FLOW HIJACKED · ADHD

INTO THE TASK

ADHD, Attention, and the Dynamics of Cognitive Control

THE ORGANISING QUESTION

What happens when a brain must repeatedly move from internally generated activity into stable, goal-directed control—and why is that transition different in ADHD?

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Scope, rights, and educational boundary

This publication is a scientific and educational lecture. It is not a diagnostic instrument, a substitute for a comprehensive clinical assessment, or individualized medical, psychological, educational, occupational, or legal advice. ADHD cannot be established from a scan, a single cognitive test, a social-media checklist, a subjective response to a stimulant, or the presence of concentration problems alone. Diagnosis requires developmentally appropriate clinical evaluation, evidence of impairment, attention to onset and course, and consideration of alternative or co-occurring explanations.

Medication is discussed at molecular, neural, cognitive, behavioral, and clinical levels. This discussion does not recommend a particular medicine, formulation, dose, combination, initiation, continuation, or discontinuation for any individual. Treatment decisions require a qualified prescriber who can consider age, cardiovascular status, sleep, appetite and growth where relevant, anxiety, mood, tics, substance-use risk, psychosis or mania vulnerability, pregnancy, other medicines, and the person's goals and preferences. Abrupt medication changes should not be made on the basis of this lecture.

Psychotherapy and behavioral interventions are discussed with the same seriousness as medication. Evidence for symptom reduction, functional compensation, family or school effects, organizational skill, emotional regulation, and neural change is kept separate. A plausible neural mechanism is not presented as demonstrated merely because an intervention is clinically useful.

The research substrate contains 531 deduplicated peer-reviewed records, including a 266-paper high-impact core selected through notable-researcher and citation-impact gates, 218 records from 2022-2026, and 244 records carrying a contradiction, limitation, null result, boundary condition, or alternative interpretation. These counts describe the acquisition system; they are not measures of certainty. Highly cited work can be foundational and still methodologically limited. Recent work can be important and still await replication.

Gabor Maté and Huberman Lab are treated as public explanatory sources, not terminal scientific authorities. Consequential claims are separated from phenomenological insight and traced, where possible, to primary research. The Maté passage-level audit remains limited wherever a complete legally accessible text was unavailable. Guideline recommendations are distinguished from mechanistic neuroscience.

All mathematical models in this lecture are explanatory and testable abstractions. They are not literal portraits of a person's brain and are not diagnostic models. In particular, the application of non-normal dynamics, pseudospectra, resolvent analysis, and transient amplification to ADHD is identified as a Flow Hijacked hypothesis because direct ADHD evidence has not established those operators or quantities.

Person-first and non-stigmatizing language is used throughout. Lived experience can illuminate meaning and stakes; it does not, by itself, establish prevalence, mechanism, cause, prognosis, or treatment effect.

Abstract

ADHD is usually introduced through inattention, hyperactivity, and impulsivity. Those features are clinically necessary, but they do not exhaust the phenomenon. Many people can perform a demanding task well in one context and struggle to begin or sustain a modest task in another. They may be highly distractible when reward is delayed yet remain intensely engaged when interest, urgency, novelty, or immediate consequence is high. This variability is often misread as an absence of effort. Scientifically, it raises a different question: not only how much attention a person has, but how cognition is allocated, assembled, stabilized, interrupted, recovered, and released across time.

This lecture builds that question from the clinical phenotype outward. ADHD is treated as a heterogeneous neurodevelopmental condition whose manifestations change with age, demands, compensation, sleep, stress, comorbidity, and environment. Executive dysfunction overlaps with ADHD but is not synonymous with it. Nor does every concentration problem indicate ADHD: sleep deprivation, anxiety, depression, PTSD, bipolar disorder, substance effects, autism, medical conditions, environmental overload, and technology-associated fragmentation require their own assessment.

The neural account moves beyond a contest between a pathological Default Mode Network and a single Task-Positive Network. The Default Mode Network supports adaptive internal cognition, including autobiographical memory, simulation, planning, and self-related thought. Goal-directed behavior recruits changing coalitions involving frontoparietal control, dorsal and ventral attention, salience, cingulo-opercular, corticostriatal, thalamocortical, cerebellar, motor, sensory, and memory-related systems. The important questions therefore concern timing and coordination: which configuration is present, how stable it is, what changes transition probability, what precedes a lapse, what enables re-entry, and what permits an appropriate switch when the task is complete.

Dynamic evidence is promising but incomplete. Some studies report differences in functional connectivity, state occupancy, dwell time, transitions, response-time variability, oscillatory activity, or trial-wise stability of control representations. Findings differ by age, task, analytic method, motion handling, medication history, and sample composition. There is no single diagnostic network signature, and mean activation, BOLD variability, behavioral variability, EEG variability, and metastability are not interchangeable quantities.

Dopamine and norepinephrine are presented as context-sensitive modulators of gain, working memory, arousal, effort, learning, reward, and action rather than as depleted fuel. The phrase “ADHD is low dopamine” captures the relevance of catecholamine systems but overstates a distributed and regionally specific literature. Molecular target engagement does not prove a unitary cause. Methylphenidate and amphetamine are not pharmacologically interchangeable; atomoxetine, guanfacine, clonidine, viloxazine extended release, bupropion, and modafinil have distinct mechanisms, evidence bases, regulatory contexts, and risk profiles.

Treatment is analyzed across layers. Medication can reduce core symptoms for many people and can alter some neural measures, but acute pharmaco-imaging findings do not establish durable normalization. Psychotherapy and behavioral treatment can modify cues, habits, task structure, reinforcement, metacognition, emotion regulation, organizational systems, and recovery after interruption. Functional improvement need not wait for proof of neural normalization. Combined treatment may be superior for some outcomes and circumstances, yet the attractive idea that medication opens a neural “learning corridor” for psychotherapy remains more plausible than directly demonstrated.

The final synthesis introduces the **Task-State Viability Envelope (TSVE)**: the set of distributed cognitive and neural states from which criterion-level performance on a specified task can remain viable, for a stated time horizon, under a stated perturbation regime and an admissible control budget. It separates entry latency, stabilization, unwanted departure, recovery and re-entry, and adaptive release. The **Dual-Exit Principle** proposes that resisting an irrelevant exit and executing a valid exit are different control achievements. Hyperfocus can therefore be modeled not as unlimited attention, but as one possible lifecycle profile: easy capture and long dwell under high value, potentially combined with slow release after the goal changes.

TSVE is a Flow Hijacked synthesis and research architecture, not a replacement diagnosis or established biomarker. Its value depends on discriminating predictions, competing models, identifiable measurements, and falsifiers. The lecture concludes that ADHD is not adequately described as simply too little attention. A deeper account is defensible when stated carefully: regulation of cognition across competing configurations differs, on average and heterogeneously, with reward, salience, catecholamines, development, learning, sleep, emotion, and environment altering the landscape. How those layers combine within an individual remains an open empirical question.

Author’s note

Writing about inconsistency without turning it into blame

The ordinary difficulty at the center of this lecture can be especially cruel because ability remains visible. A person may know what must be done, care about the consequence, possess the relevant skill, and still fail to begin at the intended time. On another day, or under a different configuration of interest, urgency, novelty, sleep, support, and reward, the same person may perform with remarkable intensity. Observers can convert that difference into a moral verdict: *If you could do it then, you could have done it now.* The verdict feels intuitive. It is also scientifically inadequate.

I do not write these pages to replace one verdict with another deterministic story about the brain. A network explanation can become dehumanizing when it is presented as destiny, and mathematical language can create false authority when its assumptions are hidden. Equations in this lecture are used to make claims more explicit and more vulnerable to disconfirmation. They do not measure the worth, intention, or effort of a person.

Nor do I want the lecture to become a contest between medication and psychotherapy. Medication is not evidence that a difficulty was “merely chemical.” Psychotherapy is not evidence that neurodevelopmental differences were “only psychological.” Environmental accommodation is not surrender, and a biological account does not eliminate agency. These interventions act at different layers and on different timescales. A medicine may change the conditions under which a task becomes more reachable. A learned strategy may change the route, cue structure, recovery policy, or cost of returning. A quieter environment may remove a perturbation that neither medicine nor willpower should be expected to defeat continuously.

The evidence does not authorize a single story for everyone with ADHD. Developmental history, symptom pattern, sex and gender, comorbidity, sleep, family and school context, work demands, medication exposure, resources, and opportunity all matter. Group differences do not specify an individual’s trajectory. A useful model must leave room for heterogeneity, compensation, growth, and the possibility that the same outward difficulty can arise through different processes.

I have therefore tried to make uncertainty visible rather than bury it in the references. Influential findings sit beside null results and methodological critiques. The Default Mode Network is not cast as an enemy. Dopamine is not presented as a tank that is simply empty. Hyperfocus is not romanticized, dismissed, or treated as proof against impairment. Public narratives are examined with respect for the insight they may offer and with equal respect for the limits of evidence.

The deepest aim is practical and humane. Better explanation should reduce blame without erasing responsibility; widen options without promising total control; and help us distinguish persistent attention from flexible, timely regulation of attention. The goal is not a person who focuses continuously. It is greater freedom to enter, sustain, recover, and release cognition when life actually requires it.

How to read the evidence

The lecture uses explicit labels so that a confident voice cannot silently turn a possibility into a fact.

EMPIRICAL RESULT

What the reported data directly show within the study's sample, design, measures, comparator, and analysis. An empirical result can be reliable without supporting the strongest interpretation attached to it.

AUTHORS' INTERPRETATION

The explanation proposed by the investigators. It deserves accurate representation, but it remains distinct from the measured result.

SUPPORTED SCIENTIFIC INTERPRETATION

A conclusion supported across several studies or methods, with its heterogeneity and boundary conditions preserved. This category is stronger than a single-study interpretation and weaker than a universal mechanism.

FLOW HIJACKED SYNTHESIS

An explicit integration of findings into the Flow Hijacked framework. It may be scientifically plausible and useful while remaining absent from the original studies.

NEW HYPOTHESIS

A falsifiable proposal that current ADHD evidence has not established. TSVE formalization and the proposed relevance of non-normal transient amplification enter this category whenever they exceed direct findings.

OPEN RESEARCH QUESTION

An uncertainty that available evidence cannot yet resolve. A good open question specifies the observation or comparison that would change the conclusion.

COUNTEREVIDENCE

A serious null, negative, contradictory, or alternative result. Counterevidence is not a decorative caveat. It changes the confidence, scope, or formulation of the claim.

CLINICAL BOUNDARY

A reminder that population evidence and mechanistic models do not determine an individual's diagnosis or treatment plan.

Reading rules

- Association is not described as causation.
- Acute change is not described as long-term reorganization.
- A statistically significant group difference is not described as a diagnostic biomarker.
- "Normalization" is used only with a named measure, comparator, age group, task, and timescale.
- Lack of detected neural change is not equated with lack of clinical benefit.
- Symptom reduction is separated from executive function, academic or occupational function, relationships, emotional regulation, safety, quality of life, and long-term outcome.
- Influence and reliability are graded separately. Citation count helps identify an intellectual backbone; it does not replace design quality, replication, directness, or recency.

The route through the lecture · I-VI

I. The paradox of available but unreliable attention

The lecture begins with the discrepancy between ability and reliable access to that ability. Task initiation, persistence, interruption, hyperfocus, and performance variability create a problem that a simple capacity model cannot solve. The moral interpretation of inconsistency is separated from the scientific question.

II. What ADHD is - and what it is not

The diagnostic phenotype, impairment, presentations, comorbidity, and heterogeneity are established before neuroscience is introduced. ADHD symptoms are distinguished from executive dysfunction, ordinary fluctuation, sleep loss, stress, anxiety, depression, PTSD, bipolar disorder, substance effects, autism, medical mimics, and technology-associated fragmentation.

III. A developmental condition with a fluctuating course

Child, adolescent, and adult ADHD are not merged. Cortical, striatal, cerebellar, white-matter, and network development are examined alongside persistence, partial remission, recurrence, compensation, late recognition, sex differences, and transitions in environmental demand.

IV. Causal architecture without destiny or blame

Heritability, common polygenic liability, rare variants, genetic correlation, prematurity, prenatal and environmental risks, adversity, stress, family context, attachment, and socioeconomic conditions are considered without reducing ADHD either to genes or to childhood relationships. Etiology, present state, and treatment target remain different questions.

V. Attention is not one faculty

Selection, vigilance, working memory, response inhibition, proactive and reactive control, prospective memory, task initiation, effort, delay, timing, mind wandering, switching, and hyperfocus are decomposed into operations with different measures and failure modes.

VI. The network cast - beyond “default versus task-positive”

The Default Mode, frontoparietal control, dorsal and ventral attention, salience, cingulo-opercular, reward, corticostriatal, thalamocortical, cerebellar, motor, sensory, hippocampal, and memory-related systems are introduced. A task is treated as a temporary configuration of systems, not the activation of one uniform network.

The route through the lecture · VII-XII

VII. From internal activity to goal-directed control

The historical default-mode interference hypothesis is recovered and then revised. The focus shifts to rest-to-task and task-to-rest transitions, frontoparietal representation, dorsal-attention selection, salience and cingulo-opercular arbitration, reward valuation, lapse precursors, successful engagement, and spontaneous departure.

VIII. The brain across time - variability, states, and metastability

Mean activation gives way to response-time variability, BOLD and electrophysiological variability, dynamic connectivity, state occupancy, dwell, transition probability, hidden-state models, trial-wise representational stability, local sleep-like activity, criticality, and metastability. Measurement differences and analytic flexibility remain visible.

IX. Why context can transform the same person

Reward timing, effort cost, novelty, emotional salience, interoception, arousal, sleep, circadian phase, stress, and task demand can change the same person's performance. Incentive-dependent improvement is not taken as proof that impairment was voluntary. Hyperfocus is examined as high capture, strong persistence, impaired release, or some combination.

X. Dopamine and norepinephrine as control parameters

Dopamine synthesis, release, transporters, receptor families, regional pathways, tonic and phasic signaling, reward prediction, locus-coeruleus norepinephrine, alpha-2A signaling, signal-to-noise, gain, and inverted-U relationships are connected to cognition without presenting ADHD as a global catecholamine deficiency.

XI. Pharmacological treatment - distinct molecules, distinct timescales

Methylphenidate, dexmethylphenidate, amphetamine formulations, lisdexamfetamine, atomoxetine, guanfacine, clonidine, viloxazine extended release, bupropion, and modafinil are compared across mechanism, efficacy, function, age, dose, onset, coverage, adverse effects, discontinuation, and long-term uncertainty. Therapeutic use is distinguished from diversion and nonmedical use.

XII. Medication as network modulation

Acute target engagement is separated from chronic adaptation. Evidence concerning the Default Mode Network, control and attention systems, salience and cingulo-opercular function, reward circuitry, thalamic and cerebellar measures, EEG, connectivity, flexibility, dwell, responder differences, and prediction is examined without assuming that every beneficial change is "normalization."

The route through the lecture · XIII-XVII

XIII. Psychotherapy, behavior, and the architecture around attention

ADHD-adapted CBT, metacognitive and organizational work, problem solving, emotion-regulation approaches, behavioral parent training, school interventions, psychoeducation, motivational work, mindfulness, acceptance-based approaches, coaching, telehealth, digital therapeutics, cognitive training, and neurofeedback are graded by target, symptom effect, functional effect, persistence, and neural evidence.

XIV. Psychotherapy and medication together - different layers of control

The limited direct psychotherapy-neuroscience corpus is separated from clinical evidence. Major multimodal trials and follow-ups are interpreted by outcome and timescale. Complementarity, possible dose-sparing effects, and the proposed medication-enabled "learning corridor" are considered without claiming an unmeasured neural synergy.

XV. Public narratives and clinical authorities under audit

Gabor Maté's developmental and relational account is treated with intellectual and humane seriousness while its causal claims about heredity, attachment, trauma, and healing are graded against contemporary evidence. Huberman claims about networks, dopamine, stimulants, attentional blinks, visual focus, omega-3, modafinil, meditation, and smartphones are mapped toward primary sources. Guidelines are compared as clinical recommendations, not mechanistic proof.

XVI. The contradiction chamber

The emerging account faces spatial nonconvergence, null findings, small and distributed effects, motion, medication history, vascular and preprocessing confounds, age and sex differences, comorbidity, publication bias, reverse inference, analytic flexibility, and the absence of a single diagnostic biomarker. The synthesis is revised where the evidence resists it.

XVII. Flow Hijacked synthesis - the Task-State Viability Envelope

Entry, stabilization, unwanted departure, recovery, re-entry, and adaptive release are integrated in a task- and context-specific state-space framework. Fast neural dynamics are separated from slower learning and development. Metastability is used only where operationalized. Non-normality, pseudospectra, resolvent gain, and transient amplification are presented as explicit hypotheses. The part ends with predictions, competing explanations, falsifiers, and a humane answer to the governing question.

The governing logic

The question held constant

What happens when a brain must repeatedly move from internally generated activity into stable, goal-directed control - and why is that transition different in ADHD?

The question does not presuppose a single transition deficit. It organizes measurements that are too often studied separately.

The cumulative argument

1. A capacity-only account cannot explain large context-dependent variation.
2. The clinical object must be defined before neural mechanisms are assigned to it.
3. Development and multiple causal routes constrain every adult or cross-sectional interpretation.
4. “Attention” decomposes into operations that recruit different systems.
5. Goal-directed cognition is a temporary distributed configuration, not one network switching on while another switches off.
6. Timing, stability, perturbation, and transition may reveal information hidden by mean activation.
7. Reward, salience, arousal, sleep, emotion, and catecholamines alter the operating regime.
8. Medication, psychotherapy, behavior, and environment act at partly different layers and timescales.
9. Null results and methodological limits narrow the permissible synthesis.
10. TSVE converts the remaining synthesis into definitions, measurements, predictions, and falsifiers.

Questions repeated at every level

- Which system or configuration is active, and in relation to which task and time point?
- How readily is the configuration entered?
- How stable is criterion-level performance once entered?
- What internal or external perturbation changes the probability of departure?
- How quickly and at what cost can the system recover?
- Can it release efficiently when the goal changes?
- What is trait-like, what is state-dependent, and what changes with development?
- What changes under medication, psychotherapy, training, environmental modification, sleep, or reward?
- Is the evidence direct, inferred, synthesized, hypothetical, or still absent?

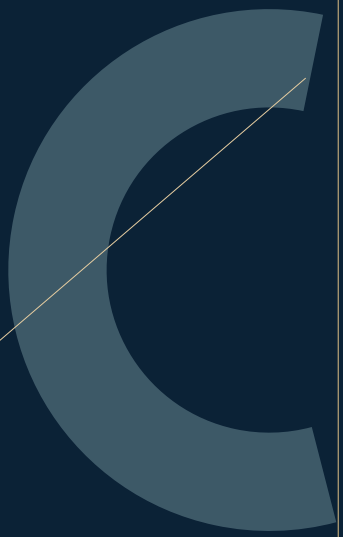
Claim boundary

The lecture can establish that ADHD is clinically and biologically heterogeneous, developmental, strongly heritable at the population level, associated with distributed and variable cognitive/neural differences, and responsive on average to several evidence-based treatments. It can support a coordination-and-regulation interpretation across multiple literatures. It can propose TSVE as a coherent research architecture. It cannot establish one neural cause, one diagnostic network signature, a universal lifecycle profile, a direct non-normal ADHD operator, or an individualized treatment prediction from the presented neuroscience.

PART I

THE PARADOX OF AVAILABLE BUT

UNRELIABLE ATTENTION



Create the contradiction that a simple capacity model cannot resolve.

Part thesis

ADHD is not well represented by a meter that is always low. The more faithful clinical puzzle is that access to attention, action, and persistence is **unevenly controllable across time and context**. A person may know exactly what to do, possess the skill to do it, care about the outcome, and still fail to assemble a durable task state. Under urgency, novelty, immediate feedback, intense interest, or social accountability, the same person may perform with remarkable speed and endurance. That contrast does not prove that ADHD is voluntary; it tells us that capacity and reliable control are different variables.

1 The unfinished ordinary task

The ordinary task is an unusually powerful clinical probe. It may be short, familiar, and objectively achievable: reply to a message, open a document, put away laundry, submit a form, begin a reading assignment. Yet it has several properties that make it difficult for many people with ADHD. Its reward is delayed. Its starting cue is weak. Its endpoint is not emotionally vivid. It offers little novelty and few intermediate consequences. It may require the person to hold an intention across competing stimuli, recover after interruption, and generate their own pacing.

Failure here is often described as a deficit of knowledge or motivation. But the person may be able to explain the task, anticipate its consequences, and perform an equivalent task when an external deadline compresses time. What varies is not necessarily the stored competence; it is the probability that the competence will be recruited at the required moment and held online long enough to matter. This distinction sits behind Barkley's separation of knowing from performing, Sonuga-Barke's motivational account, and later work emphasizing heterogeneity rather than a single executive lesion (Barkley 1997, DOI 10.1037/0033-2909.121.1.65, PMID 9000892; Sonuga-Barke 2003, DOI 10.1016/j.neubiorev.2003.08.005, PMID 14624804; Nigg 2005, DOI 10.1016/j.biopsych.2004.11.011, PMID 15950017).

The clinically important unit is therefore not "can the person pay attention?" but a sequence: can an intention survive delay; can a task state be entered; can it be protected from internally generated thought and external salience; can it be resumed after disturbance; can it be released when it is no longer useful? Later parts will translate that sequence into interacting cognitive operations and neural configurations. At this stage, it is enough to see why a binary capacity model fails.

Core sentence. The unfinished task is not proof that ability is absent; it is evidence that ability is not being made reliably available at the right time.

Figure concept — capacity versus access. Two equally high "capacity" bars feed different time series. One trace reliably enters and remains inside a task-performance band; the other repeatedly approaches, exits, and re-enters it. No brain region is labeled yet.

2 "I cannot begin" versus "I cannot stop"

Task initiation and task release can fail in opposite-looking directions. "I cannot begin" may include weak cueing, diffuse goals, high anticipated effort, delayed reward, uncertainty about the first action, or failure to maintain the intention while other events arrive. "I cannot stop" may include intense interest, immediate feedback, escalating reward, aversion to switching costs, perseveration, or failure to represent a later obligation strongly enough to terminate the current activity. Both can coexist in the same individual because neither is captured by a single quantity called attention.

This is the first reason to treat ADHD as a problem of regulation rather than a literal absence. Regulation includes selection, entry, stabilization, allocation, interruption, switching, and release. The same system can be hard to engage under one configuration and hard to disengage under another. Empirical hyperfocus work is still young and relies heavily on self-report, convenience samples, and evolving definitions, so this symmetry is a supported clinical interpretation rather than a settled neural mechanism (Hupfeld, Abagis & Shah 2019, DOI 10.1007/s12402-018-0272-y, PMID 30267329; Ashinoff & Abu-Akel 2021, DOI 10.1007/s00426-019-01245-8, PMID 31541305; Hupfeld et al. 2024, DOI 10.1038/s41598-024-70028-y, PMID 39169147).

The distinction also changes treatment questions. A timer may help a person leave a captivating task but do little to make a vague task attractive enough to enter. Breaking work into visible first actions may reduce initiation energy but not protect a state from notification capture. Medication may alter arousal, valuation, or control, while learned routines alter cueing and the environmental route into action. "Attention improved" is too coarse a description for these different effects.

