and the one claim each is remembered for; the body-first versus cognition-first axis that organises them; the currently accepted synthesis (appraisal plus interoception plus construction); and the neural correlate that grounds it all, the limbic system and the Papez circuit, the amygdala with LeDoux's two roads, and the insula for interoception. The anatomy has its deep home in the Functional Neuroanatomy & Neurophysiology notes; here it is the substrate for the psychology. Structure the answer as an evolution, not a list.

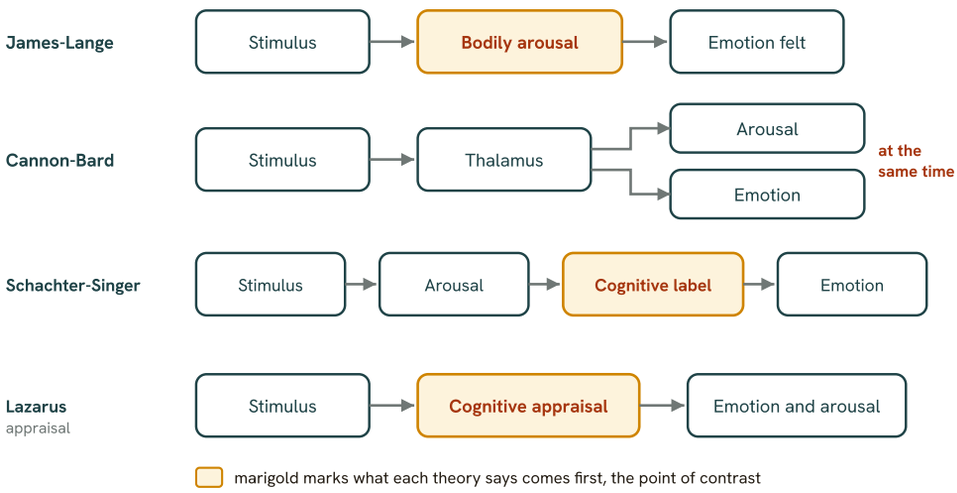


Fig 4.12 The four classic theories of emotion differ over the ORDER of arousal, cognition and feeling. James-Lange puts the bodily change first and reads emotion as the perception of it; Cannon-Bard makes arousal and feeling simultaneous outputs of the thalamus; Schachter and Singer's two-factor theory needs undifferentiated arousal plus a cognitive label; Lazarus makes an appraisal the trigger. The enduring debate is body-first versus cognition-first, which modern appraisal, interoception and constructed-emotion accounts largely reconcile.

6.1 Darwin: emotions as evolved, universal, adaptive expressions

The starting point. Charles Darwin (1872), in *The Expression of the Emotions in Man and Animals*, made the first scientific claim about emotion: that emotional expressions are innate,

evolved, and serve adaptive communicative and preparatory functions, and that the same core expressions (the bared teeth of anger, the recoil of fear) appear across human cultures and are continuous with those of other animals. **What it fixed.** It moved emotion out of philosophy and theology and into biology, framing it as a product of natural selection rather than a moral or spiritual state. **What it left debated.** Darwin described the *output* (the expression) and its evolutionary purpose, but said nothing about the internal *mechanism*: what actually generates the felt emotion inside the organism, and in what order its parts arise. That mechanistic question is what the next century fought over (Kaplan and Sadock 2024).

6.2 James-Lange: the body changes first, emotion is its perception

The bodily-feedback theory. William James (1884) and, independently, the Danish physiologist Carl Lange proposed the counter-intuitive **james-lange** theory: an emotion is not the cause of bodily change but the *perception* of it. James put it in his famous inversion of common sense: we do not tremble because we are afraid, we are afraid because we tremble. In his own words, "we meet a bear, are frightened and run . . . the more rational statement is we feel afraid because we tremble" (James 1884). The sequence is therefore: stimulus, then bodily and autonomic response (racing heart, sweating, fleeing), then perception of that response, which *is* the emotion. A strong prediction follows: each distinct emotion must have a distinct bodily signature, since the feeling is nothing but the read-out of the body. **What it fixed.** It gave Darwin's output an internal mechanism and made emotion an embodied, testable process rather than a disembodied mental event. **What it left debated.** It required different emotions to map onto reliably different visceral patterns, and it made the body the sole source of feeling, both of which the next theory attacked head-on (Kaplan and Sadock 2024).

6.3 Cannon-Bard: body and feeling arise together, driven by the thalamus

The central (thalamic) theory. Walter Cannon (1927), later developed by his student Philip Bard, mounted three empirical objections to james-lange and replaced it with the **cannon-bard** theory. His evidence: surgically isolating the viscera from the brain did not abolish emotional behaviour in animals; artificially inducing visceral changes (for example an adrenaline injection) did not by itself produce a genuine emotion; and autonomic responses are too slow and too uniform to account for the speed and variety of felt emotion. Cannon concluded that an emotional stimulus produces *two parallel outputs*: the thalamus (in modern terms, the thalamus and hypothalamus) simultaneously and independently sends one signal up to the cortex, producing the conscious feeling, and one signal down to the body, producing the autonomic arousal. The sequence is therefore: stimulus, then feeling and bodily change *at the same time*, neither causing the other. **What it fixed.** It broke the requirement for unique bodily signatures and located emotion in the brain rather than the periphery, giving it a neuroanatomical seat. **What it left debated.** By making arousal and feeling wholly parallel and independent, it left no role for how the arousal is *interpreted*, the very gap the next theory exploited (Kaplan and Sadock 2024).

6.4 Schachter-Singer: two factors, arousal plus a cognitive label (the adrenaline study)

The two-factor (arousal-cognition) theory. Stanley Schachter and Jerome Singer (1962) proposed that an emotion requires *two* ingredients: undifferentiated physiological arousal, plus a cognitive **label** that interprets that arousal in light of the situation. The same racing heart is felt as fear in a threatening context and as euphoria in a joyful one; the arousal supplies the intensity, the cognition supplies the identity. Their classic **schachter** experiment tested this: participants were injected with adrenaline (epinephrine) or saline and then placed with a confederate who acted either euphoric or angry. Crucially, some were correctly informed of the drug's arousing effects, some were told nothing, and some were misinformed. Those who had an *unexplained* arousal (told nothing or misinformed) took on the emotion modelled by the confederate, describing themselves as euphoric or angry to match; those who could correctly *attribute* their pounding heart to the injection did not. The arousal was constant; only the available cognitive explanation varied the emotion. This is the origin of *misattribution of arousal*. **What it fixed.** It reconciled james-lange and cannon-bard: the body supplies the arousal (james-lange) but is too undifferentiated to specify the emotion alone (cannon-bard's critique), so cognition does the specifying. **What it left debated.** It treated the cognitive label as a post-hoc read of an already-present arousal, and never fully specified *when* and *how* the appraisal happens, which the next debate addressed (Kaplan and Sadock 2024).

TRAP Schachter-Singer is **not** cognition-first. The undifferentiated arousal comes first and is then labelled by context, so it is body-first with cognition supplying only the identity; the same racing heart is fear beside a threat and euphoria beside joy.

6.5 Lazarus versus Zajonc: does appraisal come before feeling, or can affect be primary?

The cognition-first theory and its challenger. Richard Lazarus (1966, 1991) pushed cognition all the way to the front with the cognitive **appraisal** (cognitive-mediational) theory: an appraisal, an evaluation of the event's meaning for the self, is *necessary and prior*, and it determines both the emotion and the bodily response that follow. The **lazarus** sequence is: stimulus, then appraisal, then emotion (and its physiology) together. He distinguished *primary* appraisal (is this relevant and is it a threat, harm, or benefit to me?) from *secondary* appraisal (can I cope with it?), and it is the appraisal, not the event, that explains why the same lecture invitation delights one student and frightens another. Magda Arnold (1960) had first introduced "appraisal"; Lazarus built the full model. **The counter.** Robert Zajonc (1980, 1984) argued for *affective primacy*: some affect arises fast, automatically, and *independently of, or prior to,* full cognitive appraisal ("preferences need no inferences"), as when we flinch at a sudden loud sound or feel an instant, unexplained liking. This Lazarus-Zajonc debate is the classic exam contrast. **What it fixed and left open.** Lazarus explained individual and cultural differences in emotion to the same event; Zajonc showed appraisal cannot be the whole story because affect can outrun it. The tension between them, fast automatic affect versus slower deliberate appraisal, was resolved neurally rather than psychologically, by LeDoux's two roads (6.8), and both are folded into the modern synthesis (Kaplan and Sadock 2024).

6.6 Basic-emotion versus dimensional and constructed-emotion accounts

The modern structural debate: how many emotions, and are they given or built? Two rival modern camps carry Darwin's legacy forward.

Basic (discrete) emotion: Ekman

Paul Ekman (1970s onward), extending Darwin, holds that a small set of *basic emotions* are innate, biologically hard-wired, and universally recognised from the face across cultures, each with its own program and expression. The classic six are anger, disgust, fear, happiness, sadness, and surprise (later expanded to include contempt and others). Emotions are natural kinds the brain comes equipped with.

Dimensional (circumplex): Russell

James Russell (1980) argued emotions are not discrete categories but points in a continuous two-dimensional space, the *circumplex model*, whose axes are *valence* (pleasant to unpleasant) and *arousal* (activated to deactivated). Fear and excitement share high arousal but differ in valence; contentment and depression share low arousal. Emotion words label regions of this space rather than separate machines.

Constructed emotion: Barrett

Lisa Feldman Barrett (2017) advanced the *theory of constructed emotion*: emotions are not triggered but *constructed* in the moment by the brain, which uses concepts and past experience to make meaning of raw interoceptive and sensory signals (core affect) via predictive processing. The identical churning stomach becomes "hunger" in a bakery and "dread" in a waiting room, depending on the brain's prediction. This is the current cutting edge and directly extends the two-factor idea: arousal is given, the categorising concept builds the emotion.

Ekman says emotions are discrete and given by evolution; Russell and Barrett say they are constructed from underlying dimensions of affect.

6.7 The currently accepted account: appraisal plus interoception plus construction

Not one theory but their integration. The *currently accepted* view is that no single classical theory is right and each captured a real piece. An emotional episode begins when an event is *appraised* for its significance to the self (Lazarus), often through a fast automatic route that can precede conscious appraisal (Zajonc); this appraisal drives an autonomic and endocrine *bodily* response whose sensing, *interoception*, is a genuine constituent of the feeling (the modern vindication of james-lange, via Damasio's *somatic marker hypothesis*, in which bodily signals bias decision-making); and the brain then *constructs* the specific, named emotion by categorising this core affect using learned concepts and context (Schachter-Singer's label, formalised by Barrett's constructed emotion within a predictive-processing framework). In short: appraisal sets it off, interoception gives it its felt body, and conceptual construction gives it its identity. This synthesis dissolves the body-first versus cognition-first war by making both continuously and reciprocally involved (Kaplan and Sadock 2024).

6.8 Neural correlate: the limbic system and the Papez circuit

The historical anatomical model. The neural correlate of emotion begins with the **limbic** system. James **papez** (1937, formalised 1939), building on Cannon's work, proposed that emotion is generated by a specific reverberating circuit, the *Papez circuit*: hippocampus, then via the fornix to the mammillary bodies of the hypothalamus, then via the mammillothalamic tract

to the anterior thalamic nuclei, then to the cingulate gyrus (the seat of conscious emotional experience in his scheme), and back to the hippocampus, closing the loop. Paul MacLean (1949, 1952) extended this into the modern *limbic system* as the "visceral brain," adding the **amygdala**, the septal area, and the orbitofrontal and prefrontal cortex. The Papez circuit's clinical footprint is memory as much as emotion: lesions anywhere along it (classically the mammillary bodies and dorsomedial thalamus in Korsakoff syndrome) produce amnesia, tying this topic to the Functional Neuroanatomy & Neurophysiology notes anatomy (Kaplan and Sadock 2024).

6.9 Neural correlate: the amygdala (LeDoux's low and high roads) and the insula

The fear hub and its two routes. The single most important structure for emotion, especially fear, is the **amygdala**. Joseph LeDoux (1996) mapped how a threat reaches it by two parallel pathways from the sensory thalamus. The *low road* is a fast, direct, "quick and dirty" thalamo-amygdala projection that triggers a defensive response on a crude sketch of the stimulus before the cortex has finished processing it, the neural basis of Zajonc's affective primacy and of jumping at a stick that might be a snake. The *high road* is a slower thalamo-cortico-amygdala route that delivers a detailed cortical analysis which either confirms the threat and sustains the response or cancels it as a false alarm, the neural basis of Lazarus's appraisal. This two-road architecture resolves the appraisal-versus-primacy debate anatomically: both routes are real and run in parallel. The amygdala also tags experiences for emotional memory (why emotionally charged events are remembered vividly) and is hyperresponsive in PTSD and anxiety disorders. Alongside it, the *insula* (insular cortex) is the cortical hub for *interoception*, mapping the internal bodily state, and is the neural home of the james-lange and Barrett strand: it is central to disgust and to the felt bodily quality of emotion. The *orbitofrontal and ventromedial prefrontal cortex* integrate emotion with value and regulate the amygdala (Damasio's somatic-marker substrate); the *ventral striatum and mesolimbic dopamine* system carries reward and positive affect (Kaplan and Sadock 2024, Companion to Psychiatric Studies 2010).

HOLD THIS

LeDoux's two roads settle the appraisal-versus-primacy debate anatomically. The fast low road (thalamo-amygdala) fires before the cortex finishes (Zajonc's primacy); the slow high road (thalamo-cortico-amygdala) delivers the appraisal (Lazarus). Both run in parallel.

CLINICAL ANCHOR

The amygdala model is directly clinical. In PTSD the low road becomes sensitised: trauma reminders drive an exaggerated amygdala response with deficient prefrontal (high-road) regulation, so the fear fires before appraisal can veto it. The Kluver-Bucy syndrome (bilateral amygdala and anterior temporal damage) shows the mirror image: loss of fear and rage, placidity, hyperorality and hypersexuality, proving the amygdala is necessary to attach threat-value to stimuli. Panic disorder and specific phobia are understood as amygdala-centred fear circuits, and exposure therapy works by strengthening prefrontal extinction of that response.

COMMON TRAP

Do not confuse the two "simultaneous" theories with the sequential ones. James-lange is strictly body-first (arousal, then feeling); cannon-bard is simultaneous-and-independent (arousal and feeling together, neither causing the other); schachter-singer is arousal-then-label (body-first but needs cognition to name it); lazarus appraisal is cognition-first (appraisal, then feeling and body together). A frequent error is to call schachter-singer "cognition-first": it is not, the arousal comes first and is then interpreted. Also, Papez proposed the *circuit*; MacLean coined and extended the *limbic system* and added the amygdala.

6.10 Worked example: the snake on the path

One stimulus, read by every theory. You are walking and a coiled shape lunges at your foot. *Darwin:* your face and body throw an evolved, universal fear display (widened eyes, recoil) that readies you and warns others. *James-lange:* your body jerks back and your heart pounds first, and it is your perception of that pounding-and-fleeing body that *is* the fear. *Cannon-bard:* the thalamus fires two signals at once, so you feel fear and your heart races simultaneously and independently. *Schachter-singer:* you feel a surge of undifferentiated arousal and, reading the context (a snake), you label it "fear"; the same surge on a rollercoaster you would label "thrill." *Lazarus appraisal:* a lightning appraisal ("that thing can harm me") comes first and generates both the fear and the racing heart; had you appraised it as a garden hose, no fear would arise. *Zajonc and LeDoux, resolved neurally:* the low road fires the amygdala and yanks your foot back before you consciously know what it is (affective primacy); a heartbeat later the high road delivers the cortex's verdict, "only a rope," and the prefrontal cortex quenches the amygdala and the fear subsides. *Currently accepted synthesis:* the fast appraisal via the amygdala, the interoceptive body-signal sensed by the insula, and the concept "snake-fear" that your brain constructs from context together make the single experience you would call terror. **Same snake, one integrated fear, assembled from appraisal, body, and construction.**

GOOD TO REMEMBER

- **Darwin (1872):** emotional expressions are innate, evolved, adaptive and universal across cultures and species; describes the output, not the mechanism.
- **James-Lange (James 1884, Lange):** body-first; emotion is the *perception* of bodily/autonomic change ("we are afraid because we tremble"); predicts a unique bodily pattern per emotion.
- **Cannon-Bard (Cannon 1927, Bard):** thalamic theory; arousal and feeling occur *simultaneously and independently*; critiqued james-lange (visceral isolation preserves emotion, arousal too slow and uniform).
- **Schachter-Singer (1962):** two-factor = physiological arousal + cognitive label; the adrenaline (epinephrine) and confederate study; origin of *misattribution of arousal*.
- **Lazarus (1966, 1991):** cognitive appraisal (cognitive-mediational) theory; appraisal is prior and necessary; primary appraisal (threat/harm/benefit) and secondary appraisal (coping). Arnold (1960) first named "appraisal."
- **Zajonc (1980):** affective primacy; some affect precedes/bypasses cognition ("preferences need no inferences"); the classic counter to Lazarus.
- **Ekman:** basic (discrete) emotions, innate and universal from the face; classic six = anger, disgust, fear, happiness, sadness, surprise.
- **Russell (1980):** circumplex / dimensional model; two axes = valence (pleasant-unpleasant) and arousal (activated-deactivated).
- **Barrett (2017):** theory of constructed emotion; emotions are built from core affect plus concepts via predictive processing; current cutting edge.
- **Currently accepted:** appraisal (Lazarus) + interoception (james-lange revived; Damasio somatic markers) + construction (Schachter-Singer label, Barrett); dissolves body-first vs cognition-first.
- **Papez circuit (Papez 1937/1939):** hippocampus, fornix, mammillary bodies (hypothalamus), mammillothalamic tract, anterior thalamic nuclei, cingulate gyrus, back to hippocampus. Lesions cause amnesia (Korsakoff). Cross-ref the Functional Neuroanatomy & Neurophysiology notes.
- **MacLean (1949):** named the limbic system ("visceral brain"); extended Papez to add the amygdala, septal area and prefrontal cortex.
- **Amygdala (LeDoux 1996):** fear hub; *low road* = fast thalamo-amygdala (primacy); *high road* = slow thalamo-cortico-amygdala (appraisal); tags emotional memory; hyperactive in PTSD; Kluver-Bucy = its loss.
- **Insula:** interoceptive cortex, felt bodily quality of emotion and disgust; the modern seat of the james-lange/Barrett strand.

7 · Consciousness and altered states

Consciousness is the most slippery construct in the whole of psychology and the one the exam most reliably rewards for clean structure. The single organising move, without which nothing else makes sense, is to split the word in two. **Level versus content.** **Level of consciousness** is *arousal*: the global on-off dimension that runs from alert wakefulness down through drowsiness, clouding, stupor, and coma, and is a property of brainstem and thalamic machinery. **Content of consciousness** is *awareness*: the actual perceptions, thoughts, and feelings present to the mind at a given moment, a property of the cortex. The two are dissociable, which is exactly why the distinction earns its keep: the vegetative-state patient has arousal (eyes open, sleep-wake cycles) with no demonstrable content, while REM-sleep dreaming and vivid hallucination are rich content at a reduced or altered level (Parvizi and Damasio 2001).

For the exam the payload is fourfold and this fragment follows the standard evolution-of-theories spine. First the definitions and the philosophical problem that frames the field. Then the theories *in the order they appeared*, each fixing what its predecessor left unexplained: James's stream, the psychodynamic topography, and the two modern cognitive accounts, Global Workspace and Integrated Information. Then the *currently accepted* position and its **neural correlate**, the ascending reticular activating system, thalamocortical loops, and the default-mode network. Finally the map of **altered states**, from normal sleep and dreaming (sleep architecture proper is the Functional Neuroanatomy & Neurophysiology notes, cross-refer there) through hypnosis, meditation, and drug states to the clinical altered states, delirium, dissociation, and the disorders of consciousness (coma, vegetative and minimally conscious states).

7.1 Definitions: the two axes, and the hard problem

Consciousness has a quantity and a quality. The clinically indispensable framing (Parvizi and Damasio 2001) is that consciousness varies along two orthogonal axes. *Level* (arousal, wakefulness) is the quantitative dimension graded from full alertness to coma; it is generated subcortically and is what a Glasgow Coma Scale measures. *Content* (awareness) is the qualitative dimension, the specific things one is conscious *of*; it is generated by the cortex. Normally the two rise and fall together, but disorders of consciousness are precisely the states where they come apart.

Level (arousal)

The global degree of wakefulness. A single continuum: alert, drowsy, clouded, stuporous, comatose. Subcortical (reticular activating system, thalamus).

Content (awareness)

The set of things present to experience at a moment, the "buzzing, booming stream" (James's phrase, quoted approvingly by Kaplan and Sadock 2024). Cortical, and highly differentiated.

Self-awareness (reflexive)

Awareness that *it is I* who am experiencing: the higher-order sense of a subject. Selectively disrupted in depersonalisation and dissociation.

The "hard problem"

Chalmers's (1995) term for the question that survives every mechanistic advance: why is there *something it is like* to be conscious at all, why does information processing generate subjective experience (qualia)? He contrasted it with the "easy problems" (explaining discrimination, integration, report), which are hard in practice but conceptually tractable. The distinction marks the boundary of what any neuroscience can currently claim to have solved.

RULE **Split the word first: level versus content.** Level is arousal (subcortical, coma-to-alert); content is awareness (cortical). They are dissociable, which is the whole point of the distinction.

7.2 William James: the stream of consciousness

The first psychological description. William James, in *The Principles of Psychology* (1890), gave consciousness its founding characterisation as a **stream of consciousness**, a continuous, ever-changing, personal flow rather than a chain of discrete "ideas." He fixed four properties that still

anchor phenomenological accounts: consciousness is *personal* (always belonging to a self), *continuous* (no gaps felt from within, even across sleep), *constantly changing* (never twice the same state), and *selective* (attention foregrounds some contents and lets the rest fall away). **What it fixed.** It replaced the atomistic "ideas" of the British associationists with a lived, flowing process, and put selective attention at the centre. **What it left debated.** It was pure introspective description with no mechanism and no account of the unconscious, and introspection itself was soon attacked as unreliable, the gap the next tradition filled from the clinic (Kaplan and Sadock 2024).

7.3 The psychodynamic topography: conscious, preconscious, unconscious

Most of the mind is out of view. Freud's topographic model (1900, 1915) reframed consciousness as only the surface of the mind, and did so by dividing mental content by its *accessibility to awareness*. The **conscious** system holds what is in awareness now. The **preconscious** holds material not currently in mind but readily retrievable by directing attention (your mother's name a second before you are asked). The **unconscious** holds material actively barred from awareness by repression, dynamic rather than merely dormant, and knowable only through its derivatives: dreams (the "royal road"), slips of the tongue (parapraxes), symptoms, and free association. **What it fixed.** It gave introspection's blind spots a systematic cause and made the inaccessible mind a legitimate object of study, and it grounds the whole clinical use of dreams and defences. **What it left debated.** The topography was later folded into the structural model (id, ego, superego, the Freud and psychoanalysis topic), and the dynamic unconscious remains empirically contested; cognitive science kept the idea of non-conscious processing while discarding the repression mechanism (Kaplan and Sadock 2024).

7.4 Global Workspace theory (Baars): consciousness as broadcast

Consciousness is a stage that broadcasts. Baars's (1988) **Global Workspace theory** was the first cognitive-science account to specify a *function* for consciousness rather than merely describe it. The mind runs a vast number of specialised, parallel, unconscious processors; most of their work never becomes conscious. A given content becomes conscious when it wins the competition for access to a limited-capacity *global workspace* and is then *broadcast* widely, making it available to all the other processors at once (the "theatre" metaphor: a spotlight of attention on a stage, broadcasting to a dark auditorium of unconscious modules). Consciousness, on this view, is what integration and global availability look like from inside. Dehaene's *global neuronal workspace* (2001 onward) gave it a neural implementation: conscious access corresponds to a sudden, all-or-none "ignition" of long-range fronto-parietal networks. **What it fixed.** It made consciousness a testable information-processing function (global availability) and predicted the empirical signature of conscious versus unconscious stimuli. **What it left debated.** It arguably explains *access* consciousness (report, availability) while sidestepping Chalmers's hard problem of *why* broadcast should feel like anything, the gap the next theory attacks head-on (Kaplan and Sadock 2024).

7.5 Integrated Information theory (Tononi): consciousness as integrated information

Consciousness is how much a system integrates information. Tononi's (2004 onward) **Integrated Information theory** (IIT) inverts the usual approach: it starts from the felt properties of experience and asks what a physical system must be like to have them. Its claim is that consciousness *is* integrated information, quantified as **phi** (the "i"-with-a-line symbol Tononi used), the amount of information a system generates *as a unified whole* over and above the information of its parts considered separately. A system is conscious to the degree that it is both highly *differentiated* (many possible states) and highly *integrated* (irreducible to independent parts). **What it fixed.** It offers, in principle, a measure that explains why the thalamocortical system is conscious while the cerebellum (equally many neurons, but modular and feed-forward) is not, and it motivated the clinically promising perturbational complexity index used to detect covert awareness. **What it left debated.** Phi is effectively incomputable for real brains, and IIT's willingness to attribute graded consciousness to any sufficiently integrated system (a panpsychist flavour) draws sharp criticism; it remains a rival to, not a replacement of, workspace accounts (Kaplan and Sadock 2024).

7.6 The currently accepted position

A pragmatic convergence, not a solved problem. There is no settled theory of consciousness, and the honest exam answer says so. The *currently accepted* working position combines three things. First, the level/content distinction is treated as foundational and clinically decisive. Second, at the mechanistic level the field converges on the idea that conscious content requires *large-scale integration and global availability* across the cortex (Global Workspace and IIT are the two leading, competing formalisations of that single intuition), gated by a functioning arousal system. Third, the "easy problems" of access, report, and integration are regarded as tractable and actively yielding to neuroscience, while Chalmers's hard problem of subjective experience is acknowledged as unresolved. In short: consciousness is operationally split into arousal (a brainstem-thalamic level) plus awareness (a cortical, integrated, globally broadcast content), and that operational split, not any single grand theory, is what current clinical and research practice runs on (Kaplan and Sadock 2024).

7.7 The neural correlate: arousal system, thalamocortical loops, default-mode network

Level and content have different substrates. The neurobiology maps cleanly onto the two axes, which is why the correlates are worth memorising as a pair.

Arousal (level): the ascending reticular activating system

The **ascending reticular activating system** (ARAS), a network of brainstem tegmental nuclei (cholinergic, noradrenergic, serotonergic, and the histaminergic tuberomammillary and orexinergic hypothalamic components) projecting up through the thalamus and basal forebrain to the cortex, sets the global level of wakefulness. Focal damage here, or to the paramedian thalamus it drives, abolishes arousal and produces coma; it is the on-switch for consciousness (the web-cache reviews call it the basic mechanism of awareness).

Content (awareness): thalamocortical loops

Recurrent **thalamocortical** loops, the reciprocal circuits between specific and intralaminar thalamic nuclei and the cortex, are the substrate of conscious content and of its integration. Loss of

thalamocortical integration (deep anaesthesia, slow-wave sleep, vegetative state) abolishes awareness even when some arousal persists; their integrity is what IIT's complexity measures probe.

The self and internal awareness: the default-mode network

The **default-mode network** (medial prefrontal cortex, posterior cingulate and precuneus, and lateral parietal cortex) is most active during rest and internally directed cognition (mind-wandering, self-reference, autobiographical thought). Its activity tracks the self-related, narrative stream of content, is suppressed by demanding external tasks, and is characteristically disrupted in the altered states below (deep meditation, psychedelics, and disorders of consciousness).

7.8 Normal altered states: sleep, dreaming, and the transitional states

The baseline already shifts nightly. Not every altered state is exotic; the ordinary sleep-wake cycle is the reference case. An *altered state of consciousness* is a recognisable, marked departure from the ordinary waking baseline in perception, cognition, emotion, and sense of self (Vaitl 2012). Sleep is the paradigm: *non-REM* sleep is a low-arousal, low-content state, while *REM* sleep pairs a highly activated, "wake-like" brain with vivid, bizarre, poorly-remembered *dreaming*, the classic dissociation of high internal content from external disconnection. Between wake and sleep sit the brief *transitional* states: *hypnagogic* (falling asleep) and *hypnopompic* (waking) imagery, and everyday *daydreaming* and reverie. **Cross-reference.** The detailed sleep architecture, the NREM stages, the REM cycle, the EEG signatures, and the neurobiology of the sleep-wake switch, is covered in the Functional Neuroanatomy & Neurophysiology notes; here it functions only as the exemplar altered state (Kaplan and Sadock 2024).

7.9 Hypnosis: the state versus non-state debate and susceptibility

A trance, or just role and expectancy? Hypnosis is a state of focused, absorbed attention with heightened suggestibility and reduced peripheral awareness, naturally distributed through the population (Tasman 2015 describes it as "a natural state of attentive, focused concentration"). The central theoretical fault-line is whether it is a distinct altered state at all.

POSITION	CORE CLAIM	KEY NAMES / EVIDENCE
State (special-process) theories	**Hypnosis is a genuinely altered state of consciousness, involving a real dissociation of control and monitoring from awareness**	Hilgard's *neodissociation* theory and the "hidden observer"; a divided consciousness in which one stream registers pain the reporting stream denies
Non-state (socio-cognitive) theories	**No special state is needed; effects arise from ordinary suggestion, expectancy, motivation, and role enactment**	Barber, Spanos, Sarbin; hypnotic responses reproducible in motivated non-hypnotised subjects

The debate is unresolved; both camps agree on the phenomena and disagree on whether they require a distinct state.

Susceptibility is the stable, measurable variable. The best-replicated fact about hypnosis is that responsiveness (*hypnotisability* or hypnotic susceptibility) is a trait-like, roughly normally distributed, and stable individual difference, measured by standardised scales, the *Stanford Hypnotic Susceptibility Scales* and the *Harvard Group Scale*. It correlates with the trait of *absorption* (the tendency to become fully immersed in imaginative experience) and predicts

clinical response; a minority are highly hypnotisable, a minority essentially refractory, most intermediate (Tasman 2015; Kaplan and Sadock 2024).

7.10 Meditation and drug-induced states

Two deliberate routes to an altered state. **Meditation** is a family of self-regulation practices that intentionally alter consciousness through the control of attention; the two broad styles are *focused-attention* meditation (sustained concentration on a single object, the breath, a mantra) and *open-monitoring* or mindfulness meditation (non-reactive awareness of whatever arises). Its neural signature centres on altered *default-mode network* activity, reduced self-referential mind-wandering in experienced meditators, alongside changes in prefrontal and insular regulation of attention and interoception. **Drug-induced states** are altered states produced pharmacologically, understood by drug class and shared phenomenology: classic *psychedelics* (LSD, psilocybin, mescaline; serotonin 5-HT2A agonists) disorganise and reduce default-mode network integration, correlating with ego-dissolution; *dissociatives* (ketamine, PCP; NMDA antagonists) uncouple perception from self; sedatives and general anaesthetics collapse thalamocortical integration to abolish awareness. One influential integrative account is *transient hypofrontality* (Dietrich), which explains several altered states (the runner's high, flow, some drug and meditative states) as a temporary down-regulation of prefrontal function (Kaplan and Sadock 2024; ScienceDirect *Encyclopedia of Consciousness* 2009).

- **Psychedelics** - LSD, psilocybin, mescaline; 5-HT2A agonists; reduce default-mode network integration (ego-dissolution).
- **Dissociatives** - ketamine, PCP; NMDA antagonists; uncouple perception from self.
- **Sedatives / anaesthetics** - collapse thalamocortical integration to abolish awareness.

INDIA

The contemplative traditions the exam frames as "meditation" are indigenous to the subcontinent, dhyana and samadhi in the yogic tradition, vipassana in the Buddhist. Transcendental Meditation and mindfulness-based programmes now used clinically are secularised derivatives. Worth naming in a viva both for cultural literacy and because Indian psychiatry has an active research base in yoga-based interventions.

7.11 Clinical altered states: delirium and clouding of consciousness

The commonest pathological altered state on the ward. A reduction in the *level* of consciousness, short of coma, is the core of **delirium** and is described on a graded vocabulary the exam expects verbatim. **Clouding of consciousness** is the mildest: a state ranging from barely perceptible impairment to definite drowsiness in which the person reacts incompletely to stimuli, with impaired attention, concentration, and memory, disturbed orientation, and muddled thinking; it is the *defining feature of delirium* (Shorter Oxford, Harrison et al. 2018). Delirium adds to this clouding an acute onset, a *fluctuating* course (worst at night, "sundowning"), inattention as the cardinal deficit, and perceptual disturbance (illusions and visual hallucinations, which are far more likely when the level of consciousness is reduced). It is the exemplar of an organic altered state and a medical emergency.

COMMON TRAP

"Stupor" is a false friend across specialties. In *psychiatry*, stupor means a state in which the patient is immobile, mute, and unresponsive but appears *fully conscious* (eyes open, following objects, reflexes normal), as in catatonia. In *neurology*, stupor implies an *impairment of the level* of consciousness, a state of reduced arousal from which the patient can be roused only by vigorous stimulation. State which sense you mean (Shorter Oxford, Harrison et al. 2018).

7.12 Clinical altered states: dissociation

A splitting of content, not a lowering of level. **Dissociation** is a disruption of the normal *integration* of consciousness, memory, identity, emotion, perception, and body awareness, with arousal typically preserved. Where delirium lowers the level, dissociation fragments the content: functions that normally stream together, the sense of self, the ownership of memories, the reality of perception, come apart. The clinical forms mark which integration has failed: *depersonalisation* (detachment from one's own self, "as if a robot") and *derealisation* (detachment from surroundings, "as if a film"), dissociative *amnesia* (loss of access to autobiographical memory), and, at the severe end, dissociative *identity* disorder. Trauma is the classic antecedent, and high hypnotisability links dissociation back to 7.9, the same capacity for absorbed, divided awareness underlies both (Kaplan and Sadock 2024).

7.13 Disorders of consciousness: coma, vegetative and minimally conscious states

Where level and content dissociate completely. Severe brain injury produces a graded family of disorders of consciousness that the level/content framework organises perfectly, running from no arousal and no awareness up to fluctuating awareness.

STATE	AROUSAL (LEVEL)	AWARENESS (CONTENT)	HALLMARK
Coma	Absent	**Absent**	Eyes closed, no sleep-wake cycle, unrousable; ARAS or bilateral cortical failure. Time-limited (days to weeks), evolving to recovery, VS, or death.
Vegetative state (unresponsive wakefulness)	Present	**Absent**	Eyes open, sleep-wake cycles return, but no reproducible sign of awareness. The defining dissociation: arousal without content. "Persistent" if prolonged.
Minimally conscious state	Present	**Present but minimal and fluctuating**	Inconsistent but reproducible signs of awareness (command-following, visual tracking, appropriate emotion). Better prognosis than VS.
Locked-in syndrome	Present	**Fully present (not a disorder of consciousness)**	The trap: full awareness and arousal but near-total motor paralysis (ventral pons lesion), often only vertical eye movements. Consciousness is intact; the deficit is output.

Coma is transient; the vegetative state is the pure dissociation of arousal from awareness; locked-in syndrome is intact consciousness misread as unconsciousness.

Level of consciousness at the bedside is quantified by the *Glasgow Coma Scale* (Teasdale and Jennett 1974), scoring eye-opening, verbal, and motor responses to a total of **3** (deepest coma) to **15** (fully alert). Emerging techniques (task-based fMRI, the perturbational complexity index derived from IIT) can now detect *covert* awareness in a subset of behaviourally unresponsive patients, the clinical pay-off of the integration theories above (Kaplan and Sadock 2024).

7.14 Worked example: the vegetative-state patient and the two axes

One bedside picture that makes the whole topic cohere. A young man survives a severe traumatic brain injury. After two weeks in coma (no eye-opening, unrousable, GCS 5) he begins to open his eyes and cycle between sleep and apparent wakefulness, yet he tracks nothing, follows no command, and shows no reproducible response to his family. He is in a *vegetative state*: his ascending reticular activating system has recovered enough to restore *arousal* (level), but his thalamocortical integration has not recovered enough to generate *awareness* (content). This single dissociation, eyes open but no one home, is the clinical proof that level and content are separate axes with separate substrates, and it is why the family's intuitive question ("he's awake, so is he

conscious?") has the counter-intuitive answer "awake is not the same as aware." Months later he begins, inconsistently, to squeeze a hand on request and to smile at his mother: fluctuating, reproducible signs of content have appeared, and he has crossed into the *minimally conscious state*, a better-prognosis category. A task-based fMRI showing him imagining playing tennis on command would be evidence of covert awareness, content detectable by the brain when behaviour cannot express it (Kaplan and Sadock 2024).

HOLD THIS

The vegetative state is the pure dissociation: arousal present, awareness absent. "Eyes open but no one home" is why awake is not the same as aware, and it proves level and content have separate substrates (ARAS versus thalamocortical loops).

GOOD TO REMEMBER

- **Level versus content (Parvizi and Damasio 2001):** level = arousal/wakefulness (subcortical, coma-to-alert); content = awareness (cortical). Dissociable; the master distinction.
- **Hard problem (Chalmers 1995):** why is there subjective experience (qualia) at all, versus the tractable "easy problems" (discrimination, integration, report).
- **William James (1890):** stream of consciousness; four properties: personal, continuous, constantly changing, selective.
- **Freud topographic model (1900, 1915):** conscious / preconscious (retrievable) / unconscious (repressed, dynamic; known via dreams, slips, symptoms).
- **Global Workspace theory (Baars 1988; Dehaene global neuronal workspace):** content becomes conscious by winning access to a limited workspace and being broadcast widely ("theatre/spotlight"); explains access consciousness.
- **Integrated Information theory (Tononi 2004):** consciousness = integrated information, measured as phi; needs differentiation plus integration; explains why cortex is conscious and cerebellum is not.
- **Currently accepted:** no single theory; convergence on integration plus global availability for content, gated by arousal; hard problem unresolved.
- **Neural correlate:** ascending reticular activating system (ARAS, brainstem-thalamus) = arousal/level; thalamocortical loops = content integration; default-mode network (mPFC, posterior cingulate/precuneus, lateral parietal) = self-referential internal content.
- **Altered state (Vaitl 2012):** marked departure from waking baseline in perception, cognition, emotion, self; sleep is the paradigm; hypnagogic/hypnopompic are transitional.
- **Hypnosis debate:** state (Hilgard neodissociation, "hidden observer") versus non-state / socio-cognitive (Barber, Spanos, Sarbin: suggestion, expectancy, role).
- **Hypnotisability:** stable, trait-like, roughly normally distributed; Stanford and Harvard scales; correlates with absorption.
- **Meditation:** focused-attention versus open-monitoring (mindfulness); alters default-mode network activity.
- **Drug states by class:** psychedelics (5-HT2A agonists, reduce DMN integration, ego-dissolution); dissociatives (NMDA antagonists, ketamine/PCP); sedatives/anaesthetics (collapse thalamocortical integration). Transient hypofrontality (Dietrich) as an integrative account.
- **Clouding of consciousness:** mild reduced level with impaired attention/orientation and muddled thinking; the defining feature of delirium; delirium adds acute onset, fluctuating course, inattention, visual hallucinations.
- **Stupor (false friend):** psychiatry = immobile/mute but fully conscious (catatonia); neurology = impaired level, rousable only by vigorous stimulation.
- **Dissociation:** failed integration of content with arousal preserved; depersonalisation, derealisation, dissociative amnesia, dissociative identity disorder; trauma-linked.
- **Disorders of consciousness:** coma (no arousal, no awareness; transient); vegetative/unresponsive wakefulness (arousal present, awareness absent); minimally conscious state (minimal, fluctuating awareness); locked-in syndrome (full consciousness, motor output lost, ventral pons).
- **Glasgow Coma Scale (Teasdale and Jennett 1974):** eye, verbal, motor; total 3 (deepest coma) to 15 (fully alert).

8 · Creativity and divergent thinking

Creativity is the general-psychology topic the exam most often pairs with intelligence, because the two capacities overlap but are not the same, and the discriminator (an intelligent person converges on the one right answer, a creative person generates many) is exactly what a viva examiner wants you to draw. It is worth teaching as its own clean evolution-of-theories story: a

definition, then the models in the order they appeared, each fixing something the last one missed, ending in the currently accepted componential and systems view, its neural correlate, and a clinical anchor. That clinical anchor is the reason creativity earns a place in a psychiatry syllabus at all, the century-old and much-abused "mad genius" question, and specifically the link between the bipolar spectrum and creative achievement, which the modern evidence reframes soberly rather than romantically. **One question runs through the whole topic: what kind of thinking produces something both new and useful, and does it sit near, or apart from, ordinary intelligence and ordinary mental health?**

Ground text for the psychological models is the standard creativity literature (Guilford 1950, 1967; Torrance 1974; Wallas 1926; Sternberg and Lubart 1991; Csikszentmihalyi 1996), synthesised from the general-psychology canon and cross-checked against the Simonton definition used in modern reviews (Simonton 2012). The clinical link is grounded in the DSM-5-TR (2022) and Kaplan and Sadock (2024), and the historical clinical literature (Andreasen 1987; Jamison 1993). The threshold hypothesis and the neuroscience are drawn from the contemporary creativity-neuroscience literature (Guilford; Carson and colleagues 2003; Beaty and colleagues 2016).

8.1 Creativity defined: novel and useful, and the surprise criterion

Creativity is the ability to produce work that is both *novel* (original, statistically rare, not an obvious derivation) and *useful* (valuable, appropriate to the task, or effective as a solution). This two-part definition is the one the exam wants, because either half alone fails: a bizarre response that solves nothing is odd, not creative, and a workable idea everyone already had is competent, not creative. The modern refinement (Simonton 2012), adapted from the three criteria the US Patent Office uses to grant a patent, adds a third quality, *surprise* (the idea should be nonobvious, not a step-by-step deduction from existing expertise). Crucially all three are quantitative, matters of degree with a zero point, and an idea scoring zero on any one criterion has zero creativity: reinventing the wheel is useful but not original, so it is not creative; a parachute made of reinforced concrete is original and surprising but useless, so again not creative. Hold the working definition as *novel and useful*, and add *surprising* for the fuller account.

Novelty (originality)

The idea is statistically rare or unique, low in prior probability; not an obvious derivation.

Usefulness (appropriateness)

The idea is valuable, effective, or fit for the problem; it actually works.

Surprise (nonobviousness)

The idea does not follow step by step from acquired expertise (Simonton 2012, from the patent criteria).

RULE **Creativity needs both novel and useful (add surprising).** Each criterion has a zero point, so a zero on any one means zero creativity: reinventing the wheel is useful but not original; a concrete parachute is original but useless.

8.2 Guilford's turn: divergent versus convergent thinking

The founding move of the scientific study of creativity is J. P. **guilford**'s 1950 American Psychological Association presidential address, which put creativity on the research map and located it in a distinctive kind of thinking. He contrasted two modes. **Convergent thinking** narrows many possibilities down to the single best or correct answer, the mode intelligence tests reward (there is one right response, and speed and accuracy in reaching it are scored). **Divergent thinking** does the opposite: it fans outward from a starting point to generate many varied possibilities, with no single correct answer, and it is the cognitive engine Guilford proposed underlies creative production. What Guilford *fixed* was the prior assumption that creativity was just a by-product of high IQ, giving it a separate cognitive definition (divergent generation) and a way to measure it. What he *left debated* is whether divergent-thinking scores actually predict real-world creative achievement, a validity question that still qualifies every divergent-thinking test.

FEATURE	CONVERGENT THINKING	DIVERGENT THINKING
Goal	Reach the one correct or best answer	**Generate many varied possible answers**
Direction	Narrows inward to a single point	**Fans outward from a starting point**
Right answer?	Yes, one defined solution	**No, an open field of options of varying value**
Measured by	IQ tests; the Remote Associates Test (RAT)	Unusual Uses Task; Torrance Tests (TTCT)
Scored on	Accuracy and speed	Fluency, flexibility, originality, elaboration
Maps to	Intelligence (mostly)	**Creativity (the generative engine)**

Guilford's core distinction: intelligence tests reward convergence on one answer, whereas creativity rests on divergence into many, which is why IQ tests systematically miss it.

8.3 The four scores of divergent thinking: fluency, flexibility, originality, elaboration

Guilford operationalised **divergent** thinking through open-ended tasks, the classic being the **Unusual Uses Task** (name as many uses as you can for a common object such as a brick), and he scored the output on four dimensions that every subsequent test inherits. This quartet is high-yield and worth memorising as a set.

Fluency

The sheer number of appropriate responses generated (how many uses for the brick).

Flexibility

The number of distinct conceptual categories the responses span (using the brick as a weight, a weapon, a building block, and an art object crosses more categories than five uses that are all "as a weight").

Originality

The statistical rarity or unusualness of the responses (an answer few other people give scores higher).

Elaboration
The amount of detail and development added to each idea (how fully the use is worked out).

A related and equally examinable measure is the **Remote Associates Test** (RAT, Mednick 1962), which frames creativity as the ability to link ideas that sit far apart conceptually: given three cue words (widow, bite, monkey) the respondent finds the single word that connects them all (spider). Note that the RAT is convergent in form (one right answer) but taps the associative reach that creativity theorists prize, which is why it survives alongside the divergent tasks.

TRAP The Remote Associates Test is **convergent in form** (one right answer), not a divergent test, even though it is used to probe creativity. Divergent tasks (Unusual Uses, TTCT) fan out to many answers.

8.4 Guilford's structure-of-intellect: where divergent thinking lives

guilford embedded divergent production in a larger and famously over-ambitious map of the mind, the **structure-of-intellect (SOI) model** (1967). It treats every intellectual ability as the crossing of three facets: *operations* (what the mind does, including cognition, memory, evaluation, and the two production types, convergent production and divergent production), *contents* (the material worked on, such as figural, symbolic, semantic, behavioural), and *products* (the form of the result, such as units, classes, relations, systems). Multiplying the facets yielded a large grid of distinct abilities (in its expanded form up to 150). What SOI *fixed* was the placing of creativity firmly inside a theory of intellect rather than treating it as a mysterious spark: divergent production is one operation among several, no more mystical than memory. What it *left debated*, and where it was ultimately rejected, is that the model was too fine-grained and its many hypothesised abilities were not empirically independent, so SOI is remembered chiefly for the enduring convergent-versus-divergent distinction it carried, not for its 150-cell grid.

8.5 Torrance: the tests that made divergent thinking measurable

E. Paul **torrance** translated Guilford's ideas into the field's most widely used instrument, the **Torrance Tests of Creative Thinking (TTCT, 1966, 1974)**. The TTCT comes in verbal and figural forms (the figural form asks the child or adult to complete or build pictures from incomplete figures) and is scored on the Guilford-derived dimensions, principally fluency, flexibility, originality, and elaboration, later refined to emphasise originality and elaboration plus qualities such as resistance to premature closure and abstractness of titles. What Torrance *fixed* was the practical measurement problem: he gave educators and researchers a standardised, normed, scorable creativity test suitable for children, and his longitudinal follow-ups offered some of the first evidence that early divergent-thinking scores relate to later creative achievement. What he *left debated* is the ceiling of that predictive validity (divergent-thinking scores correlate with, but are far from equal to, real creative accomplishment) and the persistent worry that timed tick-box scoring captures only a thin slice of what creativity means.

8.6 Wallas's four-stage creative process

Alongside the ability tradition runs a process tradition, asking not how much creativity a person has but what steps a creative act passes through. The canonical scheme is Graham **Wallas**'s four-

stage model (*The Art of Thought*, 1926), which still frames how the creative process is taught.

Preparation
Conscious, effortful work: defining the problem and saturating oneself in the relevant knowledge and attempted solutions.

Incubation
The problem is set aside and worked on unconsciously; no deliberate effort, often during rest or unrelated activity.

Illumination
The sudden "aha," the insight arriving whole into consciousness (the moment the solution appears).

Verification
Conscious testing, elaboration, and refinement to confirm the insight actually works and to render it usable.

What Wallas *fixed* was the naive view that creation is one instantaneous flash: he showed it is a sequence in which conscious preparation and unconscious incubation both do necessary work before the flash, and verification does the unglamorous work after. What he *left debated* is the mechanism of incubation (is it genuine unconscious processing, mere forgetting of misleading fixed sets, or spreading activation during the pause) and whether the stages are truly discrete or overlapping and recursive. Note the deliberate link to the thinking topic: Wallas's *illumination* is the same Gestalt *insight* ("aha," sudden restructuring) met under problem-solving (cross-ref: Thinking, problem-solving and intelligence, insight).

8.7 Investment and systems theories: creativity as more than a trait

By the 1990s the field had moved from asking "what mental ability is creativity" to "what constellation of factors, inside and outside the person, produces creative work," giving two influential accounts. Robert **Sternberg and Todd Lubart**'s **investment theory** (1991) uses a market metaphor: creative people "buy low and sell high," pursuing ideas that are novel and undervalued (out of favour), developing them, and moving on. It names six convergent resources a creative act requires, namely intellectual abilities, knowledge, thinking styles, personality (tolerance of ambiguity, willingness to take sensible risks), intrinsic motivation, and a supportive environment. Mihaly **Csikszentmihalyi**'s **systems model** (1988, 1996) goes further outward, arguing creativity is not a property of a person at all but of a system with three parts in interaction: the *individual* (who produces a variation), the *domain* (the body of knowledge and symbols, such as mathematics or music, that the individual draws on and changes), and the *field* (the gatekeepers, editors, critics, and experts who decide whether the variation is accepted into the domain). On this view an idea is creative only when the field validates it and the domain absorbs it. What these theories *fixed* was the individualistic narrowness of the ability tradition, showing creativity depends on motivation, personality, and above all social validation, not on divergent thinking alone. What they *leave debated* is measurement: systems and investment accounts are rich but far harder to quantify than a divergent-thinking score.

8.8 Csikszentmihalyi's flow: the subjective state of creative work

Csikszentmihalyi's second major contribution, distinct from the systems model but examinable alongside it, is the concept of **flow** (1975, 1990): the fully absorbed, optimal state of consciousness in which a person is completely immersed in an activity, action and awareness merge, self-consciousness and the sense of time fall away, and the activity becomes intrinsically rewarding (autotelic). Flow arises specifically at the balance point where the *challenge* of the task matches the person's *skill*: too much challenge for the skill breeds anxiety, too little breeds boredom, and only the matched zone produces flow. Flow is the phenomenology of engaged creative (and skilled) activity and connects the creativity literature to positive psychology and to the "engagement" pillar of well-being (cross-ref: Motivation and emotion; positive psychology).

8.9 The threshold hypothesis: how much intelligence creativity needs

The relationship between creativity and intelligence is not "more is always more," and the exam-relevant summary is the **threshold hypothesis** (associated with Guilford and elaborated by later work). It holds that intelligence and creativity are positively correlated up to a point, but only up to a threshold conventionally placed around an **IQ** of **120**: below the threshold, a certain baseline of general intelligence is genuinely necessary for creative achievement (you cannot be creative in a domain you lack the cognitive resources to grasp), so the two rise together. Above the threshold the correlation weakens or disappears: among already-bright people, further increases in IQ do not predict more creativity, which now depends on other factors (divergent thinking, personality, motivation, opportunity). The lesson to carry is that creativity requires *some but not maximal* intelligence: high intelligence is a near-necessary but not sufficient condition, and the most creative individuals are reliably above average in IQ but are not necessarily the very highest scorers. (The precise threshold value is contested and some large modern studies fail to find a clean cut-off, so treat 120 as the classically taught figure rather than a hard constant, flagged under gaps.)

> **COMMON TRAP**
>
> Do not equate creativity with intelligence, and do not treat the threshold hypothesis as saying "the smarter you are, the more creative you are." It says the opposite above the threshold: past roughly IQ 120 the correlation flattens, so the genius-level IQ is neither required nor predictive of creative output. Equally, do not confuse convergent with divergent thinking. Convergent thinking (and the RAT, which is convergent in *form*) narrows to one right answer; divergent thinking (Unusual Uses, TTCT) fans out to many. Intelligence tests measure mostly convergent ability, which is exactly why they miss creativity.

8.10 The creativity-psychopathology question: the "mad genius" debate, stated soberly

The oldest clinical claim about creativity, from Aristotle through the Romantics to Lombroso, is that genius and madness are linked. The modern evidence supports a real but *narrow and non-linear* association, concentrated on the **bipolar spectrum** rather than on severe mental illness in general, and it must be stated carefully to avoid both romanticisation and stigma. The landmark studies are Nancy **Andreasen**'s (1987) controlled interview study of the Iowa Writers' Workshop, which found substantially higher rates of mood disorder (especially bipolar and depressive

spectrum) among eminent writers than controls, and Kay Redfield **Jamison**'s (1989, 1993) work documenting elevated rates of mood disorder and creative productivity tied to mild elevations of mood. The plausible mechanism is that mild hypomania supplies exactly the ingredients divergent thinking needs: increased fluency and speed of thought, expansiveness, reduced need for sleep, heightened energy, confidence, and looser associations, all of which can raise idea generation, provided the mood elevation stays mild.

The sober qualifications are the examinable core, and the DSM-5-TR (2022) states them plainly. First, the relationship is *non-linear*: it is *milder* forms of bipolar disorder, not full severe mania, that associate with greater lifetime creative accomplishment (florid mania and depression are disorganising and disabling, and destroy productive work). Second, higher creativity is found in the *unaffected first-degree relatives* of people with bipolar disorder, which points to a shared genetic or temperamental substrate (a creative "endophenotype") rather than illness itself being the cause. Third, creativity is listed among the *trait-like features* associated with bipolar I (alongside hyperthymic and cyclothymic temperament and reward sensitivity), again framing it as a dispositional correlate, not a product of episodes. The clinically vital and non-obvious point the DSM adds: a patient's attachment to the heightened creativity of hypomania can drive ambivalence about treatment and poor adherence, because they fear that a mood stabiliser will flatten the creative edge (cross-ref: the Social, Learning & Personality Psychology notes bipolar disorder; and note the lithium-and-creativity adherence problem).

HOLD THIS

The mad-genius link is real but narrow and non-linear. It is *milder* bipolar forms, not full mania, that associate with creative accomplishment; higher creativity in unaffected first-degree relatives points to a shared substrate, not illness itself.

CLINICAL ANCHOR

A patient with bipolar II resists lithium, saying it "kills my writing." The evidence lets you answer honestly without either dismissing him or endorsing the romantic myth: the creativity that matters is linked to *mild* hypomanic states and to his underlying temperament, not to full episodes, which are disorganising; unaffected relatives share the creative edge, so it is not the illness "giving" him talent; and untreated mood swings threaten far more of his output than a stabiliser does. Framing treatment as protecting his productive capacity from the disorganising extremes, not confiscating his gift, is the adherence-preserving move the DSM-5-TR flags as the crux.

8.11 Currently accepted account: an interaction of process, person, and system

There is no single grand theory that has won the field the way CHC has won intelligence, but the *currently accepted* synthesis is a componential and interactionist one: creativity is best understood not as one ability but as the interaction of a cognitive process (divergent generation to produce candidate ideas, followed by convergent evaluation to select and refine the good ones), a set of personal resources (adequate but not maximal intelligence past the threshold, relevant domain knowledge, openness to experience, tolerance of ambiguity, sensible risk-taking, and intrinsic motivation), and a social system (the domain that supplies the material and the field that validates

the product, per Csikszentmihalyi). In short, the modern consensus keeps Guilford's divergent-convergent cycle at the cognitive core, wraps it in the investment theory's personal resources, and situates the whole thing in the systems model's social context. The practical upshot for assessment is that no single test captures creativity, and divergent-thinking scores (TTCT) are treated as one indicator among several, not a definitive measure.

8.12 Neural correlate: reduced latent inhibition and network dynamics

The **neural correlate** of creativity has two well-supported strands the exam can ask for by name. The first is **reduced latent inhibition**. Latent inhibition is the normal, adaptive brain process by which stimuli previously experienced as irrelevant are automatically filtered out of conscious attention. Carson, Peterson, and Higgins (2003) showed that *reduced* latent inhibition, a leakier filter that lets nominally irrelevant information into awareness, is associated with higher creative achievement, but specifically in people who *also* have high intelligence and working memory to manage the extra input. This is the mechanistic bridge to psychopathology: the same reduced filtering, without the cognitive resources to harness it, appears in the positive-symptom dimension of psychosis and in schizotypy, so creativity and psychosis-proneness may share a substrate (leaky filtering) whose outcome depends on the intellectual control brought to bear on it. Dopaminergic tone, particularly in the mesolimbic and prefrontal systems, is the leading neurochemical candidate for tuning this filter.

The second strand is **large-scale network dynamics** (Beaty and colleagues 2016 and after). Creative cognition is not localised to a "right brain" but emerges from the flexible cooperation of usually antagonistic networks: the *default-mode network* (medial prefrontal cortex, posterior cingulate, and associated regions), engaged in spontaneous, associative, self-generated idea production, and the *executive control network* (dorsolateral prefrontal and parietal regions), engaged in the goal-directed evaluation, constraint, and refinement of those ideas. The salience network (anterior insula, anterior cingulate) is thought to switch between them. Highly creative people show stronger and more flexible *coupling* between the default-mode (generative) and executive (evaluative) networks, the neural version of the generate-then-select cycle described in 8.11. The old "right-brain equals creative" claim is a myth; creativity is a whole-brain, between-network phenomenon.

8.13 Worked example: the brick, from generation to product

Trace one everyday act through the whole apparatus. Asked for unusual uses of a brick, a person who lists "doorstop, paperweight, weapon, bookend, garden border, art object, water-displacement in a cistern, ground into pigment" is doing *divergent* thinking, and each Guilford score is visible: eight responses (fluency), spanning several conceptual categories from tool to art to material (flexibility), including a rare answer like pigment (originality), and one worked out in detail (elaboration). The generation phase runs on default-mode associative activity with a relatively leaky attentional filter (reduced latent inhibition letting the odd "pigment" idea surface). Then convergent, executive evaluation selects which uses actually work and are worth reporting. Map the same brick onto Wallas: *preparation* is understanding the task, *incubation* is the pause where the pigment idea forms unbidden, *illumination* is its sudden arrival, *verification* is checking

that a ground brick really does make usable pigment. And the systems check: the idea counts as creative only if it is both novel and useful, and, for genuine domain-changing creativity, only once a relevant field accepts it. The brick test is trivial; the machinery it exercises is the whole topic.

MNEMONIC

FFOE for the four divergent scores; "PI-IV" for Wallas

FFOE = **F**luency, **F**lexibility, **O**riginality, **E**laboration (the four Guilford / Torrance divergent-thinking scores). **Wallas = PI-IV**: **P**reparation, **I**ncubation, **I**llumination, **V**erification, in that order (the two "I" stages, incubation then illumination, sit in the middle).

GOOD TO REMEMBER

- **Creativity:** novel + useful (add surprising / nonobvious, Simonton 2012 from patent criteria); zero on any one criterion = zero creativity.
- **Guilford (1950 APA address):** founded the field; divergent (fans out, many answers) vs convergent (narrows to one right answer) thinking.
- **Four divergent scores (FFOE):** Fluency (number), Flexibility (categories), Originality (rarity), Elaboration (detail); measured by the Unusual Uses Task.
- **Remote Associates Test (Mednick 1962):** find the word linking three cues (widow/bite/monkey = spider); convergent in form, taps associative reach.
- **Guilford structure-of-intellect (1967):** operations x contents x products grid (up to 150 abilities); divergent production is one operation; rejected as over-fine but carried the convergent/divergent split.
- **Torrance Tests of Creative Thinking (TTCT, 1966/1974):** verbal + figural; scored on Guilford's dimensions; the standard creativity test, usable in children.
- **Wallas four stages (1926, PI-IV):** Preparation, Incubation, Illumination, Verification; illumination = the Gestalt insight / "aha."
- **Investment theory (Sternberg and Lubart 1991):** "buy low, sell high"; six resources = intellect, knowledge, thinking styles, personality, motivation, environment.
- **Systems model (Csikszentmihalyi 1988/1996):** individual x domain x field; the field (gatekeepers) validates, the domain absorbs.
- **Flow (Csikszentmihalyi 1975/1990):** total absorption; challenge matched to skill (too much = anxiety, too little = boredom); autotelic.
- **Threshold hypothesis:** intelligence and creativity correlate only up to about IQ 120; above it, creativity depends on other factors. Some, not maximal, intelligence needed.
- **Mad-genius / bipolar link:** Andreasen (1987, Iowa Writers' Workshop) and Jamison (1993); real but non-linear; *milder* bipolar forms associate with more creative accomplishment; higher creativity in unaffected relatives (shared substrate); a DSM-5-TR trait-like feature; attachment to hypomanic creativity harms treatment adherence.
- **Currently accepted:** creativity = interaction of process (divergent generation + convergent evaluation) + person (resources, above-threshold IQ, openness) + system (domain and field).
- **Neural correlate:** reduced latent inhibition (Carson et al. 2003; leaky filter, creative only if paired with high IQ; shared with psychosis-proneness; dopaminergic); flexible coupling of default-mode network (generation) with executive-control network (evaluation), salience network switching (Beaty et al. 2016). Not "right brain."

9 · Emotional intelligence

Emotional intelligence (EI, popularly EQ) is the capacity to perceive, understand, use, and regulate emotions, in oneself and in others, and to harness that emotional information to guide thinking and action. Salovey and Mayer, who coined the term in its modern scientific form, defined it as "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" (Salovey and Mayer 1990). It sits at the junction of intelligence and personality, and the whole topic is a single argument about which of those two it really is: an *ability* you can be tested on like IQ, or a cluster of *traits and dispositions* you can only self-report. **Ability or trait.** Every named model is a different answer, and each fixed a specific gap in the one before it.

For the exam the payload is fourfold: the ordered lineage of models with their authors and the one claim each is remembered for; the ability-versus-trait axis that organises them together with how each is measured (performance test versus self-report); the incremental-validity critique that is the field's central controversy; and the neural correlate, the "social brain" of ventromedial prefrontal cortex, amygdala, and insula. Structure the answer as an evolution, not a list, and end on where alexithymia and the therapeutic alliance make EI clinically real.

9.1 Thorndike: the first seed, "social intelligence"

The starting point. The idea long predates the term. Edward Thorndike (1920) distinguished, alongside abstract (academic) and mechanical intelligence, a **social intelligence**: "the ability to understand and manage men and women, boys and girls, to act wisely in human relations." **What it seeded.** It first proposed that the ability to read and handle people is a real form of intelligence, separate from the logical-verbal ability that IQ tests measure. **What it left debated.** Thorndike named the construct but could not operationalise or measure it, and social intelligence proved almost impossible to separate from general IQ with the tools of the day, so the idea lay largely dormant for decades (Salovey and Mayer 1990).

9.2 Gardner: intrapersonal and interpersonal intelligences within multiple intelligences

Reviving the personal. Howard Gardner (1983), in his theory of **multiple intelligences**, argued that the single general factor of traditional testing was too narrow and proposed several independent intelligences. Two of them are the direct ancestors of EI: *intrapersonal intelligence*, the capacity to access and understand one's own inner emotional life and use it to guide behaviour, and *interpersonal intelligence*, the capacity to read the moods, motives, and intentions of other people. **What it fixed.** It gave Thorndike's neglected social ability a formal place inside a serious theory of intelligence and split it into a self-facing and an other-facing half. **What it left debated.** Gardner's intelligences were broad and hard to measure empirically, and he never welded the two personal intelligences into a single testable emotion-specific construct, which is exactly what the next authors did (Kaplan and Sadock 2024).

9.3 Mayer and Salovey: the four-branch ability model

The scientific core. Peter Salovey and John Mayer (1990) fused Gardner's two personal intelligences into one and named it emotional intelligence, then refined it into the **four-branch**

ability model (Mayer and Salovey 1997), the model to know cold. EI is treated as a genuine cognitive ability, correlated with but distinct from general intelligence, built of four hierarchically arranged branches from lowest (most basic) to highest:

1. Perceiving emotion

The most basic branch: accurately identifying emotion in faces, voices, pictures, music, and in oneself. The entry skill on which the others depend.

2. Using (facilitating) emotion

Harnessing emotion to assist thought: letting mood prioritise attention, and using emotional states to aid reasoning, problem-solving, and creativity (for example, a positive mood widening idea generation).

3. Understanding emotion

Grasping emotional knowledge: how emotions blend, progress, and transition (that contempt mixes anger and disgust, that grief can shade into anger), and reading their causes and vocabulary.

4. Managing (regulating) emotion

The highest branch: regulating emotion in oneself and others to promote growth and reach goals, staying open to feeling while modulating it.

The four branches run lowest to highest: perceive, use, understand, manage. Mnemonic PUUM (see box).

What it fixed. It turned a loose popular idea into a precise, componential, and above all *measurable* ability that meets standard criteria for an intelligence (Mayer, Caruso and Salovey 1999). **What it left debated.** By insisting EI is a pure ability testable by performance, it drew a hard line that a rival tradition, treating EI as personality-like traits, would soon cross (Kaplan and Sadock 2024).

9.4 Goleman: the mixed (competency) model that popularised EI

The bestseller model. Daniel Goleman's 1995 book *Emotional Intelligence: Why It Can Matter More Than IQ* brought the concept to the world and made the striking claim that EI predicts life and career success better than IQ. Goleman built a **mixed model** (also called a competency model), so named because it mixes ability-type emotional skills with personality traits, motives, and social competencies. His framework distils to five domains (later reorganised into competency clusters): *self-awareness*, *self-regulation*, *motivation*, *empathy*, and *social skill* (Goleman 1998). **What it fixed.** It made EI intuitive, teachable, and workplace-relevant, driving a huge applied and training literature. **What it left debated.** By folding in motivation, optimism, and conscientiousness, the mixed model overlaps heavily with established personality traits and risks becoming an "everything but IQ that matters" grab-bag, the core of the incremental-validity critique in 9.7 (Kaplan and Sadock 2024).

9.5 Bar-On: the emotional-social intelligence (ESI) model and the EQ-i

The other mixed model. Reuven Bar-On, who is credited with the abbreviation "EQ," proposed a model of **emotional-social intelligence** (ESI): an array of interrelated emotional and social competencies, skills, and facilitators that determine how effectively we understand and express ourselves, understand and relate to others, and cope with daily demands (Bar-On 2006). His

model is organised into competency areas (intrapersonal, interpersonal, adaptability, stress management, and general mood) and is operationalised by the *Emotional Quotient Inventory (EQ-i)*, the first commercially published, peer-reviewed self-report EI test (Bar-On 1997). **What it fixed.** It gave the trait-and-competency tradition a well-validated, widely used self-report instrument and an explicit link to well-being and adaptation. **What it left debated.** Like Goleman's, it is a mixed model measured by self-report, so it inherits the same overlap-with-personality and self-report-bias problems (Kaplan and Sadock 2024).

9.6 The ability-versus-trait debate and its two measurement families

The organising split. Petrides and Furnham (2001) crystallised the field into two conceptually and psychometrically distinct constructs, distinguished chiefly by *how they are measured*.

FEATURE	ABILITY EI	TRAIT EI
Core claim	EI is a cognitive ability, a form of intelligence	EI is a constellation of emotion-related self-perceptions and dispositions ("trait emotional self-efficacy")
Where it sits	Alongside cognitive abilities	**At the lower levels of the personality hierarchy**
Key proponents	Mayer, Salovey, Caruso	Petrides and Furnham; overlaps Goleman, Bar-On
How measured	**Maximum-performance test with correct answers (MSCEIT)**	**Self-report questionnaire (TEIQue, EQ-i, Goleman inventories)**
Scoring truth-standard	Consensus or expert scoring (there is a "right" answer)	No right answer; measures self-perception
Correlation between them	**Low; empirically they behave as two different constructs**	

Ability EI is tested like IQ (right answers, performance); trait EI is self-reported and lives inside personality. The two correlate only weakly.

The flagship ability measure is the **MSCEIT** (Mayer-Salovey-Caruso Emotional Intelligence Test, V2.0), which scores actual performance on the four branches against consensus or expert norms (Mayer, Salovey, Caruso and Sitarenios 2003). The trait measures (EQ-i, Goleman's inventories, the TEIQue) are self-report and therefore assess belief about one's own emotional competence rather than demonstrated skill. A trait score can be inflated by social desirability or by the very lack of insight it claims to measure, the self-report paradox in emotion research (Kaplan and Sadock 2024).

RULE **Measurement decides the construct.** Ability EI is a performance test with right answers (MSCEIT); trait EI is self-report inside personality (EQ-i, TEIQue). The two correlate only weakly and behave as different constructs.

9.7 The incremental-validity critique

The central controversy. The sharpest scientific challenge to EI is whether it predicts anything *over and above* what we already measure cheaply with IQ and the Big Five personality traits, that is, whether it has **incremental validity**. Critics (notably Locke 2005; and Matthews, Zeidner and Roberts) argue that EI, especially the mixed and trait models, is conceptually overinflated and largely redundant: strip out general intelligence and the Big Five and little unique variance is left, so EI may be old constructs under a fashionable new name. The rebuttal is measurement-specific: performance-based ability EI (MSCEIT) shows the strongest case for genuine incremental prediction of social and clinical outcomes because it is not just relabelled personality, whereas self-report trait EI overlaps most with existing personality scales (Brackett and Mayer 2003). **The verdict for the exam.** EI is a real and useful construct, but its incremental validity is real chiefly when measured as an ability, and Goleman's popular claim that "EI matters more than IQ" is not supported at that strength (Kaplan and Sadock 2024).

HOLD THIS

Salovey and Mayer coined and defined EI; Goleman only popularised it. Ability EI has the strongest case for incremental validity beyond IQ and the Big Five; "EI matters more than IQ" is Goleman's claim, not established fact.

9.8 Neural correlate: the "social brain" of vmPFC, amygdala, and insula

Where EI lives in the brain. The *neural correlate* of emotional intelligence is a core "social brain" network, and the strongest evidence comes from lesion studies: damage to specific nodes selectively degrades EI while sparing general IQ (Hogeveen, Salvi and Grafman 2016). Three structures anchor it. The **ventromedial prefrontal cortex** (vmPFC), including the orbitofrontal cortex, integrates emotion with value and social meaning and regulates the limbic system; its lesions produce the classic dissociation of preserved abstract IQ with collapsed emotional and social decision-making (the Phineas Gage and Damasio vmPFC pattern), impairing the "using" and "managing" branches. The **amygdala** is the hub for perceiving emotional salience, especially detecting fear and threat in faces, the neural basis of the perceiving-emotion branch; amygdala damage impairs recognition of fearful expressions. The **insula** is the cortical seat of *interoception*, the sensing of one's own bodily-emotional state, and is central to empathy and to feeling disgust, grounding self-awareness and the perception of emotion in the body. Together, vmPFC (integration and regulation), amygdala (salience and perception), and insula (interoception and empathy) form the substrate on which the four branches are built (Hogeveen et al. 2016, Kaplan and Sadock 2024).

9.9 Clinical relevance: alexithymia, and EI in the therapeutic alliance

Where it becomes clinical. EI's clinical mirror-image is **alexithymia** (Sifneos 1973), literally "no words for feelings": a difficulty identifying and describing one's own emotions, distinguishing feelings from bodily sensations of arousal, and an externally oriented, concrete cognitive style. Alexithymia is essentially the low-EI end of the perceiving-and-understanding branches made pathological, and it is common in somatoform and functional disorders, substance use, eating disorders, and post-traumatic and personality disorders; it predicts poorer treatment response

and is a target of mentalisation-based and emotion-focused work. On the clinician's side, EI matters for the *therapeutic alliance*: the therapist's ability to accurately perceive a patient's affect, to attune and respond to it, and to regulate their own emotional reactions (countertransference) is EI in action, and higher clinician emotional competence is linked to stronger alliance and better engagement. This is why emotional-competence and empathy training is increasingly built into medical and psychiatric education (Kaplan and Sadock 2024).

9.10 Worked example: the patient who cannot name the feeling

One consultation, read through the models. A man presents with recurrent chest tightness and headaches; every investigation is normal. *Perceiving:* asked how he feels, he reports only the physical sensations and cannot label an emotion, high on somatic complaint, low on the perceiving branch, the signature of alexithymia. *Understanding:* he cannot connect the tightness to the fact that it began the week his father was hospitalised, a failure of the understanding branch to link emotion to cause. *Using and managing:* unable to name or modulate the feeling, he cannot use it to problem-solve and it discharges through the body. *Ability versus trait:* a self-report EI questionnaire might even rate him "fine" because he lacks the insight to report the deficit, exactly why an ability measure like the MSCEIT, or the clinician's own trained perception, catches what self-report misses. *Neural read:* the picture fits weak interoceptive and insular processing feeding a vmPFC that cannot translate bodily signals into labelled, regulable emotion. *The alliance as intervention:* the therapist uses their own EI to name the affect the patient cannot ("this started when your father fell ill, that must have been frightening"), and the therapy itself becomes emotion-labelling training. **Same patient, one somatic complaint, decoded as an emotional-intelligence deficit and treated by borrowing the clinician's EI until his own grows.**

MNEMONIC

Four branches: "PUUM" (Perceive, Use, Understand, Manage)

Read low to high, PUUM climbs the ability model: **P**erceive emotion, **U**se emotion to aid thought, **U**nderstand emotion, **M**anage emotion. Perceiving is the floor, managing is the ceiling.

COMMON TRAP

Do not blur the models. Mayer and Salovey = pure *ability* model (measured by performance, the MSCEIT). Goleman and Bar-On = *mixed* models that fold in personality and motivation (measured by self-report). Petrides = the explicit *trait* EI construct inside personality. A frequent error is crediting Goleman with defining EI: he popularised it, but Salovey and Mayer coined and defined it (1990). Another is claiming "EI predicts success better than IQ" as established fact, it is Goleman's popular claim and the incremental-validity data do not support it at that strength.

GOOD TO REMEMBER

- **Thorndike (1920):** first proposed "social intelligence," the ability to understand and manage people; named it but could not measure it.
- **Gardner (1983):** multiple intelligences; the two EI ancestors are *intrapersonal* (understanding one's own inner life) and *interpersonal* (reading others).
- **Salovey and Mayer (1990):** coined "emotional intelligence" and gave the founding definition; monitor own/others' emotions, discriminate, and use to guide thought and action.
- **Four-branch ability model (Mayer and Salovey 1997):** Perceive, Use (facilitate), Understand, Manage emotion; hierarchical, lowest to highest; EI as a genuine ability.
- **Goleman (1995, 1998):** mixed/competency model; five domains = *self-awareness, self-regulation, motivation, empathy, social skill*; claimed EI can matter more than IQ.
- **Bar-On (1997, 2006):** emotional-social intelligence (ESI); coined "EQ"; operationalised by the self-report EQ-i.
- **Petrides and Furnham (2001):** formalised the *trait EI* construct (trait emotional self-efficacy), sitting in the personality hierarchy.
- **Ability vs trait:** ability EI = performance test with right answers (MSCEIT); trait EI = self-report (EQ-i, TEIQue); the two correlate only weakly.
- **MSCEIT (Mayer-Salovey-Caruso, V2.0, 2003):** the flagship performance measure of the four branches, consensus/expert scored.
- **Incremental-validity critique (Locke 2005; Matthews, Zeidner and Roberts):** does EI predict beyond IQ + Big Five? Case is strongest for ability EI, weakest for self-report/mixed EI.
- **Neural correlate ("social brain"):** ventromedial prefrontal cortex (integration/regulation of value and emotion), amygdala (emotional salience, fear-face perception), insula (interoception, empathy); lesion evidence from Hogeveen, Salvi and Grafman (2016).
- **Alexithymia (Sifneos 1973):** difficulty identifying and describing feelings, externally oriented thinking; the low-EI pole, common in somatoform, substance-use, eating, trauma, and personality disorders.
- **Therapeutic alliance:** clinician EI (accurate affect perception, attunement, countertransference regulation) strengthens alliance; a rationale for empathy/EI training in medical education.

10 · Sensory deprivation and the mind-body problem

This is the philosophy-of-psychiatry topic, and it earns its place in the exam because it is where a clinical phenomenon and a two-thousand-year metaphysical puzzle turn out to be the same question asked twice. **Take away the world and the mind starts to invent one.** That single observation, from the isolation-tank experiments, is the empirical hook; the deeper question it forces is the one Descartes named: what exactly is the relation between the **mind** and the **body** (the brain)? The topic pairs the two deliberately. **Sensory deprivation** shows the mind is not a passive receiver of the world but an active constructor of it, which is exactly why perception is prediction (cross-refer the Perception topic); and the **mind-body problem** is the framework a psychiatrist needs to hold the biological and the psychological together without collapsing one into the other.

For the exam the payload is two halves that meet in the middle. First, sensory deprivation: the classic Hebb/McGill and Lilly experiments, the perceptual and cognitive effects, the hallucinations they produce, and the modern clinical relevance (REST, solitary confinement, the intensive-care unit). Second, the mind-body problem proper: the map of positions from

Cartesian **dualism** to the various **monisms**, the explanatory gap and qualia, and then why it all matters at the bedside: reductionism versus the biopsychosocial model, the brain-disease debate, and free will and responsibility. Ground text is Kaplan and Sadock (2024) for the philosophy-of-mind and sensory-deprivation material, with the New Oxford and Companion for the dualism-in-medicine framing and Engel (1977) for the biopsychosocial answer.

10.1 Sensory deprivation: definition and the classic experiments

Strip out the input and perception destabilises. Sensory deprivation is the drastic and sustained reduction of patterned sensory input across modalities. Humans normally operate in what Hartmann called an "average expectable environment," a certain level and variety of stimulation for which the nervous system is primed; remove it, and the brain, still generating predictions with nothing to correct them against, begins to produce its own content (Kaplan and Sadock 2024). Two lines of experiment defined the field. The **Hebb / McGill studies** (Bexton, Heron and Scott 1954, in Donald Hebb's laboratory at McGill University) paid student volunteers to lie on a bed in a lightproof, soundproof cubicle wearing translucent goggles and cardboard cuffs that abolished patterned touch; most could not tolerate more than two or three days, and they reported deteriorating concentration, disturbed thinking, and vivid visual hallucinations. The **Lilly isolation tank** (John C. Lilly, from 1954) took the reduction further: the subject floated, near-weightless, in a tank of body-temperature salt water in total darkness and silence, removing even gravity and proprioception. Lilly used it to explore altered states and the "higher levels of consciousness" the near-total silencing of input could produce (Psychotherapy Guidebook, Suedfeld). Together they established that the deprivation of stimulation is itself a potent alterer of the mind.

10.2 Perceptual, cognitive and affective effects

A reproducible syndrome, not random noise. The effects of prolonged sensory deprivation form a recognisable cluster that the exam expects enumerated.

Perceptual

Illusions first, then hallucinations, most often visual, progressing from simple flashes and geometric forms to complex, dramatic scenes; also somatic and auditory distortions and disturbances of body image. The three-scientists observation (below) captures the striking individual variability.

Cognitive

Impaired concentration and sustained attention, disorganised and drifting thinking, difficulty with directed thought, distortions of the sense of time, and increased suggestibility.

Affective and behavioural

Rising restlessness, irritability, anxiety and, in some, frank distress and an urge to escape the situation; a smaller group finds it relaxing or absorbing, which is what REST later exploited therapeutically.