3 Variable performance is not absence of ability

ADHD is strongly associated with performance variability, but variability must be named precisely. On reaction-time tasks, group differences are often expressed not only in mean speed or accuracy but in a broader, more positively skewed distribution: many ordinary responses interspersed with unusually slow responses. A mean can therefore conceal the temporal structure of performance. Two people can have the same average response time while one is consistently moderate and the other alternates between very fast and very slow trials.

This pattern matters because it suggests that the mechanism may lie partly in fluctuating state control rather than a uniformly weakened computation. Yet even "reaction-time variability" is not a single biological object. The standard deviation, coefficient of variation, ex-Gaussian tail parameter, frequency-domain oscillation, drift-diffusion parameter, and trial-level neural predictor each answer different questions. Recent trial-wise work stresses that group-averaged BOLD variability cannot simply be equated with behavioral variability (Tamm et al. 2025, DOI 10.1016/j.ynirp.2025.100263, PMID 40511327). The safe claim is that performance stability is an important phenotype; the unsafe claim is that one named network fluctuation has been proven to cause every slow trial.

Variability also exposes a moral mistake. Observers tend to treat a person's best performance as evidence of what should be continuously available. But a maximum is not a measure of reliable control. A singer who can reach a note once does not necessarily have stable vocal technique; a network that briefly forms an effective configuration does not necessarily maintain it under ordinary perturbation. Clinical impairment arises from the distribution of performance across real time, not from the existence of isolated peaks.

Contradiction boundary. Some neural studies find increased variability in ADHD; others find system-specific reductions, unchanged variability, or no direct mediation of reaction-time variability. Behavioral variability, BOLD signal variability, connectivity flexibility, entropy, and EEG variability must never be collapsed into one axis.

4 Hyperfocus challenges deficit-only language

Hyperfocus refers broadly to episodes of unusually intense or prolonged absorption, often accompanied by reduced awareness of time or competing demands and difficulty disengaging. Surveys suggest that people with elevated ADHD symptoms report such episodes more often, and newer questionnaires attempt to separate dispositional tendencies from isolated experiences (Hupfeld et al. 2019, PMID 30267329; Groen et al. 2020, DOI 10.1016/j.ridd.2020.103789, PMID 33126147; Hupfeld et al. 2024, PMID 39169147). This literature is scientifically useful because it makes a deficit-only account visibly incomplete.

It does not follow that hyperfocus is unique to ADHD, uniformly beneficial, or generated by a known dopamine signature. Deep absorption also occurs in flow, expertise, gaming, creative work, autism, obsessive-compulsive phenomena, and ordinary high-interest activity. Current measures vary in whether they emphasize duration, intensity, productivity, neglect of bodily needs, loss of temporal awareness, or switching difficulty. Many samples are self-selected, and some contain few clinically diagnosed participants. Direct neural studies of ADHD-specific hyperfocus are essentially absent.

The responsible conclusion is narrower and more interesting: high sustained attention in selected contexts can coexist with serious impairment in flexible, goal-congruent allocation. Hyperfocus may sometimes be productive flow; in other episodes it may be capture—attention is stable, but the stability serves the wrong horizon. The key questions are what initiated the state, what keeps it stable, whether the person can voluntarily redirect it, and what costs accumulate outside the focus.

5 The moral error: inconsistency mistaken for unwillingness

Inconsistent performance is socially legible as choice. If someone succeeds on Tuesday, failure on Wednesday can look like defiance, indifference, laziness, manipulation, or lack of character. The inference is understandable because ordinary social prediction assumes relatively stable access to intention. It becomes harmful when variability itself is part of the disorder.

This does not mean that every missed obligation is neurologically inevitable or that responsibility disappears. It means responsibility should be engineered around the actual control problem. Accountability can be paired with external cueing, shorter feedback loops, reduced ambiguity, planned re-entry, sleep care, medication when appropriate, and skills for sequencing and time representation. Shame supplies salience, but it does not reliably supply a task architecture. In fact, shame can increase avoidance and consume the working-memory and emotional-regulation resources required to act.

The humane formulation is also the more testable one. Instead of asking whether a person "wanted it enough," ask which task properties changed behavior: immediacy, novelty, structure, interest, risk, social presence, fatigue, time of day, or emotional load. Context-dependent changes become data about a control system. They can guide treatment without pretending that the person is either powerless or simply choosing every lapse.

6 The central transition question

This lecture is organized around one transition: **what happens when a brain must repeatedly move from internally generated activity into stable, goal-directed control, and why is that transition different in ADHD?** The wording matters. Internally generated activity is not noise; it includes autobiographical memory, simulation, planning, self-evaluation, imagination, and spontaneous thought. Goal-directed control is not one "task-positive network"; it requires temporary coordination among sensory selection, working memory, valuation, action, error monitoring, and sustained-set systems.

The transition can fail at several points. The intended task may never become sufficiently valuable or concrete to recruit control. The required configuration may assemble but remain shallow and easily displaced. External novelty or internal thought may win an arbitration process. A lapse may begin before conscious awareness. Re-entry after interruption may require rebuilding the goal model. Conversely, an absorbing state may become so stable that adaptive release is delayed.

These are hypotheses to be separated from established findings. ADHD is clinically established as a heterogeneous developmental disorder. Group differences exist across cognition, structure, function, reward, timing, and catecholamine-sensitive treatment. Evidence that some samples show altered state occupancy, dwell time, connectivity, or representational stability is emerging. A unified nonlinear state-space mechanism is not yet established; it is a synthesis to be tested.

7 The epistemic legend for the whole lecture

Every major statement in the lecture belongs to one of five categories.

1. **Empirical result:** what a specific study directly measured in its sample under its design.
2. **Authors' interpretation:** the causal or mechanistic meaning proposed by that study's authors.
3. **Broader scientific inference:** a conclusion supported across studies but not directly measured in any single experiment.
4. **Flow Hijacked synthesis:** an organizing model that connects established findings without claiming to have been directly observed as a whole.
5. **New hypothesis:** a falsifiable proposition whose direct ADHD evidence is absent or preliminary.

These categories prevent three common errors. A statistically reliable group difference is not an individual diagnostic test. A treatment's molecular target is not proof that the untreated disorder is caused by deficiency at that target. A metaphor that organizes multiple findings is not automatically a mechanism. Highly cited work receives historical weight, but citation count is not a risk-of-bias assessment. Recent evidence can qualify canonical models, and null findings are part of the substrate rather than obstacles to the story.

The lecture also maintains a nonclinical boundary. It explains evidence and treatment principles; it does not diagnose an individual, recommend a personal prescription, or replace evaluation of sleep, mood, trauma, substances, medical conditions, and context.

A closer reading of inconsistency

The central paradox becomes clearer if capacity is separated from access. Capacity asks what a person can do under favorable conditions. Access asks how reliably that capacity can be recruited at the required time, under the actual combination of delay, ambiguity, fatigue, distraction, emotion, and competing value. A single successful performance establishes that the operation is possible; it does not establish that the same operation is equally reachable across contexts. Conversely, one failed performance does not reveal an absent capacity. The clinically relevant object is therefore a distribution of task lifecycles rather than a verdict derived from one moment.

Consider two people with the same average accuracy. One enters promptly, remains stable, and makes small corrections. The other spends a long time outside the task, enters abruptly when urgency rises, performs intensely, then leaves after an interruption and cannot recover. The average can conceal the difference that determines daily functioning. This is why initiation latency, dwell time, perturbation sensitivity, recovery time, and release after completion must be kept separate.

This distinction also protects against a moral error. Context sensitivity does not make a difficulty voluntary. Every biological control system is context sensitive; the scientific task is to identify which contextual variables change reachability and stability, for whom, and at what cost. Responsibility remains meaningful, but it shifts from accusation toward designing conditions, skills, and treatments that make intended action more reliably available.

Reliability is a phenotype, not a footnote

A capacity model usually asks whether an operation can be performed under a standardized condition. A regulation model asks a harder family of questions: how often the operation becomes available when it is needed, how long access survives, how much external support is required, and what follows after interruption. These are not cosmetic additions to a test score. They distinguish a system that is consistently adequate from one that reaches the same peak only intermittently or at disproportionate cost.

Imagine repeated samples from the same person across a week. On each occasion the nominal task is identical, but sleep pressure, reward proximity, emotional load, competing intentions, and recent errors differ. Accuracy on completed trials may remain high while entry latency and abandonment vary widely. If analysis conditions on trials that were successfully initiated, it can select away the very instability that matters clinically. A study of attention must therefore record failures to enter, delays before the first valid action, interruptions, re-entry attempts, and the work left unfinished—not only responses made after the task has already captured the person.

Reliability also has a cost dimension. Two people may achieve the same outcome, while one uses routine effort and the other recruits deadline-driven arousal, repeated self-correction, environmental isolation, or prolonged recovery afterward. Equal performance does not imply equal control demand. This matters when interpreting apparently “normal” laboratory performance, because a short, novel, supervised experiment may supply cues, urgency, social accountability, and immediate feedback that daily life does not.

The useful comparison is therefore not competent versus incompetent. It is a family of conditional distributions: performance given entry, probability of entry given context, dwell given perturbation, and recovery given departure. ADHD can affect one distribution more than another. A person may show intact selection once engaged but unreliable initiation; another may enter promptly yet be unusually vulnerable to internal capture; a third may sustain attention but fail to release it when priorities change.

This reframing preserves agency without moralizing. Agency is not an all-or-none force standing outside biology. It is expressed through policies, environments, learned cues, and available control resources. The practical objective is to make intended action more reachable and less expensive across ordinary conditions. That objective is compatible with medication, psychotherapy, behavioral scaffolding, sleep intervention, and environmental redesign because these approaches can act on different terms in the same task lifecycle.

Four identical averages, four different control problems

Suppose four people complete the same proportion of work. The first enters quickly and works steadily. The second delays, then completes everything under deadline pressure. The third begins promptly but departs after every interruption and repeatedly reconstructs the task. The fourth remains absorbed after the task is no longer the highest priority. A weekly completion average makes them look equivalent, although the relevant intervention differs in each case.

The comparison shows why performance must be indexed by phase. Entry requires a first-passage measure; stability requires dwell and perturbation measures; recovery requires detection and re-entry measures; release requires a criterion for justified disengagement. Effort and after-cost should accompany each phase. A model that captures only completed output can reward crisis dependence, conceal exhaustion, and misclassify inflexible persistence as successful attention.

The clinical question is therefore not merely whether a person can focus. It is whether intended cognition can be allocated, stabilized, recovered, and released with sufficient reliability across the conditions that life actually supplies.

Read the apparent contradiction as four separate clocks

The practical question is not whether attention exists. It is how long entry takes, how long a useful configuration survives, how quickly it can be recovered after displacement, and whether it can be released when priorities change. Two people can show the same missed deadline while differing on every one of those clocks. The lecture therefore follows transitions and conditional reliability rather than treating a single successful episode as proof that regulation is intact.

PART II

WHAT ADHD IS — AND WHAT IT IS NOT

Establish the actual clinical phenotype and prevent the network model from swallowing every concentration problem.

Faraone · Posner · Nigg · Cortese · Barkley

Part thesis

ADHD is a clinically defined, developmentally anchored pattern of impairing inattention and/or hyperactivity–impulsivity. It is not a result on a scan, a low score on one executive task, an amount of dopamine, or a synonym for any concentration problem. The phenotype is real and consequential, but heterogeneous: people reach similar diagnostic descriptions through partially different cognitive and biological pathways.

8 Diagnostic phenotype and functional impairment

A diagnosis begins with behavior over development and across situations. Symptoms must be developmentally inappropriate, sufficiently persistent, present in more than one relevant context, and associated with clinically meaningful impairment. History matters because the same current complaint—"I cannot concentrate"—can arise from sleep deprivation, anxiety, depression, trauma-related intrusions, substance effects, pain, medication, or a recent environmental change. Collateral information and old records can be especially valuable when adult recall is incomplete.

Symptoms and impairment are related but not identical. A highly structured family, small classroom, supportive employer, or occupation matched to rapid novelty can conceal impairment; a transition to university, parenthood, independent work, or complex administration can expose it. Conversely, severe impairment in one domain can arise from another disorder even when several ADHD-like symptoms are present. Diagnosis therefore requires a developmental formulation, not simple symptom counting in isolation (Faraone et al. 2015, DOI 10.1038/nrdp.2015.20, PMID 27189265; Posner, Polanczyk & Sonuga-Barke 2020, DOI 10.1016/S0140-6736(19)33004-1, PMID 31982036; Faraone et al. 2021, DOI 10.1016/j.neubiorev.2021.01.022, PMID 33549739).

Operational diagnostic box: DSM-5-TR and ICD-11 are similar, not identical

Dimension	DSM-5-TR	ICD-11 CDDR
Core pattern	persistent inattention and/or hyperactivity–impulsivity that interferes with functioning or development	persistent inattention and/or hyperactivity–impulsivity outside expected variation for age and intellectual development, with direct functional cost
Duration and threshold	at least six months; at least six of nine symptoms in either domain through age 16, or at least five from age 17 onward	ordinarily at least six months; requires several clinically significant symptoms, but does not impose the DSM numerical count
Developmental onset	several symptoms were present before age 12; later recognition does not imply later onset	evidence of significant symptoms before age 12, although clinical recognition may occur later
Settings and impairment	several symptoms occur in two or more settings, with clear interference or reduced quality of social, academic, or occupational functioning	manifestations are evident across multiple situations or settings and directly impair academic, occupational, or social functioning
Exclusion and differential	not confined to a psychotic disorder and not better explained by another mental disorder	not better explained by another mental, behavioral, or neurodevelopmental disorder and not due to a substance or medication
Presentations	predominantly inattentive, predominantly hyperactive–impulsive, or combined; presentation and severity are current descriptors	predominantly inattentive, predominantly hyperactive–impulsive, combined, other specified, or unspecified

This table is an operational summary, not a self-diagnosis checklist. Neither framework permits a rating scale, symptom count, retrospective impression, or stimulant response to replace clinical history, collateral information, impairment assessment, and differential diagnosis. DSM-5-TR uses explicit counts; ICD-11 relies more on clinical judgment about several significant symptoms and developmental deviance. Sources: American Psychiatric Association, *DSM-5-TR* (2022, DOI 10.1176/appi.books.9780890425787); World Health Organization, *Clinical Descriptions and Diagnostic Requirements for ICD-11 Mental, Behavioural and Neurodevelopmental Disorders* (2024); Wolraich et al. (2019, PMID 31570648).

No current neuroimaging, cognitive, electrophysiological, genetic, or biochemical test has adequate validity to diagnose ADHD in an individual. Group-level research can reveal mechanisms and stratification candidates without replacing clinical assessment. This boundary will recur whenever a compelling brain image appears.

9 Inattention, hyperactivity and impulsivity

Inattention includes more than looking away. It can appear as omissions, losing the task rule, difficulty sustaining effort, incomplete follow-through, disorganization, losing materials, failure to register speech, or rapid capture by competing stimuli and thoughts. Hyperactivity can be gross motor activity in a child, but in adolescents and adults it may become inner restlessness, constant small movement, excessive talking, or discomfort with low-stimulation states. Impulsivity includes acting before sufficient sampling, interrupting, difficulty waiting, steep preference for immediate outcomes, or rapid decisions under emotion.

These domains interact but should not be fused. A person may be primarily inattentive, prominently hyperactive–impulsive, or show both clusters; expression changes across development and context. The current presentation is a snapshot of a

trajectory, not a permanent subtype carved into the nervous system. Ratings also depend on observer and setting: a teacher sees group-task demands, a parent sees mornings and evenings, an adult sees private administrative failure that colleagues may never notice.

The most useful language describes patterns and costs. “Inattention” should not imply lack of perception; “hyperactivity” should not imply constant movement; “impulsivity” should not imply absence of thought. Each name compresses multiple processes that later sections will disassemble.

10 Executive dysfunction overlaps with ADHD but is not synonymous

Executive functions are a family of operations used to maintain goals, inhibit prepotent responses, update working memory, shift sets, monitor error, sequence actions, and allocate effort. Many people with ADHD show difficulties in one or more of these domains. Barkley’s inhibition-centered theory was historically influential because it connected observable symptoms to self-directed action over time (Barkley 1997, PMID 9000892). Nigg’s critical review and subsequent work showed why no single executive deficit can define the disorder (Nigg 2005, PMID 15950017).

Group effects on laboratory tasks are generally moderate and heterogeneous, with substantial overlap between ADHD and comparison distributions. Some diagnosed individuals perform within ordinary limits on formal executive testing yet struggle dramatically in open-ended life. Laboratory tasks supply clear instructions, novelty, immediate experimenter presence, short duration, and frequent feedback—the very scaffolding missing from many daily tasks. Conversely, poor executive-test performance can occur in sleep deprivation, depression, traumatic stress, brain injury, learning disorders, and many other conditions.

Thus the relation is neither “executive tests are irrelevant” nor “ADHD is an executive-function test deficit.” Executive constructs help decompose mechanisms and design supports. Diagnosis remains clinical, and functional performance in natural contexts must not be inferred from a single controlled task.

Contradiction box — the neuropsychological normal performer. Normal scores do not refute ADHD; abnormal scores do not establish it. The distributions overlap, tasks vary in reliability, and real-world demands differ from test conditions.

11 Working memory, inhibition, organization and persistence

Working memory keeps goal-relevant information available while the world changes: the instruction just given, the next step, the reason one entered a room, the relation between a present action and a later outcome. Inhibition prevents a dominant or newly salient response from displacing that representation. Organization externalizes structure across objects, time, and steps. Persistence keeps behavior coupled to the longer-horizon goal when reward and feedback are sparse.

These operations are mutually supportive but dissociable. A person may remember the goal yet fail to suppress a competing response; inhibit successfully but lose the goal after interruption; plan accurately but not begin; begin but fail to persist; persist yet continue beyond the adaptive stopping point. Modern EEG work likewise separates early attentional selection from later response control rather than treating inhibition as one instant (Gholamipourbarogh et al. 2026, DOI 10.1016/j.bpsc.2025.05.001, PMID 40350038). The study is promising, not a biomarker: its sample and tensor-decomposition choices limit generalization.

This decomposition matters clinically. An intervention that makes steps visible targets working-memory load and organization. Response-cost or contingency procedures target the consequences surrounding behavior. Medication can change the probability that representations remain functionally influential, but it does not automatically create a filing system, calendar habit, or task sequence. Similar symptom improvement can therefore arise through different layers.

12 Emotional dysregulation: important yet transdiagnostic

Rapid frustration, emotional impulsivity, rejection sensitivity, prolonged recovery, and difficulty modulating high-arousal states are common and impairing in ADHD. Meta-analytic and review evidence supports elevated emotional dysregulation in both children and adults, and it predicts relationship and functional burden beyond a narrow count of core symptoms (Graziano & Garcia 2016, DOI 10.1016/j.cpr.2016.04.011, PMID 27180913; Faraone et al. 2019, DOI 10.1111/jcpp.12899, PMID 29624671; Beheshti, Chavanon & Christiansen 2020, DOI 10.1186/s12888-020-2442-7, PMID 32164655).

But emotional dysregulation is not specific to ADHD. It is central to mood, anxiety, trauma-related, personality, autism-spectrum, and substance-related presentations, among others. Some diagnostic systems place it outside the formal core criteria; proposals to treat it as a core dimension remain debated. A person’s anger or overwhelm should not be retrospectively assigned to ADHD without examining triggers, duration, episodicity, trauma, sleep, relationships, and comorbid disorders.

Within the lecture's dynamical frame, emotion is a source of state-dependent gain and salience. That is a useful inference, not evidence that one salience-network abnormality explains emotional dysregulation. Emotion changes what captures attention, which goals remain available, and how expensive re-entry feels. Treatment outcome should therefore track emotional regulation separately from core symptom ratings.

13 Presentations, severity, comorbidity and heterogeneity

The diagnosis is a family-resemblance category. Two people can meet criteria with partially different symptom combinations, cognitive profiles, comorbidities, sleep patterns, developmental histories, and treatment responses. Symptom thresholds create a categorical decision for care and communication, while the underlying liability is distributed dimensionally. Presentation labels can change when overt activity declines, demands rise, or observers change.

Comorbidity is not statistical clutter. Anxiety may increase internal threat capture; depression may reduce vigor and expected reward; autism may alter sensory load and shifting; learning disorders may make particular tasks predictably aversive; substance use may both emerge from risk and alter current attention. These pathways can produce the same outward omission for different reasons. A network model that absorbs every pathway into "ADHD dysconnectivity" becomes unfalsifiable.

Heterogeneity does not mean the diagnosis is arbitrary. It means average effects need a layered interpretation. A small group mean can be reliable while offering little individual classification; a large symptom response in a trial can coexist with varied functional outcomes; a mechanistic subgroup can be important without defining all ADHD. The 2023 annual research review by Sonuga-Barke and colleagues explicitly frames progress as moving from characterization toward causal pathways while retaining plurality (Sonuga-Barke et al. 2023, DOI 10.1111/jcpp.13696, PMID 36220605).

14 Dimensional liability versus categorical diagnosis

Population studies and molecular genetics support continuity between ADHD traits and clinical diagnosis. The first genome-wide significant case–control study found strong concordance between diagnosed ADHD and quantitative population symptom measures; later GWAS expanded the locus count and reinforced highly polygenic architecture (Demontis et al. 2019, DOI 10.1038/s41588-018-0269-7, PMID 30478444; Demontis et al. 2023, DOI 10.1038/s41588-022-01285-8, PMID 36702997). This is compatible with a liability continuum.

Clinical categories nevertheless remain useful because impairment, developmental context, risk, and access to treatment are not determined by a trait score alone. A threshold does not imply that people just below it have no difficulties, or that everyone above it is biologically identical. It is a decision boundary imposed on continuous and partly heterogeneous dimensions.

The apparent conflict between dimensional science and categorical practice dissolves when their jobs are separated. Dimensional models describe variation and shared liability. Categorical diagnosis organizes decisions under constraints. Neither licenses biological essentialism: a diagnosis is not a single brain type, and a continuous trait is not proof that disorder is merely ordinary behavior renamed.

15 Normal attentional variability versus disorder

Every mind wanders. Boredom reduces persistence; interruption creates re-entry costs; fatigue worsens vigilance; high-value stimuli capture attention. ADHD is not diagnosed because these experiences occur, but because a developmentally anchored pattern is unusually frequent, difficult to regulate, cross-situational, and impairing.

The boundary cannot be drawn by moral intuition. Modern environments expose nearly everyone to engineered novelty, rapid reward, and frequent switching. A person without ADHD can develop fragmented habits and feel subjectively less able to sustain reading. A person with ADHD can also be affected by the same environment, sometimes more strongly. The correct comparison is not "biological disorder versus environment" but trait liability interacting with an attentional ecology.

Clinical reasoning asks what changed, when, and where. A new concentration problem after weeks of restricted sleep has a different temporal signature from lifelong disorganization visible across school reports. A complaint confined to one intolerable job differs from broad impairment across school, home, relationships, driving, and administration. Ordinary variability and disorder meet on a continuum; persistence, developmental history, and consequences determine whether clinical evaluation is warranted.