Individual variability is the examinable subtlety. Kaplan and Sadock (2024) record the classic demonstration: three scientists floated in sensory-deprivation tanks for long periods; one had a few illusions and no hallucinations, the second had many illusions and a few faint hallucinations, and the third had vivid, dramatic, complex visual and auditory hallucinations. Identical

deprivation, radically different output, which foreshadows the point that what is "released" depends on the perceiver, not just the situation.

10.3 Hallucinations under deprivation: the mechanism (link to perception)

Less input, not more, breeds the hallucination. This is the counter-intuitive fact and the bridge back to the Perception topic. The **perceptual release theory** (Hughlings Jackson; developed by West 1962) holds that a steady stream of sensory input normally suppresses stored perceptual traces, memories and images, from reaching awareness; when input falls (sensory deprivation, blindness, deafness) or arousal-gating fails, those stored images are *released* and experienced as hallucinations located in outer space (Kaplan and Sadock 2024). A complementary framing is the **supersensitivity deprivation hypothesis**: deprived of expected input, the perceptual apparatus over-interprets any faint stimulation as evidence of the needed object. In the modern predictive-processing language of the Perception topic, both say the same thing: when bottom-up sensory evidence is weak, top-down priors dominate and the brain perceives what it expects. This is exactly why the blind develop Charles Bonnet hallucinations, the deaf develop musical hallucinations, and the sensory-deprived subject sees scenes in the dark, and it is the same imbalance, tipped further, that the predictive account gives for psychotic hallucination.

RULE **Less input, not more, breeds the hallucination.** When bottom-up sensory evidence is weak, top-down priors dominate and the brain perceives what it expects, which is why reduced input drives hallucination on the ward.

CLINICAL ANCHOR

The principle generalises to the ward. Any state that *reduces* sensory input or the capacity to process it heightens the risk of hallucination: the intensive-care unit at night, the post-operative patient, the cataract or hearing-impaired elderly patient, and the delirious patient (in whom impaired attention functions as an internal deprivation). It is a practical argument for windows, clocks, spectacles, hearing aids and daylight in delirium prevention.

10.4 REST and clinical relevance: therapy, solitary confinement, the ICU

The same manipulation, three very different valences. Sensory deprivation is neither uniformly harmful nor uniformly benign; its meaning depends on control, duration and consent.

CONTEXT	FORM	EFFECT AND VALENCE
REST (therapeutic)	Restricted Environmental Stimulation Therapy: chamber confinement or flotation-tank immersion, minutes to hours, voluntary and monitored (Suedfeld)	**Deliberately controlled and brief; used for relaxation, smoking cessation and habit change, pain and anxiety; the reframing of deprivation as treatment**
Solitary confinement	Involuntary, prolonged social and sensory isolation in incarceration	**Harmful: the "SHU syndrome," anxiety, perceptual disturbance, hallucination, cognitive impairment and paranoia; a recognised human-rights and forensic-psychiatry concern**
Intensive care unit	Unintended: monotonous, windowless, day-night-blurred environment with immobilisation and impaired attention	**Contributes to ICU delirium; both under-stimulation (monotony) and over-stimulation (alarms, procedures) operate, so the fix is patterned, oriented stimulation, not simply "more" or "less"**

One manipulation, three valences: controlled and consented deprivation heals, imposed and prolonged deprivation harms, and unintended deprivation in the ICU drives delirium.

10.5 The mind-body problem: the question and why it framed medicine

How does the mental relate to the physical? The **mind-body problem** is the question of the relation between mental phenomena (thoughts, feelings, subjective experience, intentions) and physical phenomena (the brain and body). Its modern statement is owed to Rene Descartes (1596 to 1650), whose **substance dualism** split reality into *res cogitans* (thinking, non-extended mind) and *res extensa* (extended, mechanical body), a term the exam attributes to Descartes via Damasio (1994). This is not idle metaphysics for a psychiatrist: the split hardened into the division of illness into "medical" (bodily pathology, treated by physicians) and "psychiatric" (an abnormal mental state, treated by psychiatrists), the very **mind-body dualism** that the New Oxford's "Deconstructing dualism" chapter argues has created obstacles to integrated care (Sharpe and Walker; Companion to Psychiatric Studies). The whole point of studying the positions below is to be able to hold biology and psychology together without falling into that clinically damaging split.

10.6 Dualism: the varieties

Mind and body are, in some sense, two. Dualist positions hold that the mental is not simply identical to the physical. They differ over whether mind is a separate *substance* or only a separate *property*, and over which way causation runs.

Substance dualism (interactionism)

Descartes's view: mind and body are two distinct kinds of substance that causally interact (he proposed, wrongly, at the pineal gland). Mind moves body (I decide, my arm rises) and body affects mind (injury causes pain). The fatal objection is the *interaction problem*: how can a non-physical mind push a physical brain without breaking the conservation of energy?

Epiphenomenalism

Body affects mind but not the reverse: mental states are causally inert by-products of brain activity, like the whistle of a steam engine that plays no part in driving the train. It preserves physics (only the physical causes) but at the price of making consciousness a passenger with no effect, which clashes with the intuition that our reasons cause our actions.

Property dualism

The one substance is physical, but it has two irreducibly different *kinds of property*, physical and mental. Kaplan and Sadock (2024) state this as their working position: the brain and the mind are different *levels of description* of one phenomenon (mechanism versus subjective experience), and because they are different levels they have different properties. It is distinguished sharply from substance dualism: nothing extra exists, but the mental cannot be read off the physical alone.

10.7 Monism: the varieties

There is only one kind of stuff. Monist positions deny a fundamental mind-body split; in psychiatry the relevant monisms are all forms of *physicalism* (everything is physical). They differ over how tightly the mental reduces to the physical.

Identity theory (type physicalism)

Mental states simply *are* brain states: to be in pain *is* to have a particular kind of neural activity (the slogan is "C-fibre firing"). Elegant and thoroughly physical, but criticised for chauvinism about *multiple realisability*: if an octopus or a silicon machine could feel pain with entirely different hardware, pain cannot be identical to one specific human brain state.

Functionalism

The fix for multiple realisability: a mental state is defined not by what it is made of but by its *functional role*, its causal relations to inputs, other states and outputs. Pain is whatever plays the pain-role, in a brain or in principle in silicon. This is the reigning framework in cognitive science, but it is charged with leaving out the felt quality of experience (the "absent qualia" worry).

Emergentism

Mind is a genuinely novel, *emergent* property of sufficiently complex and organised matter, real and causally efficacious yet not predictable from, or reducible to, the properties of the parts. Kaplan and Sadock (2024) note psychological phenomena are "emergent properties of lower-order constituents" (circuits, neurons, genes); consciousness is often described the same way. Emergentism sits between reductive physicalism and property dualism.

10.8 Reductionism: constitutive versus eliminative

Not all reduction is the same, and the difference is clinically loaded. Kaplan and Sadock (2024) draw the line the exam wants. **Constitutive reductionism**, reducing a complex entity to its component parts to *facilitate study*, is uncontroversial and is ordinary science. **Eliminative reductionism** goes further and insists that everything mental will *ultimately be explained away* at the material level, eliminating the need for a psychological level of analysis at all. The text rejects the eliminative move: valuable information is lost when you descend from mental states to neurons, and one may reasonably ask why the reduction should stop at the brain rather than continue to physics. The image they use is Shakespeare: the words on the page are material, but a chemical analysis of the ink will never capture the meaning of the play.

COMMON TRAP

The **treatment-etiology fallacy** (Kaplan and Sadock 2024): the fact that a treatment at one level works does *not* prove the cause lies at that level. An antidepressant helping depression no more proves depression is "a chemical imbalance" than aspirin curing a headache proves the headache was caused by an aspirin deficiency. Cognitive-behavioural therapy is at least as effective as medication for many depressions; both act, neither localises the cause. Do not slide from "responds to a drug" to "is a brain disease."

10.9 The explanatory gap and qualia

The residue no physical account has closed. Even granting full physicalism, a gap remains between the objective description of a brain process and the subjective feel of the experience it produces. This is the **explanatory gap** (Levine 1983) and, in its sharpest form, Chalmers's (1995) *hard problem of consciousness*: why is there *something it is like* to undergo a brain process at all? The felt qualities themselves, the redness of red, the ache of pain, are the **qualia**; Kaplan and Sadock (2024) describe them as subjective secondary qualities interpreted by the mind and attributed to the world, and identify "the subjectivity of experience, the so-called qualia of consciousness" as precisely what separates living consciousness from even the best computers. The philosophical thought-experiments the exam may cite, Nagel's "What is it like to be a bat?" (1974) and Frank Jackson's "Mary the colour scientist" (1982, who knows every physical fact about colour but learns something new on first seeing red), are both arguments that physical facts leave the qualia unexplained. This gap is the honest limit: no current position, dualist or monist, closes it, which is why the field defaults to a pragmatic property-dualist stance rather than a solved theory. (The full theories-of-consciousness sequence, James, Freud, Global Workspace, Integrated Information, is the Consciousness topic; here the gap functions only as the unresolved core of the mind-body problem.)

10.10 Why it matters for psychiatry I: the biopsychosocial model

The clinical answer to the mind-body problem. The discipline's practical resolution is not to pick a metaphysics but to adopt a working model that refuses the dualist split. George Engel's **biopsychosocial model** (Engel 1977) reframed illness as the product of interacting biological, psychological and social levels, a general-systems view in which no single level is privileged as "the real" cause (Tasman 2015). It is the direct clinical descendant of property dualism and emergentism: the levels are all real, none reduces to another, and formulation must move across them. Its virtue is integration and its recognised weakness is looseness (it can become a checklist rather than an explanation), but it remains the field's standard rebuke to both eliminative brain-reductionism and to a psychology that ignores biology. In a viva, "the biopsychosocial model is how psychiatry escapes Cartesian dualism in daily practice" is the line that ties the whole topic together.

HOLD THIS

The mind is a real, emergent, causally potent level of a physical system. Not reducible to its neurons and not a separate ghost; the biopsychosocial model (Engel 1977) is psychiatry's practical, principled escape from Cartesian dualism.

10.11 Why it matters for psychiatry II: the brain-disease debate and free will

Where the metaphysics touches responsibility. Two live controversies show the stakes are not academic. First, the *brain-disease* framing of addiction: Kaplan and Sadock (2024) criticise the neurocentric NIDA model ("addiction is a chronic, relapsing brain disease") precisely as eliminative reductionism, because it leaves the addicted *person*, the agent who retains substantial control and whose choices meditate recovery, in the shadows; the corrective is that neural correlates and voluntariness coexist. Second, *free will and responsibility*: if the mind is nothing but neurons obeying physical law (hard determinism, and the natural reading of epiphenomenalism), the ground for holding people responsible seems to vanish, which matters directly for forensic psychiatry and the insanity defence. Most psychiatrists work with a *compatibilist* stance, that meaningful agency and responsibility are consistent with a physical brain, which is again the property-dualist / biopsychosocial position applied to the will: the person is a real causal level, not an illusion painted over the neurons.

MNEMONIC

"SIP-EF" for the positions: Substance, Interactionism, Property (dualism); Epiphenomenalism between; then the monist Family (Identity, Functionalism, Emergentism)

Read left to right it is a ladder from "most separate" (substance dualism) to "least separate" (identity theory), with property dualism and emergentism as the clinically preferred middle where mind is real but not a separate stuff.

PEARL

The two halves are one argument. Sensory deprivation shows the mind actively constructs experience rather than passively receiving it, which is why removing the world produces hallucination, not blankness. The mind-body problem asks what that constructing mind *is*. The psychiatric answer to both is the same: the mind is a real, emergent, causally potent level of a physical system, not reducible to its neurons and not a separate ghost. Hold that, and you can say why the ICU patient hallucinates, why "chemical imbalance" is a half-truth, and why the biopsychosocial model is not woolly but principled.

GOOD TO REMEMBER

- **Sensory deprivation:** drastic sustained reduction of patterned input; the brain, still predicting, generates its own content.
- **Hebb / McGill studies (Bexton, Heron and Scott 1954):** lightproof-soundproof cubicle, goggles and cuffs; volunteers quit within days; impaired thinking and visual hallucinations. [verify author-year and design details]
- **Lilly isolation tank (John C. Lilly, from 1954):** flotation in body-temperature salt water, total dark and silence; altered states, "higher consciousness." [verify start year]
- **Effects triad:** perceptual (illusions then complex hallucinations, mostly visual), cognitive (impaired attention, disorganised thought, time distortion, suggestibility), affective (restlessness, anxiety, urge to escape; some find it relaxing).
- **Three scientists in tanks (K&S 2024):** one few illusions/no hallucinations, one many illusions/faint hallucinations, one vivid complex hallucinations; individual variability is the point.
- **Perceptual release (Hughlings Jackson; West 1962):** reduced input plus lost gating releases stored images as hallucinations; supersensitivity-deprivation hypothesis is the complement.
- **Clinical relevance:** REST (therapeutic, controlled, Suedfeld); solitary confinement (harmful, "SHU syndrome"); ICU (contributes to delirium; needs patterned oriented stimulation).
- **Mind-body problem:** relation of mental to physical; modern statement from Descartes (1596 to 1650), substance dualism, res cogitans vs res extensa (term via Damasio 1994).
- **Dualism, substance / interactionism (Descartes):** two substances causally interact; fails on the interaction problem (energy conservation).
- **Epiphenomenalism:** brain causes mind, mind causes nothing (the whistle, not the engine); makes consciousness causally inert.
- **Property dualism (K&S 2024's working stance):** one physical substance, two irreducible property-types; brain vs mind = different levels of description.
- **Identity theory (type physicalism):** mental state = brain state ("C-fibre firing"); criticised via multiple realisability.
- **Functionalism:** mental state defined by functional/causal role, not substrate; solves multiple realisability; charged with omitting qualia.
- **Emergentism:** mind a novel, real, non-reducible emergent property of complex organised matter.
- **Reductionism:** constitutive (study by parts, uncontroversial) vs eliminative (explains the mental away; rejected by K&S; the Shakespeare-and-ink image).
- **Treatment-etiology fallacy:** a treatment working at a level does not prove the cause lies there.
- **Explanatory gap (Levine 1983) / hard problem (Chalmers 1995):** why is there something it is like to be conscious; qualia = felt subjective qualities. Nagel's bat (1974); Jackson's Mary (1982).
- **Biopsychosocial model (Engel 1977):** interacting biological, psychological, social levels; psychiatry's practical escape from Cartesian dualism; strength = integration, weakness = looseness.
- **Brain-disease / free-will debate:** eliminative "addiction is a brain disease" critiqued (neural correlates and voluntariness coexist, K&S 2024); most psychiatrists compatibilist on responsibility.

The three depth-psychology schools

11 · Freud and psychoanalysis

The first of the depth schools. Psychoanalysis is both a theory of mind and a treatment. Freud proposed that behaviour is governed by unconscious wishes and conflicts, that early childhood shapes the adult, and that these hidden forces can be reached and modified through a disciplined

verbal method. Every later depth-psychology school (Adler, Jung, Erikson, object relations, self psychology) defines itself by what it kept from Freud and what it rejected, so the exam expects you to hold his two models of mind, the five psychosexual stages with their ages and fixations, the core techniques, and the story of the circle that carried and then splintered the movement.

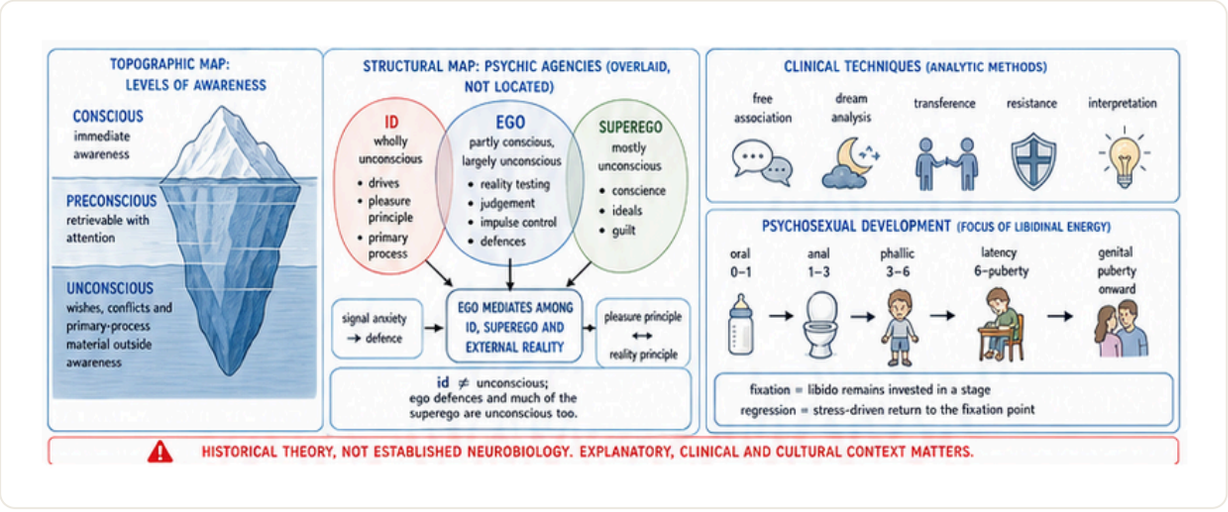


Fig 4.13 Freud's two maps of the mind.

Psychoanalysis rests on three assumptions Freud held throughout (Kaplan & Sadock 2024): *psychological determinism* (no mental event is accidental; symptoms, dreams and slips have meaning), *unconscious mental processes* (much of mind is outside awareness), and *unconscious psychological conflict* (neurosis arises from clashing psychic forces). Note at once: this is a stage-and-concept theory, not one of the general cognitive functions, so it is examined as a system to be enumerated rather than as an evolution toward a currently accepted mechanism.

11.1 The topographic model: three systems of mind

Ucs, Pcs, Cs. Freud's first structural picture (from *The Interpretation of Dreams*, 1900) classified mental contents by their relation to awareness into three systems (Kaplan & Sadock 2024). The **unconscious** (Ucs) holds repressed wishes and drive-representations; it obeys the *pleasure principle* and works by *primary process* thinking (timeless, illogical, tolerating contradiction, using condensation and displacement, seeking immediate discharge). The **preconscious** (Pcs) holds material that is not conscious now but can be summoned; it obeys the *reality principle* and *secondary process* thinking (logical, verbal, tolerating delay). The **conscious** (Cs) is the small surface in immediate awareness. In this model the therapeutic aim was simply to lift repression, making the unconscious wish conscious.

11.2 The structural model: id, ego, superego

The tripartite mind (1923). Freud found the topographic model inadequate because the forces producing resistance and guilt were themselves unconscious, so the ego could not simply equal consciousness. In *The Ego and the Id* (1923) he introduced the **structural model** (the tripartite theory) of three agencies (Kaplan & Sadock 2024). The **id** is wholly unconscious, the primordial reservoir of sexual and aggressive drive energy, ruled by the pleasure principle and primary process. The **ego** is the executive mediator between id, superego and external reality; it is partly conscious but largely unconscious, and it carries out reality testing, judgment, impulse control,

affect regulation and the deployment of defences. The **superego** holds internalised parental and social morals, ideals and prohibitions; it is the seat of conscience and guilt and is again mostly unconscious. Crucially id and Ucs are not synonymous, because ego defences and most of the superego are also unconscious.

TRAP **"Id" and "unconscious" are not the same.** The id is wholly unconscious, but ego defences and most of the superego are unconscious too, so the two models classify by different criteria (awareness versus function).

11.3 Libido, drives and the two principles

The economic idea. **Libido** is the mental energy of the sexual (life) instincts, a displaceable quantity (cathexis) that presses for discharge. Freud used "sexual" in an extended sense to mean bodily pleasurable, which is why feeding and toilet control count as psychosexual. Mental life is a compromise between the *pleasure principle* (the demand for immediate gratification and tension reduction, native to id and unconscious) and the *reality principle* (the ego's capacity to postpone gratification and adapt to the external world). Maturation is broadly the shift from pleasure-principle to reality-principle governance. Cross-reference the Social, Learning & Personality Psychology notes for the full defence-mechanism catalogue and for the object-relations extension of these ideas.

11.4 The five psychosexual stages

Erogenous zones and conflicts. Freud held that libidinal energy settles successively on a leading body zone, each stage posing a developmental conflict; unresolved conflict leaves a *fixation* that colours adult character (Kaplan & Sadock 2024). Personality is largely set by about age five. The ages below are the standard textbook bands; treat them as approximate rather than sharp cut-offs.

Oral (birth to about 1 year)

Zone: mouth. Pleasure through sucking and biting; the infant is wholly dependent, so trust and dependency are at stake. Central conflict: weaning. Fixation gives oral traits: dependency, passivity or (biting phase) verbal aggression and sarcasm, and habits such as smoking, over-eating and nail-biting.

Anal (about 1 to 3 years)

Zone: bowel and bladder control. Central conflict: toilet training, autonomy versus control. Over-strict or early training yields the *anal-retentive* (orderly, parsimonious, obstinate, obsessional) character; over-lenient training yields the *anal-expulsive* (messy, wasteful, defiant) character. This stage is the classic root of obsessional traits.

Phallic (about 3 to 6 years)

Zone: genitals. The *Oedipus complex* (in boys) is the wish to possess the mother and displace the father, checked by *castration anxiety*; the analogous *Electra complex* (a term from Jung, not Freud) and *penis envy* were proposed for girls. Resolution comes through identification with the same-sex parent, which internalises parental morality and so forms the **superego**. Karen Horney countered penis envy with the concept of *womb envy*.

Latency (about 6 to puberty)

Sexual drives are relatively dormant and repressed; energy is channelled into schooling, skills, hobbies and same-sex peer relations. Ego and superego consolidate. Fixation impairs later social competence and intimacy.

Genital (puberty onward)

Libido re-emerges and, if earlier stages resolved, matures into stable heterosexual object-love with a capacity to work and to care for others. In Freud's scheme the well-resolved adult can love and work.

Fixation and regression. *Fixation* is arrested libido that stays partly invested in an earlier stage; *regression* is a retreat, under stress, to an earlier fixated stage. The two link: the point of fixation determines the point to which one regresses, which is how psychoanalysis tied adult symptom pictures back to specific childhood stages. Karl Abraham later refined the schema, splitting the oral stage into sucking and biting phases and the anal stage into destructive-expulsive (anal-sadistic) and mastering-retaining (anal-erotic) phases.

HOLD THIS

Five stages by body zone: oral, anal, phallic, latency, genital; the superego forms at the Oedipal resolution. Fixation is energy left at a stage; regression is retreat to the fixation point under stress, and the fixation point sets where one regresses to.

11.5 Core techniques of classical analysis

How the method works. Classical psychoanalysis makes the unconscious conflict available for interpretation through a small set of tools (Kaplan & Sadock 2024).

Free association

The *fundamental rule*: the patient reports whatever comes to mind without censoring. Breaks and blocks in the flow mark *resistance*, pointing to where defended material lies.

Dream analysis

Dreams are "the royal road to the unconscious." The remembered *manifest content* is decoded, via the dreamer's associations, to the underlying *latent content* (the disguised wish); the disguising work uses condensation, displacement, symbolisation and secondary revision.

Transference

The patient unconsciously redirects feelings and templates from important early figures onto the analyst. Rather than a nuisance, the *transference neurosis* is the central working material, letting old conflicts be re-lived and interpreted in the room.

Countertransference

The analyst's own emotional reactions to the patient. Freud first saw it as interference; modern analysis treats it as a source of information about what the patient evokes.

The analytic frame

The fixed conditions that make the method possible: the couch with the analyst out of view, high session frequency, a stable time and fee, and the analyst's stance of *neutrality* and *abstinence*. Interpretation and *working through* (repeated interpretation across contexts until insight holds) do the therapeutic work.

11.6 The circle and the Wednesday Society

From a Vienna sitting-room to a movement. In 1902 Freud gathered a handful of physicians for weekly discussion in the **Wednesday** Psychological Society, meeting in his waiting room; early members included Alfred Adler, Wilhelm Stekel, Otto **Rank** (its long-serving secretary) and Hanns **Sachs**, with Paul Federn joining soon after. In 1908 the group was formally reconstituted as the **Vienna psychoanalytic** Society, and the circle widened internationally to Sandor **Ferenczi** in Budapest, Karl **Abraham** in Berlin, **Ernest Jones** in Britain, Max Eitingon, and, most prominently, Carl Jung in Zurich, whom Freud favoured as heir and installed as first president of the International Psychoanalytical Association (1910). To guard doctrinal orthodoxy after the early breaks, Jones proposed a *secret committee* (1912 to 1913) of trusted loyalists, to whom Freud gave engraved Greek intaglio rings.

The defections. The movement fractured over the primacy Freud gave to sexuality and libido. Alfred Adler left in 1911, replacing libido with the striving for superiority and the inferiority complex (individual psychology); Stekel departed the same period (1912) over orthodoxy; Carl Jung broke in 1913, recasting libido as a general psychic energy and adding the collective unconscious and archetypes (analytical psychology); and Otto Rank drifted away in the mid-1920s after emphasising the birth trauma. These splits are examined the Social, Learning & Personality Psychology notes and in the Adler and Jung topics as the birth of the rival depth schools.

PEARL

Two models, one mind: the topographic model classifies mental contents by *awareness* (Ucs, Pcs, Cs), the structural model by *function* (id, ego, superego). They coexist rather than the second erasing the first. The ego and superego straddle both, which is exactly why "unconscious" and "id" are not the same thing.

COMMON TRAP

The *Electra complex* and *penis envy* are frequently miscredited to Freud in full. Freud described the girl's phallic conflict and penis envy; the term "Electra complex" was coined by Jung. Also do not confuse *fixation* (energy stuck at a stage) with *regression* (retreat to an earlier stage under stress).

CLINICAL ANCHOR

Psychosexual character types still cue clinical pattern recognition: anal-retentive traits (orderliness, parsimony, obstinacy) map onto the obsessional character, and oral fixation onto dependency and substance-seeking. These are heuristics, not diagnoses; the fixation ages themselves are not empirically validated, so cite them as Freudian theory.

MNEMONIC

Old (Oral) Age (Anal) Pensioners (Phallic) Love (Latency) Grapes (Genital)

Reads the five stages in order. For the ego's job, remember it serves "three masters": the id, the superego, and external reality.

GOOD TO REMEMBER

- **Topographic model (1900):** unconscious (pleasure principle, primary process), preconscious, conscious (reality principle, secondary process).
- **Structural model (1923, *The Ego and the Id*):** id (drives, pleasure principle), ego (mediator, reality testing), superego (conscience, formed at Oedipal resolution).
- **Oral:** birth to about 1 year, zone mouth, conflict weaning; fixation gives dependency, smoking, over-eating.
- **Anal:** about 1 to 3 years, zone bowel/bladder, conflict toilet training; fixation gives retentive (obsessional) or expulsive character.
- **Phallic:** about 3 to 6 years, zone genitals, Oedipus/Electra complex, castration anxiety and penis envy; superego forms here.
- **Latency:** about 6 to puberty, drives dormant, social and skill development.
- **Genital:** puberty onward, mature object-love, capacity to love and work.
- **Fixation vs regression:** fixation = energy left at a stage; regression = retreat to the fixation point under stress.
- **Techniques:** free association (fundamental rule), dream analysis (manifest to latent), transference, countertransference, the analytic frame (couch, neutrality, abstinence, working through).
- **Wednesday Psychological Society:** founded 1902 in Freud's waiting room.
- **Vienna Psychoanalytic Society:** renamed 1908; International Psychoanalytical Association founded 1910 (Jung first president).
- **Circle members:** Adler, Stekel, Rank, Sachs, Federn, then Ferenczi, Abraham, Ernest Jones, Eitingon, Jung.
- **Secret committee (1912 to 1913):** Jones's loyalist inner ring, marked by Freud's engraved rings.
- **Defections over primacy of sexuality/libido:** Adler 1911 (individual psychology), Stekel 1912, Jung 1913 (analytical psychology), Rank mid-1920s (birth trauma).

12 · Adler and individual psychology

Adler is the **second primary school** of the psychodynamic tradition and, for the exam, the cleanest contrast case to Freud: where Freud made the unconscious sexual drive the engine of the mind, Adler made a conscious, forward-pulling **striving** the engine, and made the person's embeddedness in a social world the measure of health. His system is called **individual psychology**, a name that is routinely misread. It does not mean a psychology of the isolated individual; it comes from the Latin *individuum*, meaning **indivisible,** and asserts that the person is a single unified whole (holism) that cannot be split into warring drives and agencies the way Freud split the psyche. Adler (1870 to 1937), an Austrian general physician, was one of the original members of Freud's Vienna circle from 1902, rose to president of the Vienna Psychoanalytic Society, and in 1911 broke away, the first of the inner circle to leave, because he rejected the primacy of the libido and the sexual origin of neurosis (Kaplan & Sadock 2024).

The examinable core is a small chain of concepts that hang together: an **inferiority feeling** is universal, it drives a **striving for superiority** (better read as striving for competence or perfection), that striving is organised by a self-chosen goal (fictional finalism) into a consistent **style of life**, and the whole enterprise is healthy only insofar as it is turned outward toward others as **social interest**. Learn the chain and you can place any Adlerian term. Because this topic names a theorist, dated events, and a set of hard classifications (inferiority versus superiority complex, birth-order positions, safeguarding tendencies), it closes with a good-to-remember box that enumerates them (Kaplan & Sadock 2024; The Psychotherapy Guidebook 1976).

12.1 Individual psychology: the person as an indivisible, goal-directed whole

Holism plus teleology is the frame. Adler's two founding commitments are that the person is a *unit*, not a collection of drives divided against themselves, and that behaviour is *future-directed*. He called the second principle **dynamism**: in every individual the psyche moves toward a goal, and once the goal is set the whole psychic apparatus, memories, dreams, perceptions, shapes itself to attain it. This is a **teleological** account (explanation by final cause, the goal ahead) and it is the sharpest break from Freud's causal, backward-looking model in which the past determines the present. For Adler the person is not pushed from behind by instinct but pulled from in front by a chosen aim, and because the goal is chosen it can be changed, which is what makes therapy possible (Kaplan & Sadock 2024).

RULE **Adler is teleological, Freud causal.** Freud is pushed from behind by buried sexual conflict; Adler is pulled from in front by a chosen goal, and "individual" means indivisible whole (holism), not the isolated individual.

12.2 Organ inferiority: the biological seed

Adler's earliest idea, and the root of the whole system. Before the psychology came the medicine. In his *Study of Organ Inferiority* (Adler 1907), a constitutionally weak or defective organ (poor eyesight, weak lungs, poor eye-hand coordination) was shown to provoke **compensation**: the organism, or the person, works to overcome the deficit, sometimes overshooting into **overcompensation** and turning the weak point into a strength. The classic illustration is the stammerer who becomes an orator. Adler then generalised this bodily principle into a psychological law: the felt weakness drives the striving that builds the personality. Organ inferiority is thus the concrete biological seed from which the broader *inferiority feeling* grows (Kaplan & Sadock 2024).

12.3 The inferiority feeling and the striving for superiority: the great upward drive

This is the master motive of the whole theory. Every child begins life small, weak, and dependent among larger, more capable adults, so a **feeling of inferiority** is universal and normal, not pathological. The response to it is the single dynamic force Adler placed at the centre of personality: the **striving for superiority**, better translated as striving for significance, competence, mastery, or perfection, the "great upward drive" from a felt minus toward a felt plus. Adler was explicit that this is the one master motive to which all traits and drives are subordinated: standing before the unknown, each person strives to become more perfect and

complete. Note the exam point that Adler *himself* shifted the emphasis over his career, from raw compensation for weakness toward a positive striving for self-realisation, so "superiority" here means self-perfection, not domination over others (The Psychotherapy Guidebook 1976; Kaplan & Sadock 2024).

12.4 Inferiority complex versus superiority complex: the two pathological outcomes

Distinguish the normal feeling from the pathological complex. The universal inferiority *feeling* is the engine of healthy growth. It becomes pathological when the person cannot move from the felt minus to a felt plus and instead becomes stuck. The two failures are mirror images and are a favourite discriminate.

Inferiority complex

An exaggerated, entrenched sense of inadequacy in which the normal inferiority feeling is not overcome but overwhelms the person, producing discouragement, avoidance, and a retreat from life's tasks. The term entered ordinary language; Adler coined it.

Superiority complex

A defensive overcompensation: the person masks deep inferiority behind a facade of arrogance, boastfulness, vanity, or a drive to dominate. It is not the opposite of the inferiority complex but its concealment, the same wound covered by bluster.

> **COMMON TRAP**
>
> Do not equate the *inferiority feeling* (universal, normal, motivating) with the *inferiority complex* (pathological, entrenched, disabling). The feeling drives healthy striving; the complex is striving that has failed and calcified. And the superiority complex is not the healthy striving for superiority: it is a mask *over* inferiority, so a boastful, domineering patient is showing you a hidden inferiority complex, not confidence.

12.5 Fictional finalism: the guiding self-ideal

The goal that organises everything is an invented one. Adler borrowed from the philosopher Hans Vaihinger the idea that people live by useful fictions, "as if" propositions that are not literally true but guide action. The person's central fiction is a **guiding self-ideal** or **final goal**, an imagined picture of the self as complete, significant, and secure, toward which all behaviour is aimed. This is **fictional finalism** (also called the guiding fiction): the final goal is subjective and largely out of awareness, yet it is the true cause of the person's movements. Two people with the same objective circumstances live utterly differently because they aim at different fictional goals. This is the mechanism that makes Adler teleological in practice: understand the patient's fictional final goal and the apparently disparate pieces of the life snap into a single pattern (Kaplan & Sadock 2024; The Psychotherapy Guidebook 1976).

12.6 Style of life: the unique, early-set signature of striving

The consistent pattern by which a person pursues the final goal. The **style of life** (lifestyle) is the individual's characteristic, unified way of striving toward significance, the personal method of solving the three great tasks of life, work, friendship (society), and love (sexuality). It forms early, by roughly age four to five, out of the child's constitution, family atmosphere, and creative

interpretation of its situation, and then runs as a single theme through everything the person perceives and does; it is, in effect, the person's perceptual style. Crucially the style of life is not simply stamped in by heredity or environment. Adler insisted on the **creative self** (creative power): the child actively, creatively interprets and responds to its circumstances, so two children in the same family build different lifestyles. If you grasp a patient's style of life, their behaviour stops looking random and starts making sense (The Psychotherapy Guidebook 1976).

12.7 Social interest (Gemeinschaftsgefuhl): the index of mental health

This is the single most examinable Adlerian concept. **Social interest** renders Adler's German *Gemeinschaftsgefuhl*, literally community feeling: an innate but developable capacity to feel with and for others, to identify with the human community, and to contribute to the common good rather than pursue private superiority. For Adler this is the *criterion of mental health*. The healthy person turns the upward striving outward, into socially useful contribution; the neurotic and the criminal turn it inward, striving for a personal superiority on the "useless side of life" at others' expense. Adler summarised the whole diagnosis in one line: the more social interest a person has, the fewer feelings of inferiority they carry, and the aim of therapy is to increase the patient's sense of belonging and contribution. Distinguishing neurosis from psychosis in his system also runs on this axis: the neurotic *retains* social interest but is blocked from life goals by symptoms, whereas the psychotic *loses* social interest and retreats into a private world (Kaplan & Sadock 2024; The Psychotherapy Guidebook 1976).

> **PEARL**
>
> If one word survives from Adler into the exam, it is *social interest* (Gemeinschaftsgefuhl) as the yardstick of mental health. Freud measures health by the capacity to love and to work; Adler measures it by the capacity to contribute to the community. A patient whose striving is all private ambition with no social feeling is, in Adler's terms, unwell however successful they look.

12.8 Birth order and the family constellation

Adler's most popularly known and most testable classification. Adler argued that a child's *psychological* position in the **family constellation**, not the birth date as such, shapes the lifestyle, because each position offers a different situation to interpret. He is credited as the first theorist to make birth order a serious variable in personality.

POSITION	ADLER'S CHARACTERISTIC SITUATION	TYPICAL TENDENCY
First-born (oldest)	**"Dethroned" by the arrival of a sibling, having once been the sole focus**	Tends toward conservatism, order, and authority; may become achievement-oriented or, if the loss is felt as trauma, insecure
Second / middle	Grows up with a "pacemaker" ahead to overtake, never had the parents alone	**Ambitious, competitive, often better adjusted; may become the social activist, open to change**
Youngest	Never displaced, surrounded by older models, often pampered	Can be highly driven to surpass all others, or dependent and spoiled if over-indulged
Only child	Never shares the parents; adult world is the reference	**Precocious with adults but may struggle when not the centre; risk of pampering**

Adler's birth-order positions and their characteristic situations: it is the child's interpreted *psychological* position in the family constellation, not the ordinal number, that shapes lifestyle (Kaplan & Sadock 2024).

12.9 Safeguarding tendencies and the masculine protest

Two named defensive concepts examiners like to surface. When the fictional goal of superiority is threatened, the person protects self-esteem rather than face reality, and Adler called these manoeuvres **safeguarding tendencies**, his forward-looking, self-esteem-protecting counterpart to Freud's defence mechanisms. They include *excuses* (the neurotic symptom offered as an alibi, "I would succeed, but for this"), *aggression* (depreciating others, accusation, self-accusation to secure superiority), and *distance-seeking* (moving backward, standing still, hesitating, or constructing obstacles so as never to risk the test). The **masculine protest** is his term for the overstriving, in either sex, to escape a felt "feminine", that is weak, inferior, submissive, position toward an idealised "masculine", strong, dominant one; Adler used it to reframe as a social-power struggle what Freud had explained sexually (for example penis envy), locating the drive in the culture's overvaluing of masculinity rather than in anatomy (Kaplan & Sadock 2024).

12.10 The 1911 break from Freud

Know why he left, not just that he left. Adler joined Freud's discussion circle in 1902 and became president of the Vienna Psychoanalytic Society, but he never accepted the pillars of Freud's system: the primacy of the libido, the sexual origin of neurosis, and the determining power of infantile sexual wishes. Where Freud looked backward to buried sexual conflict, Adler looked forward to a chosen goal; where Freud saw a psyche split into id, ego, and superego, Adler saw an indivisible whole; where Freud made drive central, Adler made social embeddedness central. The disagreement was irreconcilable, and in 1911 Adler resigned, taking a group of followers with him and founding individual psychology, the first major secession from psychoanalysis (Jung's followed in 1914) (Kaplan & Sadock 2024; The Psychotherapy Guidebook 1976).

12.11 Theory of psychopathology: the mistaken style of life

Neurosis is a discouraged, socially useless lifestyle, not repressed sex. For Adler, emotional disorder springs from a **mistaken style of life** built on false ideas about the self and the world and on goals of private superiority that lead away from social usefulness. The pampered child, for instance, grows up expecting others to serve them, avoids responsibility, blames others for failures, and yet feels chronically insecure because their whole worth depends on being served. When such a lifestyle meets a real challenge it cannot solve, symptoms appear, and the symptoms have a *purpose*: they protect self-esteem and provide an excuse ("I could have, but for this illness") while letting the person sidestep the task they fear. Pathology is thus discouragement plus deficient social interest, and it is correctable by insight and re-education because the goal that organises it was chosen (Kaplan & Sadock 2024).

HOLD THIS

Social interest (Gemeinschaftsgefuhl) is Adler's yardstick of mental health. The neurotic retains it but is blocked by symptoms; the psychotic loses it and retreats into a private world.