16 Sleep loss, stress, anxiety, depression and PTSD

Sleep restriction can produce slowed and variable reaction time, omissions, irritability, impulsive choice, and impaired working memory. Circadian delay and sleep disorders are common in ADHD and can be both comorbid and symptom-amplifying. Reviews and meta-analyses in adults support subjective and objective sleep differences, while pediatric guidance stresses assessment of routines, apnea, restless legs, medication timing, and co-occurring conditions (Díaz-Román, Mitchell & Cortese 2018, DOI 10.1016/j.neubiorev.2018.02.014, PMID 29477617; Becker 2020, DOI 10.1016/j.copsyc.2019.09.006, PMID 31629217; Cortese 2024, DOI 10.1080/14737175.2024.2353692, PMID 38738544).

Stress can narrow attention around urgent threats while degrading flexible working memory; anxiety can fill internal attention with worry and avoidance; depression can reduce expected reward and action vigor; PTSD can create trigger-linked intrusion, hyperarousal, dissociation, and sleep disruption. All can look like inattention from the outside. Temporal course and content matter: threat-captured cognition differs phenomenologically from neutral spontaneous thought, although both can interrupt a task.

The differential is not an exclusion contest. ADHD can coexist with every condition listed, and its presence may increase exposure to failure, conflict, and later adversity. The task is to identify multiple active processes rather than force one diagnosis to explain the whole person. Treating sleep or trauma does not invalidate ADHD; treating ADHD does not make trauma or mood irrelevant.

17 Bipolar disorder, substance effects, autism and medical mimics

Bipolar disorder and ADHD can both involve talkativeness, distractibility, activity, and impulsive action. The central discriminator is course: ADHD provides a developmental baseline, whereas mania or hypomania involves a distinct episode with changes such as decreased need for sleep, expansive or irritable activation, and other mood-syndrome features. They can coexist, and the distinction matters for pharmacological safety.

Intoxication, withdrawal, chronic substance use, and nonmedical stimulant use can alter sleep, motivation, reaction time, and impulse control. ADHD itself is associated with substance-use risk, which makes careful chronology essential. Therapeutically prescribed stimulant exposure under monitoring is not pharmacologically or behaviorally equivalent to escalating, nonmedical administration.

Autism and ADHD frequently co-occur. Executive difficulties, sensory capture, intense interests, and switching problems can overlap, while autism additionally requires its characteristic social-communication and restricted/repetitive developmental phenotype (Antshel & Russo 2019, DOI 10.1007/s11920-019-1020-5, PMID 30903299). Medical contributors—pain, anemia, thyroid disorder, seizure phenomena, sleep-disordered breathing, medication adverse effects—are investigated according to history rather than through indiscriminate testing. The rule is simple: concentration is a nonspecific endpoint.

18 Technology-associated fragmentation is not automatically ADHD

Notifications, infinite scroll, variable-ratio rewards, and rapid task switching can train habits around short feedback loops. Experimental and observational work outside ADHD shows immediate costs of interruption and attentional capture. This gives a serious environmental story without supporting the stronger claim that smartphones simply create a de novo neurodevelopmental disorder in adults.

Three distinctions are necessary. First, an exposure can worsen symptoms in people with ADHD. Second, an exposure can produce an ADHD-like complaint in people without the developmental syndrome. Third, technology use can be an outcome as well as a cause: a person seeking rapid stimulation or escape may preferentially engage with high-novelty platforms. Cross-sectional associations cannot determine direction.

The lecture should neither moralize technology nor exempt design from scrutiny. It should ask what the environment repeatedly rewards, how often it interrupts, whether cues are controllable, and how quickly a task state can be restored. “Digital hygiene” can improve attentional conditions while diagnostic claims remain anchored to developmental evidence.

19 The outcome hierarchy: symptom change is not complete recovery

Core symptom ratings occupy only one layer of outcome. Above and around them sit executive self-management, school achievement, occupational reliability, relationships, emotional regulation, driving, injury, substance-related risk, self-esteem, sleep, and quality of life. These layers correlate imperfectly. A treatment can reduce observer-rated symptoms without teaching organization; a skills intervention can improve homework completion or work systems while core symptoms remain; a supportive environment can reduce impairment without changing underlying liability.

"Response" in a trial usually means a threshold change on a selected scale over a selected interval. "Remission" may mean falling below a symptom threshold at one assessment. Neither equals sustained recovery across life domains. Longer follow-up also introduces treatment changes and selection, so randomized short-term efficacy cannot be projected uncritically across years.

This hierarchy will govern the later treatment sections. Every intervention must be asked: what endpoint changed, according to whom, for how long, at what cost, and did the result generalize beyond the treatment setting? The answer can be clinically valuable without being total.

From symptoms to a defensible clinical inference

A diagnosis is not obtained by matching a person to a vivid description. It is an inference built from developmental history, persistence, cross-situational evidence, impairment, and exclusion or characterization of alternatives. The same complaint—"I cannot concentrate"—can arise from insufficient sleep, threat monitoring, depressive slowing, elevated mood, intoxication or withdrawal, pain, medication effects, sensory overload, grief, or an environment engineered for interruption. These possibilities can coexist with ADHD rather than merely compete with it.

The distinction between symptom and mechanism matters. Forgetting an appointment is an observed outcome. It may reflect prospective-memory failure, failure to encode the intention, weak cueing, time-estimation error, avoidance, sleep loss, or an interruption during execution. A diagnostic label can organize a recurrent pattern without identifying which mechanism produced every event. Treatment planning therefore requires a second layer of formulation after diagnosis.

Dimensional and categorical views answer different questions. Symptoms and impairment vary continuously across the population, while clinical categories create decision thresholds for communication and access to care. The threshold does not imply a natural cliff in biology, and dimensionality does not make diagnosis arbitrary. The defensible position is that ADHD is a clinically useful neurodevelopmental construct whose boundaries require judgment, corroboration, and attention to context.

From a familiar description to a defensible formulation

Clinical recognition begins with phenomenology but cannot end there. "I lose focus," "I procrastinate," or "my mind never stops" are meaningful descriptions, yet each can arise from several processes. The diagnostic task is to reconstruct a developmental and functional pattern: when the difficulties began, whether they occur across settings, which demands expose them, what the person can do under structure, how impairment accumulated, and which alternative or co-occurring conditions change the explanation.

Time course is one of the strongest discriminators. Sleep deprivation can produce severe attentional instability, but its onset and fluctuation may track sleep opportunity, circadian phase, or breathing-related disturbance. Depression can reduce initiation through anhedonia, fatigue, hopeless prediction, or psychomotor slowing. Anxiety and PTSD can divert resources toward threat monitoring and intrusive material. Bipolar elevation can involve distractibility, accelerated association, reduced sleep need, and increased goal pursuit, but the episodic pattern and accompanying mood change matter. Substance effects depend on intoxication, withdrawal, dose, timing, and chronic adaptation. None of these rules out ADHD; they prevent a single complaint from deciding the diagnosis.

Cross-situational evidence also requires interpretation. A highly structured school, an attentive partner, or a job rich in novelty can conceal impairment. Conversely, one hostile or chaotic environment can produce concentration problems without a pervasive neurodevelopmental syndrome. Reports from parents, teachers, partners, and the person may disagree because they observe different demands, carry different expectations, or see different costs. Disagreement is data about context, not merely measurement failure.

Developmental history should be sought with humility. Adults may not have records, may recall childhood through present concerns, or may have been protected by high ability and family structure. Girls and women may have attracted less attention when hyperactivity was subtle, internalized, or socially contained. Late recognition is therefore not the same as proven late onset. At the same time, a retrospective story should not be treated as automatically confirmatory. The formulation should state what is well corroborated, what is probable, and what remains uncertain.

Impairment must be decomposed rather than reduced to symptom count. Missing deadlines, unsafe driving, inconsistent

medication use, relationship conflict, financial disorganization, academic underachievement, and depleted self-trust occupy different outcome layers. A symptom scale can improve while the systems needed for work, parenting, or study remain fragile. Conversely, external supports may improve functioning even when core symptoms remain measurable.

Comorbidity is often the rule rather than the exception. Autism, learning disorders, anxiety, depression, trauma-related symptoms, sleep disorders, substance problems, and tic disorders can alter both presentation and treatment. The goal is not to decide which single label "really" owns every difficulty. It is to identify interacting processes, urgent risks, modifiable contributors, and the sequence in which intervention is most likely to help.

A defensible diagnosis is consequently a calibrated inference, not a personality verdict or a biomarker reading. Network neuroscience can illuminate candidate mechanisms at a group level, but it cannot currently diagnose an individual from a scan. The clinical construct remains useful because it organizes a recurrent developmental pattern and guides evidence-based care—provided that it is coupled to a person-specific formulation rather than used as a total explanation.

A differential formulation worked through in time

Consider an adult who reports chronic procrastination, mental noise, poor sleep, and periods of intense productivity. Several narratives initially fit. ADHD may explain a childhood pattern of lost materials, delayed work, inconsistent follow-through, and impairment across school and home. Anxiety may explain prolonged checking and attentional capture by anticipated error. Depression may explain a recent fall in initiation and reward value. Circadian delay may explain severe morning difficulty. Episodic reduced sleep need, elevated mood, and accelerated goal pursuit would raise a different question from staying awake late because disengagement is difficult.

The formulation proceeds by locating each process in time. Which features were present before the current mood episode? Which track nights of insufficient sleep? Which occur during enjoyable as well as aversive tasks? Does worry precede the attentional shift, or appear after another failure? Are the productive periods organized and sustainable, or compressed into high-arousal rescue attempts? What changes when structure, immediate feedback, or another person is present?

Collateral information can alter the picture without replacing the person's account. A parent may remember quiet daydreaming rather than disruption. School reports may show strong examination performance alongside chronic missing work. A partner may observe that household tasks disappear from awareness unless made visible. Each source samples a different context and should be weighted for access, bias, and developmental distance.

The next step is not to force every observation under one label. A person can have ADHD and a sleep disorder; anxiety can develop around years of inconsistency; depression can narrow reward and initiation on top of an earlier executive pattern. The formulation should state which process appears trait-like, which is episodic, which is maintained by the current environment, and which is most urgent to address.

This temporal map changes treatment interpretation. If sleep restoration markedly reduces morning variability but lifelong organizational impairment persists, both findings matter. If stimulant treatment improves response consistency but not avoidance created by repeated shame, medication has changed one layer rather than failed globally. If CBT improves completion through external structure while symptoms remain, functional compensation is a genuine outcome.

The final diagnosis is strongest when it predicts what should vary. It should anticipate which settings expose impairment, which supports reduce it, which symptoms survive mood improvement, and which outcomes require an additional intervention. That is a more demanding standard than recognition, but it is also more humane: the person receives an account of interacting processes rather than a totalizing identity.

One complaint, several causal routes

"I cannot concentrate" may arise because a goal representation is unstable, because threat monitoring is consuming capacity, because reward has lost value, because sleep pressure is high, or because a substance state has altered arousal. The observable sentence is not the mechanism. Diagnosis requires developmental timing, cross-setting impairment, persistence, collateral information, and an account of plausible alternatives; network language enters only after that clinical work.

PART III

A DEVELOPMENTAL CONDITION WITH A FLUCTUATING COURSE

Replace a static disorder model with trajectories, compensation and changing environmental demands.

Shaw · MTA · Sibley · ENIGMA · Franke · Buitelaar

Part thesis

ADHD is developmental, but development is not a one-way march from abnormal childhood toward normal adulthood. Brain organization, demands, supports, sleep, hormones, motivation, learning, and self-knowledge all change. Symptoms may persist, diminish, recur, or become hidden by compensation. A cross-sectional child–adult difference is not a developmental trajectory, and symptom remission is not proof that a neural system has "normalized."

20 ADHD begins in development, not in a scan

To call ADHD neurodevelopmental is to make a claim about its time course and causal architecture: the pattern emerges as attention, activity, impulse control, learning, and social demands develop. It is not a claim that a radiologist can see ADHD in one image. Development is reconstructed from history, observation, records, and longitudinal data. Neuroimaging and genetics can illuminate average pathways, but their distributions overlap too extensively for individual diagnosis.

Development also changes the meaning of behavior. Leaving a seat carries different information at age six than at age thirty-six. A young child's regulation is scaffolded by adults; an adult is expected to construct schedules, maintain distant goals, sequence administrative work, and recover privately from interruption. The same underlying liability can therefore generate different visible symptoms as the environment withdraws external structure.

The World Federation consensus and major reviews support ADHD as a valid, impairing developmental disorder while emphasizing heterogeneity and the absence of a single diagnostic biomarker (Faraone et al. 2021, PMID 33549739; Posner et al. 2020, PMID 31982036). The phrase "begins in development" should never be converted into "has one fixed lesion present from birth."

21 Childhood, adolescence and adult ADHD must not be merged

Childhood combines rapid neural maturation with intensive external control. Adolescence adds reward sensitivity, peer salience, delayed sleep timing, increasing autonomy, and more complex planning. Adulthood removes many institutional supports while adding financial, occupational, relationship, caregiving, and health-management demands. Each stage changes the baseline against which ADHD is measured.

This is a methodological warning. A reduction in group difference with age could reflect maturation, selective persistence, cohort composition, medication history, scanner tolerance, or the changing validity of the task. Adult samples often contain people with long treatment histories and compensatory strategies; pediatric samples may overrepresent externally disruptive behavior. Pooling both can manufacture a tidy lifespan effect that no individual follows.

Age stratification must therefore be substantive, not cosmetic. The relevant questions include which symptoms changed, whether impairment changed, which supports were available, and whether the same person was followed. Longitudinal within-person evidence is more informative about trajectory than a comparison between unrelated children and adults, although it brings attrition and repeated-measurement problems of its own.

22 Cortical maturation and the limits of the "delay" model

Shaw and colleagues' landmark longitudinal MRI study analyzed 824 scans from 223 children with ADHD and 223 comparison participants. The reported cortical-thickness sequence was regionally similar, but peak thickness occurred later on average in ADHD, particularly in prefrontal cortex (Shaw et al. 2007, DOI 10.1073/pnas.0707741104, PMID 18024590). The study was important because it represented trajectory rather than a static smaller/larger comparison.

The finding is often expanded beyond what it can bear. It does not show that every child with ADHD is globally "three years immature," that development simply stops, or that an adult with ADHD has a child's brain. Cortical thickness is one macrostructural measure influenced by multiple cellular processes; peak timing is estimated at group level; and later large-sample morphometry generally finds small, distributed, age-sensitive differences rather than a diagnostic signature.

The enduring lesson is not a literal delay clock. It is that developmental timing can matter and that the same cross-sectional measurement can have different meanings at different ages. A region's thickness, connectivity, or activation cannot be interpreted without an age-appropriate trajectory and a measurement model.

Contradiction box — "maturational delay." Supported: some group-level cortical trajectories differ in timing. Not supported: a universal developmental age gap, a complete explanatory mechanism, or an individual maturity score.

23 Striatal, cerebellar, white-matter and network development

Development is distributed. Corticostriatal loops change with learning and reward; the cerebellum contributes to timing and prediction; white matter changes the speed and reliability of long-range signaling; cortical networks become more differentiated while retaining context-sensitive integration. ADHD research reports differences across all of these systems, but directions and anatomical locations are not fully consistent.

The ENIGMA subcortical mega-analysis aggregated thousands of participants and reported small case–control volume differences, strongest in children, across structures including accumbens, caudate, putamen, amygdala, and hippocampus (Hoogman et al. 2017, DOI 10.1016/S2215-0366(17)30049-4, PMID 28219628). Its scale improved precision, but cross-sectional multisite data cannot demonstrate each structure's developmental trajectory, and small average differences are not individual biomarkers. Scanner, ascertainment, comorbidity, and medication histories remain relevant.

Diffusion and graph studies suggest distributed white-matter and connectomic differences, yet specific tracts and directions vary. Motion is particularly dangerous because children with more hyperactivity can move more, producing apparent connectivity or diffusion differences. Recent small graph-development studies are hypothesis-generating, not grounds for a singular "underconnected brain" model (Soman et al. 2023, DOI 10.1002/hbm.26288, PMID 36988503).

24 Development of DMN segregation and control systems

Across typical development, large-scale functional organization becomes more differentiated: local and distributed relationships change, control systems refine, and the default-mode network's internal structure and coupling to attention systems mature. "Segregation" does not mean permanent isolation. Effective cognition requires both distinction and selective communication.

ADHD-specific studies report altered within- and between-network relationships in some age groups, but group effects are modest and method-sensitive. Development introduces an additional reference problem: a connection that is weak relative to one childhood stage may be ordinary later, and a child–adult difference may reflect the typical developmental baseline rather than ADHD persistence. Network labels derived from adults may also fit children imperfectly.

The responsible claim is that maturation changes the landscape through which task states are assembled. The stronger claim—that one delayed DMN–control anticorrelation causes ADHD—is not established. The lecture will later treat network segregation as one coordinate among many, alongside state occupancy, transition dynamics, reward, arousal, and task design.

25 Stable persistence, partial remission, recurrence and fluctuation

Traditional summaries often state that a fixed proportion of children "outgrow" ADHD. Longitudinal evidence gives a less tidy picture. In the Multimodal Treatment Study of ADHD follow-up, Sibley and colleagues reported that sustained full recovery by the endpoint was uncommon, while many participants moved between periods above and below diagnostic thresholds (Sibley et al. 2022, DOI 10.1176/appi.ajp.2021.21010032, PMID 34384227). A 2024 analysis further examined fluctuating patterns and their relation to changing demands (Sibley et al. 2024, DOI 10.4088/JCP.24m15395, PMID 39431909).

This does not mean that everyone remains equally impaired. Mean symptoms often decline, overt hyperactivity may soften, and individuals can develop strategies, choose better-fitting environments, or benefit from treatment. It means a single below-threshold assessment cannot be assumed to represent permanent disappearance.

Course is best represented as a time series with multiple outcomes: symptom intensity, functional burden, supports, comorbidities, and environmental demand. "Persistence" can coexist with good adaptation; "remission" can coexist with high compensatory effort; recurrence can follow loss of structure or sleep. Developmental science should model these transitions rather than forcing each person into one terminal category.

26 Symptom remission versus compensatory reorganization

Three processes can look similar from the outside. First, underlying liability may diminish. Second, a person may learn compensatory strategies: external calendars, environmental selection, rehearsed routines, delegation, or deliberate over-preparation. Third, the environment may become a better fit, reducing demands on the vulnerable operation. Each can lower observed symptoms and impairment.

Imaging cannot currently distinguish these possibilities cleanly. If an adult with remitted symptoms shows a group-average pattern closer to controls, that could reflect developmental convergence. If the pattern remains different while performance improves, it could reflect compensation. If both brain and behavior differ only under certain task conditions, state and strategy may dominate. Cross-sectional "persistent versus remitted" designs are vulnerable to selection and cannot reconstruct the path that produced the endpoint.

The term normalization should therefore be reserved for a specified metric moving toward a specified comparison distribution. It should not imply restoration of an original healthy brain or complete recovery. A compensatory system is not inferior merely because it is different; clinical value lies in stable function and tolerable effort.

27 Late recognition versus proposed adult onset

Many adults are diagnosed late because earlier environments supplied structure, academic ability masked disorganization, disruptive behavior was absent, or observers missed an inattentive presentation. Late recognition is entirely compatible with developmental onset. Retrospective history can be imperfect, so school records and collateral accounts may reveal patterns the adult did not encode as symptoms.

A distinct question is whether ADHD-like syndromes can first emerge in adulthood. Several longitudinal cohorts reported adult cases without clear childhood ADHD, including influential studies by Moffitt and colleagues and Caye and colleagues (Moffitt et al. 2015, DOI 10.1176/appi.ajp.2015.14101266, PMID 25998281; Caye et al. 2016, DOI 10.1001/jamapsychiatry.2016.0383, PMID 27192050). Subsequent debate identified challenges: childhood symptoms may be missed by thresholds or informants; adult cases may reflect substance use, mood, sleep, trauma, cognitive change, or measurement differences; and some late-emerging symptom groups may not resemble classic childhood ADHD.

The scientific position is open but constrained. Late-recognized developmental ADHD is established. Adult-onset-like presentations occur in datasets, but their nosological unity and causal relation to childhood-onset ADHD remain unsettled. Clinically, new adult symptoms demand an especially careful differential rather than automatic denial or automatic relabeling.

28 Girls, women, masking, referral bias and sex differences

Boys are diagnosed more often in childhood, particularly in clinical samples. The ratio narrows in population samples and adulthood, consistent with referral mechanisms in addition to any average biological or behavioral differences. Girls with less disruptive behavior may be noticed later, while anxiety, depression, eating pathology, or compensatory effort attracts attention first. Expert consensus highlights underrecognition and the need for lifespan-sensitive assessment (Young et al. 2020, DOI 10.1186/s12888-020-02707-9, PMID 32787804).

"Masking" should not become an unmeasurable explanation for every discrepancy. It can refer to genuine strategies and social pressures, but it requires specific history: excessive preparation, hidden exhaustion, reliance on others, avoidance of high-demand settings, or symptoms visible only after support collapses. Register and twin work finds that males may be more likely to receive diagnosis or medication at comparable levels of measured traits, supporting a referral-bias component (Mowlem et al. 2019, DOI 10.1007/s00787-018-1211-3, PMID 30097723).

Neuroscience evidence on sex-specific ADHD mechanisms remains much thinner than clinical epidemiology. Many imaging studies are underpowered for interactions and historically male-skewed. Absence of a significant sex interaction is not proof of identity, but speculative female-brain narratives are not a substitute for adequately sampled longitudinal research.

29 Hormonal, sleep, environmental and demand transitions

Puberty, menstrual cycling, pregnancy, postpartum change, perimenopause, school transitions, shift work, parenthood, and changing sleep opportunity can alter arousal, emotion, and executive demand. Clinical reports suggest symptom changes around hormonal transitions, but direct mechanistic ADHD evidence is uneven. The safe point is that biological and social transitions can change expression and treatment conditions; the unsafe point is a universal hormone-to-symptom formula.

Sleep is a particularly strong state modifier. Adolescent circadian delay collides with early schedules; stimulant timing can affect sleep; sleep problems can intensify attention and emotional symptoms; and ADHD-related disorganization can itself destabilize routines. These reciprocal arrows should be retained rather than choosing one cause.

Environmental demand is equally important. A child may appear regulated in a highly scaffolded primary classroom and struggle when secondary school requires multiple teachers, long-term planning, and self-managed materials. An adult may function in urgent team-based work and collapse under solitary paperwork. Changing phenotype can therefore reflect a changing ratio between demands and scaffolds, not a changing moral commitment.

30 Development changes both phenotype and treatment response

Treatment evidence must be age-stratified because efficacy, adverse effects, learning context, family involvement, and functional goals differ. Parent training can directly reshape the environment of a young child; organizational training becomes more self-directed with age; medication choice and monitoring differ across stages; school accommodations have no exact adult equivalent. The same symptom-scale effect can yield different developmental consequences depending on whether it enables classroom learning, driving safety, or occupational stability.

Neural response may also vary with baseline maturation, but evidence is not sufficient to infer an individual child's future from a scan. A 2026 multisite structural-connectivity study reported developmental deviations related to symptoms and differential prediction of atomoxetine outcomes, with no parallel methylphenidate prediction; this is an important emerging result that requires independent prospective replication before clinical use (Xu et al. 2026, DOI 10.1038/s41551-026-01779-4).