12.12 Therapy and legacy: encouragement, early recollections, and the line into CBT

Adlerian technique is brief, active, collaborative, and re-educative. The therapist works with the patient as an equal to uncover the style of life and its mistaken goals, then *re-orients* the patient toward socially useful living. The signature tools are **encouragement** (the therapeutic antidote to discouragement, building the patient's confidence to attempt life's tasks), **early recollections** (the earliest memories, read not as historical fact but as a projective clue to the present lifestyle, since what is remembered is selected to fit the current goal), analysis of **birth order and dreams** (dreams as an expression of present-day concerns and problem-solving, not disguised infantile wishes), and **task-setting** (assigning concrete, graded real-world tasks). Adler anticipated much of what came later: his focus on mistaken beliefs and faulty perceptions of self and world prefigured **cognitive therapy** (Beck and Ellis both acknowledged the debt); his stress on the person's inherent worth, agency, and phenomenology fed the **humanistic** tradition (Maslow, Rogers); and his attention to the family constellation and the person shaping their own interpersonal world seeded **family-systems** thinking. His techniques of *reframing* and *paradoxical intention* are now standard across schools (Kaplan & Sadock 2024).

CLINICAL ANCHOR

A high-achieving professional presents with paralysing procrastination on the one project that would confirm their talent. Freud might hunt an unconscious conflict; Adler asks what the delay *achieves*. The unfinished work is a safeguarding tendency: while the project is incomplete the fictional self-ideal of "the great talent" is never put to the test and cannot fail. Adlerian therapy names the mistaken goal (superiority without risk), reframes the procrastination as protection of a fragile self-estimate, and sets a graded real task to rebuild courage and turn striving back toward useful contribution.

INDIA

Birth-order and family-constellation reasoning translates readily to the large, multi-generational Indian joint family, where the eldest son's "dethronement" and burden of expectation, or the youngest's pampering, are lived realities rather than abstractions. Adler's *social interest* also maps onto collectivist framings of the self as embedded in family and community, which can make his community-feeling yardstick of health intuitive in the Indian setting; the caution is not to read culturally normative interdependence as pathological dependency.

MNEMONIC

I Saw For Sure Some Big Sisters Mock

Adler's eight examinable concepts in order: **I**nferiority feeling, **S**uperiority striving, **F**ictional finalism, **S**tyle of life, **S**ocial interest, **B**irth order, **S**afeguarding tendencies, **M**asculine protest. Run the sentence and you have recalled the spine of individual psychology.

GOOD TO REMEMBER

- **Alfred Adler (1870 to 1937):** Austrian physician; founder of *individual psychology* ("individual" = indivisible whole, holism).
- **Circle and break:** joined Freud's Vienna circle 1902, became president of the Vienna Psychoanalytic Society, resigned 1911 (first major secession) over the primacy of libido and the sexual origin of neurosis.
- **Organ inferiority (1907):** a weak organ provokes compensation / overcompensation; the biological seed of the theory.
- **Inferiority feeling:** universal and normal (the small child among adults); the engine of healthy striving.
- **Striving for superiority:** the single master motive; the "great upward drive" from felt minus to plus; means self-perfection / competence, not domination.
- **Inferiority complex:** entrenched, disabling sense of inadequacy (term coined by Adler).
- **Superiority complex:** arrogant overcompensation masking a hidden inferiority.
- **Fictional finalism (guiding fiction):** a subjective, mostly unconscious final self-ideal that pulls all behaviour (borrowed from Vaihinger's "as if").
- **Style of life:** the unified, unique pattern of striving; set by about age four to five; shaped by the *creative self*, not just heredity/environment.
- **Three life tasks:** work, friendship (society), and love (sexuality).
- **Social interest (Gemeinschaftsgefuhl):** community feeling; the *index / criterion of mental health*; neurosis retains it, psychosis loses it.
- **Birth order / family constellation:** psychological position shapes lifestyle, first-born "dethroned"; second/middle competitive; youngest driven or pampered; only child precocious but risk of pampering.
- **Safeguarding tendencies:** self-esteem-protecting manoeuvres (excuses, aggression, distance-seeking); Adler's forward-looking analogue of defence mechanisms.
- **Masculine protest:** overstriving to escape a felt "weak/feminine" position; his social-power reframing of Freud's sexual account.
- **Therapy tools:** encouragement, early recollections, dream and birth-order analysis, task-setting, reframing, paradoxical intention; brief, active, egalitarian, re-educative.
- **Legacy:** anticipated cognitive therapy (Beck, Ellis), humanistic psychology (Maslow, Rogers), and family-systems thinking.

13 · Jung and analytical psychology

Jung is the **third primary school** of the psychodynamic tradition and, for the exam, the school that pushed the unconscious deepest and widest: Freud made it a personal repository of repressed sexual wishes, Adler barely used it, but Jung split it into a *personal* layer and a *collective* layer inherited by the whole species. His system is called **analytical psychology** (to distinguish it from Freud's psychoanalysis and Adler's individual psychology). Carl Gustav Jung (1875 to 1961), a Swiss psychiatrist who worked under Bleuler at the Burgholzli, was Freud's chosen heir and the first president of the International Psychoanalytic Association, then broke away in 1913 over the nature of libido, and founded the school that developed the concepts of the **collective unconscious**, the **archetypes**, and the two personality attitudes **introversion** and **extraversion** (Kaplan & Sadock 2024).

The examinable spine is a layered map of the psyche plus a typology. The map runs ego at the surface, then the personal unconscious holding the **complexes**, then the collective unconscious holding the archetypes (persona, **shadow**, anima/animus, the Self, the wise old man, the great mother). The typology crosses two attitudes with four functions and is the direct ancestor of the MBTI. The goal of the whole enterprise is **individuation**. Because this topic names a theorist, a dated break, a fixed set of psychic structures, the named archetypes, and hard classifications of attitude and function, it closes with a good-to-remember box that enumerates every one (Kaplan & Sadock 2024; Companion to Psychiatric Studies).

13.1 The word-association test: Jung's empirical root and the birth of the "complex"

Start where the exam rarely does, with the data. Jung's earliest and most rigorously empirical work at the Burgholzli was the **word-association test**: a standard list of stimulus words is read aloud and the patient responds with the first word that comes to mind, while the examiner times the reaction. Jung noticed that certain words provoked disturbances, a delayed reaction time, an unusual or absent response, repetition of the stimulus, or bodily signs measured by the galvanic skin response. He inferred that these disturbances clustered around emotionally charged themes, and he named such a cluster a **complex**: a group of unconscious ideas bound together by a common emotional tone (Kaplan & Sadock 2024). This is the origin of the everyday word "complex," and it is worth stressing that Jung's central construct was born from a laboratory reaction-time procedure, not from the couch. It was this work on complexes, and its relevance to the meaning of psychotic symptoms, that first drew Freud and Jung together.

13.2 The structure of the psyche: ego, personal unconscious, collective unconscious

Learn the three-layer model as a nested map. Jung replaced Freud's id-ego-superego apparatus with a layered psyche. At the surface sits the **ego**, the centre of conscious life and the bridge to external reality (in Jungian terms the ego is itself a complex). Below it lies the **personal unconscious**, the equivalent of Freud's unconscious, a repository of an individual's own repressed or forgotten memories, and the home of the complexes. Deeper still, and this is Jung's radical addition, lies the **collective unconscious** (also called the objective psyche): a shared, inherited stratum that is not personal at all but is the residue of humankind's evolutionary and ancestral past, "much as human DNA is an aggregate of the past" (Kaplan & Sadock 2024). The

collective unconscious houses the instincts, the potential for creativity, and the archetypes. Note the exam-critical boundary: complexes live in the personal unconscious, archetypes live in the collective unconscious.

RULE **Complexes sit in the personal unconscious, archetypes in the collective.** The archetype is the inherited mould; the complex is the personal cast filled in by lived experience.

13.3 Complexes and archetypes: how the two connect

An archetype is the inherited mould; a complex is what gets cast in it. A **complex** is a group of unconscious ideas around an emotionally toned experience, endowed with psychic energy from its affective charge; the more intense the complex, the greater its pull on imagery, emotion, and action, and a dormant complex can be stimulated by an external cue (a father complex fired by an older friend, or by music that evokes father memories) and then rise to dominate consciousness (Kaplan & Sadock 2024). Crucially, complexes are built around **archetypes**: genetically determined, universal, inherited predispositions to perceive and act in typically human ways (nurturance, aggression). The archetype supplies the inborn template; lived experience fleshes it out into a personal complex. Jung's own illustration is the *earth mother*: every infant is born with a dim, universal model of an all-nurturing caretaker (the mother archetype), and the individual's actual mother complex emerges as that template meets real mothering. Archetypes surface in dreams, myths, and fantasies as **primordial images** (the many-breasted animal as unlimited nurturance, the mandala as wholeness) that recur across cultures without transmission (Companion to Psychiatric Studies; Wolberg 1988).

13.4 The named archetypes: persona, shadow, anima/animus, the Self

These four (plus the great mother and wise old man) are the ones examiners want by name. Several universal archetypes attend the ego and structure the personality.

Persona

The public personality, the social mask that mediates between the ego and the outer world; the face one shows to others. Named after the mask of the classical actor. Over-identification with the persona (being only one's role) is a recognised pathology.

Shadow

The reverse image of the persona: the sum of traits unacceptable to the persona, whether negative or, importantly, positive. A brave persona has a fearful shadow. The shadow's archetype is the enemy or feared intruder, and its unacknowledged contents are the material most readily projected onto others.

Anima / animus

The contrasexual archetype. The *anima* is the residue of all experience of woman in a man's psychic heritage; the *animus* is the residue of all experience of man in a woman's. It connects the ego to the inner world and is projected onto partners in intimate relationships.

The Self

The archetype of wholeness and the innate ordering principle of the whole psyche, the unconscious centre that directs psychic life and gives rise to the ego. Not to be confused with the ego: the Self is the totality, the ego only the conscious fragment. Often symbolised by the mandala.

Two further named archetypes carry the personified wisdom and nurturance of the collective unconscious: the **wise old man** (the archetype of meaning, spirit, and guidance, appearing as the sage, teacher, or magician) and the **great mother** (the archetype of nurturance and of creation-and-destruction, the earth mother above) (Kaplan & Sadock 2024).

COMMON TRAP

Do not conflate the *ego* with the *Self*. In Jung the ego is only the centre of consciousness, a small part; the Self is the archetype of the whole psyche, conscious and unconscious together, and is the goal that individuation moves toward. Inflation of the ego with the Self's power (mistaking the part for the whole) is, for Jung, a route to grandiosity; being cut off from the Self yields alienation and depression. Likewise the *persona* is the outward mask and the *shadow* is the disowned inner opposite; they are complementary, not the same axis as ego and Self.

13.5 The two attitudes and four functions: Jung's typology behind the MBTI

This is the most widely known part of Jung and the highest-yield to memorise cleanly. Jung's **psychological types** (from *Psychological Types*, 1921) combine two *attitudes* of energy orientation with four *functions* of psychological activity. The two attitudes are **extraversion** (energy oriented outward, to others and the world of objects) and **introversion** (energy oriented inward, to the subject's own inner world); Jung himself described his type as an introverted intuitive. The four functions split into two pairs. The two *rational* (judging) functions are **thinking** (evaluating by logic) and **feeling** (evaluating by values and relationship, not by logic, so "feeling" here means valuing, not emotion). The two *irrational* (perceiving) functions are **sensation** (grasping a situation by assembling its concrete details, seeing the trees first) and **intuition** (grasping the whole first, seeing the forest). Everyone has all functions but a superior, most-developed one and an inferior, least-developed one (Kaplan & Sadock 2024). The **Myers-Briggs Type Indicator (MBTI)** operationalised Jung's attitudes and functions into a self-report instrument and is the most popular, most widely known descendant of his theory, though it is used detached from its Jungian roots and lacks strong psychometric standing.

POLARITY	POLE A	POLE B	WHAT IT CONCERNS
Attitude	Extraversion (energy outward)	Introversion (energy inward)	**Direction of psychic energy / object relatedness**
Rational (judging) function	Thinking (logic)	Feeling (values)	**How information is evaluated and judged**
Irrational (perceiving) function	Sensation (details, "trees")	Intuition (whole, "forest")	**How information is perceived / taken in**

Jung's typology: one attitude axis and two function axes (thinking/feeling are rational, sensation/intuition irrational); crossing them yields the eight function-attitude types operationalised by the MBTI (Kaplan & Sadock 2024).

13.6 Individuation and the transcendent function: the goal of the psyche

Individuation is Jung's word for the lifelong drive toward wholeness. Where Freud's endpoint was the resolution of infantile conflict, Jung's is **individuation**: the process by which a person becomes a whole, unique individual by integrating the unconscious (especially the shadow and

the anima/animus) into conscious life, so that the ego comes into a working relationship with the Self. Jung placed this squarely in the *second half of life*: in youth the ego builds itself and adapts to the world, but at midlife the task turns inward, toward meaning, and toward the parts of the personality left undeveloped (the inferior functions, the disowned shadow). The **transcendent function** is the mechanism of integration: it is the psychic function that unites conscious and unconscious contents, typically through a symbol that holds both opposites, so that the tension between them is resolved at a higher level rather than by one side suppressing the other (Kaplan & Sadock 2024; Companion to Psychiatric Studies). Individuation is thus not becoming self-centred; it paradoxically yields broader, more mature relationships and greater creativity.

HOLD THIS

Three Jung survivors: the collective unconscious and archetypes (unique to him), introversion/extraversion plus four functions (the root of the MBTI), and individuation as the goal. Individuation is a task of the second half of life.

13.7 Synchronicity and the compensatory unconscious

Two smaller Jungian concepts worth a line each. **Synchronicity** is Jung's term for a meaningful coincidence of an inner state and an outer event that are connected by *meaning* rather than by cause, an "acausal connecting principle." It sits at the mystical edge of his system and is one of the concepts that separates Jungian thought from mainstream scientific psychology. Second, Jung held that the psyche is self-balancing: his **law of compensation** states that for any one-sided or overly intense conscious attitude, the unconscious produces a compensating counterweight, which is why he read a dream by asking what conscious attitude it compensated for (a neglected person dreams of a huge, many-breasted mother) (Kaplan & Sadock 2024).

13.8 The 1913 break from Freud: libido as general psychic energy

Know the specific point of rupture, not just the fact of it. Jung was Freud's designated successor, but the friendship ended around 1913 over the *nature of libido*. Freud insisted libido was fundamentally *sexual* energy; Jung redefined it as a general, undifferentiated **psychic energy** or "life urge," of which sexuality was only one expression (Companion to Psychiatric Studies). From this single disagreement the rest of the split followed: Jung rejected the Oedipus complex as a universal developmental stage, minimised the causal weight of infantile sexuality, and replaced Freud's backward-looking, causal model with a teleological one in which the psyche is also pulled forward by the drive toward individuation and meaning. He further parted from Freud on the unconscious itself, adding the collective layer Freud never accepted. Jung's own turbulent period of self-analysis from 1913 to about 1918, during which he experienced quasi-psychotic imagery and used it as a spur to introspection, produced the raw material of much of his theory (Kaplan & Sadock 2024).

13.9 Therapeutic legacy: analytical psychotherapy, active imagination, dream amplification

Jungian technique is active, symbol-centred, and pitched at meaning. **Analytical psychotherapy** abandons the couch and the authoritarian analyst for a face-to-face (vis-a-vis) partnership, keeps the relationship positive and avoids fostering a transference neurosis, and

tailors technique to type (the introvert given elaborate interpretations, the extravert helped to pragmatic adjustment) (Wolberg 1988). Its signature methods are: **active imagination** (the patient deliberately enters and dialogues with unconscious images in a waking, semi-directed reverie, giving the unconscious a voice); **dream amplification** (elaborating a dream image by connecting it to parallel mythological, religious, and cultural motifs to draw out its archetypal meaning, rather than reducing it to a disguised infantile wish); and the use of drawings, paintings, mandalas, and the sand tray to externalise unconscious contents. Dreams are read as reflecting present strivings and future direction, not only the buried past. Beyond the clinic, Jung's reach is unusually wide: he seeded the MBTI, the word "complex," concepts of introversion and extraversion that entered ordinary language and later trait psychology, and a deep influence on the study of myth, religion, art, and spirituality (Wolberg 1988; Kaplan & Sadock 2024).

CLINICAL ANCHOR

A successful surgeon in his early fifties, secure in career and family, presents with a flat, purposeless depression and recurrent dreams of a locked room he cannot enter. Nothing in his life has "gone wrong." A Jungian reading treats this as a midlife individuation crisis: the ego-project of the first half of life is complete, and the Self is pressing for the neglected, unlived parts of the personality (the inferior functions, the shadow). The locked room is amplified as an image of the closed-off inner world; therapy uses dream work and active imagination to open a dialogue with it, aiming not to remove a symptom but to integrate what has been left out. This is precisely the "Who is the real me?" presentation Jungian analysis is considered well suited to (Kaplan & Sadock 2024).

PEARL

If three things survive from Jung into the exam, they are: (1) the *collective unconscious* with its *archetypes* as the one idea unique to him; (2) *introversion / extraversion* and the four functions as the root of the MBTI; and (3) *individuation* as the goal. Anchor the map with one boundary rule: complexes sit in the *personal* unconscious, archetypes in the *collective* unconscious.

INDIA

Jung engaged directly with Indian thought: the *mandala* he took as the central symbol of the Self is drawn from Hindu and Buddhist iconography, and his notion of individuation toward wholeness has been read alongside concepts of Self-realisation in Indian philosophy. For the Indian trainee this makes several Jungian symbols intuitively familiar; the exam caution is to keep the technical Jungian meanings (mandala = archetype of the Self and of psychic order) distinct from their devotional or ritual meanings.

MNEMONIC

PSA-S = Persona, Shadow, Anima/animus, Self

The four core archetypes in the order they are usually met in analysis (outermost mask to innermost centre): **P**ersona (the mask), **S**hadow (the disowned opposite), **A**nima/animus (the contrasexual bridge to the inner world), **S**elf (the archetype of wholeness at the centre). Add the two personified figures, the wise old man (meaning) and the great mother (nurturance), and you have the named archetype set.

GOOD TO REMEMBER

- **Carl Gustav Jung (1875 to 1961):** Swiss psychiatrist; worked under Bleuler at the Burgholzli; founder of *analytical psychology*.
- **Break from Freud (c. 1913):** over libido, Freud held it sexual, Jung held it a general psychic energy or "life urge"; Jung also rejected the universal Oedipus complex and added the collective unconscious.
- **Word-association test:** Jung's empirical root; origin of the term *complex* (a cluster of emotionally toned unconscious ideas, detected by disturbed reaction times).
- **Structure of the psyche:** ego (surface, centre of consciousness) → personal unconscious (holds the complexes) → collective unconscious / objective psyche (holds the archetypes).
- **Boundary rule:** complexes = personal unconscious; archetypes = collective unconscious.
- **Archetype vs complex:** archetype = inherited universal template (mould); complex = the personal cast filled in by lived experience.
- **Persona:** the social mask mediating ego and world.
- **Shadow:** the disowned reverse of the persona (positive or negative); readily projected.
- **Anima / animus:** the contrasexual archetype (anima = the feminine in a man; animus = the masculine in a woman).
- **Self:** the archetype of wholeness and the ordering centre of the whole psyche (symbol: mandala); not the same as the ego.
- **Wise old man / great mother:** personified archetypes of meaning/guidance and of nurturance.
- **Two attitudes:** extraversion (energy outward) and introversion (energy inward).
- **Four functions:** rational (judging) = thinking (logic) and feeling (values); irrational (perceiving) = sensation (details, "trees") and intuition (whole, "forest").
- **MBTI:** Myers-Briggs Type Indicator; the popular self-report descendant of Jung's attitudes and functions (used detached from Jungian theory, weak psychometrics).
- **Individuation:** the goal, integration of the unconscious into a whole, unique self; a task of the second half of life.
- **Transcendent function:** the psychic function that unites conscious and unconscious via a symbol holding both opposites.
- **Synchronicity:** meaningful (acausal) coincidence of inner state and outer event.
- **Law of compensation:** the unconscious counterbalances a one-sided conscious attitude (basis of Jung's dream reading).
- **Therapy:** analytical psychotherapy (face-to-face, active, type-tailored); active imagination; dream amplification; drawings, mandalas, sand tray. Dreams read for present and future, not only the past.
- **Key works:** *Psychological Types* (1921), *Two Essays on Analytical Psychology*, *The Archetypes and the Collective Unconscious*.

Developmental psychology

14 · Erikson psychosocial stages

The theory that took development off the couch and across the whole lifespan. Erik Erikson (1902 to 1994) is the ego psychologist every psychiatry exam expects you to command in full, because his eight-stage schema is the reference frame for adolescent identity work, midlife crisis, and the psychology of ageing, and because it is the cleanest illustration of how psychoanalysis was extended beyond the drives. Where Freud's psychosexual stages ended at the genital stage and fell back on themselves after adolescence, Erikson's **psychosocial** stages continued through youth, middle age, and old age, describing the maturing ego's relations with an ever-widening social world rather than a biological unfolding of erogenous zones (Kaplan & Sadock 2024).

For the exam hold four things: the eight stages in order with their ages, the crisis and the **virtue** that each resolves into, the **epigenetic principle** that binds the sequence together, and Marcia's four identity statuses as the empirical operationalisation of stage five. Erikson is best remembered as the man who coined the phrase **identity crisis**, drawing it explicitly from his own alienated, wandering adolescence (Kaplan & Sadock 2024).

14.1 Who Erikson was, and what he fixed

From Freud's drives to the ego's adaptation. Erikson was trained in Vienna by Anna Freud, absorbed her ego psychology (her 1936 treatise on the defence mechanisms), and carried it into a developmental theory of growth rather than pathology (Kaplan & Sadock 2024). His three landmark works map onto his own model: *Childhood and Society* (1950) laid out the life cycle; *Young Man Luther* analysed an adolescent identity crisis resolved in early adulthood; *Gandhi's Truth* demonstrated generativity at midlife. What he fixed from classical psychoanalysis was its two blind spots: it stopped at adolescence, and it read development as a biological unfolding of libido. Erikson kept the psychosexual scaffolding but recast each stage as a **psychosocial** crisis anchored in family, society, and history, and he pushed the sequence all the way to death. What he left debated was the empirical status of the stages themselves, which is exactly the gap Marcia later filled (see 14.6).

14.2 The epigenetic principle

The organising rule of the whole theory. Erikson borrowed the **epigenetic principle** from embryology: just as an organism in utero develops according to a predetermined ground plan in which each part has its time of special ascendancy, psychosocial growth proceeds in a fixed sequence of phases (Kaplan & Sadock 2024). Three consequences follow, and each is examinable. First, the elements of every stage are present from birth and merely differentiate over time. Second, each stage has its own period of quiescence and its own critical ascendancy, and depends on the proper resolution of the stages before it. Third, work on any stage is never finished; an old conflict can be reactivated by a later life event, which is why an adult can be thrown back into a trust or an identity crisis. The stages are not water-tight boxes but points along a continuum, and

the later four can be read as recombinations of the earlier ones (intimacy, for instance, fuses trust and autonomy).

14.3 Crisis, virtue, and the syntonic-dystonic balance

Each stage is a turning point, not a catastrophe. Erikson was precise that **crisis** means a turning point of heightened vulnerability and heightened potential, not a threat of disaster (Kaplan & Sadock 2024). Every stage pits a positive **syntonic** tendency against a negative **dystonic** one, and healthy resolution is not the total victory of the positive pole but a favourable ratio in which the syntonic quality predominates while a measure of the dystonic is retained. From that balance emerges a **virtue** or "basic strength", which Erikson defined as an inherent strength, the way one speaks of the virtue of a medicine. A useful refinement to quote: overshooting the positive pole produces a **maladaptation** (for example, sensory maldjustment, an over-trusting naivety), while collapse to the negative pole produces a **malignancy** (for example, withdrawal, entrenched mistrust). Both represent failed resolution of the crisis.

TRAP A crisis is a turning point of heightened vulnerability and potential, **not a catastrophe**. Healthy resolution is a favourable syntonic-over-dystonic ratio, not total victory of the positive pole.

14.4 The eight stages in order

The spine of the topic, learn it cold. The ages below follow Kaplan & Sadock (2024); note that the commonly taught bands (for example, trust to about 1 year, industry 6 to 12) are the same stages under rounder ages, and either set is acceptable in an answer so long as the sequence and virtues are exact. Stage five is the pivot of adolescent psychiatry; stages seven and eight are the ones examiners use to test the lifespan extension.

1. Trust versus mistrust (birth to about 18 months; virtue: hope)

The infant learns from consistent, responsive caregiving whether the world is dependable. The Freudian correlate is the oral stage. Failure yields basic mistrust; the malignancy is withdrawal.

2. Autonomy versus shame and doubt (about 18 months to 3 years; virtue: will)

Toilet training and mobility let the toddler exercise self-control and choice. The Freudian correlate is the anal stage. Over-control by caregivers breeds shame and self-doubt; the virtue is willpower.

3. Initiative versus guilt (about 3 to 5 years; virtue: purpose)

The child plans, initiates, and asserts through play and questions. The Freudian correlate is the phallic-oedipal stage. Excessive prohibition breeds guilt; the virtue is purpose.

4. Industry versus inferiority (about 6 to 12 years; virtue: competence)

School-age children build skills, compare themselves to peers, and derive self-esteem from accomplishment. The Freudian correlate is latency. Repeated failure or invidious comparison breeds inferiority; the virtue is competence.

5. Identity versus role confusion (adolescence, about 12 to 18 years; virtue: fidelity)

The adolescent integrates childhood identifications into a coherent, continuous sense of self and vocation. This is the identity crisis; the psychosocial moratorium is its healthy exploratory phase. Failure yields role (or identity) confusion; the virtue is fidelity, the capacity to sustain loyalties despite contradictions.

6. Intimacy versus isolation (young adulthood, about 20s to 40; virtue: love)

Having secured an identity, the young adult can fuse it with another's in genuine intimacy without fear of ego loss. Failure yields isolation and superficial relationships; the virtue is love.

7. Generativity versus stagnation (middle adulthood, about 40 to 65; virtue: care)

The adult invests in guiding the next generation through parenthood, mentorship, and productive work. Failure yields stagnation and self-absorption; the virtue is care.

8. Ego integrity versus despair (old age, about 65 to death; virtue: wisdom)

The elder reviews the life lived and either accepts it as meaningful and inevitable (integrity) or is overwhelmed by regret and the shortness of remaining time (despair). The virtue is wisdom, a detached yet active concern with life in the face of death.

14.5 Freud beside Erikson: the psychosexual-to-psychosocial extension

Same childhood scaffold, then Erikson keeps going. The single most common comparison question asks how Erikson relates to Freud (Tasman 2015). The two theories run in parallel through childhood, then Freud's stops and Erikson's continues for three more stages across the whole adult life.

AGE BAND	FREUD (PSYCHOSEXUAL)	ERIKSON (PSYCHOSOCIAL)	VIRTUE
0 to ~1.5 y	Oral	Trust vs mistrust	**Hope**
~1.5 to 3 y	Anal	Autonomy vs shame and doubt	**Will**
~3 to 5 y	Phallic (oedipal)	Initiative vs guilt	**Purpose**
~6 to 12 y	Latency	Industry vs inferiority	**Competence**
Adolescence	Genital	Identity vs role confusion	**Fidelity**
Young adulthood	**(Freud stops here)**	Intimacy vs isolation	**Love**
Middle adulthood	**(no Freudian stage)**	Generativity vs stagnation	**Care**
Old age	**(no Freudian stage)**	Ego integrity vs despair	**Wisdom**

The discriminator: Freud's map ends at the genital stage in adolescence, whereas Erikson adds three adult stages (intimacy, generativity, integrity), which is precisely his lifespan extension of psychoanalysis.

14.6 Marcia's four identity statuses: the empirical extension

The evidence base examiners want attached to stage five. James Marcia (1966) operationalised Erikson's identity-versus-role-confusion crisis into a testable paradigm, crossing two dimensions: **exploration** (the presence or absence of a crisis, an active period of trying out alternatives) and **commitment** (whether the person has settled on values, vocation, and beliefs). The two-by-two grid yields four **identity statuses**, and this cross-tabulation is the single most examinable diagram in the topic.

STATUS	EXPLORATION (CRISIS)	COMMITMENT	CHARACTER
Identity achievement	**Yes (explored)**	**Yes (committed)**	Confident, self-directed; the mature resolution
Moratorium	**Yes (in active crisis)**	**No (not yet committed)**	Anxious but open, actively searching
Foreclosure	**No (no crisis)**	**Yes (committed)**	Conformist; commitments taken wholesale from parents or authority without questioning
Identity diffusion	**No**	**No**	Aimless, detached, no direction; the least adaptive status

Foreclosure is the classic trap: commitment without exploration. Diffusion is neither; achievement is both; moratorium is the healthy exploratory phase Erikson himself lived through.

The clinical and cultural nuance to add. Diffusion carries the highest risk for internalising and externalising problems and for suicidality, whereas achievement predicts higher subsequent intimacy, generativity, and integrity (longitudinal data). Marcia noted that in some cultural and gender contexts foreclosure can be socially adaptive, so the statuses are not a simple ranking from bad to good.

HOLD THIS

Erikson psychosocialised Freud and ran him across the whole lifespan; Marcia then made stage five empirical. The four statuses cross exploration (crisis) with commitment: achievement (both), moratorium (crisis only), foreclosure (commitment only), diffusion (neither).

14.7 Worked clinical example

Reading a case through the schema. A 19-year-old who abruptly abandons the engineering course his parents chose, drops his social group, and describes feeling "there is no real me under all this" is presenting a stage-five failure: an unresolved **identity versus role** crisis. In Marcia's terms he has moved out of *foreclosure* (a borrowed, unexamined commitment) into *moratorium* (active exploration without a new commitment). The developmentally correct clinical stance is not to rush him to a decision but to protect the psychosocial moratorium, because premature foreclosure would only re-create the problem. If, decades later, the same man at 68 sits in your clinic consumed by regret that he "wasted his life" and terrified of dying, you are looking at stage eight, despair rather than **integrity**, and the therapeutic task is a supported life review toward acceptance and wisdom. The same theory frames both encounters, which is exactly why Erikson endures in clinical psychiatry.

COMMON TRAP

Do not swap the virtues between stages: initiative gives *purpose* (not competence) and industry gives *competence* (not purpose); intimacy gives *love* and generativity gives *care*. And do not confuse Marcia's *moratorium* status (active exploration, no commitment) with *foreclosure* (commitment without exploration): foreclosure is the one that looks settled but has skipped the crisis.

PEARL

The one-line integration for an examiner: Erikson psychosocialised Freud and extended him across the whole lifespan under the epigenetic principle, and Marcia then made the adolescent identity stage empirical by crossing exploration with commitment. Name that arc (Freud to Erikson to Marcia) and you have framed the entire topic.

MNEMONIC

Virtues: "Hope Will Push Children Fully Loving Caring Wisely"

Stage virtues in order: **H**ope, **Wi**ll, **P**urpose, **C**ompetence, **F**idelity, **L**ove, **C**are, **Wi**sdom. For the statuses, remember the crisis-by-commitment grid: achievement (both), moratorium (crisis only), foreclosure (commitment only), diffusion (neither).

GOOD TO REMEMBER

- **Stage 1, trust vs mistrust:** birth to about 18 months; virtue *hope*; Freudian oral stage.
- **Stage 2, autonomy vs shame and doubt:** about 18 months to 3 years; virtue *will*; Freudian anal stage.
- **Stage 3, initiative vs guilt:** about 3 to 5 years; virtue *purpose*; Freudian phallic-oedipal stage.
- **Stage 4, industry vs inferiority:** about 6 to 12 years; virtue *competence*; Freudian latency.
- **Stage 5, identity vs role confusion:** adolescence (about 12 to 18 years); virtue *fidelity*; the identity crisis and psychosocial moratorium.
- **Stage 6, intimacy vs isolation:** young adulthood; virtue *love*.
- **Stage 7, generativity vs stagnation:** middle adulthood (about 40 to 65); virtue *care*.
- **Stage 8, ego integrity vs despair:** old age (about 65 to death); virtue *wisdom*.
- **Epigenetic principle:** fixed, predetermined sequence; each stage present from birth, ascendant in turn, dependent on prior resolution.
- **Crisis:** a turning point of heightened vulnerability and potential, not a catastrophe (Erikson).
- **Virtue / basic strength:** the ego strength emerging from a favourable syntonic-over-dystonic ratio.
- **Maladaptation vs malignancy:** too much positive pole (maladaptation) vs collapse to the negative pole (malignancy); both are failed resolution.
- **Marcia (1966) statuses:** achievement (crisis + commitment), moratorium (crisis, no commitment), foreclosure (commitment, no crisis), diffusion (neither).
- **Extension of Freud:** Erikson made the stages psychosocial and added three adult stages past the genital stage (intimacy, generativity, integrity).
- **Key works:** *Childhood and Society* (1950), *Young Man Luther*, *Gandhi's Truth*.

15 · Piaget cognitive development, Vygotsky and theory of mind

The map of how thinking is built. Jean Piaget (1896 to 1980) gave psychiatry its dominant account of how the child's mind is constructed, stage by qualitatively distinct stage, from reflex to abstract reason. The exam wants three things held together and often contrasted: Piaget's **constructivist** stage theory (the mechanisms, the four periods with their ages and signature tasks, and the standard critiques), Lev Vygotsky's rival **sociocultural** theory (learning as socially mediated, the zone of proximal development, scaffolding), and the **theory of mind** tradition that grew out of the egocentrism question and reset the age at which a child grasps that others hold false beliefs.

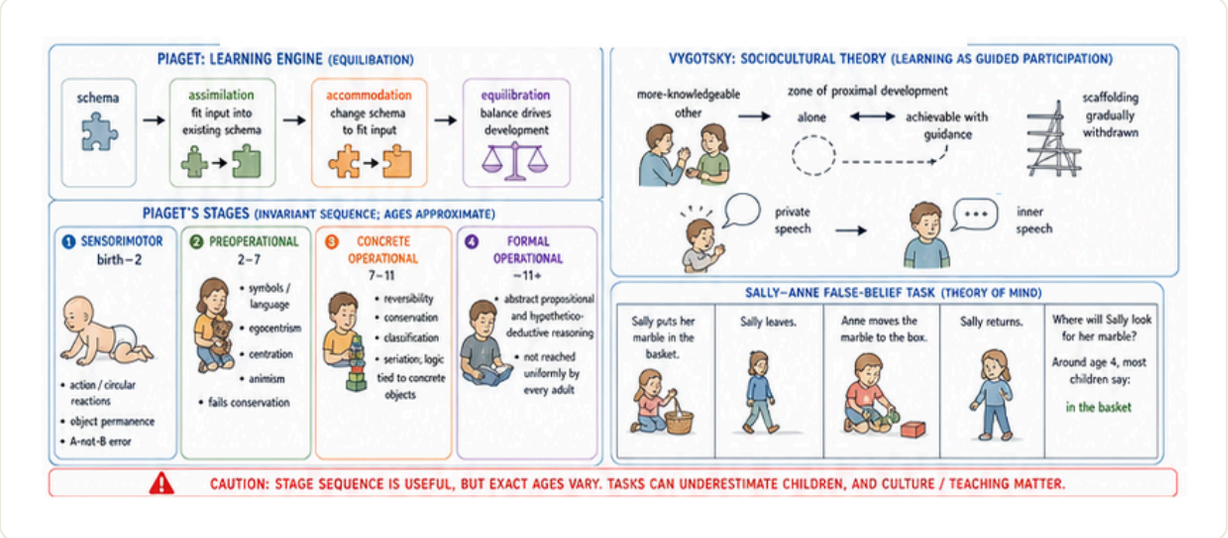


Fig 4.14 Cognitive development: from action to abstract thought.

Piaget held that the child's mental life is *qualitatively* different from the adult's, not merely a smaller version of it (Companion to Psychiatric Studies). The child is an active builder, an epistemologist: by acting on the world the child constructs internal structures, and those structures, not the environment itself, govern how the child thinks (Kaplan & Sadock 2024). This is a stage-and-concept theory, so it is examined as a system to enumerate rather than as an evolution toward a single currently accepted mechanism; treat the ages below as the standard textbook bands, not sharp cut-offs.

15.1 The building blocks: schema, assimilation, accommodation, equilibration

Functional invariants. A **schema** (scheme) is a unit of cognition: the organised structure of an action, generalised by repetition to analogous situations, from the infant's grasping reflex to the adolescent's logical operation (Kaplan & Sadock 2024). Schemata change through two complementary processes that operate at every level of development. In **assimilation**, the child incorporates new input into an existing schema: a child who meets a dachshund for the first time assimilates it into the schema "dog" (Tasman 2015). In **accommodation**, a novel stimulus that will not fit forces the schema to expand or reorganise: the schema "all four-legged animals are dogs" must be altered when the child meets a cat. **Equilibration** is the self-regulating drive that balances assimilation against accommodation; Piaget called it "compensation for an external disturbance," the internal factor that structures developing intelligence and pushes it toward

wider adaptation. Biological maturation, learning and social interaction feed into development and crystallise through equilibration.

TRAP In **assimilation** the input is bent to fit the schema (a dachshund fits "dog"); in **accommodation** the schema is bent to fit the input (the schema changes when a cat will not fit "dog"). Assimilation keeps the schema, accommodation changes it.

15.2 Sensorimotor stage (birth to about 2 years): object permanence

Knowing through action. In the **sensorimotor** period the child constructs schemata purely through perception and bodily movement, with no symbols or representational thought yet (Kaplan & Sadock 2024). Piaget divided it into six substages, tracked through the infant's growing repertoire of *circular reactions*, repeated actions that reproduce an interesting result: *primary* circular reactions centre on the infant's own body (repeating a chance motor act), *secondary* circular reactions act on external objects (shaking a rattle to reproduce a sound), and *tertiary* circular reactions in stage 5 explore variation deliberately (using a stick to move a distant object), the hallmark of active experimentation and discovery. The crowning achievement is **object permanence**, the knowledge that objects exist independently of the child's perception of them; Piaget called it the first victory of conservation and the foundation of all future knowledge. Early on, a toy dropped out of sight simply ceases to exist; by around 12 months the child searches for a hidden object. The classic error is the *A-not-B error* of stage 4: after an object is repeatedly hidden and found at point A, the infant keeps searching at A even after watching it hidden at point B.

15.3 Preoperational stage (about 2 to 7 years): symbols without logic

Representation arrives, operations do not. The **preoperational** subperiod opens with the *semiotic (symbolic) function*, the ability to let a signifier stand for something absent (Kaplan & Sadock 2024). Piaget flagged it by five behaviours emerging in the second year: deferred imitation, symbolic (pretend) play, drawing, mental imagery and language. Thought is now representational but not yet logical, limited by several features:

Egocentrism

The child cannot separate its own viewpoint from another's and assumes others share its perceptions and tastes; a toddler covers its own eyes and says "now you can't see me." Demonstrated by the *three-mountains task*, where the child fails to report how the scene looks from a doll's position.

Centration

Narrow focusing on one salient dimension of a situation while ignoring others; the child judges a quart of milk poured into two smaller containers as "less" because it attends only to the containers' smaller size (Tasman 2015).

Animism

Attributing life, feelings and intentions to inanimate objects (the sun "wants" to shine).

Lack of conservation

The child does not grasp that a quantity stays invariant across a change in appearance; poured into a tall thin glass, the same liquid is judged to be "more."

15.4 Concrete operational stage (about 7 to 11 years): logic on the concrete

Reversibility unlocks conservation. The **concrete operational** child can now perform mental *operations*, which are interiorised actions that are *reversible* and organised into a system (Kaplan & Sadock 2024). Reversibility, the ability to mentally undo a transformation (pour the liquid back), is what lets the child achieve **conservation**: the certainty that quantity, mass, number, weight or volume stays invariant despite a perceptual change. Piaget noted a fixed order within the stage, a *horizontal decalage*: conservation of number and quantity around 7, of weight around 9 to 10, and of volume only around 11 to 12. Two further operations appear: *classification* and *class inclusion* (holding a superordinate class in mind while perceiving subordinate ones, so the child grasps that there are more "pets" than "dogs"), and *seriation* (ordering rods by length, which underlies dimensional thinking). Thought is logical but tied to concrete, present objects; the child still struggles with the purely abstract or hypothetical.