Development therefore changes the system, the task, and the meaning of success. A lifespan account must preserve all three.

Development changes both the person and the task

Developmental interpretation requires two moving reference frames. The nervous system changes, but so do the tasks used to evaluate it. A child may be supported by external schedules, repeated prompts, short work intervals, and immediate feedback. An adolescent is expected to coordinate several teachers, distant deadlines, peer demands, sleep-phase shifts, and increasing autonomy. An adult may need to construct the very scaffolding that was previously supplied. A rise in impairment can therefore occur without a simple worsening of the underlying trait.

The reverse is also possible. Reduced overt hyperactivity or improved inhibition does not necessarily mean that every vulnerability has normalized. People may acquire strategies, select environments that fit them better, rely on external systems, or expend more effort to achieve the same visible result. Remission of diagnostic criteria, reduction of impairment, compensation, and neural convergence are different outcomes and should not be used interchangeably.

Longitudinal evidence is consequently more informative when it follows trajectories rather than a single group mean. Persistence, partial remission, recurrence, and context-dependent expression can arise through different combinations of maturation, learning, comorbidity, treatment, opportunity, and environmental demand. A developmental model should predict change within people and acknowledge that childhood and adult samples are not interchangeable snapshots of one static condition.

Development is a moving relation between regulation and demand

The developmental question is not whether an ADHD brain simply "catches up." Regulation, brain organization, social support, and environmental demand all change at once. A child who performs adequately with one classroom, one backpack, short deadlines, and repeated adult prompts may encounter a very different control problem when adolescence introduces several teachers, delayed projects, peer evaluation, circadian delay, and unsupervised digital access. An adult then has to build schedules, reminders, and task boundaries that were previously supplied by others.

This means that impairment can increase while some cognitive capacities improve. Working memory, inhibitory control, planning, and cortical organization may mature, yet demands can rise faster than the supports available to meet them. The opposite is also possible: symptoms can remain while functioning improves because the person acquires routines, selects a suitable occupation, shares responsibilities, or uses treatment. Developmental outcome is therefore a relation among capacity, compensation, context, and cost.

Longitudinal neuroimaging reinforces the need for trajectories. Group differences in cortical thickness, surface area, subcortical measures, white matter, or functional organization are typically small and heterogeneous. They are not a fixed anatomical signature carried unchanged from childhood into adulthood. Apparent convergence may reflect maturation, selective persistence, medication history, motion differences, compensatory reorganization, or who remains in the sample. Cross-sectional age comparisons cannot by themselves determine which process occurred within a person.

Symptom remission must also be separated into components. Overt motor hyperactivity may decline or become an internal sense of restlessness. Impulsivity may become less visible as consequences and strategies accumulate. Inattention can persist as disorganization, prospective-memory failure, inconsistent initiation, or time-management difficulty. Falling below a diagnostic threshold, experiencing less impairment, and showing neural similarity to a comparison group are distinct outcomes; none should be substituted for another.

Sex and gender shape recognition and exposure without defining two separate disorders. Referral pathways can favor disruptive behavior, while internalized distress or compensatory compliance receives less attention. Hormonal transitions, pregnancy, the postpartum period, menopause, caregiving roles, and unequal environmental demands may alter symptom expression or treatment decisions, but the evidence is uneven. Responsible teaching distinguishes replicated sex-linked findings from plausible clinical considerations and from gaps created by underrepresentation.

Development also includes accumulated learning about the self. Repeated inconsistency can generate avoidance, shame, defensive certainty, or dependence on crisis-level urgency. These learned adaptations are not reducible to the original neurodevelopmental liability, yet they can later become major determinants of entry and persistence. Psychotherapy may be especially relevant at this layer: it can change prediction, planning, self-talk, recovery after failure, and the design of the environment even when it does not erase the underlying trait.

The strongest developmental model will therefore predict multiple paths: persistence, partial remission, compensation, recurrence when demands rise, and improvement through better fit. It will measure not only symptoms but effort, supports, opportunity, comorbidity, and real-world function. “What changed?” must be answered at each layer before the word normalization is used.

A longitudinal reading requires at least four axes

Every follow-up should distinguish symptom expression, environmental demand, compensatory support, and control cost. A student may report fewer symptoms after entering a highly structured program while depending on intensive reminders. Another may retain symptoms yet function better after choosing work with rapid feedback. A third may meet fewer criteria only because family members have absorbed the organizational burden. These trajectories are not equivalent.

Neural measures add a fifth axis but do not settle the others. Convergence in one cortical or connectivity measure can coexist with persistent impairment; persistent group difference can coexist with successful compensation. The study therefore needs repeated behavior, context, treatment exposure, effort, and function alongside imaging. Attrition must be modeled because participants with the greatest instability may be least likely to complete long follow-ups.

The developmental claim becomes precise when it states the level and timescale: a symptom changed, a skill was learned, a demand fell, a support increased, or a neural measure shifted. Only then can persistence, remission, compensation, and reorganization be compared without collapsing them into the single word outcome.

Development changes both the controller and the world it must control

A developmental trajectory is an interaction between maturing systems and a changing task ecology. Increasing autonomy removes external prompts at the same time that school, work, relationships, and sleep schedules become harder to coordinate. Apparent remission may therefore reflect neural maturation, learned compensation, environmental fit, reduced demand, or a different mixture of symptoms. Longitudinal interpretation must measure these possibilities rather than naming every decline in symptom count “normalization.”

PART IV

CAUSAL ARCHITECTURE WITHOUT

DESTINY OR BLAME

Establish multiple causal routes into a heterogeneous phenotype and separate etiology from current treatment targets.

Demontis · PGC · Faraone · Franke · Nigg

Part thesis

ADHD has substantial genetic liability and multiple environmental modifiers and risks. Neither fact supports a single-gene destiny model or a universal story of early emotional injury. Genes influence developmental probabilities, environments are partly selected and evoked, and observational associations mix causal directions. Etiology, present mechanism, and treatment target are different questions.

31 Heritability is a population statistic, not personal destiny

Twin and family studies consistently indicate high heritability for ADHD traits, with syntheses often placing it near three quarters of population variance under the sampled conditions (Faraone & Larsson 2019, DOI 10.1038/s41380-018-0070-0, PMID 29892054). Heritability is the proportion of variation statistically associated with genetic differences in a population and environment. It is not the percentage of an individual's ADHD "caused by genes."

High heritability does not mean immutability. Height is highly heritable but responds to nutrition and disease; phenylketonuria is genetic but environmentally treatable. Heritability can change when environments become more or less uniform. It also says nothing by itself about which biological pathway mediates risk.

The correct conclusion is strong familial and genetic contribution at the population level. The incorrect conclusions are that outcome is fixed, that environment is unimportant, or that a polygenic score can diagnose a person. Genetic evidence rejects simple parent-caused accounts while leaving substantial room for developmental context, reciprocal processes, and intervention.

32 Polygenic liability and many small common-variant effects

Genome-wide association studies compare common variants across very large samples. The first genome-wide significant ADHD loci were reported in 2019; a larger 2023 analysis of 38,691 cases and 186,843 controls identified 27 risk loci and implicated multiple cognitive and developmental domains (Demontis et al. 2019, PMID 30478444; Demontis et al. 2023, PMID 36702997). A 2025 meta-analysis combining childhood diagnosis and symptom measures extended this architecture (van der Laan et al. 2025, DOI 10.1038/s41588-025-02295-y, PMID 40962958).

The central result is polygenicity: thousands of common variants each contribute very small changes in probability. No common "ADHD gene" determines the phenotype. Loci do not map one-to-one onto symptoms, networks, or drug response; variant association is the beginning of mechanistic work, not its completion.

GWAS also supports dimensionality because quantitative population traits share genetic signal with diagnosed cases. But the samples have ancestry imbalances, diagnosis and symptom measures differ across cohorts, and statistical associations do not specify cellular causation. Highly significant is not the same as individually predictive.

33 Rare variants and larger effects in a minority

Copy-number variants and rare coding variants can carry larger relative effects than common variants, especially in neurodevelopmental contexts, while remaining uncommon and heterogeneous. A 2026 large rare-variant study reported high-risk variants and convergent neuronal-developmental signals (Demontis et al. 2026, DOI 10.1038/s41586-025-09702-8, PMID 41224997). This advances biological resolution but does not transform ADHD into a monogenic disorder.

Rare-variant studies are sensitive to ascertainment, ancestry, sequencing coverage, annotation, and the presence of broader developmental difficulties. A statistically high relative risk may correspond to a modest absolute probability because the variant is rare and penetrance incomplete. The same variant can influence multiple outcomes.

The lecture should use rare variants to show causal plurality: some people may carry relatively large-effect developmental risks, while the population phenotype is mostly shaped by many small effects and contextual interactions. Neither route yields a deterministic biography.

34 Genetic correlations and pleiotropy

ADHD genetic liability correlates statistically with multiple psychiatric, educational, sleep, substance-related, and metabolic traits. These correlations indicate shared inherited influences across measured phenotypes. They do not show that ADHD causes each correlated outcome or that one disorder is a subtype of another.

Pleiotropy complicates all single-pathway accounts. A variant may influence early neural development, temperament, sleep, learning, or exposure to environments, thereby affecting several measured outcomes. Genetic correlation can also reflect imperfect diagnostic boundaries or mediated effects. It does not identify the direction, developmental stage, cell type, or network operation that matters.

This is why a causal graph is more useful than a list of correlations. Nodes include inherited variants, prenatal factors, temperament, cognition, family responses, school fit, sleep, adversity, symptoms, and treatment. Multiple arrows can connect them, including feedback. The graph is not proof of any particular arrow; it is protection against pretending that one association settles direction.

35 Gene–environment correlation and interaction

Environments are not always external exposures randomly assigned to genetically unrelated people. Parents transmit both genes and environments. A child's activity, emotional intensity, or disorganization can evoke responses from adults and peers. Older individuals select settings that fit or amplify their traits. These passive, evocative, and active gene–environment correlations can create associations between family conditions and symptoms without a single one-way environmental cause.

Gene–environment interaction asks whether the effect of an exposure differs by liability, or vice versa. Demonstrating it robustly is difficult: large samples are needed, exposures are measured noisily, and multiple testing can generate unstable findings. "Genes load the gun, environment pulls the trigger" is too binary for polygenic, recurrent development.

A better image is a trajectory repeatedly constrained and redirected. Genetic differences alter probabilities; environments provide demands, protections, learning, stress, and opportunity; the developing person changes the environment in return. This transactional framing is consistent with Hinshaw's multilevel review (Hinshaw 2018, DOI 10.1146/annurev-clinpsy-050817-084917, PMID 29220204), but each proposed interaction still requires direct evidence.

36 Prematurity and prenatal or perinatal risk

Preterm birth and several prenatal or perinatal complications are associated with later ADHD. These risks are not specific: they can influence broad neurodevelopment, learning, motor function, and health. Association also varies with gestational age, neonatal complications, socioeconomic context, and survival or ascertainment.

Prenatal smoking, alcohol, stress, obesity, medication, and pollutant exposures are frequently reported as correlates. Ordinary observational comparisons can be confounded by inherited liability and family characteristics. Sibling comparisons, negative controls, and genetically informed designs often attenuate apparently simple causal effects. An umbrella review concluded that confidence varies and familial or genetic confounding explains part of several prominent associations (Kim et al. 2020, DOI 10.1016/S2215-0366(20)30312-6, PMID 33069318).

The scientifically useful formulation is "risk marker or possible contributing exposure under specified evidence," not "prenatal cause of ADHD." Prevention claims require stronger causal designs than association claims.

37 Environmental exposures and causal-inference problems

Environmental research faces confounding, reverse causation, measurement error, selection, and correlated exposures. Socioeconomic disadvantage, pollution, nutrition, stress, healthcare access, sleep, and school quality cluster. Statistical adjustment can remove true pathways or leave residual confounding. Mendelian randomization adds assumptions rather than magical randomization, and sibling designs address shared family factors while introducing other limitations.

A useful evidence ladder distinguishes temporality, dose–response, specificity, negative controls, quasi-experiments, sibling comparisons, genetically informed models, and convergent mechanisms. No single rung guarantees causality. The stronger the public claim, the more of this ladder it should survive.

This protects both science and families. Weak causal language can stigmatize parents, pregnant people, or communities while diverting attention from modifiable current conditions. Qualified evidence can still justify reducing toxic exposures or improving sleep and schooling for broad health reasons; it does not need an overstated ADHD-specific mechanism.

38 Stress, adversity, trauma and socioeconomic context

Adverse childhood experiences are associated with ADHD diagnosis, symptoms, and impairment. A 2022 meta-analysis included 70 observational studies and nearly four million participants, demonstrating that the association is not trivial (Zhang et al. 2022, DOI 10.1002/brb3.2748, PMID 36068993). The causal interpretation remains complex.

Adversity may worsen attention, sleep, emotion, and functioning; increase clinical contact; or contribute to a partly overlapping phenotype. ADHD-related behavior and parental ADHD can also increase family conflict, accident exposure, school exclusion, and later adversity. Shared genetic and socioeconomic factors can influence both. Trauma-related symptoms can be misidentified as ADHD, and the two can coexist.

Socioeconomic context affects chronic stress, environmental toxins, nutrition, school resources, diagnostic access, and the feasibility of treatment. It can magnify impairment without being a single origin. A humane lecture acknowledges environmental suffering while refusing to erase inherited liability or imply that all ADHD is a scar of trauma.

39 Parenting and attachment: consequence, modifier and uncertain causal direction

Parenting is clinically important because family contingencies, routines, conflict, scaffolding, and parental well-being alter daily function. Behavioral parent training can improve interactions and outcomes. This therapeutic relevance does not prove that parenting caused the neurodevelopmental disorder. Child behavior influences caregivers, parental ADHD affects organization, and stress cycles become reciprocal.

Insecure attachment has been associated with ADHD in a limited and heterogeneous literature. A 2021 review by Wylock and colleagues is consistent with association, not with the proposition that attachment disruption is the primary cause of ADHD. Diagnostic overlap, referral patterns, parental symptoms, child temperament, and shared adversity complicate direction.

The distinction is crucial for interpreting Gabor Maté's *Scattered Minds*. His emphasis on emotional attunement, stress, relational safety, and compassionate self-understanding can contain valuable phenomenology and clinical framing. His stronger causal prioritization of early environment over genetic architecture is in tension with contemporary twin, genomic, and genetically informed evidence. This audit must be passage-specific once a complete legal text is available; the present corpus supports only a proposition-level assessment, not verbatim adjudication.

Assessment. Relationship and stress can modify regulation and healing: supported. Attachment disruption as a universal or primary cause of ADHD: unproven and inconsistent with current genetic evidence. Parent blame: scientifically and clinically unjustified.

40 Why neither "all genes" nor "all childhood environment" survives scrutiny

An all-genes model cannot explain why symptoms vary with sleep, task structure, incentives, learning, relationships, and developmental demand. An all-environment model cannot explain high twin similarity, molecular genetic association, rare-variant risk, and ADHD traits visible across diverse environments. Both fail because they ask one factor to occupy every causal level.

Multiple developmental routes can converge on similar behavior. Genetic liability can affect catecholamine regulation, learning, arousal, motor control, or timing; adversity can alter sleep and threat processing; a learning disorder can make school tasks punishing; family support can buffer all of these. Convergence at the phenotype does not imply convergence at one biological lesion.

The integrated position is not a vague compromise. It makes sharper predictions: causal effects should vary by subgroup and developmental period; genetically informed designs should change some environmental estimates; interventions can help without reversing etiology; and the same present symptom can require different treatment priorities.

41 Etiology, current state and treatment target are different questions

Etiology asks how a vulnerability developed. Current-state mechanism asks what is producing impairment now. Treatment target asks what can be changed safely and effectively. These sets overlap, but they are not identical. A genetic contribution can be treated through environmental scaffolding; a trauma history can coexist with a current sleep disorder; a medication can improve control without correcting an original cause.

This distinction prevents reverse pharmacological inference. Methylphenidate's benefit does not prove that ADHD was caused by methylphenidate-sensitive dopamine deficiency, just as analgesic response does not identify the origin of pain. It also prevents psychotherapy from being misrepresented as proof of environmental causation. Learning new strategies can alter present behavior regardless of how the vulnerability arose.

For the Flow Hijacked synthesis, causal variables become parameters that shape a state landscape across different timescales. That is an organizing abstraction, not a replacement for molecular, developmental, and social evidence. Its value will depend on whether it produces measurable predictions rather than merely redescribing complexity.

Causal layers: origin, expression, and leverage

Three questions are often collapsed: What contributed to the development of ADHD liability? What changes symptom expression today? What can be modified to improve life now? The answers need not be the same. A factor can be etiologically important yet difficult to change, while another factor may not have caused the condition but may strongly influence current impairment and treatment response.

Heritability is a population statistic defined within a particular range of environments. It does not measure how "genetic" an individual is, specify a single biological route, or imply immutability. Polygenic liability can influence temperament, learning, sleep, activity, and the environments people evoke or encounter. Environmental exposures can operate before birth, through health and stress pathways, through educational opportunity, or by changing the demands placed on regulation. Correlation among these levels complicates simple causal stories.

Attachment, parental attunement, adversity, and emotional climate can matter profoundly for regulation and wellbeing without serving as a universal cause of ADHD. This is where compassionate clinical insight must be separated from etiological proof. A useful causal model permits multiple routes, bidirectional influence, resilience, and change. It avoids blaming families, avoids genetic fatalism, and directs intervention toward modifiable conditions even when those conditions were not the original source of liability.

Causation requires more than choosing genes or environment

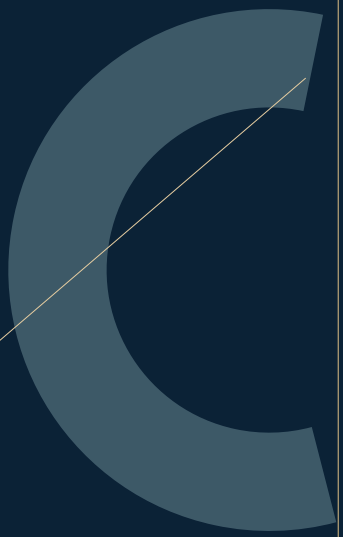
Heritability, molecular association, prenatal exposure, family stress, and attachment describe different levels of explanation. They cannot be placed on one simple percentage scale. High heritability within a population does not imply a single genetic route, does not determine an individual's future, and does not make environments irrelevant. Polygenic liability can influence development through many small pathways, while environments can alter expression, compensation, and access to care.

The same caution applies to environmental claims. Association with adversity may reflect causal exposure, shared familial liability, bidirectional effects, selection into environments, or measurement differences. Strong causal language requires designs capable of separating at least some of these possibilities. Attachment and emotional attunement can be profoundly important for regulation and wellbeing without being established as universal causes of ADHD.

For the lecture, the productive distinction is among origin, present expression, and leverage. A factor need not have caused ADHD to be a powerful treatment target today. Sleep, task structure, family interaction, school fit, trauma treatment, and economic stress can change the system's operating conditions. This is a non-blaming, non-deterministic causal architecture: inherited liability and developmental context interact, while intervention remains possible at several layers.

PART V

ATTENTION IS NOT ONE FACULTY



Turn ‘difficulty paying attention’ into separable cognitive operations with different failure modes.

Barkley · Nigg · Sonuga-Barke · Hart · Bozhilova

Part thesis

"Pay attention" compresses a chain of distinct operations. The nervous system must choose information, construct a goal, maintain it, suppress or postpone competitors, value future outcomes, allocate effort, monitor error, update after feedback, resume after interruption, and eventually disengage. ADHD can affect different links in different people and moments. No single task measures the chain, and no single failure mode explains the diagnosis.

42 Selection of relevant information

Selection amplifies information relevant to the current goal and limits the influence of competitors. It can be spatial—one location rather than another—feature-based—red objects rather than blue—or conceptual—one rule rather than a tempting alternative. Selection occurs at multiple stages, from sensory gain to working-memory prioritization.

Distractibility is not proof that early perception is globally weak. A distractor can receive too much priority because it is novel, rewarding, threatening, or currently congruent with another goal. Alternatively, the active task representation may be too unstable to bias competition. These possibilities predict different neural and behavioral signatures. Strong sensory responses can coexist with poor goal-directed selection; weak sustained control can coexist with intact momentary orienting.

The classic distinction between dorsal goal-directed and ventral stimulus-driven attention was foundational, but network boundaries have since become more nuanced (Corbetta & Shulman 2002, DOI 10.1038/nrn755, PMID 11994752). In ADHD, meta-analytic task-fMRI findings are distributed and heterogeneous rather than a single broken selection module. A selection error should therefore be described by task phase and stimulus conditions, not merely assigned to an "attention network."

43 Sustained attention and vigilance

Sustained attention is the capacity to maintain task-relevant processing over time, especially when events are infrequent and stimulation is low. Vigilance tasks create precisely the conditions that reveal instability: long intervals, repetitive stimuli, weak immediate reward, and rare targets. ADHD groups often show more omissions and more variable responses under these conditions.

Yet sustained attention is not a reservoir that drains linearly. Performance can show slow drift, abrupt lapses, periodic fluctuations, strategic speed–accuracy shifts, fatigue effects, and local stimulus history. Time-on-task effects can also reflect motivation, arousal, learning, or mind wandering. Averaging the first and last half of a task erases many of these dynamics.

A formal representation treats performance as an observation (y_t) generated by an unobserved state (z_t):

$$y_t \sim p(y_t \mid z_t,\, s_t), \qquad z_{t+1} \sim p(z_{t+1} \mid z_t,\, c_t),$$

where (s_t) is the current stimulus and (c_t) includes fatigue, reward, and context. This is a modeling scaffold, not evidence that one latent state exists in the brain. It forces the correct question: did the computation become uniformly weaker, or did the probability of entering a poor-performance state change?

44 Working-memory maintenance

Working memory keeps a limited representation active or readily retrievable while it is used. In real tasks, the fragile item may be the next action, the rule, the reason a distraction should be ignored, or a future intention. Difficulty can arise during encoding, maintenance, protection from interference, updating, or retrieval; a single span score cannot locate the problem.

ADHD groups show average working-memory difficulties, but effect size varies with modality, load, age, comorbidity, medication status, and task design. Laboratory structure can reduce real-world demands by making the goal explicit and the trial short. Daily life instead requires self-generated rehearsal and prospective organization across minutes or days.

Working-memory failure can therefore amplify every later operation. If the future goal loses representational strength, a present reward need not be abnormally strong to win. Externalizing the goal—written next actions, visible time, placed materials, reminders at the point of action—changes the competition without claiming to alter the underlying storage capacity. This is one reason behavioral scaffolding can improve function even when a neuropsychological test changes little.

45 Response inhibition and action cancellation

Inhibition includes withholding a prepared response, cancelling an action already initiated, resisting distractor interference, and delaying choice long enough to sample evidence. Go/no-go, stop-signal, Stroop, and interference tasks do not measure identical mechanisms. Stop-signal performance, for example, depends on assumptions about independent go and stop processes; violations can distort the inferred stop time.

Barkley's theory made inhibition a central developmental bottleneck linking ADHD to working memory, self-regulation, and action across time (Barkley 1997, PMID 9000892). It remains influential, but the broader literature does not support a universal inhibition deficit that is necessary or sufficient for ADHD. Some individuals perform normally; motivational and timing pathways contribute independently; task-fMRI meta-analyses implicate distributed systems with modest convergence.

Recent EEG tensor decomposition separates an early posterior selection component from later response-control activity in clinically relevant inhibition deficits (Gholamipourbarogh et al. 2026, PMID 40350038). This supports temporal decomposition, not diagnostic classification. The safe conclusion is that inhibitory control is one important family of operations within a heterogeneous disorder.

46 Proactive versus reactive control

Proactive control maintains the goal before conflict arrives. Reactive control is recruited after a conflict, error, or salient cue. A person can succeed reactively—recovering when an alarm, deadline, or visible error appears—while failing to sustain the anticipatory configuration needed to prevent the problem. This difference helps explain why external urgency can transform performance.

Proactive control is expensive because it occupies representational and energetic resources without immediate evidence that they are needed. It therefore depends on expected value, uncertainty, fatigue, and the reliability of future payoff. Reactive control can be effective but late, creating a life organized around crisis.

The distinction is useful clinically and experimentally, though direct ADHD evidence varies by paradigm. Cue–target intervals, conflict adaptation, pupil-linked arousal, and preparatory neural activity can separate modes better than overall accuracy. In the Flow Hijacked frame, proactive support raises the probability that the appropriate configuration exists before perturbation; reactive support changes recovery after departure. These are hypotheses to operationalize, not labels to apply retrospectively to every behavior.

47 Task initiation and prospective memory

Task initiation is not a standard cognitive module. It is the behavioral outcome of intention formation, prospective memory, valuation, sequencing, arousal, and action selection. The "first step" may remain abstract; the cue may not arrive at the right moment; the anticipated effort may dominate a delayed reward; or another activity may have high switching costs.

Prospective memory asks a system to remember to act later. It requires an intention to survive while attention is elsewhere and to be retrieved when a time, event, or context occurs. ADHD research suggests difficulties, but the literature is smaller than work on inhibition or working memory and direct neural evidence is sparse. Failures are particularly likely when cues are nonfocal and monitoring must be self-initiated.

External systems work by altering this architecture. "At 15:00, open the tax folder and find the first missing document" is a stronger event–action mapping than "do taxes." A reminder delivered away from the place of action may merely create another intention to remember. Treatment outcome should distinguish knowing the plan, initiating it, and completing it.

Figure concept — the initiation chain. Intention → cue detection → goal retrieval → first-action selection → motor commitment. Annotate distinct failure and intervention points; avoid one "motivation" box.

48 Effort allocation and persistence

Effort is allocated when expected benefits justify control costs. Contemporary control theory often expresses this as a comparison between expected performance gain and subjective cost. A generic objective is

$$u_t^* = \arg\max_{u \in \mathcal{U}} \Big(\mathbb{E}[R_{t:t+H} \mid u, c_t] - C(u \mid a_t) \Big),$$

where (u) is control intensity, (R) future reward, (C) subjective cost, (a_t) arousal, and (H) the represented horizon. The equation is a normative scaffold; it does not identify a literal calculator in the brain.

In ADHD, low persistence may reflect reduced benefit from a distant outcome, elevated cost of maintaining control, unstable representation of the horizon, insufficient arousal, or noisy execution after a sensible choice. Work by Winter and colleagues explicitly asks whether atypical effort behavior reflects decision-making or execution (Winter, Ben-Pazi & Pollak 2019, DOI 10.1177/1087054716654569, PMID 27329487).

This distinction undermines "not trying." A person can value the final outcome while the momentary expected value of control repeatedly falls below competing alternatives. Immediate feedback, social presence, shorter horizons, visible progress, or medication may change different terms in the objective. No single manipulation works universally because the governing term can differ.

49 Delay discounting and delay aversion

Temporal discounting describes how subjective value declines with delay. A common hyperbolic form is

$$V(D) = \frac{A}{1 + kD},$$

where A is reward magnitude, D delay, and $k > 0$ the discount rate. Larger estimated k means stronger preference for immediacy under that model. ADHD groups show steeper monetary delay discounting on average in case–control meta-analysis, but distributions overlap and estimates depend on reward type, real versus hypothetical outcomes, delay range, and model (Jackson & MacKillop 2016, DOI 10.1016/j.bpsc.2016.01.007, PMID 27722208).

Delay aversion is related but distinct. It proposes that waiting acquires negative value and behavior seeks to escape or avoid it, especially when alternatives exist (Sonuga-Barke 2003, PMID 14624804). A person can estimate time accurately yet dislike delay, or misestimate duration without preferring immediacy. Combining both under "impulsivity" loses mechanism.

Reward-related behavior is heterogeneous. Ventral-striatal differences are most consistently discussed during reward anticipation, but task phase, incentive, and sample alter findings (Plichta & Scheres 2014, DOI 10.1016/j.neubiorev.2013.07.012, PMID 23928090). Incentive-dependent performance improvement is evidence of context modulation, not voluntary symptom production.

50 Interval timing, time estimation and "time blindness"

Temporal processing includes perceiving duration, producing an interval, comparing intervals, synchronizing movement, estimating how long a task will take, and representing a future deadline. These processes recruit partially different sensory, striatal, cerebellar, and prefrontal mechanisms. "Time blindness" is a vivid clinical phrase for failures of temporal self-management; it is not a single standardized biological construct.

Meta-analysis in children and adolescents reports group differences in time perception, often more apparent at longer intervals, with heterogeneity across methods (Zheng et al. 2022, DOI 10.1177/1087054720978557, PMID 33302769). A task-fMRI meta-analysis identified distributed timing-related differences and medication-sensitive moderators, but the literature was small and coordinate-based (Hart et al. 2012, DOI 10.1016/j.neubiorev.2012.08.003, PMID 22922163). Adult review likewise finds a decade of mixed tasks rather than one deficit (Mette 2023, DOI 10.3390/ijerph20043098, PMID 36833791).

Temporal self-management also depends on working memory and prospective memory. A distant future can exert little control if it is not represented at the moment of choice. Visible clocks, intermediate deadlines, and precommitment can improve the mapping between future intention and present action without proving that an internal clock was repaired.

51 Response-time variability and performance fluctuation

Let reaction time T have density $p(T)$. A single mean $\mu = \mathbb{E}[T]$ ignores dispersion, skew, and temporal dependence. Ex-Gaussian models write $T = X + Y$, with $X \sim \mathcal{N}(\mu, \sigma^2)$ and $Y \sim \text{Exp}(1/\tau)$, so τ captures a long right tail. Drift-diffusion models instead attribute choices and times to latent evidence accumulation, boundary separation, nondecision time, and trial variability. These parameterizations are not interchangeable explanations.

ADHD research often finds increased intra-individual response-time variability, especially a larger slow tail. The tempting interpretation is periodic attentional lapse. That is plausible, but motor variability, speed–accuracy policy, arousal, mind wandering, learning, and measurement error can contribute. Trial order matters: independent slow trials imply something different from clustered or oscillatory lapses.

Recent trial-level neuroimaging work warns that a brain measure differing on average between groups may not predict the trials on which a given person slows (Tamm et al. 2025, PMID 40511327). A valid mechanism should connect within-person neural state to within-person behavior, survive out-of-sample testing, and not depend on motion or flexible preprocessing. Variability is therefore central evidence for dynamics and a central source of methodological caution.

52 Mind wandering, perceptual decoupling and meta-awareness

Mind wandering is thought that departs from the current external task. It can be deliberate or spontaneous, rich in content or blank, future-oriented or autobiographical. Perceptual decoupling refers to reduced processing of external input while internal cognition dominates. Meta-awareness is awareness that the mind has wandered. These dimensions predict different consequences.

ADHD is associated in several studies with more spontaneous task-unrelated thought and weaker context regulation, motivating a mind-wandering perspective on the disorder (Bozhilova et al. 2018, DOI 10.1016/j.neubiorev.2018.07.010, PMID 30036553; Bozhilova et al. 2021, DOI 10.1177/1087054720956714, PMID 32942934). Experience-sampling EEG work begins to link reported state to event-related dynamics (Bozhilova et al. 2022, DOI 10.1016/j.nicl.2022.103068, PMID 35696811).

Mind wandering is not equivalent to DMN activation, and DMN activity is not inherently a lapse. Internally generated thought supports planning, memory, creativity, and self-understanding. The dysfunction lies in insufficient control over timing, content, or reorientation. A 2022 adolescent study found DMN connectivity related to delay aversion and discounting but not reported mind wandering, a useful contradiction to one-to-one mapping (Broulidakis et al. 2022, DOI 10.1016/j.ijpsycho.2022.01.007, PMID 35032471).

53 Interruption, re-entry and task switching

An interruption does more than consume its duration. It replaces the active goal, changes working-memory contents, and may leave an unfinished intention competing for retrieval. Re-entry requires reconstructing where one was, what mattered, and what comes next. If the original goal representation was fragile, the restart cost can exceed the interruption itself.

Switching has at least two components: disengaging from the current set and configuring the next. A person may switch too readily toward salient novelty yet resist leaving an absorbing activity. There is no contradiction if entry and exit hazards depend on the current state, reward, and switching cost. “Distractible” and “stuck” can be two directions of inflexible allocation.

ADHD-specific naturalistic re-entry data remain limited, so the lecture should distinguish general interruption science from ADHD inference. Measurable outcomes include resumption lag, error after resumption, loss of place, and probability of never returning. Environmental design can reduce these costs through interruption barriers, restart notes, protected blocks, and cues placed at the re-entry point.

54 Hyperfocus, flow, perseveration and unresolved boundaries

Flow is commonly defined by deep absorption, a balance between challenge and skill, clear goals, immediate feedback, and a sense of fluent control. Hyperfocus is usually described by intensity and duration, sometimes with loss of time awareness and difficulty disengaging. Perseveration emphasizes continuation despite a changed rule or declining utility. The phenomena can overlap without being identical.

Empirical hyperfocus studies find associations with ADHD traits, distractibility, and executive-function complaints, but operational definitions are still developing (Hupfeld et al. 2019, PMID 30267329; Zhang et al. 2023, DOI 10.1371/journal.pone.0292215, PMID 37878578; Garcia Pimenta et al. 2024, DOI 10.1016/j.ridd.2023.104639, PMID 38039699). The AHQ-D improves measurement structure but was validated with only a small diagnosed-ADHD subgroup and provides no direct neural mechanism (Hupfeld et al. 2024, PMID 39169147).

The defensible synthesis is that hyperfocus challenges a pure capacity deficit and points toward allocation, capture, persistence, and release. It does not yet justify a specific dopamine curve, network state, or ADHD-exclusive mechanism. The crucial outcome is not simply hours focused; it is whether focus matches the person's chosen goal, remains responsive to changing priorities, and can be left without disproportionate cost.

End-of-part synthesis. Attention is a controlled sequence across time. ADHD can alter the reliability of that sequence through partially separable executive, motivational, temporal, arousal, and contextual routes. The next part must therefore introduce multiple networks and ask how they form temporary coalitions, rather than search for one anatomical "attention system."

55 Parts I–V evidence boundary and hand-off

Established evidence: ADHD is a clinically defined, impairing, heterogeneous developmental disorder with strong polygenic liability; symptoms and functioning vary with development and context; average differences occur across executive, motivational, timing, emotional, sleep, and variability measures.

Supported interpretation: For many people, impairment is better described as unreliable recruitment, maintenance, and flexible allocation of control than as the total absence of attentional capacity.

Plausible synthesis: Developmental liability and current state variables jointly change the probability that goal-relevant operations become available when needed.

Not established: A unitary executive lesion; one dopamine deficiency; one attachment cause; one "time blindness" mechanism; a known neural signature of hyperfocus; or an individual diagnostic biomarker.

Open questions: Which within-person state changes precede real-world task departure? Which mechanisms distinguish initiation failure from release failure? Which developmental trajectories are convergence, compensation, or environmental fit? Which causal subgroups predict differential benefit from medication, psychotherapy, sleep treatment, and scaffolding?

Decomposing a failed task

"Attention failed" is usually too coarse to guide measurement. Before a task begins, the person must represent the goal, estimate time, value a delayed outcome, inhibit an easier alternative, and cross an initiation threshold. During performance, the system must maintain the rule, select relevant input, monitor conflict and error, pace effort, and protect the task from internal and external capture. After disruption, it must detect departure, reconstruct context, and re-enter. At completion, it must release the old set and transition to the next demand.

Different laboratory tasks sample different slices of this sequence. A response-inhibition task does not measure organization in daily life; a continuous-performance task does not isolate motivation; a working-memory span does not by itself reveal why an intention was never encoded. Even apparently objective measures contain task-specific assumptions about speed, strategy, fatigue, and the value of errors.

The practical implication is a process-level formulation. Instead of asking only whether a person "has executive dysfunction," ask where the lifecycle becomes fragile, which contexts expose that fragility, and what compensatory route already works. This decomposition makes room for dissociation: someone may select information accurately once engaged yet struggle to initiate, or may enter easily but fail to recover after interruption. Treatment can then target the weak operation rather than an undifferentiated faculty.

A process trace is more informative than the word attention

Consider the apparently simple act of submitting a form. The person must notice the requirement, represent the future consequence, estimate how long the task will take, locate the materials, inhibit an easier alternative, begin before urgency becomes extreme, maintain the rule while reading, detect errors, tolerate boredom, and remember to press the final button. A failure at any link can be reported afterward as "I could not focus."

This trace separates control operations that laboratory tasks often blend. Response inhibition, working-memory maintenance, prospective memory, temporal estimation, effort valuation, and error monitoring are related but not interchangeable. A person can perform normally on one while struggling on another; a task can improve through strategy without changing the underlying operation that first appeared to be deficient.

Treatment becomes more precise when it targets the weak transition. A visible first action may reduce entry cost. Timed external cues may protect prospective memory. Immediate feedback can stabilize an early task state. A distraction plan can accelerate re-entry. Medication may alter the operating conditions under which several of these policies become usable. The phrase executive dysfunction is useful only when it is followed by this finer process map.

One ordinary task, observed from cue to release

Take a task that is common and consequential: answering an important email. At time zero the message is noticed. The person must classify its significance, decide whether a response is required, preserve the intention while gathering information, and assign the task a place in time. If the response is deferred, the system must create a cue strong enough to reactivate the intention later. Failure can occur before any writing begins.

Entry then requires reducing the action space. “Answer the email” is not yet an executable operation. Opening the thread, locating the requested document, writing one factual sentence, or setting a ten-minute draft interval is. A visible next action reduces retrieval and choice demands. The intervention is not motivational rhetoric; it changes the representation from an abstract obligation to a reachable transition.

During composition, working memory holds the communicative goal while language, social prediction, error monitoring, and inhibition compete for access. Perfectionistic checking can consume the same control resources as distraction. A new notification can displace the draft, while an internally generated concern can do so without any external event. The outward behavior—no sent message—does not reveal which route occurred.

Re-entry is a separate operation. The person has to notice departure, reopen the correct window, reconstruct what has been written, recover the intended tone, and identify the next missing unit. A short re-entry note written before switching can preserve this state information. Environmental design and metacognitive skill can therefore reduce recovery cost even if the probability of interruption is unchanged.

Completion is not the end of control. The draft must cross a sufficiency threshold, the send action must occur, and the system must release the task. Endless revision is not successful persistence if it prevents adaptive completion. Conversely, rapid sending without error monitoring may be an impulsive exit. The criterion depends on the task, not on maximal speed or maximal dwell.

This single trace yields distinct measurements: cue-to-open latency, open-to-first-word latency, uninterrupted dwell, number and cause of departures, re-entry duration, revision count, send time, subjective effort, and recovery afterward. Different treatments can improve different variables. The phrase “better attention” should be reserved for a pattern whose operational meaning has been stated.

Worked decomposition: producing a consequential report

Consider a report due in three weeks. At the moment it is assigned, prospective memory must preserve a future intention without allowing it to dominate every present action. Temporal estimation must translate an abstract deadline into a plausible sequence of work intervals. Valuation must make an outcome that is delayed and uncertain competitive with immediate alternatives. None of these operations is identical to selecting a relevant stimulus on the screen.

Entry begins when the person converts “write report” into an executable next action. The relevant failure may be ambiguity rather than ignorance: the goal has too many unresolved branches, no visible stopping rule, and no cue specifying where to begin. Task decomposition, a prepared document, an external start time, or another person’s presence can reduce this boundary complexity. Their effectiveness does not prove that the underlying condition is motivational or environmental; it shows that performance is jointly produced by person, task, and scaffold.

Once work starts, several controls must coexist. Working memory maintains the current claim, selective attention protects the evidence being read, inhibition limits a tempting response, and monitoring detects when a paragraph no longer serves the argument. A lapse may be external capture, spontaneous thought, confusion, fatigue, or a strategic pause. Those events can look identical in a reaction-time series while requiring different corrections.

Recovery is its own operation. After an interruption, the system must reconstruct what was being attempted, recover the unresolved subgoal, and suppress the attractive thread introduced by the interruption. Measuring only total time hides whether poor completion arose from frequent exits or from a very high cost of each return. A person with few but prolonged derailments may need a different intervention from someone with many brief lapses and rapid recovery.

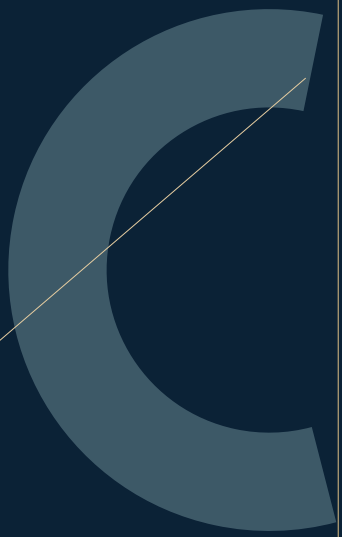
Release also matters. Continuing to polish after the decision-relevant threshold has been reached can impair performance elsewhere. Intense persistence is not automatically adaptive merely because it produces long dwell time. The criterion is context-sensitive control: remain when marginal work retains value, switch when another priority becomes dominant, and preserve enough state information to resume later.

This decomposition creates falsifiable treatment questions. Medication might shorten entry latency without teaching task decomposition. Cognitive-behavioral treatment might improve cue construction and re-entry while leaving laboratory inhibition largely unchanged. Sleep treatment might reduce late-session collapse. A reward manipulation might alter initiation yet have little effect after a state is established. “Attention improved” is therefore the beginning of analysis, not its conclusion.

PART VI

THE NETWORK CAST — BEYOND ‘DEFAULT

VERSUS TASK POSITIVE’



Give the audience the component systems needed to understand coordination without inventing one task-positive network.

Raichle · Corbetta · Seeley · Dosenbach · Menon · Power

Part proposition

The brain does not contain a single attention module that becomes globally weak in ADHD. Nor does it contain one internally oriented network that must be defeated by one "task-positive" opponent. Goal-directed performance is produced by a temporary configuration: sensory systems represent what matters; dorsal attention systems bias selection; frontoparietal systems hold and update rules; cingulo-opercular systems maintain set and monitor performance; salience and reorienting systems change priorities; corticostriatal loops evaluate and select policies; thalamic and neuromodulatory systems regulate access and gain; cerebellar systems predict timing and error; motor systems prepare and execute the response; memory systems preserve the goal across interruption. The configuration differs from task to task and from moment to moment.

The central move is therefore from **network opposition** to **configuration adequacy**. The scientific question is not simply whether default-mode activity is high and task activity is low. It is whether the required coalition can be assembled, stabilized, revised, and released at the right time.

56 What a large-scale network is — and is not

At the scale of fMRI, a network is usually inferred from patterned covariation: regions whose signals co-activate during tasks, correlate at rest, or share a statistical component. At the scale of EEG or MEG, it may be inferred from phase, amplitude, directed dependence, or source-space coupling. At the scale of anatomy, it may refer to white-matter tracts and recurrent loops. These are related descriptions, not interchangeable measurements.

Represent a parcellated brain by a time-indexed graph

$$G(t) = (V, E(t), W(t)),$$

where V is a set of regions, $E(t)$ the estimated edges at time t, and $W(t) = [w_{ij}(t)]$ their weights. A "network" may mean a subset of vertices, a community detected from W, or a canonical label transferred from another atlas. Its apparent borders therefore depend on parcellation, acquisition duration, preprocessing, thresholding, state, and task. Yeo et al. (2011) and Power et al. (2011) gave the field influential but nonidentical cortical partitions. Neither is a final anatomical dictionary.

ESTABLISHED EVIDENCE

Large-scale systems can be reproducibly identified at a coarse level, and their interactions vary with cognitive demand (Raichle et al., 2001; Seeley et al., 2007; Dosenbach et al., 2007; Yeo et al., 2011; Power et al., 2011; Cole et al., 2013).

Boundary. A functional edge is not a synapse, correlation is not communication, and temporal precedence in BOLD data is not proof of neural causation. A difference between two diagnostic groups is not a biomarker for an individual.

CORE SENTENCE A network name is a coordinate system for inquiry, not an autonomous object inside the head.

Figure concept 6A — One brain, three descriptions

A three-layer plate shows anatomical tracts, functional correlations, and time-varying effective models over the same nodes. Identical colors indicate correspondence; dotted boundaries show that the partitions do not coincide exactly. Caption: "The map changes with the measurement."

57 The default-mode network as adaptive internal cognition

The default-mode network (DMN) became visible not because the brain became inactive at rest, but because a coherent set of regions often showed lower average activity during externally demanding tasks than during unconstrained conditions. Canonical nodes include medial prefrontal cortex, posterior cingulate/precuneus, angular gyrus and lateral temporal cortex, with important interactions with hippocampal and parahippocampal systems (Raichle et al., 2001; Buckner et al., 2008).

Calling it "default" never meant useless. DMN activity participates in autobiographical memory, imagining futures, constructing social models, semantic integration, self-related appraisal, and linking the present to longer temporal horizons. Those functions can help a task. Planning an essay, understanding a character, considering another person's intention, or remembering why a goal matters may require cooperation between DMN and control systems. Some externally oriented tasks suppress selected DMN components; other tasks recruit them.

This matters ethically and scientifically. If internally generated thought is described as neural failure, creativity, memory and self-reflection are pathologized. The regulatory problem is **contextual fit**: is internal cognition serving the present goal, coexisting with it, or displacing the sensory and control processes the task presently requires?

ESTABLISHED EVIDENCE

The DMN is an adaptive set of interacting systems, and task-related attenuation is component- and demand-specific (Raichle et al., 2001; Buckner et al., 2008).

Rejected simplification. "ADHD is an overactive DMN." ADHD studies report both stronger and weaker within-DMN coupling, altered modulation, and small cross-network differences whose direction depends on node, age, state, and method (Castellanos et al., 2008; Uddin et al., 2008; Gong et al., 2019; Sütçübaşı et al., 2020; Cortese et al., 2021; Norman et al., 2023; Shi et al., 2026).

58 DMN subsystems: memory, self, simulation, and planning

The DMN should not be taught as a single scalar $D(t)$. Posterior medial, medial temporal, and dorsomedial subsystems contribute differently to memory construction, contextual simulation, social cognition, and self-referential evaluation. Their participation changes with task semantics and temporal horizon. Even the posterior cingulate and medial prefrontal cortex need not move together.