~7 y	~9 to 10 y	~11 to 12 y
CONSERVE NUMBER/QUANTITY	CONSERVE WEIGHT	CONSERVE VOLUME

15.5 Formal operational stage (about 11 years onward): hypothetico-deductive reasoning

The possible over the real. In the **formal operational** stage, the relationship between the real and the possible reverses: for the adolescent the possible has priority and the actual is treated as one instance of what could be (Kaplan & Sadock 2024). Three features follow. Thought becomes *hypothetico-deductive*, moving from a general hypothesis to its testable consequences, mirroring scientific reasoning. It becomes *propositional*, operating on abstract statements freed from concrete referents, so transitive inferences (A less than B, B less than C, therefore A less than C) can be made without demonstration. And it can *isolate variables and systematically examine all combinations*, holding other factors constant to test each cause in turn. Piaget noted a fresh burst of *adolescent egocentrism* at this transition, in which the adolescent unrealistically assumes others are as preoccupied with them as they are, feeding social anxiety and idealism.

15.6 Critiques of Piaget

Right sequence, wrong timetable and boundaries. The developmental sequence Piaget described is robustly supported and rarely reverses, but three lines of criticism are exam-standard (Companion to Psychiatric Studies; Kaplan & Sadock 2024). First, he *underestimated infants and young children*: Gibson and Walk's visual-cliff work showed depth perception by 6 months, and Margaret Donaldson's redesigned conservation task, in which "naughty teddy" rather than a deliberate adult moves the counters, let far more 4 to 6 year olds conserve, arguing that Piaget's tasks misled children rather than measuring pure incompetence. Second, *ages vary and the stages are too broad*; specific training accelerates conservation, and many adolescents and adults fail formal-operations tasks, so the timetable is not fixed. Third, there is *cultural bias*: cross-cultural work shows tasks are mastered at different ages across cultures, and the supremacy of formal over concrete operations is culturally relative. Piaget also relied heavily on the child's verbal justification, confounding logical competence with verbal skill, and gave little weight to social intelligence or to knowledge acquired by social transmission, the very gap Vygotsky fills.

15.7 Vygotsky: the sociocultural alternative

Learning is social first, individual second. Lev Vygotsky's sociocultural theory treats cognitive development as a fundamentally **social** process, not the solitary journey of discovery Piaget emphasised (Tasman 2015). Learning is driven and mediated by interaction with a *more-knowledgeable other* (parent, teacher, more capable peer), and culture shapes which skills are learned, so development varies across cultures; children internalise the "tools of intellectual adaptation" their culture supplies. Its core constructs:

Zone of proximal development (ZPD)

The gap between what a learner can do independently (actual developmental level) and what they can achieve with guidance (level of potential development). Instruction is most effective, and cognitive growth maximised, when pitched into this zone.

Scaffolding

The graduated, temporary support a more-knowledgeable other gives within the ZPD (modelling, visual aids, worked examples, one-to-one feedback), progressively withdrawn as the learner becomes able to perform the task alone. (The term is Wood, Bruner and Ross's, applied to Vygotsky's framework.)

More-knowledgeable other (MKO)

Anyone with greater mastery of the task, most often a parent, teacher or peer, who guides the learner across the ZPD.

Private speech

Self-directed audible speech (typically from about age 3) that regulates the child's own behaviour and problem-solving; for Vygotsky it is a transitional stage between social external speech and silent inner speech (from about age 7), and thought and language, initially separate, merge around this age. Contrast Piaget, who read the same self-talk as immature egocentric speech that simply fades.

15.8 Piaget versus Vygotsky

DIMENSION	PIAGET	VYGOTSKY
Engine of development	**Individual construction: the lone child acting on the world**	**Social mediation: guided interaction, then internalisation**
Role of culture	Universal, culture-general stages	Central; development varies across cultures
Role of language	A product of thought; egocentric speech is immature	The root of learning; private speech regulates and builds thought
Learning and development	Development leads; readiness gates learning	Learning leads development within the ZPD
Adult / other	Peers spur cognitive conflict; direct teaching can constrain	The MKO actively scaffolds new competence

Two constructivisms: Piaget builds the mind from the inside out, Vygotsky from the social world in.

15.9 Theory of mind and the false-belief task

Knowing that others can be wrong. **Theory of mind** is the ability to attribute mental states (beliefs, desires, intentions) to oneself and others and to use them to predict behaviour, and to grasp that beliefs can be true or false and that different people can hold different beliefs (Companion to Psychiatric Studies). It is tested with the **false-belief** task, which Wimmer and Perner introduced in 1983 (the "Maxi" task, in which a child must predict where a character will look for chocolate that was moved in his absence). Simon Baron-Cohen, Alan Leslie and Uta Frith adapted it into the *Sally-Anne task* (1985): Sally places a marble in a basket and leaves; Anne moves it to a box; the watching child is asked where Sally will look on returning. Children of about 3 and under answer "the box," the marble's true location, failing to separate their own knowledge from Sally's; from about *4 years* children answer "the basket," correctly tracking Sally's false belief. This resets Piaget's egocentrism finding: the shift out of egocentrism on a belief task happens nearer 4 than the 7 years Piaget implied for perspective-taking. Its clinical weight is in autism: Baron-Cohen, Leslie and Frith found children with autism selectively failed the Sally-Anne task despite adequate mental age, giving rise to the influential *mindblindness* account of autism as a specific theory-of-mind deficit, with theory-of-mind impairment later also implicated in schizophrenia (Frith).

HOLD THIS

False belief emerges about age 4, resetting Piaget's egocentrism. Object permanence is sensorimotor; conservation is concrete-operational; the Sally-Anne autism study is Baron-Cohen, Leslie and Frith (1985), the paradigm Wimmer and Perner (1983).

CLINICAL ANCHOR

Theory-of-mind testing sits directly in the autism assessment. A child with intact general ability who selectively fails false-belief tasks fits the mindblindness profile; theory-of-mind deficits also feature in the social cognition literature on schizophrenia. Piagetian stage is a useful frame for pitching psychoeducation: a concrete-operational child reasons about present, tangible facts, so explanations of illness or medication should be concrete rather than abstract until formal operations are in place.

COMMON TRAP

Do not confuse the ages: object permanence in the *sensorimotor* stage, conservation in the *concrete operational* stage. Do not credit "scaffolding" to Vygotsky as a term (it is Wood, Bruner and Ross; the underlying ZPD is Vygotsky's). And the false-belief milestone is about *4 years*, not the 7 years Piaget gave for perspective-taking; the Sally-Anne autism study is Baron-Cohen, Leslie and Frith 1985, while the false-belief paradigm itself is Wimmer and Perner 1983.

MNEMONIC

Some People Can Fly = Sensorimotor, Preoperational, Concrete, Formal

Reads Piaget's four periods in order. Anchor one signature to each: Sensorimotor to object permanence, Preoperational to egocentrism (no conservation), Concrete to conservation, Formal to hypothetico-deductive abstraction.

GOOD TO REMEMBER

- **Schema:** unit of cognition; changed by assimilation (fit new input to old schema) and accommodation (alter schema to fit new input), balanced by equilibration.
- **Sensorimotor:** birth to about 2 years; action-based, circular reactions (primary, secondary, tertiary); achieves object permanence; A-not-B error.
- **Preoperational:** about 2 to 7 years; symbolic/semiotic function; egocentrism (three-mountains task), centration, animism, no conservation.
- **Concrete operational:** about 7 to 11 years; reversibility gives conservation, plus classification, class inclusion and seriation; logic tied to the concrete.
- **Formal operational:** about 11 years onward; abstract hypothetico-deductive and propositional thought, isolating variables; adolescent egocentrism.
- **Conservation order (decalage):** number/quantity about 7, weight about 9 to 10, volume about 11 to 12.
- **Piaget critiques:** underestimated infants (Donaldson's naughty-teddy task; Gibson and Walk visual cliff), ages vary and stages too broad, cultural bias.
- **Vygotsky (sociocultural):** zone of proximal development, scaffolding, more-knowledgeable other, private speech; learning is socially mediated and culture-dependent.
- **Piaget vs Vygotsky:** individual construction vs social mediation; Piaget development leads learning, Vygotsky learning leads development.
- **Theory of mind:** attributing mental states and grasping false belief; emerges about 4 years.
- **False-belief task:** Wimmer and Perner 1983 (Maxi); Sally-Anne = Baron-Cohen, Leslie and Frith 1985, relevant to autism (mindblindness).

16 · Kohlberg moral development

Where it sits. Lawrence **Kohlberg** (1958, 1969, 1984) took Piaget's two-phase account of moral judgment (the young child's **moral realism**, in which rules are fixed and sacred and wrongness equals the size of the damage, giving way to the older child's **moral relativism** or autonomy, in which rules are negotiable agreements and intention counts) and built it into a full **six-stage, three-level** theory of moral *reasoning*. Piaget wrote *The Moral Judgment of the Child* but did not develop the area further; Kohlberg's extension is, in Kaplan and Sadock's phrasing, "the first and perhaps best-known attempt to extend Piaget theory" (Kaplan & Sadock 2024).

For the exam this is the single most examinable moral-development theory: know the three level names, the six stage names, that it is elicited by the **Heinz dilemma**, that it is the *reasoning and not the answer* that fixes the stage, that progression is invariant and forward-only but that most people never reach the top, and that it draws two famous critiques, Gilligan's ethic-of-care/gender-bias critique and the cross-cultural critique. The stages presuppose Piagetian

cognitive stages: conventional reasoning needs concrete operations, principled reasoning needs formal operations (Kaplan & Sadock 2024).

16.1 The method: moral dilemmas and the Moral Judgment Interview

What Kohlberg measured. He adopted Piaget's storytelling technique but standardised it into the **Moral Judgment Interview** (MJI): each participant was read a set of ten hypothetical dilemmas, each engineered to pit one ethical norm against another (property versus life, law versus compassion, loyalty versus honesty), and then probed with follow-up questions asking *why* a course of action was right or wrong. The original sample was 72 Chicago boys aged 10 to 16 years, of whom 58 were followed at roughly three-yearly intervals for 20 years (Kohlberg 1984). Kohlberg was deliberately indifferent to the participant's final choice: development pertained to the *form* of the thinking, not the content of the solution (Kaplan & Sadock 2024).

16.2 The Heinz dilemma

The stimulus. Heinz's wife is dying of a cancer that a new drug might cure. The chemist who discovered it charges ten times its cost, far more than Heinz can raise even with help. The chemist refuses to sell cheaper or to accept later payment, so Heinz breaks in and steals the drug. *Should Heinz have stolen it, and why?* The genius of the design is that "yes" and "no" answers appear at every level, so it is only the **justification** that reveals the stage: fear of jail (preconventional), a good husband's duty (conventional), or the relative worth of life over property (postconventional). This is the load-bearing exam point, the same answer can be stage 1 or stage 6 depending on the reason.

RULE **It is the reasoning, not the answer, that fixes the stage.** Two people who both say Heinz should steal can be a stage apart; two who disagree on the verdict can share a stage.

16.3 Level I: Preconventional morality (moral authority is external)

The child accepts an outside code. Typically the mode until about age 9, and grounded in the anticipated consequence of the act to oneself. There is no internal sense of right and wrong yet; "right" is what avoids punishment or brings reward (Kaplan & Sadock 2024).

Stage 1 : Punishment and obedience orientation

Rules are fixed and absolute; an act is "bad" purely because it is punished. Intent is ignored. Heinz should not steal because he could be jailed. The defining test of "right" becomes being able to get away with it.

Stage 2 : Instrumental exchange (naive hedonism, self-interest)

The child recognises that different people have different interests and acts to serve personal need. Reciprocity is transactional, "an eye for an eye," "you scratch my back," "what's in it for me." Heinz may steal if the wife's survival serves him, not from any principle.

16.4 Level II: Conventional morality (moral authority is internalised but unquestioned)

The standards of the group become one's own. Prevalent from adolescence; the person internalises the moral standards of valued adults and the norms of the group, and reasons to maintain relationships and social order. Authority is taken on board but not interrogated (Kaplan & Sadock 2024).

Stage 3 : Good-boy / good-girl, interpersonal conformity

Morality is being seen as good by others: trust, loyalty, living up to what a nice person in one's role would do. Heinz should steal because a devoted husband is *expected* to do everything to save his wife; the motive is approval and the maintenance of the relationship.

Stage 4 : Law-and-order, authority and social-order maintenance

The frame widens from the immediate circle to society as a whole. One obeys laws, respects authority and does one's duty because the social system depends on it. Heinz should not steal because upholding the law prevents the chaos that would follow if everyone broke it.

16.5 Level III: Postconventional morality (moral authority is self-chosen principle)

Principles come to outrank both the group and the law. Reached, if at all, in late adolescence or early adulthood, and only by a minority: Kohlberg held that roughly 10 to 15 percent of people ever reason predominantly at this level, because it demands the abstract, formal-operational thought needed to weigh competing rights (Kohlberg 1984).

Stage 5 : Social contract and individual rights

Laws are seen as social agreements serving the greatest good, but as fallible and revisable when they conflict with fundamental rights. Heinz should steal because the preservation of life is a more basic value than the chemist's property right; the law here works against a legitimate individual interest.

Stage 6 : Universal ethical principles

Reasoning rests on self-chosen, universal principles of justice, equality and the dignity of human life that apply to everyone and override any law. The person will act on them, and accept punishment, even against the whole of society (non-violent civil disobedience is the paradigm). Kohlberg himself doubted that many people ever reach stage 6 and in later work questioned whether it could be reliably identified.

16.6 The structure of the sequence: invariant, forward-only, not universal in attainment

How the stages behave. The levels form an invariant sequence; a person passes through them in fixed order and each new stage replaces the reasoning of the one before, so stages cannot be skipped and there is no regression (Kaplan & Sadock 2024). Progress is driven by cognitive **disequilibrium**, the discomfort of meeting a viewpoint one's current reasoning cannot handle, and by improving perspective-taking. Crucially, Kohlberg did *not* claim that all or even most people reach the highest levels: attainment is capped by cognitive development and by exposure, and the top level is rare. Colby and Kohlberg's (1983) longitudinal re-analysis of the original cohort, tested repeatedly over more than two decades, supported the fixed-order claim.

16.7 Scoring: how a stage is assigned

The 50 percent rule. Responses across the ten dilemmas are coded and a person is formally classified at a stage only if they reason at that stage 50 percent or more of the time, so the stage represents their dominant, preferred mode rather than a single answer. The standardised scoring manual (Colby & Kohlberg 1983) defined explicit stage criteria and sharply improved inter-rater reliability, addressing an early complaint that scoring was subjective.

72	50%	10 to 15%
CHICAGO BOYS, ORIGINAL SAMPLE	REASONING TO BE SCORED AT A STAGE	EVER REACH POSTCONVENTIONAL

16.8 Gilligan's critique: an ethic of care versus an ethic of justice

The gender-bias objection. Kohlberg's original sample was entirely male, and his data suggested men more often progressed past stage 4, which read as though women were morally deficient (typically "stuck" at stage 3). His research associate Carol **Gilligan** (1977, 1982, *In a Different Voice*) argued the theory was androcentric: it defined morality narrowly as abstract justice and so mis-scored a genuinely different, equally mature **ethic of care** centred on relationships, responsibility and context, more common in women. In the Heinz dilemma a care voice attends to consequences for the marriage (if Heinz is jailed his wife loses him) rather than ranking abstract rights. Gilligan's charge is that women reason from care and connection, men from justice and fairness, and that Kohlberg mistook difference for deficiency (Kaplan & Sadock 2024).

COMMON TRAP

Do not present Gilligan's critique as the settled last word. Kaplan and Sadock note that *subsequent empirical research showed women score as high as, or higher than, men* on Kohlberg's stages, so the original claim of a female deficit did not hold up, which paradoxically weakens the premise Gilligan was attacking while leaving her positive point (that care is a legitimate moral orientation) intact. The examinable nuance: state the care-versus-justice distinction AND the finding that the sex difference in stage scores was not replicated.

16.9 The other criticisms: content, verbal skill, ecological validity and culture

Beyond gender. Kaplan and Sadock (2024) list several further objections. First, the moral *subject* was criticised as detached from moral *content*, and individual differences in reasoning stage did not correlate strongly or consistently with actual moral *behaviour* (reasoning and conduct diverge). Second, the method may have confounded verbal skill and general intelligence with moral reasoning, since higher stages simply require more articulate justification. Third, the dilemmas are artificial and hypothetical and so lack ecological validity (Rosen 1980); ten-to-sixteen-year-old boys had never been married or faced anything like Heinz's plight. The **cross-cultural critique.** Kohlberg's work was criticised as culturally biased toward the Western middle-class male: postconventional, individual-rights reasoning reflects an individualist liberal ethic, and members of collectivist and traditional societies who reason from communal duty, family honour or religious law are systematically scored lower, which many regard as an artefact of the instrument rather than genuinely lower morality (Kaplan & Sadock 2024).

HOLD THIS

Progression is invariant and forward-only, but attainment is not universal. Conventional reasoning needs concrete operations, principled reasoning needs formal operations; the theory is justice-centred and Western, which Gilligan and the cross-cultural critics attacked.

INDIA

The cross-cultural critique matters directly in the Indian setting. In collectivist, family-centred and duty-oriented moral cultures, an appeal to *dharma*, filial obligation or the maintenance of family and social order (which Kohlberg codes as conventional, stage 4) is often the most mature and considered response available, yet the MJI grades individual-rights reasoning as superior. Shweder and colleagues' Indian work on the "big three" ethics (autonomy, community, divinity) is the classic demonstration that Kohlberg's justice-and-rights scheme captures only the autonomy ethic and undervalues community and divinity moralities. Read Kohlberg's hierarchy as culture-bound, not as a universal ranking of moral worth.

16.10 Clinical and exam relevance

CLINICAL ANCHOR

Moral-reasoning frameworks surface in child and adolescent psychiatry (assessing conduct disorder and callous-unemotional traits, where the question is whether reasoning is delayed versus behaviourally uncoupled from reasoning), in forensic and personality-disorder assessment, and in medical ethics teaching. Beck's cognitive therapy of antisocial personality disorder explicitly draws on Kohlberg's model, framing treatment as helping the patient move from egocentric, preconventional cost-benefit reasoning toward more perspective-taking, mutual-benefit reasoning (Beck, Freeman & Davis). In Young's schema therapy, the Self-Sacrifice schema is located as a higher moral level than Subjugation precisely by reference to Kohlberg's stages, one surrenders one's needs from an inner standard rather than from external coercion.

MNEMONIC

"Pre-Con-Post" outer to inner · stages 1 to 6 = "Please Stop Getting Little Stupid Points"

Levels move from an **outside** code (Preconventional) to the **group's** code (Conventional) to a **self-chosen** code (Postconventional). For the six stages: **P**unishment, **S**elf-interest, **G**ood-boy, **L**aw-and-order, **S**ocial-contract, **P**rinciples. Pair each level with its Piagetian floor: conventional needs concrete operations, principled needs formal operations.

LEVEL	STAGE	RIGHT IS DEFINED BY	HEINZ JUSTIFICATION
I Preconventional (to ~age 9)	1 Punishment / obedience	Avoiding punishment; rules absolute	**Don't steal, he'll be jailed**
	2 Instrumental exchange	Self-interest, transactional reciprocity	**Steal if the wife is useful to him**
II Conventional (adolescence on)	3 Good-boy / conformity	Approval, being a good person in one's role	**Steal, a good husband would**
	4 Law-and-order	Duty, obeying law, social order	**Don't steal, uphold the law**
III Postconventional (10 to 15% only)	5 Social contract	Laws as revisable agreements; rights	**Steal, life outranks property**
	6 Universal principles	Self-chosen universal justice, dignity	**Steal, sanctity of life is absolute**

Kohlberg's three levels and six stages, with the same dilemma scored differently at each stage: the reasoning, not the verdict, fixes the level.

PEARL

The one line that answers most viva questions: *"It is the reasoning, not the answer, that determines the stage."* Two people who both say Heinz should steal can be a stage apart; two who disagree on the verdict can share a stage. Add the two headline caveats, progression is invariant but attainment is not universal (only 10 to 15 percent reach postconventional), and the theory is justice-centred and culturally Western, which is exactly what Gilligan and the cross-cultural critics attacked.

GOOD TO REMEMBER

- **Theorist:** Lawrence Kohlberg (1958 onward); built on Piaget's moral realism to relativism shift.
- **Elicited by:** the Heinz dilemma, scored via the Moral Judgment Interview (10 dilemmas).
- **Original sample:** 72 Chicago boys aged 10 to 16; 58 followed for 20 years (Kohlberg 1984).
- **Level I Preconventional (to ~age 9):** Stage 1 punishment-and-obedience; Stage 2 instrumental exchange / self-interest.
- **Level II Conventional (adolescence onward):** Stage 3 good-boy interpersonal conformity; Stage 4 law-and-order / social-order maintenance.
- **Level III Postconventional (only 10 to 15% reach it):** Stage 5 social contract and individual rights; Stage 6 universal ethical principles.
- **Core rule:** the reasoning, not the answer, fixes the stage; sequence invariant and forward-only; attainment not universal.
- **Cognitive floor:** conventional needs concrete operations, principled needs formal operations (Piagetian dependency).
- **Scoring rule:** classified at a stage if reasoning at it 50% or more of the time; standardised by Colby & Kohlberg (1983).
- **Gilligan critique:** androcentric, justice-biased; proposed an ethic of care (relationships, context) versus ethic of justice; note women later scored as high as or higher than men.
- **Cross-cultural critique:** Western, individualist, middle-class male bias; undervalues collectivist duty and divinity moralities (Shweder).
- **Related models:** Loevinger (ego), Fowler (faith/spiritual) as parallel adult stage theories of maturation.

17 · Attachment theory: Bowlby, Ainsworth and Harlow

The bond that builds the self. Attachment theory is the developmental account of the child's first tie to a caregiver, and it is examined as a linked chain of three names. Harry Harlow's rhesus-monkey experiments overturned the old view that the infant loves the mother because she feeds it; John Bowlby recast attachment as an evolved **behavioural system** serving survival, with the caregiver as a **secure base**; and Mary Ainsworth turned Bowlby's theory into a measurable laboratory procedure, the **Strange Situation**, that yields the attachment classifications the exam most often asks for. Hold the sequence: Harlow the empirical challenge, Bowlby the theory, Ainsworth the measurement, with the disorganised type and reactive attachment disorder as the later additions.

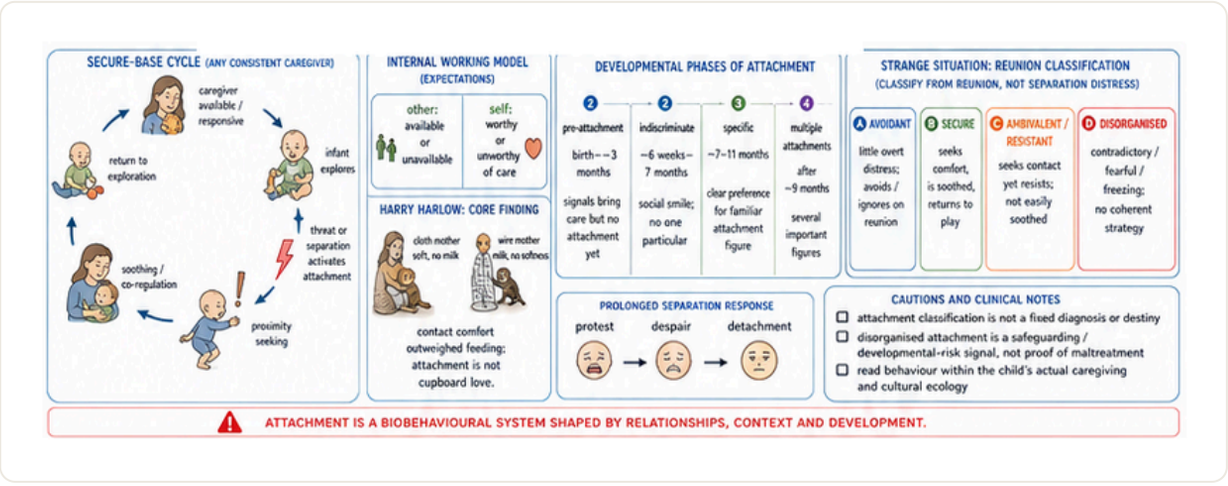


Fig 4.15 Attachment: secure base, working model and reunion.

The topic matters clinically because attachment is a major developmental-psychopathology construct: insecure and especially disorganised attachment in infancy is a replicated risk marker for later disorder, adult attachment style shapes the therapeutic relationship, and reactive attachment disorder is the diagnosable clinical extreme cross-referenced in Paper III child psychiatry (Kaplan & Sadock 2024). This is a stage-and-concept theory, so it is examined as a system to enumerate rather than as an evolution toward a single mechanism; treat the ages and percentages below as the standard textbook figures.

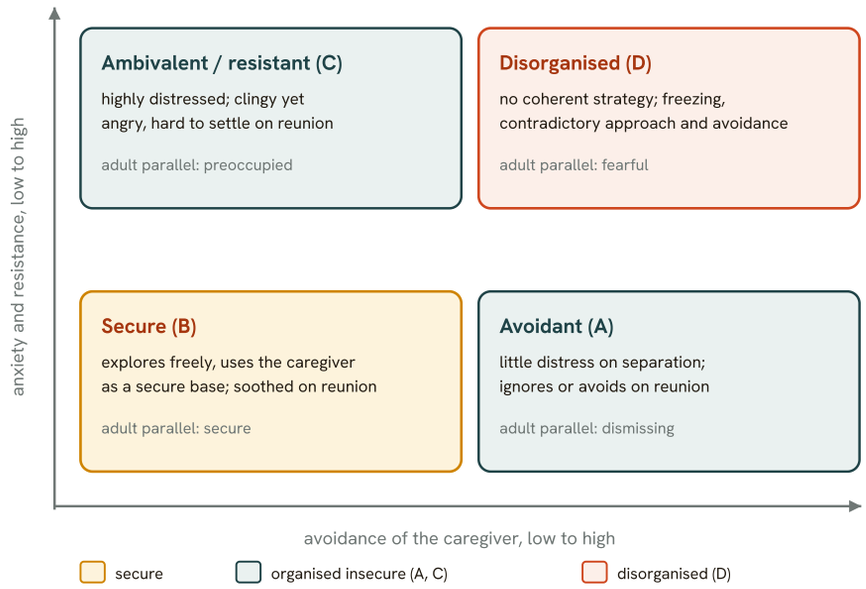


Fig 4.16 Ainsworth's strange-situation classification, read on two axes: how much the infant avoids the caregiver, and how much anxiety and resistance it shows. Secure infants (B) use the caregiver as a secure base and are soothed on reunion; avoidant infants (A) show little overt distress and turn away; ambivalent-resistant infants (C) are highly distressed and cannot be settled. Disorganised attachment (D, Main and Solomon) is the collapse of any coherent strategy and carries the greatest developmental-psychopathology risk. The adult-attachment parallels are noted in each cell.

17.1 Harlow: contact comfort overturns cupboard love

The wire mother and the cloth mother. Before Harlow, both psychoanalysis and learning theory held a **drive-reduction** (or "cupboard-love") view: the infant bonds to the mother because she reduces the primary hunger drive, so love is a secondary, learned reward for feeding (Kaplan & Sadock 2024). Harry Harlow tested this in the 1950s by rearing newborn rhesus monkeys with two surrogate "mothers," one a bare wire cylinder fitted with a feeding bottle, the other wire covered in soft terry cloth but giving no food (Harlow 1958). The prediction of cupboard love was that the infant would prefer whichever surrogate fed it. Instead, the infant monkeys spent almost all their time clinging to the cloth mother and went to the wire mother only to feed, then returned to the cloth; when frightened by a novel stimulus they fled to the cloth mother for comfort and used her as a base from which to venture out. The bond formed with the source of **contact comfort**, not the source of food. Harlow's later isolation experiments showed that monkeys reared without a real mother developed profound and lasting social, sexual and emotional deficits, evidence for a sensitive period in social development and against the idea that feeding is what matters.

PEARL

Harlow's single most exam-quoted conclusion: attachment is built on comfort and responsiveness, not on feeding. His work gave Bowlby the empirical footing to reject the psychoanalytic secondary-drive theory of the bond, and it prefigured the modern idea, carried into Emotionally Focused Therapy, that soothing physical contact directly regulates the threatened brain.

17.2 Bowlby: attachment as an evolved behavioural system

A control system for keeping the infant safe. John Bowlby (1907 to 1990), drawing on ethology, reframed attachment as a biologically evolved **behavioural system** whose set-goal is proximity to the caregiver and whose survival function is protection from predators and danger (Bowlby 1969). Attachment behaviours (crying, clinging, following, smiling, calling) are activated by fear, separation or fatigue and terminated by contact with the attachment figure. Two of Bowlby's terms recur in the exam. The **secure base** is the caregiver used as a base from which the child explores and to which it retreats when alarmed, so that attachment and exploration are reciprocally balanced. **Monotropy** is Bowlby's claim that the infant has an innate bias to form one principal, hierarchically superior attachment (usually but not necessarily the mother), which is qualitatively distinct from its bonds to other figures. Bowlby deliberately wrote "attachment figure" rather than "mother," acknowledging that fathers, grandparents and other caregivers can serve as attachment figures; the field's later focus on mothers reflected sampling convenience more than theory (Cassidy et al. 2013).

17.3 Bowlby: the internal working model

A cognitive template of self and other. The **internal working model** (IWM) is Bowlby's mechanism for how early experience persists: from repeated interactions the child builds a mental representation of whether the attachment figure is reliably available and responsive, and a complementary model of the self as worthy or unworthy of care (Bowlby 1969; Kaplan & Sadock 2024). These paired models operate largely outside awareness, guide expectations in later relationships, and are the theorised route by which infant attachment security predicts adult relational functioning. The IWM is the conceptual bridge from Ainsworth's infant classifications to the adult attachment literature and to the intergenerational transmission of attachment: a parent's own working model, captured on the Adult Attachment Interview, tends to predict the classification their infant will show in the Strange Situation.

17.4 Phases of attachment development

From indiscriminate signalling to a focused bond. Attachment is not present at birth but assembles over the first year through a described sequence of phases; the widely taught four-phase version comes from Schaffer and Emerson's longitudinal study of 60 infants (Schaffer & Emerson 1964), and maps closely onto Bowlby's own phase model.

Pre-attachment (birth to about 3 months)

No specific attachment; innate signals such as crying and smiling draw any caregiver near and are not yet directed at a particular person.

Indiscriminate attachment (about 6 weeks to 7 months)

The infant distinguishes familiar from unfamiliar people and responds more positively to primary caregivers but still accepts comfort from others.

Discriminate (specific) attachment (about 7 to 11 months)

A focused bond to one figure emerges; the infant now shows *separation protest* when parted from that figure and *stranger anxiety*, both appearing around 7 to 9 months.

Multiple attachments (after about 9 months)

Additional bonds form with other consistent caregivers (second parent, siblings, grandparents).

17.5 Maternal deprivation and separation: protest, despair, detachment

The sequence of a young child losing the caregiver. Bowlby's early work on prolonged separation described a predictable three-phase response in a young child removed from the attachment figure, for example on hospital or institutional admission (Kaplan & Sadock 2024). In **protest** the child cries, searches and refuses comfort, actively trying to recover the caregiver. In **despair** the child becomes quiet, withdrawn, hopeless and inactive, appearing to mourn. In **detachment** the child superficially recovers, engaging with surroundings and even the returning parent with apparent indifference, having defensively deactivated the attachment. Bowlby's **maternal deprivation hypothesis** linked disrupted early care to later disturbance, echoing René Spitz's earlier account of *anaclitic depression* in institutionalised infants deprived of a mothering figure (Spitz 1946). The strong "critical-period" reading of the hypothesis was later softened: outcome depends on the quality and reversibility of care, and later good caregiving can partly repair early deprivation.

17.6 Ainsworth: the Strange Situation procedure

A laboratory microcosm of attachment. Mary Ainsworth operationalised Bowlby's theory in the **Strange Situation**, a standardised observational procedure for infants of roughly 12 to 18 months (Ainsworth et al. 1978). It comprises eight brief episodes (about three minutes each) staged in an unfamiliar toy-filled room, using structured separations from and reunions with the caregiver plus the entry of a stranger, deliberately escalating mild stress to activate the attachment system. Observers rate four behavioural dimensions: *proximity and contact seeking*, *contact maintaining*, *avoidance* of proximity and contact, and *resistance* to contact and comfort, together with separation anxiety, stranger anxiety and, most diagnostically, the child's behaviour on *reunion*. The classification rests principally on the reunion episodes, not on how much the child cries at separation.

RULE **Read the type from reunion, not separation.** Both secure (B) and ambivalent (C) infants are highly distressed at separation, so separation distress alone never classifies.

17.7 The attachment classifications

Three original patterns plus a fourth. Ainsworth's analysis yielded three patterns, one secure and two insecure; Mary Main and Judith Solomon later added a fourth, **disorganised**, for infants who did not fit the original coding (Main & Solomon 1986).

TYPE	LABEL	EXPLORATION / SEPARATION	REUNION BEHAVIOUR (THE DISCRIMINATOR)	TYPICAL CAREGIVING
B	Secure	Explores freely using caregiver as a base; distressed at separation	**Actively seeks and is readily comforted by caregiver, then returns to play**	Sensitive, consistently responsive

TYPE	LABEL	EXPLORATION / SEPARATION	REUNION BEHAVIOUR (THE DISCRIMINATOR)	TYPICAL CAREGIVING
A	Insecure-avoidant	Explores with little reference to caregiver; little or no distress at separation	**Avoids or ignores caregiver on return; treats stranger and caregiver similarly**	Rejecting, dismissing of needs
C	Insecure-ambivalent / resistant	Clingy, explores little; intensely distressed at separation	**Seeks contact yet resists it, may arch away or push the caregiver away; not settled**	Inconsistent, unpredictable
D	Disorganised	No coherent strategy for managing distress	**Contradictory, odd or fearful acts on reunion: freezing, dazed expression, approaching then backing away**	Frightening / frightened; abuse or neglect

The reunion column is what separates the four types; separation distress alone does not, since both secure and ambivalent infants are distressed.

Distribution. In Ainsworth's original middle-class US sample the classic split was roughly secure 70 percent, avoidant 15 percent, ambivalent 15 percent, before the disorganised category existed (Ainsworth et al. 1978). A large modern meta-analysis of 285 studies and over 20,000 infant-caregiver pairs gives a global distribution of secure 51.6 percent, avoidant 14.7 percent, resistant 10.2 percent and disorganised 23.5 percent (Madigan et al. 2023). The A, B, C patterns are described as **organised** strategies (each a coherent, if insecure, way of managing an available or unavailable caregiver), whereas D reflects a breakdown of strategy.

51.6%	14.7%	10.2%	23.5%
SECURE (B)	AVOIDANT (A)	RESISTANT (C)	DISORGANISED (D)

COMMON TRAP

Do not equate crying at separation with insecurity: a securely attached infant is typically distressed when the caregiver leaves and comforted on return, whereas the avoidant infant shows little separation distress. The classification is read from *reunion*, not separation. Keep the letters and their labels aligned: A is avoidant, B is secure, C is ambivalent/resistant, D is disorganised. And attribute the fourth category correctly: the original three are Ainsworth's, the disorganised type is Main and Solomon.

17.8 Adult attachment, intergenerational transmission and psychopathology risk

The IWM carried forward and across generations. The infant patterns have adult counterparts assessed on the Adult Attachment Interview (autonomous corresponding to secure, dismissing to

avoidant, preoccupied to ambivalent, and unresolved/disorganised to disorganised), and a parent's classification statistically predicts their infant's, the phenomenon of **intergenerational transmission** of attachment; the imperfect link between parental state of mind and observed caregiving is the well-known "transmission gap" (Cassidy et al. 2013). Clinically, **disorganised** attachment is the pattern of greatest concern: it is over-represented in maltreated infants and is a robust early risk marker in developmental psychopathology, prospectively associated with later externalising problems, dissociation and personality pathology (Tasman 2015). Attachment concepts also underpin mentalization-based treatment, which locates the capacity to understand mental states within the security of early attachment relationships (Bateman & Fonagy).

HOLD THIS

Harlow theory, Bowlby framework, Ainsworth measure; disorganised (D) carries the greatest psychopathology risk. Harlow showed contact comfort beats feeding; the disorganised type (Main & Solomon) is over-represented in maltreated infants and is a safeguarding cue.

17.9 Reactive attachment disorder: the clinical extreme

When a selective attachment fails to form. **Reactive attachment disorder** (RAD) is the diagnosable disorder at the far end of the attachment spectrum, cross-referenced in Paper III (Kaplan & Sadock 2024). In DSM-5-TR and ICD-11 it requires a developmental age of at least **9 months** (the level at which selective attachment first becomes possible), onset before age 5, and a documented history of grossly insufficient care: social neglect, repeated changes of caregiver that prevent stable bonds, or rearing in settings with high child-to-caregiver ratios. The child shows an *emotionally withdrawn, inhibited* pattern: minimal seeking of or response to comfort when distressed, blunted positive emotion, and unexplained irritability, sadness or fearfulness. Autism spectrum disorder must be excluded. Its former "disinhibited" subtype is now the separate **disinhibited social engagement disorder** (DSED), marked by indiscriminate over-familiarity and reduced stranger wariness, and increasingly regarded as distinct from attachment as such. The evidence base is the English and Romanian Adoptees study and the Bucharest Early Intervention Project, which showed RAD signs recede within weeks of adequate care, whereas DSED can persist; neuroimaging in RAD has found reduced visual cortex volume and altered thalamic and white-matter measures (Kaplan & Sadock 2024).

CLINICAL ANCHOR

Attachment thinking is used at the bedside well beyond the RAD diagnosis. A child's attachment status frames how it will use a hospital admission or a new caregiver, and Bowlby's protest to despair to detachment sequence still describes the young inpatient separated from a parent. Adult attachment style shapes the therapeutic alliance: a dismissing patient may minimise distress and disengage, a preoccupied patient may over-seek reassurance, and an unresolved/disorganised state of mind flags trauma to be handled carefully. Disorganised attachment in an infant is a safeguarding cue, since it clusters with maltreatment.

INDIA

The Strange Situation was normed on Western nuclear families, and its coding of "avoidance" and independent exploration can misread culturally valued behaviour; in multiple-caregiver and joint-family settings common in India, distributions and the very meaning of a single monotropic figure may differ. Read a child's attachment behaviour against its actual caregiving ecology rather than against the original US base rates.

MNEMONIC

"A Avoids, B is Best, C Clings, D is Disordered"

Maps the four Strange-Situation letters to their signature: A avoidant (avoids the caregiver on reunion), B secure (the best-adjusted, comforted on reunion), C ambivalent/resistant (clings yet resists), D disorganised (no coherent strategy, odd or fearful reunion).