A better reduced description is a vector

$$\mathbf{d}(t) = (d_{\text{pm}}(t), d_{\text{mtl}}(t), d_{\text{dm}}(t), \ldots),$$

with task performance depending not on minimizing $\|\mathbf{d}(t)\|$, but on realizing an appropriate pattern of within-DMN and cross-network coupling. In a prospective-memory task, medial-temporal/DMN processes may preserve a future intention while FPN maintains the current rule. During stimulus discrimination, the same internal construction could become interference if it decouples processing from the sensory stream.

SUPPORTED INTERPRETATION

ADHD may involve difficulty regulating which internally oriented components remain coupled to control and which become decoupled from present demands. The evidence currently supports distributed coordination differences more securely than it supports any subsystem-specific causal lesion.

OPEN QUESTION

Do spontaneous task departures in ADHD contain more autobiographical simulation, more unconstrained semantic association, more "mind blanking," or different mixtures by arousal state? Experience sampling suggests heterogeneity; neuroimaging rarely identifies thought content precisely enough to answer.

59 Frontoparietal control network: flexible rules, not generic effort

Frontoparietal control network (FPN) regions, including lateral prefrontal and posterior parietal areas, participate flexibly across many tasks. Their connectivity can reconfigure with the rule, target, and uncertainty. Cole et al. (2013) characterized such regions as flexible hubs: their value lies partly in changing partners rather than remaining permanently attached to one task module.

FPN should not be equated with "willpower." It represents and adjusts task-relevant mappings: what counts as a target, which rule is active, which response is permitted, which feature deserves weight, and when a strategy should change. A person may understand a rule but fail to keep it stable; maintain it but fail to translate it into motor policy; or implement it until an unexpected salient event changes network priorities.

Task-fMRI meta-analysis moved ADHD away from a single frontostriatal lesion toward distributed systems differences (Cortese et al., 2012). More recent work reports mixed mean activation but altered network organization, trial-to-trial representational stability, and rest-to-task reconfiguration. In children, reduced temporal and spatial stability of salience/FPN activity patterns has been related to fluctuating control performance (Gao et al., 2025). In another pediatric study, network organization changed differently as cognitive demands increased (Michael et al., 2025).

SUPPORTED INTERPRETATION

"Inconsistently assembled or stabilized control representations" is more faithful than "underactive prefrontal cortex."

Boundary. Both recent studies are cross-sectional and method-sensitive; a group difference in multivariate stability does not tell us why a given individual missed a deadline.

60 Dorsal attention network: selecting what to sample

The dorsal attention network (DAN), classically involving intraparietal sulcus/superior parietal cortex and frontal eye fields, supports goal-directed selection of spatial locations and features (Corbetta & Shulman, 2002; Petersen & Posner, 2012). It biases sensory processing toward what the current goal declares relevant. It is neither identical to FPN nor sufficient for task performance.

ADHD findings include altered coupling among DAN, DMN, frontal eye fields, visual cortex, and control systems, but regional activation effects are not directionally uniform. Large samples find slightly less negative DMN–DAN coupling on average in youth, while some task-connectivity studies identify specific frontal-eye-field coupling differences and no ventral-attention effect (Norman et al., 2023; Metin et al., 2024; Norman et al., 2025). The effect in large samples is real at the group level but very small.

ESTABLISHED SMALL EFFECT. Average DMN–DAN segregation differs slightly in several large datasets.

Not established. That difference cannot diagnose ADHD, explain every lapse, or prove that the networks are locked in a zero-sum contest. Anticorrelation is shaped by preprocessing, and collaboration between DMN and DAN can be useful in tasks that join internal models to external sampling.

61 Ventral attention and reorienting systems: interruption can rescue or derail

The ventral attention network (VAN) is often described as a right-lateralized system that responds when behaviorally relevant events violate expectations and require reorientation (Corbetta & Shulman, 2002). Depending on atlas and paper, parts of temporoparietal junction, inferior frontal cortex, anterior insula, and operculum are assigned differently to VAN, salience, or cingulo-opercular systems. The labels should not be silently merged.

Reorienting is not intrinsically pathological. The same machinery can rescue a person from perseverating on the wrong problem, or pull the person away from a fragile task state toward a notification. Its value depends on the precision of salience assignment: how strongly an event is weighted, how much uncertainty it resolves, and whether it advances the active goal.

Adults with ADHD have shown weaker VAN/salience–DMN anticorrelation and altered auditory coupling; in that study, stronger VAN/salience–auditory segregation related to better distraction resistance (Blomberg et al., 2022). Yet atlas overlap, small samples, and unmeasured arousal prevent a clean “VAN deficit” conclusion.

SUPPORTED INTERPRETATION

Interruptibility can be understood as context-sensitive reorienting with altered thresholds or downstream stabilization, not simply as a weak capacity to concentrate.

62 Salience network: arbitration, not a literal master switch

The salience network is commonly centered on anterior insula and dorsal anterior cingulate, with subcortical partners. It integrates signals about novelty, bodily state, uncertainty, error, reward, and affective significance (Seeley et al., 2007; Menon & Uddin, 2010). Sridharan et al. (2008) reported that right fronto-insular activity preceded changes between default and executive systems, motivating a switching account.

The word “switch” is helpful only if it is not literalized. A light switch has two discrete states and one controller. A brain transition is distributed, noisy, graded, and context dependent. The insula can be an influential hub without being an executive homunculus. ADHD studies report salience-centered connectivity differences, greater temporal variability, altered state occupancy, and associations with symptoms or stimulant response. Cai et al. (2018) found replicated time-varying salience-centered interactions related more strongly to inattention than static averages. Acute methylphenidate shifted salience–FPN–DMN dynamics in a small randomized crossover study (Mizuno et al., 2022; Cai et al., 2023).

Counterevidence matters: some paradigms find preserved anterior-insula switching responses; salience, VAN, and cingulo-opercular definitions overlap; directions vary by task and development.

SUPPORTED INTERPRETATION

ADHD may involve altered arbitration among candidate network configurations.

Not established. There is no proven single “broken switch.”

63 Cingulo-opercular systems: holding the set across time

Dosenbach et al. (2007) distinguished a rapid, adaptive frontoparietal control system from a cingulo-opercular system associated with stable task-set maintenance and performance monitoring. The distinction is imperfect across atlases, but conceptually important. Flexible adjustment and tonic maintenance are different demands.

A learner can recruit the correct rule after each reminder yet fail to keep the rule active across a long interval. Conversely, a person can maintain a set rigidly and fail to adapt when circumstances change. ADHD research often compresses both into "executive dysfunction." Large connectome work and task studies implicate distributed cingulo-opercular connectivity and differentiation, while direct causal and treatment-specific evidence remains limited (Mooney et al., 2024; Michael et al., 2025).

SUPPORTED INTERPRETATION

Some performance variability may arise not at rule discovery but during sustained set maintenance, error monitoring, or recovery after error.

OPEN QUESTION

Which aspect—tonic maintenance, performance monitoring, post-error adjustment, or coupling to arousal—best predicts spontaneous task exit within individuals? Existing group studies rarely sample all four at adequate temporal resolution.

64 Reward and corticostriatal loops: value enters the control equation

Corticostriatal organization is plural. Ventral loops involving nucleus accumbens contribute to reward anticipation, incentive salience, and motivated engagement. Dorsal caudate/putamen loops contribute to action selection, habit, motor policy, timing, and cognitive control. Prefrontal, limbic, and motor territories overlap and interact rather than forming sealed channels.

Meta-analytic work has reported average ventral-striatal hyporesponsiveness during reward anticipation in ADHD, with a medium standardized difference in an early synthesis (Plichta & Scheres, 2014). The effect is not universal and changes with reward phase, task design, age, comorbidity, and medication. Dorsal striatal structure and function also show small, age-dependent differences. Medication-naïve pediatric seed studies helped expand the field beyond DMN-only accounts (Zang et al., 2009).

SUPPORTED META-ANALYTIC GROUP SIGNAL. Early synthesis supports an average difference in anticipatory ventral-striatal response, while the wider corticostriatal literature is heterogeneous across reward phase, task, age, comorbidity, and medication.

Unsupported leap. Ventral-striatal findings do not establish a single reward-deficiency syndrome, explain hyperfocus directly, or prove that low motivation is voluntary.

65 Thalamocortical gating: access, precision, and arousal

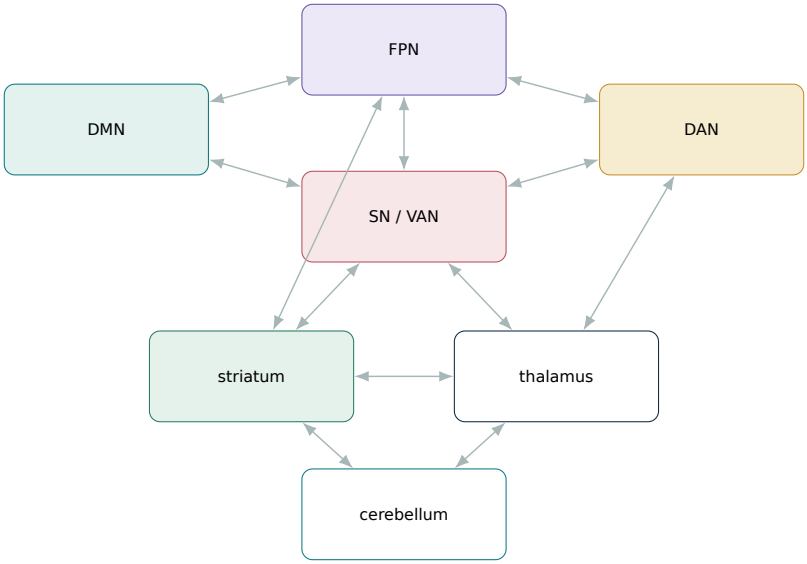
The thalamus is not a uniform relay. Distinct nuclei participate in sensory transmission, cortical coordination, arousal, and cortico-thalamo-cortical loops. ADHD studies report thalamic connectivity differences with attention, visual, default, and fronto-opercular systems, but the literature is less replicated than for cortical and striatal systems. Dynamic insular connectivity with thalamus has also been reported in children (Fateh et al., 2022).

One possible role is gating: controlling which signals receive sufficient precision or gain to influence a current network configuration. Another is timing and coordination across cortical systems. These are plausible mechanistic interpretations, not ADHD-specific causal findings.

EMERGING EVIDENCE. Thalamocortical coupling is implicated in some ADHD cohorts.

Boundary. Directed-connectivity or transfer-entropy estimates derived from short BOLD scans do not establish physiological direction. Nucleus-specific conclusions require acquisition and parcellation capable of resolving thalamic substructure.

A task is a temporary network coalition



Edges mean possible coordination, not fixed wiring or a measured ADHD effect.

66 Cerebellar timing, prediction, and coordination

The cerebellum contributes beyond movement. It supports temporal prediction, error-based learning, sensorimotor calibration, and closed-loop interactions with prefrontal and striatal systems. Structural and task meta-analyses have repeatedly implicated cerebellar regions in ADHD, although localization varies and effect sizes are generally small (Cortese et al., 2012; broader corpus synthesis).

This system matters for a dynamical account because stable task engagement requires prediction: when a target will appear, how long a response should be withheld, how an action's consequence updates the next action, and how pacing should change. Cerebellar timing differences could contribute to response variability without being a primary "attention" deficit.

ESTABLISHED EVIDENCE

Cerebellar involvement is supported across structural, task, and connectivity literatures.

OPEN QUESTION

Which cerebellar computations—interval prediction, error correction, arousal coupling, or motor timing—are most responsible for ADHD-related functional impairment? Current imaging does not justify one answer.

67 Motor preparation and response systems

Attention experiments usually end with an action: press, withhold, speak, or move the eyes. Variation in the measured reaction time therefore mixes perception, decision, motor preparation, and execution. Somatomotor connectivity and inhibition-related recruitment differ in some ADHD samples and dynamic states. These effects can be informative, but they are also uniquely vulnerable to head-motion artifact.

Let an observed response time be decomposed conceptually as

$$RT_k = T_k^{\text{enc}} + T_k^{\text{dec}} + T_k^{\text{motor}} + \varepsilon_k.$$

The equation is not an identifiable model without additional measurements. Its purpose is to prevent a category error: a long or variable RT_k does not reveal which latent interval changed.

SUPPORTED INTERPRETATION

Some "attentional" variability may arise in action-system timing or the translation from control policy to response.

Method warning. Because hyperactivity and micromovements can contaminate fMRI connectivity, apparent somatomotor dysconnectivity must survive stringent motion analysis rather than be treated as self-validating.

68 Sensory networks and distractor gain

Sensory cortices are not passive cameras. Their responses are shaped by attention, expectation, arousal, and the statistical structure of the environment. Visual and auditory network coupling can predict resistance to distraction, but ADHD findings are mixed. In some contexts atypical coupling may support better performance rather than represent deficiency.

In a gain-control shorthand,

$$y_i(t) = g_i(t)s_i(t) + \eta_i(t),$$

where s_i is sensory evidence, g_i its context-dependent gain, and η_i unmodeled input/noise. The scientific problem is not simply high noise. A distractor can win because its gain is too high, the target's gain is too low, or higher-order control fails to preserve the relevant weighting.

EMERGING EVIDENCE. Performance-linked sensory-network segregation and control coupling differ in some ADHD studies (Blomberg et al., 2022; Michael et al., 2025).

Boundary. BOLD variance, neural entropy, and behavioral inconsistency cannot be collapsed into the single phrase "noisy brain."

69 Hippocampal and memory-related systems

Maintaining a task is partly a memory problem. The present goal must survive competing thoughts; after interruption, context must be reconstructed; prospective intentions must become active at the right future cue. Hippocampal and medial-temporal systems interact with DMN during scene construction and future simulation, and with control networks during retrieval and prospective memory.

ADHD-specific network evidence here is limited compared with FPN, DMN, and striatum. Behavioral prospective-memory difficulties are plausible contributors to missed intentions and failed task resumption, but direct links from hippocampal dynamics to spontaneous lapses remain sparse.

OPEN QUESTION

Does task re-entry fail because the control state is costly to rebuild, because the goal trace is weak, because interruption overwrites context, or because the re-entry cue lacks salience? These mechanisms predict different interventions.

70 Network definitions vary with atlas, task, and method

A result labeled "salience" in one paper may be labeled "ventral attention" or "cingulo-opercular" in another. A seed-based study asks about one chosen region; independent-component analysis estimates spatial sources; graph analysis depends on node definition and threshold; task activation and resting correlation answer different questions. Even anticorrelation can change when global signal regression is included.

Power et al. (2012) demonstrated that small head movements can produce systematic functional-connectivity artifacts. This is especially consequential in ADHD, where motion is related to the phenotype. Aggressive censoring can also create selection bias by disproportionately excluding the most symptomatic participants. There is no single preprocessing choice that erases the problem.

The 2021 preregistered resting-state meta-analysis found no significant spatial convergence across 30 studies and 978 participants (Cortese et al., 2021). A 2026 pediatric meta-analysis found convergence in seed-based but not non-seed-based analytic families (Shi et al., 2026). Large participant-level mega-analyses nevertheless recover very small distributed effects (Norman et al., 2023, 2025).

ESTABLISHED EVIDENCE

Method family changes the apparent ADHD network map.

Lecture consequence. Show uncertainty as part of the picture: solid lines for replicated coarse effects, shaded fields for variable localization, and explicit "not an individual test" labels.

71 A task is a temporary configuration, not activation of one network

Suppose a task T requires a configuration $C_T(t)$ over multiple systems. We can write a schematic performance functional

$$P_T(t) = \mathcal{F}_T(\mathbf{a}(t), \mathbf{W}(t), \mathbf{z}(t), \mathbf{c}(t)),$$

where **a** denotes regional activity, **W** coupling, **z** slower internal states such as arousal and fatigue, and **c** context. The subscript on $\mathcal{F}_T$ is essential: the useful configuration for mental arithmetic is not the useful configuration for autobiographical planning.

"Task positive" can be retained as a historical description of voxels that increase in a contrast. It should not be treated as an anatomically uniform network. FPN, DAN, VAN, salience, cingulo-opercular, sensory, motor, reward, thalamic, cerebellar, and memory systems make dissociable contributions.

CORE SENTENCE A task is not one network turning on; it is a coalition becoming adequate for a particular purpose.

Figure concept 6B — Configuration, not combat

Show four snapshots of the same network map: autobiographical planning, low-value vigilance, rewarded inhibition, and re-entry after interruption. Node size represents recruitment; line width represents coupling. The DMN remains meaningfully engaged during planning, selectively attenuates during vigilance, and reconnects during goal reconstruction. No frame is labeled "healthy" or "ADHD"; a second row later shows empirically supported small probability shifts rather than caricatured on/off states.

Teaching matrix 6C — Keep the systems dissociated

System	Dominant teaching function	Typical phase of contribution	Lecture-safe ADHD statement	Confidence
DMN	memory, simulation, self, semantic integration	internal model; goal meaning; off-task thought	coordination and modulation differ in some samples; direction is heterogeneous	moderate
FPN	flexible rule representation and adjustment	entry, rule update, strategy change	recruitment and representational stability may be altered	moderate
DAN	goal-directed sensory selection	ongoing external sampling	DMN coupling differs slightly on average; local findings vary	moderate
VAN/reorienting	detection of behaviorally relevant violations	interruption, rescue, reorientation	capture and segregation findings are emerging and atlas-sensitive	limited–moderate
Salience	weighting internal/external significance	arbitration around entry and switch	time-varying involvement is supported; no master-switch lesion	moderate
Cingulo-opercular	sustained set and performance monitoring	maintenance and error recovery	distributed involvement is supported; treatment specificity is sparse	moderate
Ventral striatum	anticipation, incentive salience, motivated engagement	entry and vigor	anticipatory response is lower on average, not universally	moderate
Dorsal striatum	policy/action selection, habit, timing	selection and execution	small, age-sensitive structural/functional differences	moderate
Thalamus	gating, relay, arousal coordination	access and state regulation	connectivity evidence is emerging; causal direction unknown	limited
Cerebellum	prediction, timing, error adaptation	pacing and calibration	involvement is replicated more than any precise mechanism	moderate
Somatomotor	preparation and execution	response	differences exist but are highly motion-sensitive	moderate
Sensory	evidence representation and gain	sampling	coupling can predict distraction resistance; direction is contextual	limited–moderate
Hippocampal/memory	context and future intention	goal retention and re-entry	plausible relevance; direct dynamic evidence is sparse	limited

A coalition, not a switch

Large-scale network names are useful coordinates, not sealed anatomical organs. The FPN, DAN, VAN, SN, CON, DMN, corticostriatal loops, thalamus, cerebellum, sensory systems, motor systems, and hippocampal formations contribute different operations whose combination depends on the task. Reading a paragraph, waiting through a delay, remembering a future intention, and stopping an already prepared movement are all "tasks," but they require different coalitions.

The DMN illustrates why binary language fails. Internally generated cognition can interrupt a monotonous external task, yet internal simulation can also preserve the goal, construct a plan, retrieve autobiographical knowledge, or imagine a future consequence. Successful control may require selective coupling between DMN components and control systems rather than

maximal suppression. Likewise, greater FPN activation can reflect effective recruitment, compensatory effort, unresolved conflict, or a more difficult task; direction alone is not interpretation.

Network findings must therefore specify nodes, edges, time scale, task epoch, comparator, preprocessing, motion control, and medication status. Static functional connectivity is not directed influence, and a parcellation boundary is not a biological wall. The stronger question is configurational: which distributed pattern supports criterion performance now, how was it assembled, how long does it remain viable, and what causes its reconfiguration?

The same network can help or hinder, depending on the configuration

Network names describe recurring patterns of covariance, not agents with single intentions. The DMN is not a generator of pathology; the FPN is not a central executive sitting above the rest of the brain; the salience network is not a literal switch; and the DAN is not synonymous with every externally directed task. Each label contains multiple nodes, subdivisions, and time-dependent relationships whose contribution changes with the cognitive demand.

Take prospective planning. Remembering a future goal may require internally generated simulation and autobiographical memory associated with DMN components, a control representation supported by frontoparietal systems, salience assignment to the relevant cue, hippocampal retrieval, and corticostriatal valuation of delayed consequences. Suppressing all internal activity would damage the operation. The useful configuration is selective cooperation: internally generated content remains coupled to the current goal while competing streams are constrained.

A continuous performance task requires another coalition. Sensory systems represent the stream, dorsal attention supports selection, cingulo-opercular systems help sustain the set and monitor errors, motor circuits prepare and withhold responses, thalamic pathways regulate transmission, and cerebellar systems contribute timing and prediction. DMN activity may rise around lapses, but the inference depends on timing: activity before an error, after an error, and during a self-report probe cannot be treated as the same event.

Even the phrase anticorrelation requires caution. Its magnitude depends on preprocessing, global-signal treatment, task design, parcellation, and the precise nodes averaged together. Lower anticorrelation can mean reduced segregation, greater cooperation, common arousal influence, motion artifact, or a shift in only one component. A group difference does not identify which interpretation is correct without converging measures.

The strongest ADHD account is therefore configurational and conditional. It asks which coalition is assembled for this task, whether recruitment occurs at the right epoch, whether the pattern predicts criterion performance, and how stable it remains under perturbation. Mean activation can contribute to the answer, but activation direction alone cannot tell whether a region is efficient, compensating, conflicted, fatigued, or simply responding to a harder condition.

This also changes the meaning of treatment-related imaging. If medication moves one connection toward a control-group average, that is a descriptive convergence, not proof that the network was repaired or that the change mediated clinical benefit. A credible mechanism requires target engagement, temporal precedence, dose or exposure information, behavioral linkage, and replication. Network vocabulary should make the causal standard more exact, not provide a modern-sounding shortcut around it.

Epochs matter more than a single network contrast

A cue period, early configuration, stable performance, detected lapse, error correction, and release are different epochs. Averaging them can cancel effects or reverse their apparent direction. Increased salience-network activity may be useful when a task cue must win access, disruptive when an irrelevant stimulus captures the system, and reactive when it follows an error. The anatomical label is unchanged; the computational role is not.

The same temporal discipline applies to the DMN and control networks. Coupling that supports prospective planning before entry may become maladaptive if unrelated autobiographical content dominates during execution. Frontoparietal recruitment may predict successful correction after a lapse even when its average across the block shows no group difference. Event-locked and state-conditioned analyses are therefore essential to the coordination story.

A task configuration is a coalition, not a switch

The useful unit is a temporary coalition: sensory selection, control, salience, memory, action, valuation, and monitoring contribute with weights that change across task phases. DMN participation can be harmful during an unbidden lapse and useful during planning or autobiographical simulation. The scientific question is whether coordination is appropriate to the moment.

PART VII

FROM INTERNAL ACTIVITY TO

GOAL-DIRECTED CONTROL

Answer the central question at a first mechanistic level by replacing the on/off metaphor with coordinated transition.

Sonuga-Barke · Castellanos · Liddle · Norman · Cai

Part proposition

Entering a task is a transition, not a binary command. The brain must preserve enough internal model to know the goal, weight incoming information, recruit a rule, establish a motor policy, and resist irrelevant perturbations. Leaving the task is also a transition, and its causes are not the reverse image of entry. The ADHD question is therefore directional: what raises or lowers the probability of a successful **rest-to-task transition**, a stable **within-task trajectory**, an unwanted **task exit**, and a rapid **task re-entry**?