GOOD TO REMEMBER

- **Harlow (1958):** rhesus monkeys; cloth (contact-comfort) mother preferred over wire (feeding) mother, disproving cupboard-love / drive-reduction.
- **Bowlby (1907 to 1990):** attachment as an evolved behavioural system; secure base, monotropy, internal working model.
- **Internal working model:** mental template of caregiver-availability and of self-worth; route to adult and intergenerational transmission.
- **Separation response:** protest to despair to detachment (Bowlby); anaclitic depression (Spitz 1946).
- **Phases of attachment:** pre-attachment (0 to 3 mo), indiscriminate (6 wk to 7 mo), discriminate/specific (7 to 11 mo, separation protest and stranger anxiety), multiple (after ~9 mo).
- **Ainsworth (1978):** Strange Situation, infants ~12 to 18 months, 8 episodes; classification read from reunion.
- **Type B, Secure (~70% original):** distressed at separation, readily comforted on reunion; sensitive caregiving.
- **Type A, Insecure-avoidant (~15%):** little separation distress, avoids caregiver on reunion; rejecting caregiving.
- **Type C, Insecure-ambivalent/resistant (~15%):** intense distress, seeks yet resists contact; inconsistent caregiving.
- **Type D, Disorganised (Main & Solomon 1986):** contradictory/fearful reunion behaviour; frightening caregiving, maltreatment; highest psychopathology risk.
- **Modern distribution (Madigan et al. 2023):** secure 51.6%, avoidant 14.7%, resistant 10.2%, disorganised 23.5%.
- **Reactive attachment disorder:** developmental age ≥9 months, onset before age 5, pathogenic care; withdrawn/inhibited; ASD excluded. DSED is the separate disinhibited disorder. Evidence: ERA study, Bucharest Early Intervention Project.

18 · Temperament: Thomas and Chess

The idea that a child arrives with a behavioural signature, and the environment either fits it or fights it. **Temperament** refers to the constitutionally based, early-appearing, moderately heritable and relatively stable individual differences in how a person reacts to the world and regulates that reaction. It is the raw behavioural material on which later personality is built. For

the psychiatry exam this topic is owned by two child psychiatrists, Stella Chess and Alexander Thomas, whose New York Longitudinal Study (NYLS, begun in the 1950s) gave the field its enduring vocabulary: nine temperament dimensions, three temperamental constellations, and the concept of goodness of fit (Kaplan & Sadock 2024).

Hold four things for the exam and you command the topic: the nine **dimensions** Chess and Thomas rated; the three **types** (easy, difficult, slow-to-warm-up) with their approximate proportions; **goodness of fit** as the actual predictor of outcome (not the temperament alone); and the later models that refined the picture, Kagan's behavioural inhibition, Rothbart's reactivity and self-regulation, and Cloninger's psychobiological model that bridges temperament to personality. The etymology is worth a line: temperament comes from the Latin *temperare*, "to mix", the same idea that ran through Galen's four humoral temperaments and survives today in talk of neurotransmitter balance (Kaplan & Sadock 2024).

18.1 What temperament is, and how it differs from character and personality

Three words that are not synonyms. Examiners like the distinction because textbooks warn it is habitually blurred (Kaplan & Sadock 2024). **Temperament** is the biologically given, early-emerging, heritable substrate of reactivity and self-regulation, observable in infancy and stable across years. **Character** is the acquired layer: the self-concepts, goals, and values that develop through learning and experience and mature into adulthood (in Cloninger's model, self-directedness, cooperativeness, and self-transcendence). **Personality** is the integrated whole, temperament plus character, further shaped by culture, cognition, and life experience. Most theorists treat temperament as one of the foundations of personality, with the boundary between them genuinely obscure, "somewhat akin to pinpointing exactly when someone is an adult" (Kaplan & Sadock 2024). A useful shorthand: temperament is the *how* of behaviour (style and intensity), character is the *what for* (goals and values), personality is the sum.

18.2 The New York Longitudinal Study and the nine dimensions

Where the nine came from. During the 1950s, against a climate in which both psychoanalysis and behaviourism attributed almost everything to nurture, Chess and Thomas interviewed parents and observed children over many years and proposed that infants show measurable, heritable behavioural styles from the start (Kaplan & Sadock 2024). Rating behaviour, not underlying motive, they extracted **nine dimensions**. Each is a continuum, and the profile across all nine defines the child.

1. Activity level

The proportion of active to inactive periods; the child's overall motor tempo and vigour.

2. Rhythmicity (regularity)

The predictability of biological functions: sleep, hunger, and bowel habit falling into a regular schedule or not.

3. Approach or withdrawal

The nature of the first response to a new stimulus, person, food, or place: does the child move toward it or pull back?

4. Adaptability

How readily the initial response is modified in the desired direction once the novelty is no longer new; ease of settling into change.

5. Intensity of reaction

The energy level of a response, positive or negative, irrespective of its quality or direction.

6. Threshold of responsiveness

The strength of stimulation needed to evoke a discernible response (sensory threshold to light, sound, touch, and social cues).

7. Quality of mood

The balance of pleasant, joyful, friendly behaviour against unpleasant, crying, unfriendly behaviour.

8. Distractibility

The degree to which extraneous stimuli divert the child from ongoing behaviour.

9. Attention span and persistence

How long an activity is pursued (span) and whether it is continued despite obstacles or interruption (persistence); treated as one paired dimension.

18.3 The three constellations: easy, difficult, slow-to-warm-up

The person-centred layer that made the study famous. Beyond the nine variables, Chess and Thomas noticed that certain dimensions cluster into recognisable constellations, and named three types (a fourth group could not be classified). The proportions below are the NYLS figures and are examinable (Kaplan & Sadock 2024). Note that later writers, uneasy with judgemental labels for infants, renamed the types (flexible, feisty, cautious), and either set is acceptable.

TYPE (ALTERNATIVE NAME)	APPROX. PROPORTION	DEFINING TEMPERAMENTAL PROFILE
Easy child (flexible)	**~40%**	Regular rhythmicity, positive approach to novelty, high adaptability, mild-to-moderate intensity, predominantly positive mood; settles into routines quickly.
Difficult child (feisty)	**~10%**	Irregular rhythmicity, withdrawal from the new, poor (slow) adaptability, high intensity of reaction, predominantly negative mood; the low-threshold, intense, hard-to-soothe child.
Slow-to-warm-up child (cautious)	**~15%**	Initial withdrawal and slow adaptability like the difficult child, but with low activity and low-intensity reactions; warms up gradually if allowed repeated low-pressure exposure.
Undifferentiated / unclassified	~35%	A mix of characteristics not fitting any single type; positive on some dimensions, negative on others.

The discriminator between the two withdrawing types: the difficult child reacts with high intensity and negative mood, whereas the slow-to-warm-up child withdraws quietly, with low activity and low intensity; time and gentle re-exposure win the slow-to-warm child over.

Why the difficult child matters clinically. Chess and Thomas were emphatic that no type is pathology per se, but in the longitudinal follow-up it was the difficult children, roughly 10% of the sample, who most often went on to poorer adjustment and greater psychiatric disturbance (Kaplan & Sadock 2024). The precise cluster they defined as difficult was low rhythmicity, low response threshold, low adaptability, and high response intensity.

~40%	**~10%**	**~15%**
EASY	DIFFICULT (HIGHEST RISK)	SLOW-TO-WARM-UP

18.4 Goodness of fit: the real predictor of outcome

The single most important concept in the topic. Chess and Thomas' deepest contribution was to insist that temperament does not determine outcome by itself. **Goodness of fit** is the match between the child's temperament and the demands, expectations, and capacities of the environment, above all the caregivers (Kaplan & Sadock 2024). A good fit, in which environmental demands are consonant with the child's style, promotes healthy development; a poor fit, in which demands clash with the child's temperament, breeds stress, conflict, and later disturbance. The corollary is that no trait is intrinsically good or bad: a fearful, withdrawing temperament may be adaptive in a genuinely dangerous setting and maladaptive in a safe, predictable one. Outcome depends less on the child's temperament than on how the environment

responds to it, which is exactly why this construct anchors modern parent-guidance and early-intervention work.

RULE **Goodness of fit, not temperament, predicts outcome.** No type is pathology; a difficult child is only at higher risk, and that risk is realised or averted by the match between the child's style and the environment's demands.

CLINICAL ANCHOR

A "difficult" infant (irregular, intense, slow-adapting) placed with a calm, flexible, patient parent who paces transitions gently can develop well; the same infant with an anxious or rigid parent who reads intensity as defiance and escalates is set up for a coercive cycle and later behaviour problems. Rettew and colleagues showed this empirically: high child novelty-seeking predicted attention problems only when paired with a high-novelty-seeking mother, not with a low-novelty-seeking one. The lesson for the clinic is to treat the dyad, not the child alone, and to reframe temperament for parents as a style to be worked with rather than misbehaviour to be disciplined out.

18.5 Kagan's behavioural inhibition

The most heavily researched single temperamental trait. Jerome Kagan and colleagues at Harvard defined **behavioural inhibition** (BI) as the tendency of a subgroup of young children, roughly 10% to 15% of the population, to respond to novel people and situations consistently with reticence, restraint, and fear (Kaplan & Sadock 2024). Its opposite, behavioural disinhibition, is the sociable, approach-dominant response to novelty. Unlike most dimensions, BI has been studied largely as a near-categorical trait a child does or does not show. It matters because toddlers with BI carry an elevated risk of later anxiety disorders, above all social anxiety disorder. Its neural signature is durable: adults who were behaviourally inhibited at age 2 show heightened amygdala activation to novel faces on fMRI decades later, even when they report no current anxiety, evidence that the physiology of a temperamental trait can persist beneath a behaviourally regulated surface.

18.6 Rothbart's reactivity and self-regulation

The definition most textbooks now adopt. Mary Rothbart reframed temperament as "constitutionally based individual differences in **reactivity** and **self-regulation**", where reactivity is the excitability of emotional, motor, and attentional systems and self-regulation is the capacity (chiefly **effortful control**) to modulate that reactivity (Kaplan & Sadock 2024). Her structure resolves into three broad higher-order factors that recur across modern taxonomies: **surgency/extraversion** (approach, activity, positive emotion), **negative affectivity** (fear, anger, discomfort, sadness), and **effortful control** (attentional focusing and inhibitory control). What Rothbart fixed from Chess and Thomas was the addition of a genuine regulatory dimension, effortful control, which lets temperament account for how a child governs reactivity, not merely how strongly it reacts.

18.7 Cloninger: the bridge from temperament to personality

Where temperament research meets personality-disorder theory. C. Robert Cloninger's psychobiological model is the standard bridge, and it is the model that formally separates the two words this topic keeps distinguishing (Companion to Psychiatric Studies; Kaplan & Sadock 2024). His Temperament and Character Inventory (TCI) posits four heritable **temperament** dimensions, each tied to a neurotransmitter system, and three **character** dimensions that mature with experience.

Temperament (heritable, early, neurotransmitter-linked)

Novelty seeking (dopaminergic, approach to novelty), **harm avoidance** (serotonergic, behavioural inhibition to punishment), **reward dependence** (noradrenergic, sensitivity to social reward), and **persistence** (perseverance despite frustration).

Character (experiential, maturing)

Self-directedness (being responsible and goal-directed), **cooperativeness** (tolerance and helpfulness toward others), and **self-transcendence** (identification with something beyond the self).

The clinical payoff examiners want: low self-directedness and low cooperativeness (the character dimensions) are the core marker that a personality disorder is present, while the temperament profile shapes *which* disorder, for example high novelty seeking with low harm avoidance and low reward dependence maps to the antisocial/adventurous profile (Kaplan & Sadock 2024). This is how a childhood temperament construct connects to adult personality pathology.

> HOLD THIS
>
> **Temperament is the heritable early substrate (the how), character the acquired goals and values (the what for), personality the sum.** In Cloninger, low self-directedness and low cooperativeness are the core marker that a personality disorder is present.

18.8 Neurobiology of temperament

The "usual suspects" of psychiatry reappear here. Temperament is 20% to 60% heritable across twin and adoption studies, with additive polygenic effects and substantial nonshared-environmental contribution (Kaplan & Sadock 2024). The **neural correlates** map cleanly onto the three higher-order dimensions. Negative affectivity, harm avoidance, and behavioural inhibition centre on the **amygdala** and its circuitry (reduced amygdala-anterior-cingulate connectivity tracks higher harm avoidance; amygdalar hyperreactivity underlies BI), with serotonergic dorsal-raphe projections and HPA-axis dysregulation. Approach, novelty seeking, and extraversion run on **dopaminergic** mesolimbic and nigrostriatal pathways. Reward dependence and social affiliation involve **noradrenergic** locus-coeruleus output, median-raphe serotonin, and **oxytocin** at reward centres. Effortful control and persistence are mediated by **anterior/prefrontal cortex** and the **anterior cingulate** modulating subcortical drive. An EEG signature is examinable: left frontal activation tracks approach and positive emotion, right frontal activation tracks withdrawal and negative emotion.

COMMON TRAP

Do not say a "difficult" temperament causes psychopathology. Chess and Thomas explicitly denied that any type is pathology; the difficult child is only at higher *risk*, and that risk is realised or averted by goodness of fit. Equally, do not conflate temperament with personality on the exam, temperament is the heritable early substrate, personality is temperament plus acquired character. And do not confuse Kagan's behavioural inhibition (a near-categorical trait predicting social anxiety) with Chess and Thomas' slow-to-warm-up type; they overlap in withdrawal but are separate constructs from separate research programmes.

PEARL

The three big modern taxonomies converge: Rothbart's negative affectivity, Cloninger's harm avoidance, and the personality trait neuroticism describe the same amygdala-linked withdrawal dimension; Rothbart's surgency, Cloninger's novelty seeking, and extraversion describe the same dopamine-linked approach dimension; Rothbart's effortful control, Cloninger's persistence, and conscientiousness describe the same prefrontal regulatory dimension. If you can state these three axes, you can answer almost any temperament comparison question.

MNEMONIC

A RAAI TMDP

Read the nine dimensions in this order: **A**ctivity level, **R**hythmicity, **A**pproach-withdrawal, **A**daptability, **I**ntensity of reaction, **T**hreshold of responsiveness, **M**ood, **D**istractibility, **P**ersistence (attention span). For the three types, the fit is on a sliding scale: the child who fits Easily, the one who is Difficult, and the one who is Slow to warm.

GOOD TO REMEMBER

- **Chess and Thomas, New York Longitudinal Study (1950s):** the origin of the nine dimensions, three types, and goodness of fit.
- **Nine dimensions:** activity level, rhythmicity, approach-withdrawal, adaptability, intensity of reaction, threshold of responsiveness, quality of mood, distractibility, attention span and persistence.
- **Easy child (~40%):** regular, approaching, adaptable, positive mood; also called flexible.
- **Difficult child (~10%):** irregular rhythmicity, withdrawing, poorly adaptable, intense, negative mood; highest risk of later disturbance; also called feisty.
- **Slow-to-warm-up child (~15%):** initial withdrawal and slow adaptation but low activity and low intensity; warms with gentle re-exposure; also called cautious.
- **Undifferentiated (~35%):** mixed profile, unclassifiable.
- **Goodness of fit:** match between child temperament and environmental demand is the actual predictor of outcome, not temperament alone.
- **Kagan, behavioural inhibition:** ~10% to 15% of children, fearful/reticent to novelty, near-categorical, predicts social anxiety disorder; persistent amygdala signature on fMRI.
- **Rothbart:** temperament as reactivity and self-regulation; three factors, surgency/extraversion, negative affectivity, effortful control.
- **Cloninger TCI:** four temperament dimensions (novelty seeking, harm avoidance, reward dependence, persistence) plus three character dimensions (self-directedness, cooperativeness, self-transcendence); low self-directedness and cooperativeness mark personality disorder.
- **Temperament vs character vs personality:** temperament is the heritable early substrate (the how); character is the acquired goals and values (the what for); personality is the integrated whole.
- **Heritability of temperament:** about 20% to 60% across twin and adoption studies.

19 · Mahler separation-individuation

The psychological birth of the human infant, mapped month by month. Margaret Mahler (1897 to 1985), a Hungarian-born analyst working in New York, did for the first three years of life what Erikson did for the whole lifespan: she took direct, systematic observation of infants and their mothers and built from it a stage theory of how a self is born out of fusion (Kaplan & Sadock 2024). Her **separation-individuation** theory is the developmental spine of psychodynamic child psychiatry, and it is the theory examiners reach for whenever they want to test the developmental roots of borderline personality organisation. The title of her 1975 book with Fred Pine and Anni Bergman, *The Psychological Birth of the Human Infant*, is itself the thesis: biological birth and psychological birth are separate events, and the second one takes about three years.

For the exam hold four things: the two normal precursor phases (**autism** and **symbiosis**), the four subphases of separation-individuation in order with their ages, the two conceptual poles the whole process moves between (**separation**, the emergence from fusion, and **individuation**, the growth of an autonomous self), and the endpoint, **emotional object constancy**. Then attach the one clinical hypothesis every examiner wants: the rapprochement-failure account of borderline pathology (Masterson & Rinsley 1975). Mahler is a developmental map only; the fuller object-relations school that grew alongside her (Klein, Winnicott, Fairbairn) is **the Social, Learning & Personality Psychology notes** material and is signposted below, not taught here.

19.1 Who Mahler was, and what her method fixed

From reconstructed fantasy to observed behaviour. Before Mahler, most analytic accounts of infancy were reconstructions, inferred backwards from adult patients or from the analysis of older children. Mahler's contribution was methodological as much as theoretical: she and her collaborators watched mother-infant pairs directly, over time, in a naturalistic playroom setting, and derived the phases from what infants actually did (Kaplan & Sadock 2024). What this fixed was the empirical thinness of earlier drive-based accounts of the first year. What she kept from psychoanalysis was its central question, how the mind comes to distinguish self from other; what she left debated was whether her earliest phases (normal autism above all) survive scrutiny against modern infant research, which shows newborns to be far more socially oriented from birth than a phase of "objectless" autism would allow. Hold that critique for 19.8; it is the standard higher-order examiner follow-up.

19.2 Normal autistic phase (birth to about 1 month)

The closed system. In the **normal autistic phase** the newborn is described as being in a state of absolute primary narcissism, without awareness of a mothering agent, functioning as though within a closed psychological system (Kaplan & Sadock 2024). Needs are met but not yet attributed to anything outside the self; the infant does not know that the satisfaction comes from a caregiver. Mahler suggested a normal degree of autism here may be protective, buffering the immature nervous system against a flood of stimuli. This is the phase most challenged by later research, and Mahler herself, late in her career, questioned whether it should be retained; keep that caveat ready.

19.3 Normal symbiotic phase (about 1 to 5 months)

The dual unity within one common boundary. In the **normal symbiotic phase** the infant develops a dim awareness that need satisfaction comes from outside the self, and behaves as though it and the mother were "an omnipotent system, a dual unity within one common boundary" (Kaplan & Sadock 2024). Self and object are not yet distinguished; the boundary between them differentiates only momentarily, in states of **affect hunger**, and dissolves again once the need is gratified. This fused, need-satisfying matrix is the ground from which the true psychological birth will emerge. The word **symbiosis** is Mahler's, and it is the term examiners test: it names a subjective fusion, not a biological one.

19.4 Subphase 1, differentiation or hatching (about 5 to 9 months)

Breaking out of the symbiotic shell. Separation-individuation proper begins with **differentiation**, which Mahler called **hatching**: the infant gradually emerges from the symbiotic orbit and begins to sense the body-self as distinct from the mother (Kaplan & Sadock 2024). Attention turns outward, from an internal preoccupation to active curiosity about the surroundings and about the caregiver as a separate entity. The behavioural markers are the classic ones of this age: increased alertness, scanning, and comparative examination of the mother against strangers. Stranger reactions and the beginnings of exploration belong here. The two threads of the process are already visible and should be named separately: *separation* (emerging

from fusion) and *individuation* (the growth of the infant's own capacities), which advance in parallel but are not the same thing.

19.5 Subphase 2, practising (about 9 to 16 months)

The love affair with the world. The **practising** subphase is powered by upright locomotion: crawling, then walking, let the toddler physically leave the mother's orbit and return to it (Kaplan & Sadock 2024). Mahler split it into an early phase (the infant moves away by crawling but keeps visually "checking back") and a practising period proper (free upright walking). Two concepts are examinable here. The first is **emotional refuelling**: the toddler ventures out, and returns to physical contact with the mother to be recharged before venturing again, using her as a **home base**. The second is the elated, seemingly grandiose mood of this period, the toddler "intoxicated with their own faculties", relatively impervious to knocks and frustrations, which Mahler's colleague Greenacre called the toddler's "love affair with the world". Separation anxiety is at its lowest ebb here, which is exactly why the next subphase lands so hard.

19.6 Subphase 3, rapprochement (about 16 to 24 months): the crisis

The single most examinable moment in the whole theory. By the middle of the second year the toddler's growing cognitive and language ability delivers an unwelcome discovery: it is small, separate, and dependent after all. This is the **rapprochement** subphase, and its defining feature is the **rapprochement crisis** (Kaplan & Sadock 2024). The elated omnipotence of practising collapses into an acute awareness of separateness, and the child oscillates: it wants autonomy and it wants the mother, and it cannot have both without contradiction.

The behavioural signature. The child alternates between clinging to the mother (shadowing) and darting away from her (darting-off), and between demanding help and angrily refusing it. Mahler named this vacillation **ambitendency**. It generates the classic tantrums and neediness of the period, and it places a specific demand on the mother: she must remain emotionally available and tolerant of the child's ambivalence, surviving its aggression without retaliating or withdrawing. Optimal maternal availability here lets the child integrate the loving and the frustrating images of the mother into one whole. Failure of that maternal function is the hinge of the borderline hypothesis in 19.8.

RULE **Rapprochement is the crisis of the whole theory.** Practising omnipotence collapses into an awareness of separateness, and the toddler oscillates (ambitendency: shadowing and darting-off), needing the mother to survive its aggression without withdrawing.

19.7 Subphase 4, consolidation and emotional object constancy (about 24 to 36 months)

Carrying the mother inside. The last subphase is the **consolidation of individuality** and the attainment of **emotional object constancy** (Kaplan & Sadock 2024). Two achievements define it. First, a stable, integrated sense of self (individuality consolidated). Second, and the term to get exactly right, **emotional object constancy**: the capacity to hold a stable, unified internal representation of the mother as both good and frustrating, so that her image can be sustained and can comfort the child even in her absence and even when she is frustrating the child. This is distinct from Piaget's *object permanence*, which is merely knowing that a physical object continues

to exist when out of sight; a discriminator examiners love. With object constancy the child can tolerate longer separations, accept symbolic substitutes, and finally hold together love and hate for the same person. This is the true endpoint of psychological birth.

PHASE / SUBPHASE	AGE (MONTHS)	CORE TASK OR STATE	SIGNATURE MARKER
Normal autism	0 to 1	Closed system, primary narcissism	**No awareness of a mothering agent**
Normal symbiosis	1 to 5	Dual unity, one common boundary	**Fusion; boundary appears only in affect hunger**
Differentiation (hatching)	5 to 9	Body-self felt as distinct	**Hatching; outward attention, stranger reactions**
Practising	9 to 16	Locomotor exploration from a home base	**Emotional refuelling; elated "love affair with the world"**
Rapprochement	16 to 24	Awareness of separateness and dependence	**Rapprochement crisis; ambitendency, shadowing and darting**
Consolidation / object constancy	24 to 36	Stable self plus internalised whole mother	**Emotional object constancy**

The whole arc at a glance: two normal precursor phases, then four subphases of separation-individuation, ending at emotional object constancy by about the third birthday. The discriminator column carries the term most likely to be asked for each row.

19.8 The rapprochement-failure hypothesis of borderline pathology

Why Mahler is on a psychiatry syllabus at all. The clinical payoff of the theory is a developmental account of **borderline personality organisation**. Masterson and Rinsley (1975), building directly on Mahler, proposed that borderline pathology is a fixation at, or failure of, the rapprochement subphase (Bateman & Fonagy 2004). Their model runs as follows. The mother of the pre-borderline child (in their formulation, herself often borderline) rewards clinging, regressive dependence and withdraws her emotional supply, her **libidinal availability**, precisely when the child moves toward autonomy. The child is left with a lasting equation: separation and individuation bring abandonment. Because the loving and the frustrating images of the mother are never integrated, the person's inner world stays organised by **splitting** into all-good and all-bad object representations, and emotional object constancy is never securely reached (Kaplan & Sadock 2024).

What this explains, and its limits. The adult correlates fall out neatly: the terror of abandonment, the unstable and intense relationships that swing between idealisation and devaluation, the identity disturbance, and the abandonment depression Masterson placed at the centre of the disorder. This is a high-yield exam line, but state it as a hypothesis, not fact: it is a retrospective, reconstructive model, and contemporary aetiology of borderline personality disorder is multifactorial (temperament, trauma, invalidating environments, and gene-

environment interaction), with the developmental account one contributing strand rather than the whole story.

HOLD THIS

Failed rapprochement is the developmental template for borderline splitting (Masterson & Rinsley). The loving and frustrating images never integrate, so emotional object constancy is never reached and the inner world stays split into all-good and all-bad. State it as a hypothesis.

CLINICAL ANCHOR

An adult patient who cannot be alone, who idealises then abruptly devalues the same person, and who experiences any move toward independence in therapy as an abandonment, can be formulated in Mahlerian terms as arrested at rapprochement: love and hate for the object were never integrated, so object constancy fails and the inner world stays split. In the transference this shows as the therapist being all-good one week and all-bad the next. Naming that mechanism (splitting from failed rapprochement) is the developmental half of a borderline formulation; the treatment half belongs to the the Social, Learning & Personality Psychology notes object-relations therapies.

19.9 Boundary line: where Mahler ends and object-relations theory begins

Know the fence so you place each name on the right side of it. Mahler gives the developmental cartography, the observed sequence from fusion to a self. The wider **object-relations** school gives the theory of how internal images of self and other are built, split, repaired, and used, and that school is taught in full on **the Social, Learning & Personality Psychology notes**. Three names sit on the far side of that fence and should be signposted, not developed here.

Melanie Klein (the Social, Learning & Personality Psychology notes)

The paranoid-schizoid position and the depressive position; part-objects (good and bad breast), projective identification, and the origin of the object-relations view. The Kleinian "positions" are the structural counterpart to Mahler's developmental subphases.

Donald Winnicott (the Social, Learning & Personality Psychology notes)

The good-enough mother, the holding environment, the transitional object and transitional space. Winnicott's "there is no such thing as a baby, only a nursing couple" is the object-relations echo of Mahler's symbiosis.

Ronald Fairbairn (the Social, Learning & Personality Psychology notes)

The most thoroughgoing object-relations theorist: libido is object-seeking rather than pleasure-seeking, and the ego is split (central, libidinal, and anti-libidinal or internal saboteur) through frustrating early relationships.

The one link to carry across the fence: Mahler's *emotional object constancy* and Klein's *depressive position* describe the same maturational achievement from two vantage points, the integration of a whole object that is both loved and hated. Everything else about Klein, Winnicott and Fairbairn waits for the Social, Learning & Personality Psychology notes.

COMMON TRAP

Do not conflate Mahler's *emotional object constancy* with Piaget's *object permanence*. Object permanence (roughly 8 to 12 months) is the cognitive knowledge that a thing still exists when hidden; emotional object constancy (by about 36 months) is the affective capacity to hold a stable, integrated internal image of a specific person as both good and bad, and to be soothed by it in their absence. They are different constructs, different theorists, and different ages. A second trap: *symbiosis* in Mahler is a subjective psychological fusion, not the biological symbiosis of two organisms.

PEARL

The one-line integration for an examiner: Mahler mapped the psychological birth of the infant across two normal phases and four subphases, ending at emotional object constancy, and the failure of the rapprochement subphase (Masterson & Rinsley) is the developmental template for borderline splitting. Name that arc (symbiosis to rapprochement crisis to object constancy, and its borderline failure) and you have the whole topic.

MNEMONIC

Subphases: "Dear Practising Reaches Consolidation"

Differentiation (hatching, 5 to 9m), **P**ractising (9 to 16m), **R**approchement (16 to 24m), **C**onsolidation and object constancy (24 to 36m). Prefix the two normal precursors with "**A**utism, **S**ymbiosis" and the full order is A, S, then D, P, R, C.

GOOD TO REMEMBER

- **Margaret Mahler (1897 to 1985):** separation-individuation theory; book with Pine and Bergman, *The Psychological Birth of the Human Infant* (1975).
- **Normal autistic phase:** birth to about 1 month; closed system, primary narcissism, no awareness of a mothering agent.
- **Normal symbiotic phase:** about 1 to 5 months; dual unity within one common boundary; boundary appears only in affect hunger.
- **Differentiation (hatching):** about 5 to 9 months; body-self felt as distinct; outward attention, stranger reactions.
- **Practising:** about 9 to 16 months; locomotor exploration, home base, emotional refuelling, elated "love affair with the world".
- **Rapprochement:** about 16 to 24 months; rapprochement crisis; ambitendency, shadowing and darting-off; separation anxiety peaks.
- **Consolidation / emotional object constancy:** about 24 to 36 months; stable self plus integrated whole-object image of the mother.
- **Separation vs individuation:** separation = emergence from fusion; individuation = growth of the autonomous self; parallel but distinct threads.
- **Emotional object constancy vs object permanence:** affective (stable inner image of a person, by ~36m, Mahler) vs cognitive (a thing persists when hidden, ~8 to 12m, Piaget).
- **Rapprochement-failure hypothesis:** Masterson & Rinsley (1975); mother withdraws libidinal availability at moves toward autonomy; fixation at rapprochement, persistent splitting, failed object constancy; developmental template for borderline organisation (a hypothesis, not settled fact).
- **the Social, Learning & Personality Psychology notes boundary (object-relations school):** Klein (paranoid-schizoid and depressive positions), Winnicott (good-enough mother, holding, transitional object), Fairbairn (object-seeking libido, ego splitting) are taught on the Social, Learning & Personality Psychology notes, not here.

20 · Language and motor developmental milestones

The developmental yardstick. A **milestone** is a functional skill that a typically developing child acquires at a roughly predictable age, and the milestones are conventionally tracked along four parallel **streams**: gross motor, fine motor (adaptive), language, and personal-social (adaptive-social). The exam wants two things from this topic. First, the milestone ages themselves, because a psychiatrist reads them backwards: a delayed or lost milestone is the earliest sign of intellectual developmental disorder, autism, cerebral palsy or a regressive condition, and the developmental history is a fixed part of every child psychiatric assessment (Kaplan & Sadock 2024). Second, the competing theories of how one milestone in particular, spoken language, is acquired, because the Skinner-to-Chomsky argument is a set-piece and Chomsky's language acquisition device is the single most asked-about idea in this area.

Handle the two halves differently. The milestone ages are learned as a table to be enumerated, with a small set of high-yield anchor ages committed to memory. The language-acquisition theories, by contrast, follow the standard evolution-of-theories flow: Skinner's learning account, what Chomsky's nativism fixed, then the interactionist synthesis that is currently accepted, followed by the neural correlate and a worked example. Treat the ages below as the standard

textbook figures (K&S / Gesell schedule); normal children vary, and a lag of a month or two around any single milestone is not itself pathological.

20.1 The four streams and why they are read together

One age, four windows. Development is assessed across four streams because a child can be typical in one and delayed in another, and the *pattern* of delay is diagnostic. **Gross motor** covers posture and large-muscle control (head control, sitting, standing, walking). **Fine motor** or adaptive covers hand skills and eye-hand coordination (reaching, grasp, the pincer grip, tower-building, copying shapes). **Language** covers both reception and expression (cooing, babbling, first words, phrases). **Personal-social** covers interaction and self-care (social smile, stranger anxiety, feeding self, dressing). An *isolated* motor delay points to a neuromuscular or cerebral-palsy picture; an isolated language delay points to hearing loss or developmental language disorder; a *global* delay across all four streams is the developmental signature of intellectual developmental disorder, and a delay concentrated in language plus social-reciprocity flags autism spectrum disorder (Kaplan & Sadock 2024).

TRAP Do not read one milestone in isolation; it is the **pattern of delay** that is diagnostic. Isolated motor delay points to cerebral palsy, isolated language delay to hearing loss, global delay to intellectual developmental disorder, language-plus-social delay to autism.

20.2 Gross-motor milestones

Cephalocaudal progression: head, trunk, legs. Motor control descends the body, so head control precedes sitting, which precedes standing and walking. The high-yield ages are head control (steady head-holding, lifting the head to 90 degrees prone) by about 3 months; rolling over and sitting with support by about 5 months; sitting steadily without support with a straight back by about 6 to 8 months; pulling to stand and cruising around furniture by about 10 months; and walking well without support by about 14 to 15 months (Kaplan & Sadock 2024). By 2 years the child runs and climbs stairs; by 3 years climbs stairs with alternating feet and rides a tricycle.

20.3 Fine-motor (adaptive) milestones

From whole-hand rake to precise pincer. Grasp matures from a crude palmar rake toward the **pincer grasp**, the opposition of thumb and index finger that lets the infant pick up a small pellet, which appears at about 9 to 10 months and is a classic exam item because it marks a qualitative advance in hand control (Kaplan & Sadock 2024). Construction and copying then follow a fixed order used clinically to estimate developmental age: a tower of 3 to 4 cubes by about 18 months, a tower of 6 to 7 cubes and copying a horizontal line by 2 years, then copying a circle at 3 years, a cross at 4 years, a square at 5 years, a triangle at 6 years and a diamond at 7 years. The copy-a-shape sequence (circle 3, cross 4, square 5, triangle 6, diamond 7) is a favourite because the ages step up by one year.

20.4 Language milestones

Sound before words, words before sentences. Expressive language runs through a conserved sequence: vocalising apart from crying and laughing aloud by about 3 months; saying "mama, dada" and other repeated syllables non-specifically by about 9 months; the **first words** used

meaningfully at around 12 months; roughly 10 words including the child's name by 18 months; and combining two different words into simple phrases between 18 and 24 months (Kaplan & Sadock 2024). By 3 years the child uses plurals and has a fair vocabulary; by 5 years names the primary colours accurately and defines simple words. Reception runs slightly ahead of expression throughout: a 10-month-old understands "where is mama?" before it can say much itself.

20.5 Personal-social milestones

The social calendar. The **social smile**, the first smile given in response to a human face rather than reflexively, appears at about 6 to 8 weeks and is the earliest social milestone routinely asked about (Kaplan & Sadock 2024). The infant recognises the mother by about 3 months and smiles at its mirror image by about 6 months. **Stranger anxiety**, wariness or distress at an unfamiliar face, emerges at about 8 months (the range 7 to 9 months is quoted), signalling that the infant now discriminates the primary caregiver from others; separation anxiety appears in the same window. Self-care then advances: feeding self with a spoon by about 18 months, dressing with help by 3 years, and dressing without supervision by 5 years.

PEARL

Stranger anxiety at about 8 months is not a problem, it is a milestone: it means the infant has formed a specific, discriminated attachment and can tell its caregiver from a stranger. Its *absence* at the expected age is the concern. The same 8-month window is why reactive attachment disorder requires a developmental age of at least 9 months, the point at which a selective attachment (and therefore its failure) first becomes possible.

20.6 The milestone table (verified ages)

The four streams side by side. The following consolidates the high-yield ages across streams for rapid recall (Gesell schedule as reproduced in Kaplan & Sadock 2024).

AGE	GROSS MOTOR	FINE MOTOR / ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
6 to 8 weeks	Lifts head momentarily prone	**Regards / follows a face**	Vocalises, coos	Social smile
3 months	Head control (holds head, 90 degrees prone)	**Follows object past midline**	Laughs aloud	Recognises mother
6 months	Sits with support; rolls over	**Palmar (raking) grasp; reaches**	Babbles	Smiles at mirror image
8 months	Sits steadily without support	**Transfers object hand to hand**	Non-specific "mama, dada"	Stranger anxiety
9 to 10 months	Pulls to stand; cruises furniture	**Pincer grasp (thumb-index)**	Understands "where is mama?"	Responds to social play
12 months	Stands alone; may take first steps	**Neat pincer; releases object**	First words (meaningful)	Waves bye-bye

AGE	GROSS MOTOR	FINE MOTOR / ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
14 to 15 months	Walks well without support	**Tower of 2 cubes; scribbles**	Jargon; few words	Points to indicate wants
18 months	Runs stiffly; walks up stairs, hand held	**Tower of 3 to 4 cubes**	About 10 words	Feeds self with spoon
2 years	Runs well; climbs stairs	**Tower of 6 to 7 cubes; copies line**	Two-word phrases; simple sentences	Wears simple garments
3 years	Stairs with alternating feet; tricycle	**Copies a circle; tower of 9 to 10**	Plurals; fair vocabulary	Dresses/undresses with help

Anchor ages to memorise: social smile 6 to 8 wk, head control 3 mo, sits without support 6 mo, stranger anxiety 8 mo, pincer 9 to 10 mo, first words ~12 mo, walks 14 to 15 mo, two-word phrases 18 to 24 mo.

6 to 8 wk SOCIAL SMILE	**8 mo** STRANGER ANXIETY	**9 to 10 mo** PINCER GRASP	**~12 mo** FIRST WORDS

COMMON TRAP

Do not conflate the walking figure quoted in different books. One common figure gives independent walking at 14 to 15 months as the age most children walk *well*; many texts quote the wider normal range of 12 to 15 months, and the red-flag cut-off for referral is failure to walk by 18 months. State the figure with its book, and use the red flag, not the median, to decide whether a child is delayed. Likewise "first words at 12 months" is the median; the delay threshold is no single words by *2 years*.

20.7 Red-flag delays

When variation becomes concern. A single milestone reached a little late is usually normal; a red flag is a delay large enough to warrant assessment, or any *loss* of a skill already gained (regression), which is always abnormal (Kaplan & Sadock 2024). The standard motor and social red flags are: no head control by 4 months, not sitting unsupported by 9 months, not walking by 18 months, and no social smile by 3 months. The language red flags are the most examinable and come straight from ICD-11: the *absence of single words by 2 years* of age and the *failure to generate simple two-word phrases by 3 years*, especially when persistent or with a family history of language problems, are the thresholds that separate a late talker (who usually catches up) from developmental language disorder (World Health Organization ICD-11 2019). Loss of previously acquired language or social skills, at any age, warrants urgent evaluation for autism spectrum disorder or a neurodegenerative or epileptic process.

20.8 Stages of language: cooing, babbling, holophrastic, telegraphic

The universal sequence. Before the theories, fix the stages, because every account has to explain this sequence and all typically developing infants pass through it in the same order (Tasman 2015). **Cooing**, the production of vowel-like sounds, begins at about 2 months. **Babbling** proper

follows as consonants are added at about 4 to 6 months, becoming *canonical (reduplicated) babbling* with repeated consonant-vowel syllables such as "da-da-da" by about 7 months. The **holophrastic** or one-word stage begins around 12 months, when a single word ("milk") is used to carry the force of a whole utterance. The **telegraphic** or two-word stage begins at about 18 to 24 months, when the child combines two content words ("more milk", "daddy go") while omitting grammatical function words, like a telegram. The child then acquires roughly 5 to 9 new words a day through the preschool years, reaching about 5,000 words by kindergarten (Tasman 2015).

20.9 Skinner: the learning (operant) account

Language as verbal behaviour shaped by reinforcement. The first systematic theory was B. F. Skinner's, set out in *Verbal Behavior* (Skinner 1957). On this behaviourist account, language is learned like any other operant: the infant emits sounds, the caregiver *reinforces* approximations to real words with attention, praise and getting what is named, and through selective reinforcement, shaping and imitation the child's output is gradually moulded toward the adult language (Tasman 2015). There is no special language faculty; the same principles of operant conditioning (reinforcement, extinction, stimulus control) that Skinner used to explain all behaviour explain speech. *What it got right:* environmental input clearly matters, since children learn the specific language they are exposed to, vocabulary tracks the amount of speech directed at the child, and reinforcement does influence output. *What it left unexplained:* the sheer speed of acquisition, the fact that children produce grammatical forms and novel sentences they have never heard and could not have been reinforced for, and their regular *over-generalisation* errors ("goed", "foots") which are the opposite of what imitation predicts.

20.10 Chomsky: nativism and the language acquisition device

An innate grammar organ. Noam Chomsky's 1959 review of Skinner's book is the standard turning point (Chomsky 1959). Chomsky argued that language cannot be learned by reinforcement alone because of the **poverty of the stimulus**: the speech a child actually hears is finite, error-filled and degenerate, yet from it every normal child rapidly extracts an infinite generative grammar and masters most of the basic rules by about age 4 (Tasman 2015). To bridge this gap Chomsky proposed an innate, biologically given **language acquisition device** (LAD): humans are born with a domain-specific facility for acquiring language (Chomsky 1975). Its content is a **universal grammar**, a set of structural principles common to all human languages, so that the environment only has to *set the parameters* for the particular language, not teach grammar from scratch. This is the **nativist** or innateness hypothesis: at least some linguistic knowledge exists in humans at birth (Chomsky 1986; Tasman 2015). *What it fixed:* it explained the speed, the creativity (novel grammatical sentences), the universality of the stage sequence, and the ease with which children handle grammatical transformations. *What it left debated:* the strong version treats environmental input as almost irrelevant, which sits badly with the robust evidence that responsive, socially contingent talk accelerates acquisition, and the LAD itself is a postulated faculty rather than a localised structure.

COMMON TRAP

Keep the labels straight. The *LAD* is the hypothesised innate device or faculty; *universal grammar* is its content, the shared structural principles; *nativism / innateness hypothesis* is the broader position that some grammar is inborn; and *poverty of the stimulus* is the argument *for* nativism, not a synonym for it. Skinner is the learning theorist Chomsky was refuting, not a nativist. And Chomsky 1959 is the review of Skinner; the LAD is elaborated in the later works (1975, 1986).

20.11 The interactionist / social-pragmatic view (currently accepted)

Innate capacity plus social input. The **currently accepted** position is neither pure Skinner nor pure Chomsky but an **interactionist** synthesis (Tasman 2015). Interactionist theorists accept Chomsky's evidence for an innate, biologically prepared capacity for language, but hold that this capacity is realised only through environmental and, crucially, *social* input: language emerges from the interaction of the child's endowment with responsive communication tuned to the child's level. The *social-pragmatic* strand (drawing on Bruner's "language acquisition support system" and on Vygotsky) stresses that language is acquired in the service of shared social goals, scaffolded by joint attention and contingent caregiver talk; the classic experimental support is that socially contingent feedback to an infant's babble accelerates phonological learning (Goldstein & Schwade 2008). This resolves the Skinner-Chomsky opposition: the nativists were right that experience alone is insufficient and a prepared capacity is needed, and the learning and social theorists were right that input, especially interactive input, is what switches that capacity on and shapes it to the ambient language.

HOLD THIS

Language = an innate capacity switched on by social input (interactionist synthesis). Skinner (reinforcement) could not explain over-generalisation ("goed"); Chomsky's LAD and universal grammar could; the currently accepted view keeps both.

20.12 Neural correlate and a critical period

Where language lives, and when the window is open. The **neural correlate** of language is a left-hemisphere-dominant perisylvian network: *Broca's area* in the left inferior frontal gyrus for speech production and syntax, *Wernicke's area* in the left posterior superior temporal gyrus for comprehension, and the *arcuate fasciculus* connecting them (Kaplan & Sadock 2024). Consistent with the nativist claim of a biological substrate, a seed language-processing network is already detectable in the temporal cortex of newborns just a few days old, an experience-independent "attractor" template on which the mature network is built through exposure (Kaplan & Sadock 2024). Language acquisition is subject to a **critical period**: the capacity to acquire a first language effortlessly, and to attain native accent in a second, declines from childhood and closes around puberty, which is why very early deprivation of language input has lasting effects while later good input can only partly compensate.

20.13 Worked example

The over-regularisation error, read by each theory. A 3-year-old who has correctly said "went" for months suddenly starts saying "goed". Skinner's account struggles here: the child was never

reinforced for, and never heard, "goed", so imitation and reinforcement cannot have produced it. The nativist reads it as decisive evidence for an internal rule system: the child has extracted the productive past-tense rule "add -ed" from universal grammar's parameter-setting and is over-applying it to an irregular verb, generating a form it could not have copied. The interactionist adds that the child will drift back to "went" as continued interactive exposure supplies the correct irregular form and the caregiver's contingent recasts ("yes, he went") tune the rule. The single error thus captures the whole debate: it is inexplicable by input alone, it demonstrates an internal generative rule, and it is corrected by social input, which is exactly why the interactionist synthesis is accepted.

INDIA

Milestone screening in Indian practice relies on locally validated tools rather than the raw Gesell ages: the Trivandrum Developmental Screening Chart and the developmental sections of instruments such as the Vineland Social Maturity Scale (Indian adaptation) are in routine use, and the RBSK (Rashtriya Bal Swasthya Karyakram) programme screens for developmental delay at anganwadi and school level. The language red flags need cultural adjustment too: many Indian children grow up bilingual or multilingual, and a transient "delay" in one language with normal total vocabulary across languages is not developmental language disorder. Assess the child's language across all the languages it hears, not just the clinic language.

MNEMONIC

"Smile at 2 months, Sit at 6, Stranger at 8, Speak at 12"

The four social-motor anchors in month order: social *smile* at about 6 to 8 weeks (~2 months), *sits* without support at about 6 months, *stranger* anxiety at about 8 months, and first *words* ("speak") at about 12 months. For the copy-a-shape ladder: circle 3, cross 4, square 5, triangle 6, diamond 7, each a year apart.

GOOD TO REMEMBER

- **Social smile:** 6 to 8 weeks (~2 months); earliest social milestone.
- **Head control:** 3 months (holds head, 90 degrees prone). Recognises mother 3 months.
- **Rolls over / sits with support:** about 5 to 6 months; babbles ~6 months.
- **Sits without support:** about 6 to 8 months (straight back, steady).
- **Stranger anxiety:** about 8 months (range 7 to 9); marks discriminated attachment.
- **Pincer grasp:** 9 to 10 months (thumb-index opposition).
- **First words (meaningful):** around 12 months; understands "where is mama?" by 10 months.
- **Walks well without support:** 14 to 15 months; wider normal range 12 to 15 months.
- **Two-word (telegraphic) phrases:** 18 to 24 months; ~10 words by 18 months.
- **Copy-a-shape ladder:** circle 3 y, cross 4 y, square 5 y, triangle 6 y, diamond 7 y.
- **Language red flags (ICD-11):** no single words by 2 years; no two-word phrases by 3 years; any loss of skill (regression) at any age is abnormal.
- **Motor red flags:** no head control by 4 mo, not sitting by 9 mo, not walking by 18 mo, no social smile by 3 mo.
- **Language stages:** cooing ~2 mo, babbling (canonical) 4 to 7 mo, holophrastic (one-word) ~12 mo, telegraphic (two-word) 18 to 24 mo.
- **Skinner (1957):** operant / learning account; language shaped by reinforcement and imitation; no special faculty.
- **Chomsky (1959 review; LAD 1975):** nativist; language acquisition device, universal grammar, poverty-of-stimulus argument.
- **Interactionist / social-pragmatic:** currently accepted; innate capacity realised through responsive social input (Bruner LASS, Vygotsky scaffolding).
- **Neural correlate:** left perisylvian network, Broca (production/syntax), Wernicke (comprehension), arcuate fasciculus; critical period closing around puberty.

Discriminate

21 · Discriminate: the theories side by side

The step that turns a list of theorists into an answer that scores. these notes reward one skill above all others: the ability to hold two or more rival theories in the same frame and name the one line that separates them. Examiners do not ask "describe Erikson"; they ask "compare Freud and Erikson", "which theory says the body changes first", "how does assimilation differ from accommodation". This topic gathers the three comparisons the exam returns to again and again and lays them out as tables, because a table is exactly the form a discrimination question wants back. Read the individual theory topics for depth; read this one to **compare** them cold.

Three grids do the work. The first and most important is the **aligned developmental-stages** grid, which stacks Freud, Erikson, Piaget and Kohlberg down a single shared age axis so you can read across a row and see what each theorist says is happening in the same child at the same age. The second sets the four emotion theories against each other on the single axis of *sequence*, the order in which arousal, cognition and feeling arrive. The third arranges the intelligence models on the single axis of *number*, one general capacity against many. A closing trap box collects the classic mix-ups that cost marks. Ground text throughout is Kaplan and Sadock (2024), with the

New Oxford Textbook, Tasman (2015) and the Companion to Psychiatric Studies behind the individual entries.

Age	Freud psychosexual	Erikson psychosocial	Piaget cognitive	Kohlberg moral
0 to 1 infancy	Oral	Trust vs mistrust	Sensorimotor	(pre-moral)
1 to 3 toddler	Anal	Autonomy vs shame, doubt	sensorimotor to preoperational	Preconventional emerging
3 to 6 preschool	Phallic Oedipus	Initiative vs guilt	Preoperational	Preconventional stages 1 to 2
6 to 12 school age	Latency	Industry vs inferiority	Concrete operational	Conventional stages 3 to 4
12 to 18 adolescence	Genital	Identity vs role confusion	Formal operational	Conventional to postconventional
19 to 40 young adult	Genital mature	Intimacy vs isolation	formal operational	Postconventional stages 5 to 6
40 to 65 midlife	(complete)	**Generativity vs stagnation**	(complete)	(complete)
65 plus old age	(complete)	**Integrity vs despair**	(complete)	(complete)

Fig 4.17 The four stage theories aligned down one shared age axis, the flagship figure of these notes. Reading across any row shows what each theorist claims is happening at that age: at 3 to 6 years, for instance, Freud's phallic conflict, Erikson's initiative crisis, Piaget's preoperational thought and Kohlberg's earliest preconventional morality all coincide. Reading down a column gives that theorist's full sequence. The single most examinable point is visible at a glance: Freud, Piaget and Kohlberg complete their sequences by early adulthood, while only Erikson's psychosocial stages (marigold) carry through midlife and old age.

21.1 The aligned developmental-stages grid: four theorists, one age axis

The flagship comparison of the whole set of notes. Four great stage theorists mapped childhood and beyond, each along his own dimension: Freud on the moving **erogenous zone** (psychosexual), Erikson on the widening **social** task (psychosocial), Piaget on the growing **cognitive** structure, and Kohlberg on the maturing basis of **moral** reasoning. Because they share a rough age spine, they can be aligned so that a single column, say the preschool child of 3 to 5, shows Freud's phallic-oedipal drama, Erikson's initiative-versus-guilt, Piaget's preoperational egocentrism, and Kohlberg's preconventional obedience all at once. Learning the grid down the age axis, rather than four separate ladders, is the single highest-yield move for these notes, and it is the figure to draw from memory in the exam (Kaplan and Sadock 2024).

Two alignment caveats before the grid. Kohlberg's stages are keyed to moral *reasoning* and therefore lag the others: preconventional reasoning runs to roughly age 9, and the higher levels

open only in adolescence and adulthood, so the moral column is deliberately coarser than the rest. And Freud's ladder simply *stops* at the genital stage in adolescence, whereas Erikson, Piaget (formal operations) and, above all, Erikson's three adult stages carry the developmental story across the entire lifespan. The empty lower-left of the Freud column is itself an examinable fact.

AGE BAND	FREUD (PSYCHOSEXUAL)	ERIKSON (PSYCHOSOCIAL: CRISIS / VIRTUE)	PIAGET (COGNITIVE)	KOHLBERG (MORAL)
Infancy (birth to ~1.5 y)	**Oral**	Trust vs mistrust / hope	**Sensorimotor (object permanence)**	(pre-moral)
Toddler (~1.5 to 3 y)	**Anal**	Autonomy vs shame and doubt / will	**Sensorimotor into preoperational**	(pre-moral)
Preschool (~3 to 5 y)	**Phallic (oedipal)**	Initiative vs guilt / purpose	**Preoperational (egocentrism)**	Level I Preconventional (to ~age 9): punishment-obedience, then self-interest
School-age (~6 to 12 y)	**Latency**	Industry vs inferiority / competence	**Concrete operational (conservation)**	
Adolescence (~12 to 18 y)	**Genital**	Identity vs role confusion / fidelity	**Formal operational (hypothetico-deductive)**	Level II Conventional: good-boy, then law-and-order
Young adulthood	**(Freud stops here)**	Intimacy vs isolation / love	Formal operational (mature)	Level III Postconventional (only ~10 to 15%): social contract, then universal principles
Middle adulthood (~40 to 65 y)	**(no Freudian stage)**	Generativity vs stagnation / care	Formal operational	
Old age (~65 y to death)	**(no Freudian stage)**	Ego integrity vs despair / wisdom	Formal operational	

Read across a row for the same-aged child through four lenses; read down the Freud column to see it end at adolescence while Erikson runs to death. Ages are the standard textbook bands (Kaplan and Sadock 2024), not sharp cut-offs.

How to use the grid in an answer. The examiner's favourite cross-sectional question is "what is happening developmentally at age X". At the preschool column you can now say, in one breath, that the phallic-stage child working through the Oedipus complex is simultaneously exercising Eriksonian initiative, thinking in egocentric preoperational terms (three-mountains task), and reasoning morally only from fear of punishment. That four-lens sentence is worth more than any single ladder recited in isolation, and it is exactly what the aligned grid trains.

TRAP Do not expect Freud's ladder to continue past adolescence. Freud, Piaget and Kohlberg **finish by early adulthood; only Erikson runs to death**, and the empty lower-left of the Freud column is itself an examinable fact.

21.2 Emotion theories on the axis of sequence: which comes first?

One question orders all four: body-first or cognition-first? Given a bear on the path, does the pounding heart come before the fear, at the same time, or after an appraisal? Each named theory is a different answer, and the whole set is best held as a single spectrum from pure body-first (james-lange) to pure cognition-first (lazarus), with cannon-bard and schachter-singer between them (Kaplan and Sadock 2024). The discriminator is always the *order* of the three ingredients: physiological arousal, cognitive interpretation, and conscious feeling.

THEORY (AUTHOR, YEAR)	SEQUENCE IT PROPOSES	THE ONE DISCRIMINATOR
James-Lange (James 1884, Lange)	Stimulus, then bodily arousal, then perception of it = the emotion	**Body first; feeling is the read-out of the body ("we are afraid because we tremble"); needs a unique bodily pattern per emotion**
Cannon-Bard (Cannon 1927, Bard)	Stimulus, then arousal and feeling together, in parallel	**Simultaneous and independent; the thalamus fires body and cortex at once, neither causes the other**
Schachter-Singer (1962)	Stimulus, then arousal, then cognitive label = the emotion	**Two factors: undifferentiated arousal first, but cognition must name it; same arousal labelled fear or euphoria by context**
Lazarus appraisal (1966, 1991)	Stimulus, then appraisal, then feeling and arousal together	**Cognition first; appraisal of meaning-for-self is necessary and prior and generates both feeling and body**

The spectrum from body-first to cognition-first. Note the two easily-confused middle theories: cannon-bard is simultaneous-and-independent, schachter-singer is arousal-then-label (still body-first, but cognition specifies which emotion).

The pairing examiners exploit. The two most-confused theories are james-lange and cannon-bard, because both concern the body, yet they are opposites on sequence: james-lange makes the body *cause* the feeling (serial, body then feeling), cannon-bard makes body and feeling *parallel* and unlinked (simultaneous, neither causing the other). Cannon built cannon-bard precisely as a rebuttal of james-lange, on three grounds: isolating the viscera did not abolish emotion, injected arousal did not create a genuine emotion, and autonomic responses are too slow and too uniform to explain the speed and variety of feeling. Beyond the four, the *currently accepted* synthesis folds them together, appraisal (Lazarus) sets it off, interoception gives it its felt body (james-lange revived, via Damasio's somatic markers and the insula), and conceptual construction names it (Schachter-Singer's label, formalised by Barrett 2017), with the appraisal-versus-primacy tension resolved neurally by LeDoux's low and high roads (Kaplan and Sadock 2024).

21.3 Intelligence models on the axis of number: one thing or many?

The single question that orders the intelligence theories: how many intelligences are there? Every model is judged against one stubborn empirical fact, the **positive manifold**, that scores on

almost all cognitive tests correlate positively, which any theory denying a general factor has to explain away. The models run from Spearman's single *g* to Gardner's eight-or-nine, with the Cattell-Horn-Carroll hierarchy resolving the fight by making it a matter of levels rather than of count (Kaplan and Sadock 2024; Carroll 1993).

MODEL (AUTHOR, YEAR)	HOW MANY, AND WHAT	THE ONE DISCRIMINATOR
Spearman two-factor (1904)	One general factor g, plus a specific s per task	**Unitary: one g lifts every performance; explains the positive manifold directly**
Gardner multiple intelligences (1983)	Many (seven, then eight): linguistic, logical-mathematical, spatial, musical, bodily-kinaesthetic, interpersonal, intrapersonal, naturalistic	**Plural and independent; each dissociable, own neural substrate; critique: contradicts the positive manifold, abilities do correlate**
Sternberg triarchic (1985)	Three: analytical, creative, practical	**Real-world success, not just school; first to bring creativity formally inside intelligence**
Cattell-Horn-Carroll, CHC (1993)	All levels at once: g over ~8 to 10 broad abilities over many narrow abilities (three strata)	**Hierarchy dissolves the one-vs-many war; g at the apex (Spearman) above broad and narrow abilities (Thurstone); the currently accepted consensus**

The axis is number. Spearman says one, Gardner says many-and-independent, Sternberg says three-for-real-life, and CHC nests them all: g over broad over narrow. The pluralist theories that deny g cannot be the consensus because the positive manifold is real.

Why CHC wins and the pluralists do not. The exam rewards the counter-intuitive line: Gardner and Sternberg feel modern and inclusive, but they sit *outside* the empirical mainstream precisely because they deny or minimise g, which the positive manifold will not allow. CHC is the working consensus because it honours both halves of the century-old debate, a genuine general factor at the top (vindicating Spearman) sitting over a rich layer of broad and narrow abilities (vindicating Thurstone, Cattell and Horn), which is why modern tests report both a full-scale IQ and index scores (Kaplan and Sadock 2024).

21.4 The three axes in one sentence each

Carry these away. The developmental grid is organised by *age* (what four theorists say is happening in the same child), the emotion theories by *sequence* (body-first to cognition-first), the intelligence models by *number* (one general capacity to many independent ones). Name the axis first in any comparison answer and the discriminators fall into place, because each theory is only ever defined by where it sits on its axis relative to its neighbours.

HOLD THIS

Three axes: developmental theorists on age, emotion theories on sequence, intelligence models on number. Name the axis, place each theory on it, state the single discriminator; that is what converts a memorised list into a comparison answer.

COMMON TRAP

The four classic mix-ups the exam plants:

- **James-Lange vs Cannon-Bard (direction):** both are about the body, but james-lange is *serial* (arousal then feeling, the body causes the emotion) while cannon-bard is *parallel and independent* (arousal and feeling together, neither causes the other). Do not call schachter-singer "cognition-first": its arousal comes first, then the label.
- **Assimilation vs accommodation:** in *assimilation* the new input is bent to fit the existing schema (a dachshund fits "dog"); in *accommodation* the schema is bent to fit the new input (the schema changes when a cat will not fit "dog"). Assimilation keeps the schema, accommodation changes it.
- **Piaget vs Vygotsky:** Piaget is individual construction (the lone child acting on the world, development leads learning); Vygotsky is social mediation (a more-knowledgeable other scaffolds within the zone of proximal development, learning leads development). Scaffolding as a term is Wood, Bruner and Ross, not Vygotsky.
- **Freud vs Erikson stage names:** Freud's are psychosexual (oral, anal, phallic, latency, genital); Erikson's are psychosocial crises with virtues (trust-vs-mistrust / hope, and so on). They run in parallel through childhood; then Freud stops at genital while Erikson adds three adult stages (intimacy, generativity, integrity). Do not swap Erikson's virtues between stages: initiative gives *purpose*, industry gives *competence*.

PEARL

For any "compare X and Y" question, do three things in order: name the shared axis (age, sequence, or number), place each theory on it, and state the single discriminator between the two. That structure, axis then placement then discriminator, is what converts a memorised list into a comparison answer, and it is why examiners set discrimination questions in the first place.

MNEMONIC

Three axes: AGE, SEQUENCE, NUMBER

Developmental theorists align on **age** (Freud / Erikson / Piaget / Kohlberg across one child), emotion theories order on **sequence** (body-first james-lange to cognition-first lazarus), intelligence models split on **number** (one g to many). Name the axis, then the discriminator.

GOOD TO REMEMBER

- **Aligned grid, preschool column (~3 to 5 y):** Freud phallic, Erikson initiative-vs-guilt (purpose), Piaget preoperational, Kohlberg preconventional.
- **Aligned grid, school-age (~6 to 12 y):** Freud latency, Erikson industry-vs-inferiority (competence), Piaget concrete operational, Kohlberg preconventional into conventional.
- **Aligned grid, adolescence:** Freud genital (last Freudian stage), Erikson identity-vs-role-confusion (fidelity), Piaget formal operational, Kohlberg conventional.
- **Freud stops, Erikson continues:** Freud's ladder ends at the genital stage; Erikson adds intimacy (love), generativity (care), integrity (wisdom) across adult life.
- **James-Lange:** body-first, feeling is the perception of arousal ("afraid because we tremble").
- **Cannon-Bard:** arousal and feeling simultaneous and independent (thalamic theory); built as the rebuttal of james-lange.
- **Schachter-Singer (1962):** two-factor, arousal then cognitive label; same arousal, different emotion by context.
- **Lazarus (1966, 1991):** cognition-first, appraisal is prior and necessary; Zajonc (1980) counter = affective primacy.
- **Emotion axis:** body-first to cognition-first; currently accepted = appraisal + interoception + construction.
- **Spearman (1904):** one general factor g plus specific s; the positive manifold.
- **Gardner (1983):** multiple independent intelligences (seven then eight); critique = contradicts the positive manifold.
- **Sternberg (1985):** triarchic, analytical + creative + practical.
- **CHC (Carroll 1993):** three-stratum hierarchy (g over broad over narrow); the currently accepted consensus.
- **Intelligence axis:** number, one thing (g) to many; pluralists that deny g fall outside the mainstream.
- **Four classic traps:** james-lange vs cannon-bard (serial vs parallel); assimilation (keep schema) vs accommodation (change schema); Piaget (individual) vs Vygotsky (social); Freud psychosexual vs Erikson psychosocial names.

Apply and consolidate

22 · Apply: four psychology vignettes

The final step, where the theories become an answer. Psychology is only worth marks if the frameworks convert into reads of a described child or adult. Examiners increasingly favour the short clinical vignette: a two-line presentation, then "which stage", "which attachment type", "which theory explains this". This topic drills that conversion on four deliberately varied cases, one per major tool covered above, so that the *discriminator* (the single fact that decides the answer) is what you learn to hunt for. Each vignette follows the same discipline: read the presentation, name the tool the case is testing, apply it, and state the one line that carries the mark.

The four cases are chosen to span the whole of this material. The first is a **developmental-stage** read of a preschooler placed simultaneously through Piaget, Erikson and the milestone schedule. The second is a **goodness-of-fit** case pairing a difficult-temperament infant with a rigid

parenting environment. The third is an **attachment classification** from a Strange-Situation description, naming the type and the internal working model it encodes. The fourth is an **emotion-theory and intelligence** application, reading an arousal-then-label sequence by Schachter-Singer and placing a jagged ability profile on CHC and Gardner. Ground text is Kaplan and Sadock (2024), with Piaget (1952), Ainsworth and colleagues (1978) and Schachter and Singer (1962) behind the individual reads.

22.1 Vignette 1: the four-year-old who fails conservation and false belief

A developmental-stage read across three theorists at once. This case tests whether you can take a single age and place the child correctly on Piaget, Erikson and the milestone schedule together, which is exactly the four-lens sentence a cross-sectional question rewards. The discriminator is the pairing of the two failed tasks: a conservation failure and a false-belief failure are the twin signatures of preoperational thought.

CLINICAL ANCHOR

Case (vignette). A boy of 4 years is watched at play. When water from a short wide beaker is poured into a tall thin glass in front of him, he insists there is now "more water". Shown the Sally-Anne scenario, in which Sally hides a marble in a basket and leaves, Anne moves it to a box, and Sally returns, he says Sally will look in the box. He copies a cross on request but cannot yet copy a square. Place him.

The reasoning. Two failures anchor the Piagetian stage. The child cannot conserve liquid quantity because he *centrates* on the single salient dimension (the height of the column) and lacks the *reversibility* that would let him mentally pour the water back; conservation of quantity is not achieved until the concrete operational stage at about 7 years (Piaget 1952). He also fails the false-belief task, answering from his own privileged knowledge of where the marble truly is rather than tracking Sally's false belief, the marker of *egocentrism*; theory of mind on this task emerges at about 4 years (Wimmer and Perner 1983; Baron-Cohen, Leslie and Frith 1985), so at exactly 4 he can be on the cusp and still fail. Both features place him firmly in the **preoperational stage** (about 2 to 7 years).

The read. Piaget: preoperational, shown by non-conservation (centration, irreversibility) and egocentrism (false-belief failure). Erikson: at 4 the crisis is *initiative versus guilt*, virtue purpose (about 3 to 5 years). Freudian correlate: the phallic-oedipal stage. Milestones: copying a cross is the expected fine-motor item *at 4 years* (the square comes at 5), so his graphomotor development is on schedule and the cognitive "failures" are stage-appropriate, not delay. The whole answer in one line: a normally developing preoperational preschooler in Erikson's initiative-versus-guilt stage, whose conservation and false-belief failures are expected for his age.

HOLD THIS

At 4 years, non-conservation and false-belief failure are expected, not delay. The paired failure is the twin signature of preoperational thought; the milestone check (copies a cross at 4) confirms the child is on track.

22.2 Vignette 2: the difficult infant meeting a rigid parent

A temperament case that turns on goodness of fit, not on the temperament alone. The trap here is to answer "difficult temperament, poor outcome" and stop. The tool the case actually tests is Chess and Thomas' **goodness of fit**: outcome is predicted by the *match* between the child's style and the environment's demands, so the same infant does well or badly depending on the parenting it meets (Kaplan and Sadock 2024).

CLINICAL ANCHOR

Case (vignette). A 10-month-old feeds and sleeps on no predictable schedule, screams loudly and for a long time at each new food or face, takes many exposures to settle to any change, and is generally irritable. Her father, a punctual and orderly man, keeps a strict feeding and sleeping timetable, reads her intense crying as wilful defiance, and responds by tightening the routine and raising his voice. Classify the temperament and predict the trajectory.

The reasoning. The infant's profile is the classic **difficult child** constellation: irregular rhythmicity, withdrawal from novelty, poor (slow) adaptability, high intensity of reaction and predominantly negative mood (Chess and Thomas, New York Longitudinal Study). Difficult children are about 10 percent of the sample and carry the highest risk of later disturbance, but that risk is not fixed. The decisive variable is the environment she meets. Here the fit is *poor*: a rigid, timetable-driven parent who misreads intensity as defiance and escalates is maximally mismatched to an irregular, intense, slow-adapting infant, setting up a coercive cycle.

The read. Difficult temperament plus a rigid, mismatched caregiving environment equals a *poor goodness of fit*, and it is the poor fit, not the temperament, that predicts stress, escalating conflict and later behaviour problems. State the counterfactual to prove you understand the construct: the identical infant paired with a calm, flexible parent who paces transitions gently and reframes intensity as style rather than misbehaviour has a good fit and a favourable trajectory. The clinical move is to treat the dyad, not the child, and to reframe temperament for the father as a style to work with, not defiance to be disciplined out.

22.3 Vignette 3: the Strange-Situation reunion that names the type

An attachment classification read from reunion behaviour, plus the internal working model it encodes. The tool is Ainsworth's **Strange Situation**, and the whole discriminator lives in the *reunion* episode, not in how much the infant cries at separation (Ainsworth and colleagues 1978). Get the reunion behaviour, name the letter and label, then state the internal working model of self and other that the pattern encodes.

CLINICAL ANCHOR

Case (vignette). A 14-month-old in the standardised procedure explores the toys only a little and stays close to her mother. When the mother leaves she becomes intensely distressed and cannot be settled by the stranger. On the mother's return she rushes to be picked up but then arches away, kicks and cannot be comforted, alternately seeking and resisting contact, and does not return to play. The mother's caregiving history is described as warm but unpredictable. Classify.

The reasoning. Separation distress alone does not classify, since both secure and insecure-ambivalent infants are highly distressed; the answer is read from reunion. The signature here, seeking contact yet simultaneously resisting it (approaching to be held, then arching and pushing away), unsettled and not returning to exploration, is the **insecure-ambivalent / resistant** pattern, Ainsworth's *Type C*. The little pre-separation exploration and clinginess fit the same type. The typical caregiving is *inconsistent and unpredictable*, which matches the "warm but unpredictable" history: the child cannot form a stable expectation of availability, so it maximises proximity-seeking and protest to keep an unreliable caregiver engaged.

The read. Type C, insecure-ambivalent (resistant), read from the contradictory seek-and-resist reunion. Its **internal working model** (Bowlby's mental template built from repeated interactions) is a model of the caregiver as *unreliably available*, sometimes responsive and sometimes not, paired with a model of the self as having to escalate distress to secure care and as not confidently worthy of consistent comfort. Contrast to fix the answer: had she avoided and ignored the mother on reunion with little separation distress, that is Type A avoidant (a model of the caregiver as rejecting); had she sought the mother and been readily comforted then returned to play, that is Type B secure (a model of the caregiver as reliably available and the self as worthy of care). The adult counterpart of Type C on the Adult Attachment Interview is the preoccupied classification.

22.4 Vignette 4: the arousal that is labelled two ways, and the jagged ability profile

Two applications in one case: an emotion theory on the axis of sequence, and an intelligence model on the axis of number. The emotion half tests Schachter-Singer's two-factor account, where the same undifferentiated arousal is named by context; the intelligence half tests where a spiky ability profile sits on CHC versus Gardner. The discriminator for emotion is *same arousal, different label*; for intelligence it is *whether the peaks are truly independent or nest under g*.

CLINICAL ANCHOR

Case (vignette). A man is given an injection that races his heart and makes him sweat, but he is not told the drug is arousing. Placed with a cheerful companion he reports feeling euphoric; on another day, identically injected but placed with an angry companion, he reports feeling angry. Separately, a schoolboy is assessed: he reasons superbly through novel puzzles and has a large vocabulary, plays music with rare skill and is socially deft, yet on formal testing his musical and interpersonal talents do not stand apart from his general ability, which is uniformly high. Read the emotion, then place the profile.

The reasoning, part one (emotion). The arousal is constant across both days; only the available cognitive interpretation changes, and with it the reported emotion. This is **Schachter-Singer** two-factor theory (1962): undifferentiated physiological arousal supplies the intensity, and a cognitive *label* drawn from the context supplies the identity, so the same pounding heart is felt as euphoria beside a happy confederate and as anger beside a hostile one. Because the man was not informed of the drug's effects, he had an *unexplained* arousal to attribute, the origin of *misattribution of arousal*. Note the sequence to avoid the classic trap: arousal comes *first*, then the label, so this is still body-first, not cognition-first; had the case turned on an appraisal preceding any arousal it would be Lazarus.

The reasoning, part two (intelligence). The boy shows apparent peaks (music, social skill) on top of strong general reasoning and knowledge. **Gardner** would read the peaks as separate *musical* and *interpersonal* intelligences, largely independent modules an IQ test misses (Gardner 1983). But the case supplies the decisive fact: on testing his talents do *not* dissociate from his general ability, which is uniformly high. That is the **positive manifold**, the robust finding that cognitive abilities correlate positively, and it is precisely what Gardner's independence claim cannot accommodate. The profile therefore sits best on **CHC** (Cattell-Horn-Carroll): a high general factor *g* at the apex (Stratum III) expressed through strong broad abilities (Stratum II) and narrow abilities (Stratum I), so his novel-puzzle skill is fluid reasoning (Gf), his vocabulary is crystallised knowledge (Gc), and even his musical and social strengths, while real, correlate with the same underlying g rather than floating free.

The read. Emotion: Schachter-Singer two-factor, one arousal labelled two ways by context (body-first, arousal-then-label). Intelligence: a jagged-looking profile that nonetheless obeys the positive manifold belongs on the CHC hierarchy (g over broad over narrow), not on Gardner's independent multiple intelligences, because the peaks do not dissociate from g. CHC is the currently accepted consensus for exactly this reason.

COMMON TRAP

The four discriminators the vignettes turn on, and the wrong answers they punish:

- **Vignette 1:** do not call a stage-appropriate conservation or false-belief failure "developmental delay". At 4 years, non-conservation and egocentric false-belief errors are *expected* preoperational features; the milestone check (copies a cross at 4) confirms the child is on track.
- **Vignette 2:** do not answer "difficult temperament, therefore poor outcome". Temperament alone does not predict outcome; *goodness of fit* does. Name the poor fit, and state the counterfactual (same infant, flexible parent, good outcome).
- **Vignette 3:** do not classify from separation distress. Both secure (B) and ambivalent (C) infants are highly distressed at separation; the type is read from *reunion*. Seek-and-resist is C, not B.
- **Vignette 4:** do not call Schachter-Singer "cognition-first" (arousal comes first, then the label). And do not accept a spiky profile as proof of Gardner's independent intelligences unless the peaks actually *dissociate* from g; if they correlate (the positive manifold), the profile is CHC.

PEARL

Every vignette answer has the same skeleton: name the tool the case is testing, apply it to the described behaviour, and state the single discriminator that carries the mark, then prove mastery with the counterfactual (what a different answer would have looked like). The discriminator is nearly always one fact: the failed conservation-and-false-belief pair means preoperational; the poor match means bad goodness of fit; the reunion behaviour means the attachment type; the constant arousal with a changing label means Schachter-Singer; the peaks that still correlate with g mean CHC, not Gardner.

GOOD TO REMEMBER

- **Vignette 1, the tool:** developmental-stage read (Piaget + Erikson + milestones), placing one age through several lenses.
- **Vignette 1, the read:** a 4-year-old failing conservation (centration, no reversibility) and false belief (egocentrism) is *preoperational* (Piaget, about 2 to 7 y); Erikson crisis = initiative vs guilt (virtue purpose, about 3 to 5 y); copies a cross at 4 y (square at 5) = milestones on track.
- **Conservation of quantity:** achieved in concrete operational stage (about 7 y), not before.
- **False-belief / theory of mind:** emerges about 4 years (Sally-Anne, Baron-Cohen, Leslie and Frith 1985; paradigm Wimmer and Perner 1983).
- **Vignette 2, the tool:** temperament plus goodness of fit (Chess and Thomas, New York Longitudinal Study).
- **Difficult child:** irregular rhythmicity, withdrawal, poor adaptability, high intensity, negative mood; about 10 percent; highest risk of later disturbance.
- **Goodness of fit:** the match between child temperament and environmental demand is the real predictor of outcome, not the temperament alone; difficult infant plus rigid parent = poor fit = coercive cycle; same infant plus flexible parent = good fit.
- **Vignette 3, the tool:** attachment classification from the Strange Situation (Ainsworth and colleagues 1978), read from reunion.
- **Type C, insecure-ambivalent / resistant:** intense separation distress, seeks yet resists contact on reunion (approach then arch away), not settled; caregiving inconsistent/unpredictable; internal working model = caregiver unreliably available, self must escalate for care; adult counterpart preoccupied.
- **Reunion, not separation, classifies:** both B (secure) and C (ambivalent) are distressed at separation; A (avoidant) ignores caregiver on reunion; B seeks and is readily comforted.
- **Internal working model (Bowlby):** paired mental template of caregiver-availability and of self-worth, built from repeated interactions, largely outside awareness.
- **Vignette 4, emotion:** Schachter-Singer two-factor (1962), same undifferentiated arousal labelled euphoria or anger by context; body-first, arousal-then-label; origin of misattribution of arousal.
- **Vignette 4, intelligence:** a jagged ability profile whose peaks still correlate with g (the positive manifold) belongs on CHC (Cattell-Horn-Carroll, g over broad over narrow), not on Gardner's independent multiple intelligences; CHC is the currently accepted consensus.
- **Positive manifold:** cognitive abilities correlate positively; the fact any theory denying g must explain away.

23 · Consolidate: mnemonic, retrieval and synthesis

The last hour is where revision is made or lost. General and developmental psychology fails on exam morning not because the facts were never read but because they were never **consolidated** into a single retrievable structure. This closing topic does three specific jobs, each a distinct memory operation. First it gives one master **mnemonic** that chains every strand of this material, from the five schools through the general-psychology functions to the developmental theorists, so that pulling one thread pulls the rest. Second it converts the material into **retrieval practice**, a set of answer-free prompts to be worked with the answers covered, because the act of retrieving is itself what fixes a memory (Kaplan & Sadock 2024). Third it names a whole-chapter **synthesis map** to redraw from memory, aligning the developmental theorists on one age axis with the general-psychology functions and the depth-psychology schools as branches.

Why these three and not simple re-reading. The consolidation literature is unambiguous that the two most effective study strategies are **retrieval practice** (testing yourself) and **spaced practice**, and that re-reading and highlighting, though they feel productive, are among the weakest (Dunlosky et al. 2013). The **testing effect** is the finding that recalling material strengthens later retention more than restudying the same material for the same time (Roediger & Karpicke 2006). A good mnemonic supplies the retrieval cues, active recall exercises the retrieval itself, and a redrawn map forces the relations between items to be reconstructed rather than merely recognised. Use this topic as the closing loop: read the mnemonic, then cover the answers and self-test, then redraw the map on blank paper.

TRAP Re-reading and highlighting feel productive but are among the **weakest** study strategies; retrieval practice and spaced practice are the strongest, and the testing effect means recall beats restudy for the same time (Dunlosky et al. 2013).

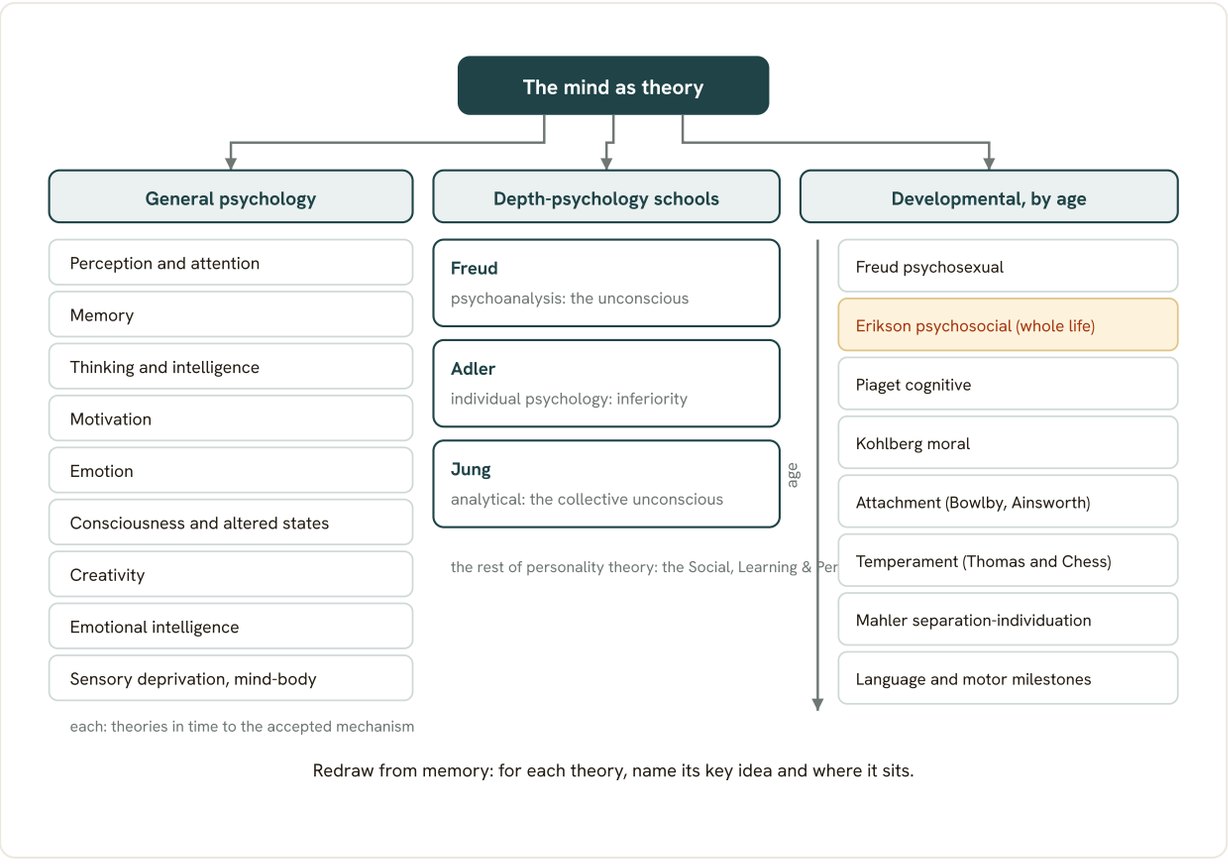


Fig 4.18 The whole chapter on one page. General psychology supplies the functions, each taught as a history of theories converging on the accepted mechanism; the three depth-psychology schools (Freud, Adler, Jung) supply the map of the unconscious; and the developmental theorists line up along a single age axis, with only Erikson spanning the whole lifespan. Cover the panels and rebuild this from memory as a retrieval test.