72 Rest is active cognition

During "resting-state" fMRI, participants are typically asked to lie still with eyes open or closed. They are not cognitively empty. They remember, plan, worry, simulate, monitor bodily sensations, become drowsy, and react to scanner noise. Resting connectivity is attractive because it avoids performance demands and can be acquired across sites; it is scientifically dangerous when interpreted as a direct sample of attention.

Let X_R denote data from rest and X_T data during task. In general,

$$p(X_T \mid \text{ADHD}) \neq p(X_R \mid \text{ADHD}),$$

and there is no reason to assume that a diagnostic contrast at rest predicts the contrast under demand. The mapping also depends on age, arousal, medication history, and task type.

ESTABLISHED EVIDENCE

Resting-state studies reveal small distributed ADHD-related differences, but rest does not substitute for task-state measurement (Gong et al., 2019; Sütçübaşı et al., 2020; Cortese et al., 2021; Norman et al., 2023; Michael et al., 2025).

Contradiction with a static narrative. In Michael et al. (2025), pediatric network organization changed with cognitive demand; effects visible during engagement need not be recoverable from rest alone.

73 The historical default-mode interference hypothesis

Sonuga-Barke and Castellanos (2007) proposed that inadequate attenuation of spontaneous default-mode activity could periodically intrude on task processes, producing the characteristic periodicity and variability of ADHD performance. The hypothesis was important because it shifted attention from mean deficit to fluctuation. Early studies found altered cingulate–precuneus connectivity, decreased network homogeneity, and reduced task-related suppression associated with distractibility (Castellanos et al., 2008; Uddin et al., 2008; Fassbender et al., 2009). Electrophysiological work also linked inadequate attenuation of very-low-frequency activity to performance (Broyd et al., 2010).

The historical model should be recovered and then revised. It preceded large multisite samples, contemporary motion control, dynamic connectivity, mature network parcellations, and the recognition that DMN contributes adaptively to complex tasks. "Intrusion" is a hypothesis about timing and functional displacement, not evidence that DMN activity is intrinsically abnormal.

ESTABLISHED HISTORICAL CONTRIBUTION. The model correctly made moment-to-moment fluctuation central.

QUALIFIED BY CURRENT EVIDENCE. Modern results favor small, distributed, state- and method-dependent differences rather than one robust DMN lesion (Cortese et al., 2021; Norman et al., 2023, 2025; Shi et al., 2026).

74 Task-related DMN attenuation

During many externally oriented tasks, average activity in parts of the DMN falls relative to a baseline. In ADHD, several small studies reported less attenuation, and Fassbender et al. (2009) linked reduced medial-prefrontal suppression to distractibility. Mowinckel et al. (2017) found greater DMN variability and weaker sustained suppression in adults with ADHD; methylphenidate changed some within-network connectivity but not the central variability effect.

Yet attenuation depends on demand. Liddle et al. (2011) found that a low-incentive group difference in DMN modulation could be removed by incentive or methylphenidate. Metin et al. (2015) reported a nonlinear, U-shaped dependence on event rate rather than a fixed suppression deficit. These studies are small, but their logic is powerful: if the difference changes with context within a person, it cannot be explained only as a fixed incapacity.

A useful quantity is not a single average deactivation but a task- and time-indexed modulation

$$M_D(t;T) = D(t \mid T) - D(t \mid B),$$

where B is a specified baseline. Changing B changes the meaning of M_D.

SUPPORTED INTERPRETATION

ADHD-related DMN modulation can be weak or unstable under some low-engagement conditions and can change under incentive or medication.

Not established. Universal failure to suppress the DMN.

75 Why maximal DMN suppression is not always desirable

Suppression is not a score whose maximum always indicates health. Reading for meaning may require semantic and autobiographical integration. Planning needs internally generated futures. Prospective memory needs a representation of what must happen later. Social cognition needs a model of people not directly observable in sensory input.

The ideal is conditional coordination. Let q_T be task quality and d DMN participation. For some tasks, $\partial q_T/\partial d < 0$ over the relevant range; for others, $\partial q_T/\partial d > 0$; often the relationship is nonlinear because some internally generated structure helps until it competes with immediate sampling.

ESTABLISHED GENERAL-COGNITION EVIDENCE. DMN supports adaptive memory, simulation, self, and meaning functions (Buckner et al., 2008).

Lecture correction. Replace "the DMN must switch off" with "DMN components must be selectively coupled or attenuated according to the computation."

76 Rest-to-task and task-to-rest are different transitions

Consider four directional quantities:

$$\begin{aligned} p_{\text{enter}} &= \Pr(S_{t+1} = T \mid S_t = R, c_t), \\ p_{\text{stay}} &= \Pr(S_{t+1} = T \mid S_t = T, c_t), \\ p_{\text{exit}} &= \Pr(S_{t+1} \neq T \mid S_t = T, c_t), \\ p_{\text{return}} &= \Pr(S_{t+1} = T \mid S_t \neq T, \text{goal retained}, c_t). \end{aligned}$$

The notation is deliberately agnostic about how states are estimated. It shows that task initiation, persistence, interruption, and re-entry are not one parameter. A person can enter quickly but exit frequently; enter slowly yet remain stable; sustain a high-interest task but struggle to release it; or recover rapidly after interruption despite frequent lapses.

SUPPORTED INTERPRETATION

ADHD heterogeneity is more intelligible when these transition directions are measured separately.

OPEN QUESTION

Which direction is altered in which presentation, age, context, and comorbidity? Most studies aggregate across a block and cannot answer.

Figure concept 7A — The four directional bottlenecks

A state diagram with Internal/Rest, Task-Ready, Stable Task, and Displaced states. Four colored arrows carry the quantities above. Around each arrow, list candidate influences: cue salience, goal memory, reward, fatigue, emotion, medication, and learned scaffolding. Caption: "The same symptom score can arise from different transition profiles."

77 FPN recruitment and control representation

Task entry requires more than increased frontal activity. The system must instantiate a task model: stimulus–response rules, decision boundaries, goals, and exceptions. In multivariate terms, the issue is whether neural patterns that discriminate the relevant rule are sufficiently separable and stable.

If $\mathbf{r}_k(t)$ is the population representation of rule k, one can define a conceptual stability measure

$$\rho_k(t, t+\Delta) = \text{corr}(\mathbf{r}_k(t), \mathbf{r}_k(t+\Delta)).$$

A lower ρ_k could arise from noisy encoding, state change, strategy change, or motion; it is not automatically neural unreliability. Gao et al. (2025) reported reduced temporal and spatial stability of control-related activity patterns in children with ADHD, associated with fluctuating performance. Michael et al. (2025) found altered reconfiguration as task demands changed.

EMERGING DIRECT EVIDENCE. Control representation and network organization can be less stable in pediatric ADHD samples.

Boundary. Cross-sectional correlations do not prove that instability causes symptoms; developmental stage, task difficulty, and prior medication remain plausible moderators.

78 DAN engagement and sensory selection

The DAN biases sensory systems in favor of task-relevant locations and features. Successful engagement requires the control representation to specify what DAN should select, and sensory evidence to update the representation. This is a recurrent loop, not a command cascade.

An observed lapse may therefore arise from at least three configurations:

1. the goal representation weakened while sensory selection remained intact;
2. the goal remained active but the wrong stimulus acquired gain;
3. selection was adequate, but response policy or motor execution failed.

Large trial-level data illustrate why this separation matters. Tamm et al. (2025) examined 5,719 children and found that trial-wise slowing recruited salience/VAN and executive systems while attenuating DMN, with weaker network competition in ADHD. This does not imply that every slow trial has one signature, but it demonstrates that averaged case–control maps discard relevant within-task variation.

SUPPORTED INTERPRETATION

Goal-directed selection in ADHD depends on coordination among DAN, control, salience, sensory, and default systems; a DAN-only explanation is insufficient.

79 Salience and cingulo-opercular arbitration

At task entry, a cue must become sufficiently significant to alter the current configuration. During persistence, cingulo-opercular systems help maintain set and track error. During interruption, reorienting/salience systems evaluate whether a competing event warrants displacement. The same system can facilitate entry, destabilize persistence, and enable adaptive exit.

This makes "distractibility" a decision problem under uncertainty, even when no conscious decision is experienced. Let $V_g(t)$ be the expected value of preserving the goal and $V_n(t)$ the estimated value or urgency of a novel event. A schematic reorientation threshold is

$$\text{reorient if } V_n(t) - V_g(t) > \theta(t),$$

where θ depends on arousal, fatigue, learning history, and context. The equation is not a literal neuronal comparator. It exposes testable components: value estimation, threshold setting, and post-switch stabilization.

Cai et al. (2018) found altered salience-centered time-varying interactions in children with ADHD, with stronger links to inattention than static measures. Yet preserved insular switching in some paradigms resists the "broken master switch" story.

FLOW HIJACKED SYNTHESIS. Salience arbitration may change the probability landscape of transitions without constituting a single damaged switch.

80 Reward systems decide whether engagement is worth sustaining

Reward signals can affect entry, vigor, persistence, learning, and release. The phrase "decide whether it is worth it" describes a distributed computation, not a conscious moral verdict. Ventral-striatal activity during anticipation is often lower on average in ADHD, whereas reward receipt and omission can yield different patterns (Plichta & Scheres, 2014). Incentives can reduce behavioral and DMN-modulation differences in some tasks (Liddle et al., 2011).

In reinforcement-learning notation, a prediction error is

$$\delta_t = r_t + \gamma V(s_{t+1}) - V(s_t),$$

but ADHD cannot be reduced to abnormal δ_t. Reward anticipation, temporal discounting, action vigor, effort cost, and salience are separable. A valuable immediate cue may stabilize a task that a distant outcome does not; a surprising notification may outcompete a meaningful but delayed goal.

ESTABLISHED CONTEXT EFFECT. Reward and incentive alter performance and some neural measures.

Boundary. Incentive-dependent improvement is not proof that the person could perform identically at all times "if they tried." Context-dependent machinery is still machinery.

81 What immediately precedes an attentional lapse

A block-average contrast compares people; a pre-lapse analysis asks what changed before a specific failure. Candidate precursors include reduced prestimulus sensory readiness, altered alpha/theta dynamics, slow fluctuations in arousal, local sleep-like slow waves, weakening of a control representation, or a change in cross-network coupling.

Bozhilova et al. (2022) combined experience sampling and EEG and reported weaker alpha modulation and theta phase consistency during demanding tasks and mind-wandering episodes in adults with ADHD. Einziger et al. (2023) found greater prestimulus neural variability in adolescents with more ADHD symptoms, but that variability did not explain reaction-time variability. Pinggal et al. (2026) reported more wake sleep-like slow waves in adults with ADHD; these related to errors, slower and more variable responses, mind wandering, and sleepiness. Horáková et al. (2026) found that mind wandering affected early sensory and P3b measures in both groups, with additional disruption of error/performance-monitoring activity in ADHD.

EMERGING EVIDENCE. Pre-lapse physiology can be measured and may reveal several routes to failure.

Boundary. Most samples are modest, mediation is not causation, and no single precursor is a validated ADHD marker.

Figure concept 7B — A pre-lapse ensemble, not a canonical trace

Use four aligned lanes: arousal/local slow wave; sensory readiness; salience/control coupling; response. Show multiple possible precursor paths converging on an omission. Empirical segments are solid; hypothesized causal arrows are dashed. Never draw one waveform as "the ADHD lapse."

82 What predicts successful engagement

Successful engagement is not merely the absence of a lapse. It can be predicted at multiple timescales: baseline sleep, momentary arousal, task value, cue clarity, goal representation, network reconfiguration, and the occurrence of task-favorable latent states.

Cai et al. (2021) reported that more frequent occupancy of a task-optimal latent state predicted lower response variability and faster evidence accumulation. In the acute randomized methylphenidate cohort, baseline dynamics predicted individual improvement, and medication shifted salience–FPN–DMN interactions toward the control pattern (Mizuno et al., 2022; Cai et al., 2023). Fisher et al. (2023) showed that cognitive and perceptual load had opposing ADHD-specific effects on network efficiency and behavioral variability.

SUPPORTED INTERPRETATION

A task-favorable configuration is conditional on demand. More integration is not always better, and more segregation is not always better.

OPEN QUESTION

Can a model trained within one person predict successful engagement across days and tasks better than a diagnostic group model? The field needs dense individual sampling and out-of-sample validation.

83 What predicts spontaneous task departure

Departure may follow internal capture, external capture, fatigue, uncertainty, error, emotional salience, or declining expected value. These pathways can converge behaviorally while differing physiologically. Experience-sampling studies show more freely moving or spontaneous off-task thought in ADHD, but thought content and meta-awareness vary (Bozhilova et al., 2018; Alperin et al., 2021; Bozhilova et al., 2022).

Define the first-exit time from a task-favorable set $\mathcal{T}$ as

$$\tau_{\text{exit}} = \inf\{t > t_0 : X(t) \notin \mathcal{T}\}.$$

The associated hazard

$$\lambda_{\text{exit}}(t \mid \mathcal{H}_t) = \lim_{\Delta t \downarrow 0} \frac{\Pr(t \le \tau_{\text{exit}} < t + \Delta t \mid \tau_{\text{exit}} \ge t, \mathcal{H}_t)}{\Delta t}$$

can depend on recent reward, error, sleepiness, emotional events, and state history $\mathcal{H}_t$. This survival formulation is a **measurement proposal**, not an established ADHD biomarker.

FLOW HIJACKED SYNTHESIS. Instead of asking whether attention is deficient, estimate when the task configuration becomes vulnerable to departure and which perturbations raise its exit hazard.

84 Coordination replaces the on/off metaphor

The evidence does not support the sentence "the task network turns on and the default network turns off." A defensible sequence is richer:

1. an external or internal cue receives salience;
2. control systems instantiate the relevant goal and rule;
3. dorsal attention and sensory systems weight task evidence;
4. cingulo-opercular systems maintain set and monitor performance;
5. corticostriatal and neuromodulatory systems shape value, vigor, and gain;
6. memory, thalamic, cerebellar, and motor systems preserve context, coordinate timing, and implement action;
7. the configuration is continuously revised as conditions change.

ADHD-related differences can occur at any transition or coupling. They are probabilistic, heterogeneous, developmental, and context dependent.

CORE SENTENCE The scientific problem is whether the appropriate configuration can be assembled, stabilized, revised, and released at the appropriate time.

Teaching matrix 7C — Directional control problems

Control problem	Observable outcome	Candidate network operation	Common confound	Strong test
Entry	latency before first goal-directed action	cue salience plus rule instantiation	unclear instructions; anxiety	within-person cue/value manipulation
Stabilization	sustained accurate performance	control representation, sensory weighting, tonic set	ceiling/floor task difficulty	trial-wise decoding plus behavior
Unwanted exit	lapse, off-task report, omission	arousal drop, capture, internal decoupling	missed perception or motor failure	pre-lapse multimodal measurement
Re-entry	time to recover after interruption	context reconstruction and goal-memory reinstatement	interruption complexity	experimentally standardized interruption
Adaptive release	leaving when goals change	salience detection plus policy update	perseveration mistaken for diligence	rewarded switch paradigm

The rows are dissociable hypotheses. A single symptom score cannot determine which row generated impairment.

The transition has stages

Moving into goal-directed control is not instantaneous. A cue must first be detected and assigned sufficient relevance. The current activity must then be interrupted or suspended, a task model must be retrieved, sensory and mnemonic priorities must be configured, an action policy must become available, and early performance must be monitored until the new state stabilizes. Failure at any stage can look like "not starting."

This staging clarifies why urgency or novelty can transform performance. A near deadline can increase salience and expected cost, reducing entry latency without necessarily improving planning or reducing later exhaustion. External structure can make the task model easier to retrieve. Immediate feedback can stabilize the early trajectory. None of these observations demonstrates that the original difficulty was chosen; they identify variables that alter transition probability.

The same logic applies after a lapse. Detecting that attention has departed is distinct from reconstructing what was being done, locating the next action, and suppressing the competing stream. A useful experiment should time-lock cues, interruptions, errors, awareness reports, and behavioral recovery so that neural activity immediately before and after the transition can be distinguished. Rest-to-task contrasts averaged across long blocks cannot resolve this sequence on their own.

PART VIII

THE BRAIN ACROSS TIME — VARIABILITY, STATES AND METASTABILITY

Supply the measurements needed for a genuinely dynamical account of ADHD.

Shappell · Cai · Gao · Park · Shine · Lurie

Part proposition

An average can conceal the phenomenon we are trying to explain. Two people can have the same mean reaction time while one performs consistently and the other alternates between fast, accurate epochs and long lapses. Two brains can have the same scan-average connectivity while occupying different configurations, dwelling in them for different durations, or traversing them in a different order. A dynamic account asks not only **where activity differs**, but **when a configuration appears, how long it persists, what precedes its exit, and how reliably it can be re-entered**.

The promise of dynamics is real. So is the danger of decorating static data with dynamical language. A clustering state is not automatically a biological attractor. Windowed correlation is not direct neural communication. "Metastability" must be operationalized, and different variability measures must never be treated as synonyms.

85 Why averages conceal the phenomenon

For trial series $y_1, \dots, y_N$, the mean

$$\bar{y} = \frac{1}{N} \sum_{k=1}^{N} y_k$$

discards order. The sequences $(1, 1, 1, 9, 9, 9)$ and $(1, 9, 1, 9, 1, 9)$ have the same mean and variance but radically different temporal organization. The first suggests a state change; the second suggests rapid alternation. Autocorrelation, run length, spectral structure, and conditional transition probabilities are needed to distinguish them.

This is not mathematical ornament. ADHD is defined partly by inconsistency across context and time. A block-average activation map can miss brief but consequential departures, while a symptom total can merge slow initiation, frequent interruption, and prolonged hyperfocus-like capture.

ESTABLISHED EVIDENCE

Intra-individual behavioral variability is elevated on average in ADHD. Dynamic neuroimaging and electrophysiology reveal state- and trial-dependent effects that static averages can miss (Cai et al., 2018, 2021; Shappell et al., 2021; Yin et al., 2022; Gao et al., 2025; Tamm et al., 2025).

Boundary. A dynamic metric is not automatically more reliable or clinically useful than a static one. More model freedom can create more apparent patterns.

86 Intra-individual reaction-time variability

Reaction-time variability is among the most replicated cognitive findings in ADHD, but it is not a single mechanism. Standard deviation and coefficient of variation summarize spread; ex-Gaussian parameters attempt to distinguish the central distribution from a long tail; diffusion models decompose evidence accumulation, boundary, and nondecision time. Each asks a different question.

For an ex-Gaussian description,

$$RT \sim \mathcal{N}(\mu, \sigma^2) + \mathrm{Exp}(\tau),$$

where τ describes the exponential tail. A higher τ may be consistent with occasional lapses, but it does not identify their neural cause. Slow trials can arise from low arousal, internal thought, cautious decision thresholds, motor delay, uncertainty, or strategic checking.

Tamm et al. (2025), in 5,719 children, demonstrated the value of trial-level analysis: response slowing was associated with a coordinated shift involving salience/VAN, executive systems, and DMN, with weaker competition in ADHD. Einziger et al. (2023), however, found that increased prestimulus EEG variability did not explain reaction-time variability.

ESTABLISHED EVIDENCE

Behavioral response variability differs at group level.

Rejected inference. It is not a direct meter of neural noise or a diagnostic signature.

87 BOLD variability is not behavioral variability

BOLD amplitude variability quantifies temporal dispersion in a regional hemodynamic signal. It is affected by neural activity, vascular dynamics, respiration, cardiac physiology, head motion, preprocessing, and the chosen frequency band. Higher variability may reflect flexible dynamic range in one context and instability in another. Lower variability can reflect rigidity or reduced responsiveness.

Let $B_i(t)$ be a preprocessed regional BOLD series. The sample variance

$$s_i^2 = \frac{1}{T-1}\sum_{t=1}^{T}\left(B_i(t) - \bar{B}_i\right)^2$$

contains no information about which source generated the variance. It should not be called "neural variability" without qualification.

Mowinckel et al. (2017) reported increased DMN variability related to reduced task performance in adults with ADHD. Other work finds system- and task-specific increases or decreases. A global "more variable ADHD brain" story therefore fails.

Boundary. BOLD variance, dynamic connectivity, entropy, representational instability, and reaction-time variability are distinct. A lecture visual must use separate axes and units.

88 EEG and MEG variability

EEG and MEG provide millisecond-scale access to oscillations, evoked responses, aperiodic activity, phase consistency, and long-range temporal correlations. They are better suited than fMRI to asking what happens immediately before a lapse, though source localization and artifact control remain difficult.

Reported ADHD effects include prestimulus variability, weaker event-related phase consistency, altered microstates, and local sleep-like slow waves. Bozhilova et al. (2022) linked mind-wandering episodes to weaker alpha modulation and theta phase consistency. Pinggal et al. (2026) linked waking slow waves to errors, mind wandering/blanking, and sleepiness. Haque et al. (2026) reported a nonlinear relationship between ADHD symptoms and MEG long-range temporal correlations, interpreted in relation to an extended critical regime.

The well-known theta/beta ratio should not be resurrected as a shortcut. A 2026 multiverse analysis in the corpus strongly challenged its robustness as an ADHD biomarker.

EMERGING EVIDENCE. Fast temporal physiology may reveal lapse precursors and arousal states.

Not established. A single electrophysiological ADHD signature.

89 Dynamic functional connectivity

Static functional connectivity estimates association over an entire scan. Dynamic functional connectivity (dFC) attempts to estimate change using sliding windows, time-varying models, edge cofluctuations, or latent states (Hutchison et al., 2013; Allen et al., 2014). If $x_i(t)$ and $x_j(t)$ are regional signals, a windowed estimate is

$$\hat{\rho}_{ij}(t; L) = \operatorname{corr}\left(x_i[t - L/2 : t + L/2], x_j[t - L/2 : t + L/2]\right),$$

where L is the window length. Short L improves temporal localization but destabilizes correlation estimates; long L smooths transitions. Apparent dynamics can arise from sampling variability even when the generating process is stationary.

ADHD dFC studies report altered salience-centered variability, occupancy of hyperconnected or less segregated states, differences by presentation, age and sex, and relationships with symptoms or behavior (Cai et al., 2018; de Lacy & Calhoun, 2019; Ahmadi et al., 2021; Shappell et al., 2021; Agoalikum et al., 2023; Luo et al., 2023; Zhu et al., 2023).

SUPPORTED INTERPRETATION

Time-varying configuration carries information not present in scan averages.

Boundary. State number, window, atlas, motion correction, scan duration, and clustering all affect the result.

90 State occupancy and dwell time

Many analyses assign each time point or window to a latent state $S_t \in \{1, \dots, K\}$. Two simple summaries are occupancy

$$\pi_k = \frac{1}{T} \sum_{t=1}^{T} \mathbf{1}(S_t = k)$$

and mean dwell time

$$d_k = \frac{1}{N_k} \sum_{m=1}^{N_k} \ell_{km},$$

where ℓ_{km} is the length of the m-th visit to state k. Shappell et al. (2021) reported that children with ADHD left a DMN–task anticorrelated state sooner, spent more time in a globally hyperconnected state, and less time in segregated states. Cai et al. (2021) found that greater occupancy of a task-optimal latent state predicted lower behavioral variability and faster evidence accumulation. Xin et al. (2025) identified entropy-defined states with group differences in occupancy and transitions.