23.1 The master mnemonic for the whole set of notes

One chain from schools to functions to theorists. This is the single memory anchor for the chapter: a three-part device whose first line seeds the five schools, whose second line seeds the general-psychology functions, and whose third and fourth lines seed the depth-psychology schools and the developmental theorists. The letters are cues, not content; each is unpacked

below to the item it must recover. Rehearse the four lines until they run without effort, then use each letter as a hook to reel in its full topic.

MNEMONIC

Big Cats Bite Prey Hungrily · Please Make Time, Matey, Every Clever Creature Excels · Freud, Adler, Jung climb the iceberg · Every Playful Kid Anxiously Tests Mother's Milestones

Line 1, the five schools, in appearance-and-argument order (Big Cats Bite Prey Hungrily). Big = *Biological* (the brain: genes, neurotransmitters, circuits, evolution). **C**ats = *Cognitive* (the computer metaphor; Neisser 1967). **B**ite = *Behavioural* (the black box; Watson 1913, Skinner). **P**rey = *Psychodynamic* (the iceberg; Freud, Adler, Jung). **H**ungrily = *Humanistic* (the growing self; Maslow, Rogers; descendant positive psychology, Seligman).

Line 2, the nine general-psychology functions (Please Make Time, Matey, Every Clever Creature Excels). Please = *Perception* (currently accepted as predictive processing; neural correlate the sensory-association cortex and the two visual streams). **M**ake = *Memory* (Atkinson-Shiffrin then Baddeley then the systems synthesis; correlate hippocampus for declarative, basal ganglia and cerebellum for procedural, amygdala for emotional). **T**ime = *Thinking and intelligence* (currently accepted CHC model; correlate parieto-frontal integration theory and processing speed). **M**atey = *Motivation* (drive to incentive to the currently accepted multi-system view; correlate mesolimbic dopamine, hypothalamus). **E**very = *Emotion* (James-Lange to Cannon-Bard to Schachter-Singer to the currently accepted appraisal-plus-interoception-plus-construction synthesis; correlate the limbic system and Papez circuit, amygdala with LeDoux's two roads, insula for interoception). **C**lever = *Consciousness* (global workspace and its neural correlate). **C**reature = *Creativity* (the componential and systems view; correlate the default-mode, executive-control and salience networks). **E**xcels = *Emotional intelligence* (Salovey-Mayer ability model versus Goleman and Bar-On mixed models; correlate the "social brain," ventromedial prefrontal cortex, amygdala, insula), and the *mind-body* problem underneath them all (dualism to identity theory to functionalism).

Line 3, the three depth-psychology schools (Freud, Adler, Jung climb the iceberg). Freud = psychoanalysis: topographic and structural models, the psychosexual stages, defence and transference. **Adler** = individual psychology: organ inferiority, the inferiority feeling, striving for superiority, style of life, social interest. **Jung** = analytical psychology: the collective unconscious, archetypes (persona, shadow, anima and animus, self), complexes, introversion and extraversion.

Line 4, the developmental strands (Every Playful Kid Anxiously Tests Mother's Milestones). Every = *Erikson* (eight psychosocial crises, each with its virtue). **P**layful = *Piaget* (four cognitive stages: sensorimotor, preoperational, concrete operational, formal operational). **K**id = *Kohlberg* (three moral levels: preconventional, conventional, postconventional). **A**nxiously = *Attachment* (Harlow, Bowlby, Ainsworth; secure, avoidant, ambivalent, disorganised). **T**ests = *Temperament* (Chess and Thomas nine dimensions and three types; goodness of fit; Kagan's behavioural inhibition). **M**other's = *Mahler* (separation-individuation: the precursor phases autistic and symbiotic, then the four subphases differentiation, practising, rapprochement, consolidation). **M**ilestones = the *developmental milestones* ladder (social smile, sitting, pincer grasp, first words, walking, the copy-a-shape sequence, and their red flags). Freud's psychosexual stages, from Line 3, are the fifth stage theorist that runs down the same age axis.

23.2 Retrieval practice: work these with the answers covered

Test yourself, do not re-read. The following are deliberately answer-free. Use **active recall**: read each prompt, say or write the full answer from memory, and only then check it against the topic it came from. This is **retrieval practice**, the single highest-yield way to convert a day of reading into exam-durable memory, and it works only if you genuinely attempt recall before checking, so cover the answers.

RETRIEVAL PRACTICE, COVER THE ANSWERS

Retrieval practice, cover the answers. Answer each aloud or on paper before you look anything up. If a prompt is blank in your mind, flag it and return to that topic; a blank on a self-test now is a mark you would otherwise have lost in the exam.

1. Name the five schools of psychology and give each one's unit of analysis and its lead figure.
2. State the historical arc: which school fixed which gap, from introspection through behaviourism to the cognitive revolution, and where the psychodynamic and humanistic traditions sit.
3. For perception, give the evolution from the classical view to the currently accepted predictive-processing account, and name its neural correlate.
4. Lay out the memory systems and map each onto its structure: declarative versus procedural versus emotional, and the model sequence from Atkinson-Shiffrin to Baddeley's working memory.
5. State the currently accepted model of intelligence and its neural correlate, and distinguish fluid from crystallised ability.
6. Trace the emotion theories in order (James-Lange, Cannon-Bard, Schachter-Singer, appraisal, constructed emotion) and name the structures of the neural correlate.
7. Contrast the ability model of emotional intelligence with the mixed models, naming their authors.
8. Give Freud's topographic and structural models and list the psychosexual stages with their ages and zones.
9. State Adler's core concepts: organ inferiority, inferiority feeling, striving for superiority, style of life, and social interest.
10. Draw Jung's structure of the psyche and name the major archetypes, and state the boundary rule for complexes versus archetypes.
11. List Erikson's eight psychosocial stages with their ages and virtues.
12. Give Piaget's four stages with ages and one signature achievement or error each, then contrast Piaget with Vygotsky.
13. State Kohlberg's three levels and six stages, the dilemma used to elicit them, and the core scoring rule.
14. Name the four attachment classifications, the discriminator that separates them, and who added the fourth type.
15. List Chess and Thomas's three temperament types with their approximate proportions, define goodness of fit, and give Mahler's two precursor phases and four subphases of separation-individuation with their ages.

23.3 The whole-day synthesis map to redraw from memory

Reconstruct the relations, do not just recognise the items. The final consolidation act is to draw the whole set of notes as one **synthesis map** on a blank sheet and to redraw from memory until it flows without prompts. Put a single horizontal *age axis* across the page, from birth on the left to old age on the right. Along it, stack the five stage theorists who share that axis so their stages line up vertically: Freud's psychosexual stages, Erikson's eight psychosocial crises, Piaget's four cognitive stages, Kohlberg's three moral levels, and Mahler's separation-individuation sub-phases, with attachment phases and the motor-language milestone ladder threaded beneath as the relational and observable strands. Then branch upward off the map two further clusters that are not age-staged: the nine *general-psychology functions* (perception, memory, thinking and intelligence, motivation, emotion, consciousness, creativity, emotional intelligence, and the mind-body problem), each labelled with its currently accepted mechanism and neural correlate, and the three *depth-psychology schools* (Freud, Adler, Jung) as the roots feeding the psychodynamic lens. Redraw this from memory once and the material is genuinely consolidated: the age axis holds the developmental theorists in register, and the two branches keep the functions and the schools attached to the same single structure. A concept SVG of this map should be drawn to anchor the redraw.

HOLD THIS

One age axis holds five stage theorists in register (Freud, Erikson, Piaget, Kohlberg, Mahler), with the functions and the depth-schools branching off. Redraw it once from memory and the chapter is genuinely consolidated.

GOOD TO REMEMBER

- **Five schools (Line 1):** Biological (brain), Cognitive (computer; Neisser 1967), Behavioural (black box; Watson 1913, Skinner), Psychodynamic (iceberg; Freud, Adler, Jung), Humanistic (growing self; Maslow, Rogers; positive psychology, Seligman).
- **Nine functions (Line 2):** perception, memory, thinking and intelligence, motivation, emotion, consciousness, creativity, emotional intelligence, mind-body; each learned as evolution of theories to currently accepted mechanism to neural correlate.
- **Perception:** currently accepted = predictive processing; correlate = sensory-association cortex and the two visual streams (dorsal "where," ventral "what").
- **Memory:** Atkinson-Shiffrin then Baddeley working memory then systems synthesis; correlate = hippocampus (declarative), basal ganglia and cerebellum (procedural), amygdala (emotional).
- **Intelligence:** currently accepted = CHC (Cattell-Horn-Carroll); correlate = parieto-frontal integration theory and processing speed.
- **Emotion:** James-Lange to Cannon-Bard to Schachter-Singer to appraisal-plus-interoception-plus-construction; correlate = limbic system and Papez circuit, amygdala (LeDoux's two roads), insula.
- **Emotional intelligence:** Salovey-Mayer ability model vs Goleman and Bar-On mixed models; correlate = the "social brain," ventromedial prefrontal cortex, amygdala, insula.
- **Freud (Line 3):** psychoanalysis; topographic and structural models; psychosexual stages (oral, anal, phallic, latency, genital); staged by body zone.
- **Adler (Line 3):** individual psychology; organ inferiority, inferiority feeling, striving for superiority, style of life, social interest.
- **Jung (Line 3):** analytical psychology; collective unconscious; archetypes (persona, shadow, anima/animus, self); complexes; introversion/extraversion.
- **Erikson (Line 4):** eight psychosocial crises, each with a virtue (trust/hope to integrity/wisdom); psychosocial, added three adult stages beyond Freud's genital.
- **Piaget (Line 4):** sensorimotor (0 to ~2 y), preoperational (~2 to 7 y), concrete operational (~7 to 11 y), formal operational (~11 y onward).
- **Kohlberg (Line 4):** preconventional (to ~9 y), conventional (adolescence on), postconventional (only ~10 to 15% reach it); Heinz dilemma; reasoning fixes the stage.
- **Attachment (Line 4):** Harlow (contact comfort), Bowlby (behavioural system, secure base, internal working model), Ainsworth (Strange Situation); types A avoidant, B secure, C ambivalent, D disorganised (Main & Solomon).
- **Temperament (Line 4):** Chess and Thomas nine dimensions, easy (~40%), difficult (~10%), slow-to-warm-up (~15%); goodness of fit; Kagan behavioural inhibition (~10 to 15%).
- **Mahler (Line 4):** normal autistic (0 to ~1 mo), symbiotic (~1 to 5 mo), differentiation (~5 to 9 mo), practising (~9 to 16 mo), rapprochement (~16 to 24 mo), consolidation/object constancy (~24 to 36 mo).
- **Milestones (Line 4):** social smile ~6 to 8 wk, sits without support ~6 to 8 mo, pincer grasp 9 to 10 mo, first words ~12 mo, walks well 14 to 15 mo; copy-a-shape circle 3 y, cross 4 y, square 5 y, triangle 6 y, diamond 7 y.
- **Consolidation science:** retrieval practice and spaced practice are the highest-yield strategies (Dunlosky et al. 2013); the testing effect beats restudy (Roediger & Karpicke 2006); re-reading and highlighting are weak.

Previously asked

Real long-essay (25-mark) and short-note (10-mark) questions from the general and developmental psychology territory, most-recent year shown.

LONG ESSAYS (25 MARKS)

- Define emotions. Discuss the various theories of emotion and the psychopathological presentations related to emotion. MUHS 2017
- Describe the physiological basis of emotions. MUHS 2018
- Describe perceptual processes and the various disorders of perception. MUHS 2014
- Define the term consciousness. Describe the differential diagnosis of unconsciousness, and how you would investigate and manage a case of suspected dissociative (hysterical) unconsciousness. MUHS 2016

SHORT NOTES (10 MARKS)

- Erik Erikson and the stages of psychosocial development. MUHS 2021
- Theories of motivation and their application in psychiatry. MUHS 2021
- Psychological development in adolescence and its relation to psychiatric disorders. MUHS 2020
- Carl Gustav Jung. MUHS 2017
- Emotional intelligence. MUHS 2018
- Principles of Gestalt psychology. MUHS 2018
- Freud's concept of the id. MUHS 2013
- Implicit memory. MUHS 2013
- Working memory. MUHS 2012
- Jean Piaget. MUHS 2011
- Sigmund Freud and his contribution to psychiatry. MUHS 2011
- Tests used to assess intelligence. MUHS 2011

Psychology is a dependable examiner's quarry: emotion theories and the physiological basis of emotion recur as full essays, and Freud, Jung, Erikson, Piaget, motivation, working and implicit memory, emotional intelligence and Gestalt appear regularly as short notes. Prepare each theorist well enough to give the core idea, the stages or components, and one clinical link in a few lines. Learning and classical or operant conditioning, theories of personality, social perception, the psychology of aggression and the psychology of rape are examined from this same territory but are taught on the Social, Learning & Personality Psychology notes; intelligence testing is taken up on the Psychometry, Assessment and Descriptive Psychopathology notes.

Quick review

The whole picture in one table	
SCHOOLS OF PSYCHOLOGY	Five lenses on the same mind: biological (brain, genes), cognitive (information processing), behavioural (observable stimulus and response), psychodynamic (the unconscious), humanistic (growth and meaning). Each arose partly to fix what the previous lens left out. The general-psychology topics below each run the same way: the theories in the order they appeared, then the currently accepted mechanism and its neural correlate.
PERCEPTION AND ATTENTION	Sensation to perception; Gestalt organisation; Gibson direct bottom-up versus Gregory constructivist top-down, now reconciled as predictive perception; signal detection (d-prime, criterion). Attention: Broadbent early filter to Treisman attenuation to Deutsch-Norman late selection to Kahneman capacity. Hallucination theories evolve from perceptual release (Hughlings-Jackson) through source monitoring and aberrant salience to predictive coding. Neural: ventral what and dorsal where streams.
MEMORY	Ebbinghaus forgetting curve; Atkinson-Shiffrin multi-store (sensory, short-term, long-term); Baddeley working memory (central executive, phonological loop, visuospatial sketchpad, episodic buffer); levels of processing; Tulving long-term taxonomy (episodic, semantic, procedural; explicit, implicit). Forgetting by decay, interference, retrieval failure. Neural: hippocampus and medial temporal lobe for declarative, prefrontal for working memory.
THINKING AND INTELLIGENCE	Heuristics and biases (availability, representativeness, anchoring); dual-process. Intelligence models: Spearman g, Thurstone primary abilities, Cattell fluid and crystallised, the Cattell-Horn-Carroll consensus, Gardner multiple, Sternberg triarchic. The argument is one thing versus many; CHC is the working consensus. Neural: parieto-frontal integration (P-FIT). Testing is on the Psychometry, Assessment and Descriptive Psychopathology notes.
MOTIVATION	Instinct to drive-reduction (Hull) to arousal or optimal-level (Yerkes-Dodson) to incentive to Maslow's hierarchy (deficiency then growth needs) to Murray and McClelland to Deci and Ryan self-determination (intrinsic and extrinsic; autonomy, competence, relatedness). Homeostasis cannot explain curiosity or achievement. Neural: mesolimbic dopamine incentive-salience.

The whole picture in one table	
EMOTION	James-Lange (body first), Cannon-Bard (simultaneous, thalamic), Schachter-Singer two-factor (arousal plus label), Lazarus appraisal (appraisal first), then basic (Ekman) versus constructed emotion (Barrett). The enduring debate is body-first versus cognition-first. Neural: limbic system and Papez circuit, amygdala (LeDoux), insula for interoception.
CONSCIOUSNESS	Level (arousal) versus content (awareness); the hard problem. Global workspace (Baars) and integrated information (Tononi). Altered states: sleep and dreaming, hypnosis, meditation, drug-induced, and clinical (delirium, dissociation, coma). Neural: ascending reticular activating system, thalamocortical loops, default-mode network.
CREATIVITY	Guilford convergent versus divergent thinking (fluency, flexibility, originality, elaboration); Torrance tests; Wallas four stages (preparation, incubation, illumination, verification); the threshold hypothesis; the creativity-psychopathology question. Neural: reduced latent inhibition, default-mode and executive dynamics.
EMOTIONAL INTELLIGENCE	Mayer and Salovey four-branch ability model (perceive, use, understand, manage) versus Goleman mixed or trait model; Bar-On. Ability versus trait debate; MSCEIT versus self-report; incremental-validity critique. Neural: ventromedial prefrontal cortex, amygdala, insula.
SENSORY DEPRIVATION AND MIND-BODY	Sensory deprivation (Hebb and McGill, Lilly): perceptual and cognitive effects, hallucinations; relevance to solitary confinement and ICU. Mind-body problem: dualism (Descartes) versus monism (physicalism, functionalism, emergentism); the explanatory gap and qualia; the biopsychosocial synthesis (Engel) as the working clinical stance.
FREUD (PSYCHOANALYSIS)	Topographic (conscious, preconscious, unconscious) and structural (id, ego, superego) models; psychosexual stages oral, anal, phallic (Oedipus), latency, genital; techniques (free association, dream analysis, transference). The Wednesday Psychological Society became the Vienna Psychoanalytic Society; Adler, Jung, Stekel and Rank defected over the primacy of sexuality.
ADLER (INDIVIDUAL PSYCHOLOGY)	Inferiority feeling driving striving for superiority; the inferiority and superiority complexes; holism and fictional finalism; the style of life; social interest as the mark of health; birth order and family constellation. Broke from Freud over libido; influenced CBT and humanistic therapy.
JUNG (ANALYTICAL PSYCHOLOGY)	Ego, personal unconscious (complexes), collective unconscious with archetypes (persona, shadow, anima and animus, the Self); introversion and extraversion with four functions (the MBTI typology); individuation as the goal; the word-association test; synchronicity. Broke from Freud over libido as general psychic energy.

The whole picture in one table	
ERIKSON (PSYCHOSOCIAL)	Eight lifespan crises with virtues: trust versus mistrust (hope), autonomy versus shame (will), initiative versus guilt (purpose), industry versus inferiority (competence), identity versus role confusion (fidelity), intimacy versus isolation (love), generativity versus stagnation (care), integrity versus despair (wisdom). Epigenetic principle; Marcia identity statuses. The only stage theory to span the whole life.
PIAGET, VYGOTSKY, THEORY OF MIND	Piaget: assimilation and accommodation; sensorimotor (object permanence), preoperational (egocentrism, no conservation), concrete operational (conservation, reversibility), formal operational (abstract). Vygotsky: sociocultural, the zone of proximal development, scaffolding (social versus individual construction). Theory of mind: the false-belief task, emerging near age 4, relevant to autism.
KOHLBERG (MORAL)	Three levels via the Heinz dilemma: preconventional (punishment-obedience, instrumental exchange), conventional (interpersonal conformity, law and order), postconventional (social contract, universal principles). The reasoning defines the stage, not the answer; not all reach postconventional. Gilligan critique: care versus justice.
ATTACHMENT	Harlow contact comfort overturned cupboard-love. Bowlby: an evolved system, secure base, monotropy, internal working model, protest-despair-detachment. Ainsworth strange situation: secure (B), avoidant (A), ambivalent-resistant (C), disorganised (D, Main and Solomon). Disorganised attachment carries the greatest psychopathology risk.
TEMPERAMENT	Thomas and Chess (New York Longitudinal Study): nine dimensions (activity, rhythmicity, approach-withdrawal, adaptability, intensity, threshold, mood, distractibility, persistence); three types (easy, difficult, slow-to-warm-up); goodness of fit between temperament and environment predicts outcome. Kagan behavioural inhibition; Rothbart reactivity.
MAHLER (SEPARATION-INDIVIDUATION)	Normal autistic (0 to 1 month) and symbiotic (1 to 5 months) phases, then four subphases: differentiation, practising, rapprochement (the crisis), and consolidation with object constancy (to 36 months). Rapprochement-failure is linked to borderline pathology. Klein, Winnicott and Fairbairn (object relations) are taught on the Social, Learning & Personality Psychology notes.
LANGUAGE AND MOTOR MILESTONES	Verified ages: social smile 6 to 8 weeks, head control 3 months, sits 6 months, stranger anxiety 8 months, pincer grasp 9 to 10 months, first words about 12 months, walks 12 to 15 months, two-word phrases 18 to 24 months. Language theory: Skinner operant versus Chomsky nativist (language acquisition device, universal grammar) versus interactionist; cooing, babbling, holophrastic, telegraphic.
DISCRIMINATE AND APPLY	Align the stage theorists (Freud, Erikson, Piaget, Kohlberg) down one age axis; only Erikson spans the whole life. Tell the emotion theories apart by the

The whole picture in one table	
	order of arousal, cognition and feeling; place the intelligence models on the one-versus-many spectrum. Apply by reading a child by stage, a temperament by goodness of fit, and an attachment by the strange situation.

References

This material is grounded in the standard texts (the source hierarchy below); each theory is attributed to its primary source, and landmark, contested or numeric claims carry a PubMed-verified journal citation. Every PMID here was checked against PubMed this build, and citations whose identifier did not resolve to the cited paper were corrected or dropped.

SOURCE HIERARCHY (TEXTBOOKS)

1. Boland R, Verduin ML, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 11th ed. Philadelphia: Wolters Kluwer; 2024. [primary depth bar; contributions of the psychological sciences, human development]
2. Sadock BJ, Sadock VA, Ruiz P. Kaplan & Sadock's Synopsis of Psychiatry. 11th ed. Philadelphia: Wolters Kluwer; 2015. [theories of personality and psychopathology; the schools of psychology]
3. Geddes JR, Andreasen NC, Goodwin GM, eds. New Oxford Textbook of Psychiatry. 3rd ed. Oxford: Oxford University Press; 2020. [psychology and human development chapters]
4. Tasman A, Kay J, Lieberman JA, First MB, Riba MB, eds. Psychiatry. 4th ed. Chichester: Wiley-Blackwell; 2015. [developmental and cognitive psychology]
5. Johnstone EC, Owens DGC, Lawrie SM, et al, eds. Companion to Psychiatric Studies. 8th ed. Edinburgh: Churchill Livingstone/Elsevier; 2010. [psychology of perception, memory, motivation, emotion]

FOUNDATIONAL PRIMARY SOURCES

1. Neisser U. Cognitive Psychology. New York: Appleton-Century-Crofts; 1967. [names cognitive psychology; the information-processing metaphor]
2. Atkinson RC, Shiffrin RM. Human memory: a proposed system and its control processes. In: The Psychology of Learning and Motivation. Vol 2. New York: Academic Press; 1968:89-195. [multi-store model]
3. Baddeley AD, Hitch GJ. Working memory. In: The Psychology of Learning and Motivation. Vol 8. New York: Academic Press; 1974:47-89. [working-memory model]
4. Maslow AH. A theory of human motivation. Psychol Rev. 1943;50:370-396. [the hierarchy of needs]
5. Freud S. The Ego and the Id. London: Hogarth Press; 1923; and Introductory Lectures on Psycho-Analysis. 1916-1917. [the structural model; psychosexual theory]
6. Adler A. The Practice and Theory of Individual Psychology. London: Routledge; 1924. [inferiority, superiority, style of life, social interest]
7. Jung CG. The Archetypes and the Collective Unconscious. Collected Works, Vol 9, Part 1. Princeton: Princeton University Press; 1959. [archetypes, individuation]
8. Erikson EH. Childhood and Society. New York: Norton; 1950. [the eight psychosocial stages]
9. Piaget J. The Origins of Intelligence in Children. New York: International Universities Press; 1952. [the four cognitive stages]
10. Vygotsky LS. Mind in Society. Cambridge: Harvard University Press; 1978. [the zone of proximal development, scaffolding]
11. Chomsky N. A review of B.F. Skinner's Verbal Behavior. Language. 1959;35:26-58. [the nativist critique; the language acquisition device]
12. Kohlberg L. Essays on Moral Development. Vol 1: The Philosophy of Moral Development. San Francisco: Harper & Row; 1981. [the six moral stages]
13. Harlow HF. The nature of love. Am Psychol. 1958;13:673-685. [contact comfort; the rhesus-monkey studies]

14. Bowlby J. Attachment and Loss. Vol 1: Attachment. London: Hogarth Press; 1969. [attachment as an evolved system]
15. Ainsworth MDS, Blehar MC, Waters E, Wall S. Patterns of Attachment: A Psychological Study of the Strange Situation. Hillsdale: Erlbaum; 1978. [the strange-situation classifications]
16. Thomas A, Chess S. Temperament and Development. New York: Brunner/Mazel; 1977. [the nine dimensions; goodness of fit]
17. Mahler MS, Pine F, Bergman A. The Psychological Birth of the Human Infant. New York: Basic Books; 1975. [separation-individuation and its subphases]
18. Gardner H. Frames of Mind: The Theory of Multiple Intelligences. New York: Basic Books; 1983. And Sternberg RJ. Beyond IQ: A Triarchic Theory of Human Intelligence. Cambridge: Cambridge University Press; 1985. [plural models of intelligence]

JOURNAL REFERENCES (PUBMED-VERIFIED, 11)

1. Schachter S, Singer JE. Cognitive, social, and physiological determinants of emotional state. Psychol Rev. 1962;69:379-99. PMID: 14497895.
2. Baddeley A. Working memory. Science. 1992;255:556-9. PMID: 1736359.
3. Tulving E. Episodic memory: from mind to brain. Annu Rev Psychol. 2002;53:1-25. PMID: 11752477.
4. Loftus EF. Planting misinformation in the human mind: a 30-year investigation of the malleability of memory. Learn Mem. 2005;12:361-6. PMID: 16027179.
5. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. Am Psychol. 2000;55:68-78. PMID: 11392867.
6. Mayer JD, Salovey P, Caruso DR. Emotional intelligence: new ability or eclectic traits? Am Psychol. 2008;63:503-17. PMID: 18793038.
7. Kapur S. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. Am J Psychiatry. 2003;160:13-23. PMID: 12505794.
8. Marcia JE. Development and validation of ego-identity status. J Pers Soc Psychol. 1966;3:551-8. PMID: 5939604.
9. Ainsworth MD, Bell SM. Attachment, exploration, and separation: illustrated by the behavior of one-year-olds in a strange situation. Child Dev. 1970;41:49-67. PMID: 5490680.
10. Wimmer H, Perner J. Beliefs about beliefs: representation and constraining function of wrong beliefs in young children's understanding of deception. Cognition. 1983;13:103-28. PMID: 6681741.
11. Baron-Cohen S, Leslie AM, Frith U. Does the autistic child have a "theory of mind"? Cognition. 1985;21:37-46. PMID: 2934210.

Index

Every entry jumps to its page. Numbers are the page of first mention.

#

22q11.2 deletion 16

A

aberrant salience 145
ACE model 25
adoption study 13
alexithymia 196
Angelman syndrome 21
anticipation 21
antisaccade 61

B

behavioural inhibition 249
biopsychosocial model 202

C

CACNA1C 40
carbamazepine 92
Carter effect 18
CHRNA7 63
collective unconscious 134
complement C4A 47
copy number variant 22
CYP2C19 89
CYP2D6 89

D

d-prime 139
de novo mutation 11
DISC1 36
DNA methylation 21

E

emotional object constancy 255
endophenotype 11
epigenetic principle 226
equal-environments assumption 29

F

Falconer's formula 28
fictional finalism 214
FKBP5 55
fragile-X syndrome 21

G

genomic imprinting 21
Glasgow Coma Scale 179
goodness of fit 249
Gottesman and Gould 60
GWAS 13

H

Heinz dilemma 236
heritability 11
hierarchy of needs 134
HLA-B*15:02 92

I

individuation 135
internal working model 244

K

Kluver-Bucy syndrome 176

L

language acquisition device 261
law of Prägnanz 140
levels of processing 150
liability-threshold model 13
linkage disequilibrium 34
LOD score 13

M

Mendelian randomization 47
mismatch negativity 61
missing heritability 14
MSCEIT 198
Myers-Briggs Type Indicator 225

O

object permanence 232
Oedipus complex 210

P

p-factor 69
P-FIT 161

P50 suppression 62
Papez circuit 172
pleiotropy 41
polygenic risk score 13
positive manifold 156
Prader-Willi syndrome 21
predictive processing 143
prepulse inhibition 61

R

reactive attachment disorder 242
Remote Associates Test 189

S

Sally-Anne task 235
self-determination theory 168
signal detection theory 139
social interest 214
somatic marker hypothesis 175
Stevens-Johnson syndrome 94
Strange Situation 242

T

Thematic Apperception Test 168
Torrance Tests of Creative Thinking 190

W

working memory 61

Y

Yerkes-Dodson law 167

Z

zone of proximal development 231

About the authors

Dr. Wilfred D'souza

MD Psychiatry (Resident) · Certified Gestalt Therapist · Weave, Centre for Integrative Psychiatry

Works in integrative psychiatry with Schema Therapy as the primary lens, alongside CBT, DBT, motivational interviewing and emotion-focused therapy, and is a certified Gestalt therapist. His clinical interests run through neurodivergence, ADHD, bipolar disorder, personality disorders, addiction and developmental psychiatry: work grounded in lived experience of attention difficulties long labelled as laziness, which made psychiatry personal before it became professional. He has been developing the Toroidal Model of Psychosis and Affect (TMoP), his computational model of mind, and TMoP thinking shaped the Claude Code AI system he builds with: clinical software, teaching tools and much of this series' production pipeline among its work, bringing psychiatry into the AI era in his own way. Lead author of the Weave Sprint series.

Dr. Niharika Reddy

Consultant Psychiatrist · Weave, Centre for Integrative Psychiatry

Consultant Psychiatrist at Weave, Mumbai, seeing people online through weave.clinic. Her work centres on relationships and family dynamics, family therapy and women's mental health, with a particular focus on neurodivergence in women and on adolescent mental health. Practises integrative, person-centred psychiatry. Co-author of this volume.

THE WEAVE LIBRARY

You revised from one. The whole shelf is open.

Field guides and references written in practice, for the people who do the work and the people living through it. Most are free to read and download.



field guides · references · for clinicians and families · free to read

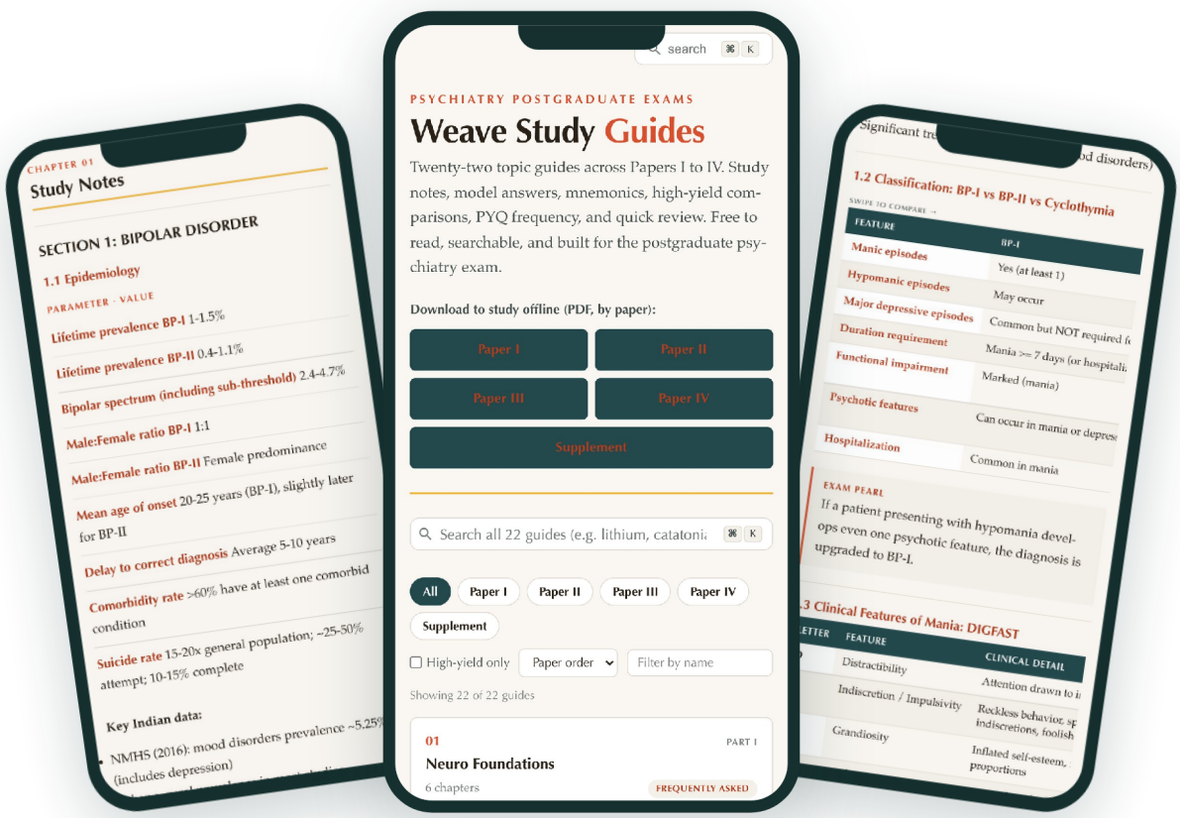
weave.clinic/library

TAP OR SCAN TO OPEN

WEAVE STUDY GUIDES

When the night is short, read the guide.

Twenty-two topic guides across all four papers. Study notes, model answers, mnemonics, high-yield comparisons and previous-question frequency. Free, searchable, built for this exam.



22 guides · all four papers · fully searchable · free to read

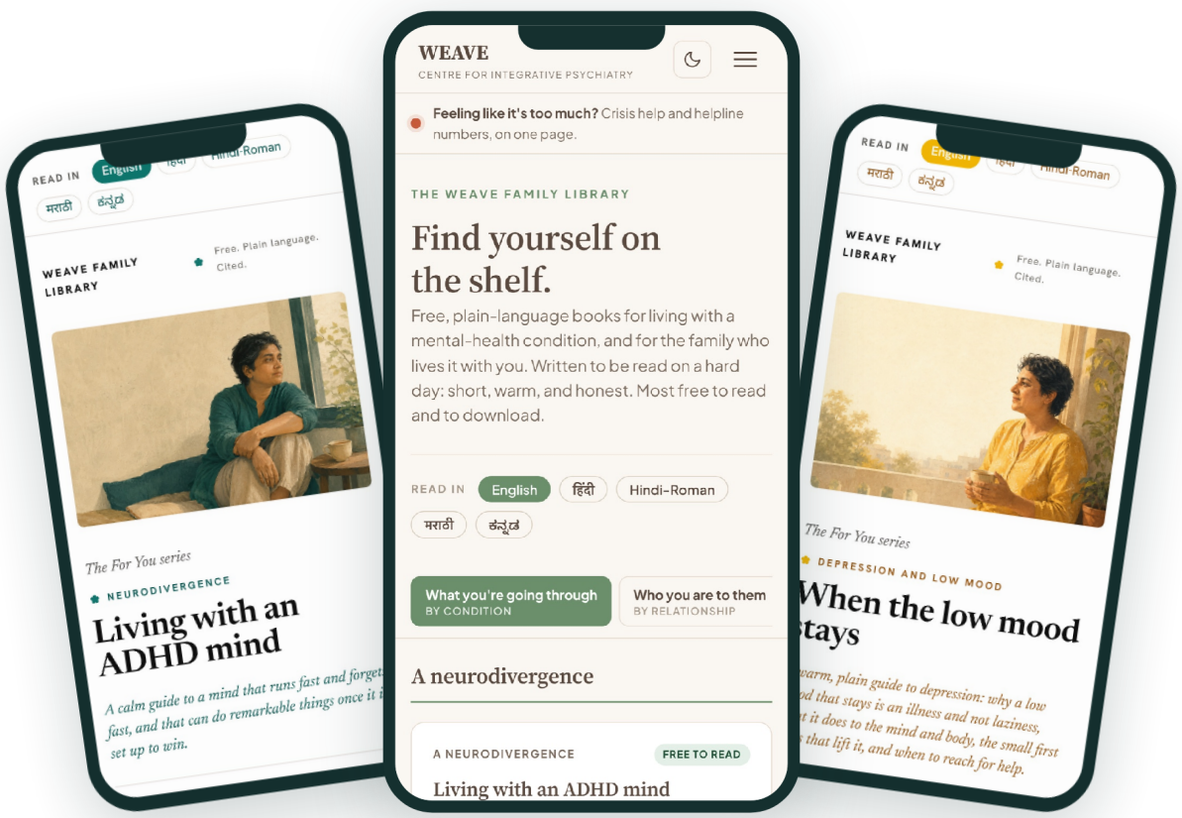
weave.clinic/study

TAP OR SCAN TO OPEN

THE WEAVE FAMILY LIBRARY

Send the family home with more than a prescription.

Free, plain-language books for living with a mental-health condition, written for patients and the people who love them. Find yours by condition, by relationship, or by situation.



plain language · patients and families · five languages · free to read

weave.clinic/family

TAP OR SCAN TO OPEN

A PAPER A DAY

The whole written exam, in one day's reach.

Every paper of the MD psychiatry written exam in one free book, with a colour memory code and clickable navigation, for the last week, the last night, the last hour before the hall.



four papers · one volume · colour-coded · free to read

weave.clinic/revision

TAP OR SCAN TO OPEN

STUDY TOGETHER

You do not have to revise alone.

These notes started as messages in a room full of residents helping each other through. That room is still open. Bring your doubts, your corrections, and the questions the textbooks do not answer.

Join the study group

https://chat.whatsapp.com/H7TsLGK2wFl4bSe2r0Zfzn?mode=gi_t

PRINTING AND DISTRIBUTION

Notes Next Door (NND), Delhi is the official printing and distribution partner for Weave Sprint. The soft-copy PDFs and the complete print-ready set are always available at weave.clinic/sprint, should you prefer to print the notes yourself. Weave Sprint is open source and free, and as part of Weave's commitment to residents it will stay that way, forever. We do, however, strongly recommend a printed set from Notes Next Door: in our experience, they have been the most reliable printing partner we have worked with.

WEAVE SPRINT · PAPER I · VOLUME TWO

Volume Two of the first paper: the genetics of psychiatric disorder, from family and twin evidence through the molecular methods to what the clinic can honestly do with a risk estimate; then general and developmental psychology, the mind studied as theory and the child studied as a sequence. Two complete sets of notes, written to be understood the first time and recalled every time after, with a colour memory code, a clickable contents and a full index.

Built to understand. Kept to revise.

All the very best for your exam.

WEAVE

weave.clinic · wilfred@weave.clinic · niharika@weave.clinic