EMERGING DIRECT EVIDENCE. Some ADHD samples differ in occupancy or dwell time.

Boundary. A state is a model-dependent partition of data. "Shorter dwell" is not identical to a shallow attractor basin, and state labels may not transfer across pipelines.

91 Transition probabilities and exit hazard

For a first-order Markov model, transition probabilities are

$$P_{ij} = \Pr(S_{t+1} = j \mid S_t = i).$$

The model assumes that the next state depends on the present state, not the full history. Brain dynamics may violate that assumption: duration, fatigue, recent errors, and reward history can matter. A hidden semi-Markov model therefore estimates state-specific duration distributions rather than forcing geometric dwell times.

An exit hazard from a task-favorable state k can be written

$$h_k(a \mid \mathbf{u}_t) = \lim_{\Delta a \to 0} \frac{\Pr(a \le D_k < a + \Delta a \mid D_k \ge a, \mathbf{u}_t)}{\Delta a},$$

where a is time already spent in the state and $\mathbf{u}_t$ contains reward, arousal, error, or stimulus covariates. This distinguishes memoryless switching from duration-dependent fatigue or stabilization.

FLOW HIJACKED SYNTHESIS. ADHD may be studied as altered transition hazards rather than as uniformly reduced activation.

OPEN QUESTION

Do ADHD differences reflect higher unwanted exit hazard, reduced entry hazard, slower re-entry, impaired adaptive release, or different combinations? Existing state studies rarely estimate these competing processes within tasks.

92 Hidden Markov and hidden semi-Markov models

In a hidden Markov model (HMM), the observed vector Y_t is generated conditionally on an unobserved state S_t:

$$p(Y_{1:T}, S_{1:T}) = p(S_1) \prod_{t=2}^{T} p(S_t \mid S_{t-1}) \prod_{t=1}^{T} p(Y_t \mid S_t).$$

The parameters can encode state-specific means, covariance, spectral content, or effective connectivity. A hidden semi-Markov model replaces the implicit geometric duration with $p(D_k = d)$, making dwell explicitly modelled.

Park et al. (2021) used HMM-defined states to examine state-dependent effective connectivity and reported ADHD-related differences in directed DMN coupling, mainly in estimated self-inhibition. Cai et al. (2023) used a Bayesian dynamical-system analysis of randomized methylphenidate data and found that medication shifted a latent-state process and state-dependent DMN hyperconnectivity toward the typically developing pattern.

EMERGING DIRECT EVIDENCE. Latent-state models can link network configurations, behavior, and acute drug perturbation.

Boundary. Hidden means statistically unobserved, not neurologically discovered. Model selection, priors, identifiability, and out-of-sample stability must be reported.

93 Trial-wise stability of control representations

Latent state analysis clusters broad configurations; representational analysis asks whether the code for a particular rule or target remains stable. Let $\mathbf{r}_t$ be a multivoxel or sensor pattern and $\mathbf{r}^*$ the task-template estimate. A simple alignment measure is

$$a_t = \frac{\mathbf{r}_t^\top \mathbf{r}^*}{\|\mathbf{r}_t\| \, \|\mathbf{r}^*\|}.$$

Low or fluctuating a_t could precede an error. Gao et al. (2025) reported less stable salience/FPN patterns in children with ADHD, related to cognitive-control fluctuation. The important advance is temporal: group differences become trajectories of representational fidelity rather than a single activation contrast.

SUPPORTED INTERPRETATION

Task persistence may require sustained representational alignment, not continuously high activity.

OPEN QUESTION

Does alignment fail because the rule representation decays, because the network changes strategy, or because competing representations become stronger? Causal perturbation and within-person replication are needed.

94 EEG microstates and oscillatory state structure

EEG microstates partition scalp topographies into brief recurring classes, often lasting tens of milliseconds. Oscillatory state models can instead cluster power, phase synchrony, or aperiodic features. These representations operate at a different scale from fMRI dFC states and should not share labels without validation.

Kember et al. (2023) preregistered resting EEG phase-synchrony and modularity predictions that were null. Longer dwell in a high-alpha/beta, low-delta/theta state related to better response control, particularly in ADHD, with tentative sex moderation. The null primary predictions are scientifically valuable: they resist the tendency to interpret every dynamic decomposition as disease-specific.

EMERGING EVIDENCE. Some EEG state durations relate to response control.

Contradiction. Preregistered network predictions can fail even when exploratory state–behavior relationships appear.

95 Local sleep-like activity during wakefulness

Wakefulness is not globally uniform. Local neuronal populations can express slow-wave-like events associated with reduced responsiveness, especially under sleep pressure. Pinggal et al. (2026) reported more waking local slow waves in adults with ADHD and associations with errors, response slowing/variability, mind wandering or blanking, and subjective sleepiness.

This result offers a direct bridge among sleep, arousal, lapse phenomenology, and fast neural dynamics. It does not imply that ADHD is a sleep disorder. ADHD and sleep disturbance can be bidirectional; medication, circadian phase, anxiety, routines, and comorbid conditions can alter both.

EMERGING DIRECT EVIDENCE. Local sleep-like events may constitute one route to momentary lapse in some adults with ADHD.

Boundary. The study is recent and modest; mediation cannot establish causal direction; replication across ages and medication states is required.

Figure concept 8A — Multiple roads to the same omission

Four converging trajectories reach the same behavioral error: local slow wave; internal thought with preserved arousal; salient external capture; control-representation decay. The graphic makes the central point that identical outcomes do not imply identical neural causes.

96 Criticality and long-range temporal correlations

A system near a critical transition can display scale-free correlations, large dynamic range, and sensitivity to perturbation. Long-range temporal correlations are often estimated by detrended fluctuation analysis (DFA). For integrated, detrended signal segments of size s,

$$F(s) \propto s^{\alpha},$$

where α indexes temporal persistence over the fitted range. This exponent is not itself "distance from criticality"; the inference requires a model and convergent observables.

Haque et al. (2026) reported nonlinear associations between MEG long-range temporal correlations and ADHD symptoms, proposing that similar symptom burdens may occur at different operating points within an extended critical regime. This is conceptually important because it rejects a one-direction deficit axis.

EMERGING EVIDENCE. A very recent cross-sectional MEG/model study links symptom variation to nonlinear temporal organization.

Not established. ADHD as a criticality disorder. Replication, longitudinal perturbation, estimator robustness, and specificity relative to sleep, medication, and comorbidity are needed.

97 Metastability: direct evidence, proxies, and overstatement risk

In dynamical systems, metastability describes temporary residence near a configuration with an ongoing tendency to reconfigure. It can arise without a permanently stable attractor. In neuroscience, the term is used for phase-coordination measures, switching among connectivity patterns, and whole-brain models (Shine et al., 2016; Deco et al., 2017; Breakspear, 2017). These operationalizations are not equivalent.

For oscillator phases $\phi_j(t)$, the Kuramoto order parameter is

$$R(t)e^{i\Psi(t)} = \frac{1}{N}\sum_{j=1}^{N} e^{i\phi_j(t)}.$$

One metastability index is the temporal variance of $R(t)$:

$$M_R = \mathrm{Var}_t[R(t)].$$

High M_R indicates fluctuation between more and less synchronized regimes under this definition. An HMM dwell time does not measure the same object.

ADHD research provides direct evidence for altered state occupancy, dwell, flexibility, entropy dynamics, and representational stability in some samples. It provides limited direct, convergent evidence for metastability in the strict dynamical-systems sense.

SUPPORTED INTERPRETATION

Task-state stability and transition structure are promising targets.

Guardrail. Do not relabel every dFC finding "altered metastability." State which metric was measured.

98 Motion, preprocessing, parcellation, and analytic flexibility

Head motion can inflate nearby correlations, reduce distant correlations, create apparent state changes, and correlate with age or symptom severity (Power et al., 2012). Respiratory and cardiac signals can mimic low-frequency network dynamics. Global signal regression changes the distribution of correlations and can produce or alter anticorrelation. Short scans produce unstable individual estimates. Atlas choice changes nodes; model order changes the number and identity of states.

A credible dynamic result should therefore report at least:

- framewise displacement distributions and group differences;
- censoring/scrubbing thresholds and remaining data per participant;
- physiological correction where possible;
- sensitivity to global signal handling;
- alternative parcellations or model orders;
- reliability or split-sample replication;

- preregistration or a multiverse when analytic degrees of freedom are large;
- out-of-sample prediction rather than in-sample separation alone.

Aggressive exclusion is not a neutral fix: it can remove the most hyperactive or youngest participants and change the target population. Motion is both artifact and phenotype-correlated behavior; analysis must address both without confusing them.

CORE SENTENCE Dynamics become explanatory only when the measured quantity, temporal scale, and inferential limits are explicit.

Figure concept 8B — Metrics are not synonyms

A matrix places behavior, BOLD amplitude, static FC, dFC, HMM occupancy, dwell, entropy, EEG microstates, DFA exponent, phase metastability, and control energy in rows; columns show temporal scale, units, assumptions, and ADHD evidence strength. Red prohibition marks prevent arrows that equate one metric with another.

Teaching matrix 8C — Evidence ladder for a dynamical claim

Claim level	Minimum observation	Additional requirement	Present ADHD status
Fluctuation	within-person variation above measurement error	reliability across sessions	established behaviorally; mixed neurally
Recurring state	reproducible multivariate configurations	stable state identity out of sample	emerging
Altered dwell/transition	group or dimensional difference in durations/transitions	robust model order and motion sensitivity	emerging direct evidence
Metastability	temporary coordination under an explicit dynamical definition	convergent phase/model measures	limited
Attractor landscape	perturbation-dependent return/escape geometry	causal or densely sampled system identification	not established in ADHD
Clinical biomarker	reliable individual prediction	external validation and added clinical value	not established

This ladder prevents a common inflation: moving from an observed change in windowed covariance to a claim about attractor pathology without testing the intervening levels.

Time-averaged equality can conceal dynamical inequality

Suppose two recordings have the same mean activation and mean accuracy. In one, the system remains near a task-supporting configuration with small fluctuations. In the other, it alternates between high-control and off-task states. The averages are equal, but the second trajectory contains longer entry delays, more transitions, and heavier recovery costs. This is the basic reason to study distributions, autocorrelation, dwell, hazard, and transition structure rather than means alone.

Dynamic measures introduce their own risks. A short sliding window can manufacture variability; a long window can erase it. Head motion can resemble state change. A clustering algorithm will return states even when the generative process is continuous. Hidden Markov and semi-Markov models depend on the number of states, emission assumptions, temporal resolution, and alignment across people. Neural entropy, BOLD variance, EEG microstates, and reaction-time variability are not interchangeable indices of one underlying "instability."

The evidential standard should therefore be predictive and multilevel. A proposed state must be reliable enough within a person, correspond to a defined task epoch or behavior, generalize to held-out data, and add information beyond symptom severity, motion, arousal, and simple performance summaries. Only then can altered occupancy or dwell be interpreted as a candidate mechanism rather than an analytic description.

What a dynamic claim must actually measure

A dynamic account begins with a simple warning: temporal variation in a measurement is not automatically variation in a neural state. Reaction times fluctuate because of attention, motor preparation, strategy, speed-accuracy tradeoff, fatigue, and measurement noise. BOLD signals fluctuate through neural, vascular, respiratory, cardiac, and motion-related processes. EEG amplitude and phase vary across arousal, eye movement, muscle activity, and cognitive events. The analytic task is to show that a proposed state variable captures reproducible structure beyond these alternatives.

Different methods answer different temporal questions. Trial-wise behavioral models can estimate lapse probability at the scale of seconds. EEG and MEG can resolve rapid changes in oscillatory coordination but localize sources indirectly. fMRI samples slower hemodynamic projections with higher spatial coverage. Experience sampling can identify thought content but perturbs the stream it measures. Wearables and digital phenotyping offer ecological duration while sacrificing experimental control. A coherent design aligns these scales instead of treating them as interchangeable views of one hidden process.

State discovery is especially vulnerable to circularity. A clustering algorithm will partition data even when the underlying

process is continuous. A sliding window will produce changing correlations even from some stationary signals. Hidden Markov models can return crisp labels whose certainty exceeds the evidence. The proposed states must therefore survive changes in window length, parcellation, motion threshold, state number, initialization, and classifier. Posterior uncertainty and out-of-sample prediction belong in the result, not in a methods footnote.

For ADHD, a useful state should predict something clinically or behaviorally consequential: an imminent omission, spontaneous mind wandering, recovery after interruption, failure to initiate, or successful completion outside the scanner. Group differences in occupancy or dwell matter more when they predict these events beyond symptom score, mean performance, sleepiness, medication status, and head motion. Otherwise the dynamic analysis may be a more elaborate description of variance rather than an explanation.

Trait and state must also be separated. A person's average transition pattern may be relatively stable, while the expression of that pattern changes with sleep, reward, menstrual or hormonal state, stress, novelty, and drug exposure. Repeated measurement permits a hierarchical decomposition into between-person differences, within-person context effects, and residual fluctuation. A single resting-state scan cannot provide that decomposition.

The Flow Hijacked synthesis becomes testable only at this level. Shorter dwell, greater perturbation sensitivity, slower re-entry, or altered transition probability are distinct predictions. They may not all move together, and ADHD may contain subgroups with opposite patterns. Metastability should therefore denote an estimable balance between persistence and flexibility, not a poetic synonym for inconsistency.

A pre-lapse experiment that could discriminate mechanisms

An informative study would combine a sustained task with intermittent thought probes, eye tracking, EEG, and a slower whole-brain measure in repeated sessions. Interruptions, reward, and time-on-task would be experimentally varied. The primary outcome would not be a mean group contrast, but the probability of an omission or reported task-unrelated thought in the next several seconds.

Candidate models would compete prospectively. One might use only recent reaction times and errors. Another might add pupil-linked arousal and gaze. A network-state model might add time-varying coordination; a semi-Markov model might distinguish transition probability from duration. The neural model earns explanatory value only if it improves held-out prediction and remains useful after motion, sleepiness, and performance history are included.

The experiment would also test direction. Does a candidate neural configuration precede the lapse, appear when the person notices departure, or follow the error? These epochs require separate regressors and sufficient events. A classifier trained on post-error recovery cannot be used as evidence that the same state caused the original lapse.

Repeated sessions allow trait-state decomposition. If a person repeatedly shows high unwanted-exit hazard across contexts, that may be trait-like. If the hazard rises specifically with sleep loss or low reward, the context interaction becomes the more precise result. Medication can then be tested against the same model: does it alter baseline occupancy, transition probability, dwell, or only task performance?

Such a design could still fail. Probes may change mind wandering, EEG states may not align with fMRI states, and ecological tasks may not reproduce scanner dynamics. Those limitations should be part of the prediction. A dynamic theory is strengthened when it specifies the observations that would show its state vocabulary is unnecessary.

Dynamics must earn their extra complexity

A hidden-state model is informative only if its states are reliable across resampling, interpretable through behavior or independent measurement, and predictive outside the observations used to construct them. More states will almost always fit training data better. The meaningful comparison is against simpler baselines on held-out people or sessions, with uncertainty around dwell time and transition estimates. Otherwise "metastability" may rename noise, motion, fatigue, or arbitrary clustering.

PART IX

WHY CONTEXT CAN TRANSFORM THE SAME PERSON

Explain why capability can appear radically different across tasks without invoking willpower or contradiction.

Sonuga-Barke · Plichta · Jackson · Volkow · Aston-Jones

Part proposition

The familiar puzzle—"How can someone fail to begin an ordinary task yet sustain intense attention elsewhere?"—is not resolved by declaring either incapacity or hidden willpower. Performance is generated by a person-in-context system. Reward timing, intrinsic interest, novelty, emotional significance, bodily state, arousal, sleep, stress, task structure, and available scaffolding all change the probability that a useful configuration will be entered and maintained.

Context dependence does not mean that ADHD is unreal. It means that the phenotype is expressed through state-dependent control. Trait liability changes the distribution of reachable states; context changes which part of that distribution is sampled.

99 Low-value and high-value tasks

"Value" includes more than money or pleasure. A task can carry intrinsic curiosity, social meaning, urgency, identity relevance, relief from uncertainty, or a clear endpoint. A low-value task may have delayed consequences, ambiguous steps, weak feedback, and high initiation cost. The same person can therefore experience a different control problem under two tasks that look equally simple to an observer.

Let the subjective action value be schematically

$$Q(a, s) = \mathbb{E}\left[\sum_{k=0}^{\infty} \gamma^k r_{t+k} \mid s_t = s, a_t = a\right] - C_{\text{effort}}(a, s),$$

where γ discounts future outcomes and C_{effort} represents anticipated cost. This is a modeling vocabulary, not a claim that the brain computes a literal scalar. Immediate, reliable feedback can raise estimated value and reduce uncertainty; distant outcomes can lose leverage.

ESTABLISHED CONTEXT EFFECT. Incentive and task structure can substantially alter ADHD performance and some network measures (Liddle et al., 2011; Fisher et al., 2023).

Moral guardrail. A neural system that responds to value is not choosing symptoms. "Can under one condition" does not entail "can identically under all conditions."

100 Reward anticipation and ventral striatum

Reward processing unfolds in phases: cue detection, anticipation, action, outcome, prediction error, and learning. Plichta and Scheres (2014) reported a medium average reduction in ventral-striatal responsiveness during reward anticipation in ADHD across the early fMRI literature. The direction and magnitude are not uniform across reward receipt, omission, probability, age, and comorbidity.

The ventral striatum receives converging information about expected outcomes, novelty, and motivational significance. Its activity can influence control vigor and task selection through corticostriatal loops. Methylphenidate has been reported to modify reward-cue discrimination in adults with ADHD (Furukawa et al., 2020), but one task-specific pharmacological effect does not establish a universal reward normalization.

SUPPORTED META-ANALYTIC GROUP SIGNAL. An average anticipatory ventral-striatal difference is supported in the early synthesis, but its magnitude, generality, and boundary conditions remain unsettled.

Boundary. Reward anticipation is not motivation as a whole, and BOLD response is not dopamine concentration.

101 Immediate versus delayed outcomes

Meta-analysis shows steeper monetary delay discounting on average in ADHD (Jackson & MacKillop, 2016). Delay aversion, however, is conceptually distinct from inaccurate interval timing. One describes preference or avoidance under delay; the other describes temporal representation. A person may estimate time accurately and still find waiting unusually costly, or estimate it poorly without preferring immediacy.

Hyperbolic discounting is often modeled as

$$V(D) = \frac{A}{1 + kD},$$

where A is delayed reward magnitude, D delay, and k discount rate. Higher k means steeper discounting. The model is descriptive; it does not locate a single neural cause.

Delayed goals create a control challenge because their representation must persist without immediate reinforcement. External milestones, visible progress, and proximal feedback can change the effective temporal structure of the task rather than merely exhorting greater effort.

SUPPORTED INTERPRETATION

Temporal discounting and delay aversion can make some useful task states less reachable or less stable.

Boundary. Group differences do not apply uniformly, and discounting depends on task design and reward domain.

102 Effort cost and behavioral vigor

Effort allocation asks whether the expected outcome justifies cognitive or physical cost. Behavioral vigor asks how rapidly and energetically an action policy is executed. These are separable from accuracy and from reward sensitivity.

The ADHD effort literature is smaller and sometimes contradictory. Winter et al. (2019) suggested that children with ADHD may not choose a different effort–reward trade-off so much as struggle to recruit the selected effort. Mitchell and Sevigny-Resetco (2020) emphasized that the relation between ADHD and effort-based decision making remained underdeveloped.

OPEN QUESTION

Is the limiting process altered cost valuation, difficulty mobilizing control after a choice, unreliable persistence once mobilized, or some combination? Different mechanisms predict different responses to incentives, task chunking, and medication.

Lecture consequence. Do not use "motivation" as an explanation that merely renames nonperformance.

103 Novelty and attentional capture

Novel events carry information. They can signal threat, reward, opportunity, or a need to update a model. Reorienting to novelty is adaptive; chronic environments designed to deliver rapid novelty can repeatedly destabilize a weakly anchored task.

A salience-weighting shorthand is

$$S_i(t) = w_r R_i(t) + w_u U_i(t) + w_e E_i(t) + w_g G_i(t),$$

where R is reward relevance, U uncertainty reduction, E emotional significance, and G goal relevance. The weights w are state dependent. An external cue can dominate because it is novel even when it is not aligned with the long-term goal.

SUPPORTED INTERPRETATION

Altered reorienting thresholds, gain, or post-capture stabilization could contribute to distractibility.

Not established. A universal novelty-seeking circuit or direct proof that smartphones create de novo adult ADHD. Rapid-switch environments can fragment attention and amplify symptoms without becoming the developmental disorder's sole cause.

104 Emotional salience

Anger, rejection, shame, anticipation, and threat can rapidly reorganize priorities. Emotional dysregulation is common and impairing in ADHD, but not a diagnostic synonym. Amygdala, insula, medial prefrontal, cingulate, striatal, and autonomic systems interact with cognitive control; the division between "emotion" and "attention" is artificial at the level of network dynamics.

Yang et al. (2021) reported time-varying amygdala-subregion coupling differences with prefrontal and other regions in children with ADHD. Rafi et al. (2025) found that lower salience-centered dynamic connectivity tracked an integrated adolescent ADHD phenotype, whereas greater global metastate variability tracked emotional reactivity.

EMERGING EVIDENCE. Emotion-related circuitry participates in time-varying ADHD network organization.

Boundary. Samples are modest, emotional measures often include self-report, and comorbid anxiety, depression, trauma, or bipolar risk can change the pattern.

105 Interoception and bodily state

The anterior insula integrates signals from the body with uncertainty, salience, and action readiness. Hunger, pain, heart rate, respiratory state, and medication side effects can therefore influence task engagement. Interoceptive signals may stabilize behavior when they accurately mark fatigue or urgency, or compete with the task when bodily discomfort becomes dominant.

SUPPORTED GENERAL MECHANISM. Salience systems integrate internal and external significance (Seeley et al., 2007; Menon & Uddin, 2010).

OPEN ADHD QUESTION. Direct evidence linking interoceptive precision to momentary ADHD task transitions is insufficient. The lecture may present interoception as a candidate moderator, not a demonstrated core mechanism.

This distinction prevents reverse inference: anterior-insula activity does not prove that an interoceptive process caused a lapse.

106 Arousal and locus-coeruleus state

The locus-coeruleus norepinephrine system has been modeled as regulating neural gain and the balance between exploitative task engagement and exploratory reorientation (Aston-Jones & Cohen, 2005). Very low arousal may weaken task representation and sensory responsiveness; excessive tonic arousal may increase distractibility or reduce selectivity. The useful regime is often described by an inverted-U relationship.

If performance P depends on effective gain g, a simple local model is

$$P(g) = P_{\max} - \alpha(g - g^*)^2,$$

where g^* is context-specific optimum. This parabola is an illustration, not a universal law. Different prefrontal operations, developmental stages, and stress levels can have different optima.

Recent large observational and precision-pharmacology work reported that stimulant-associated connectivity related more to arousal, sleep, and reward systems than to canonical attention-network connectivity, though the observational arm cannot establish causality and the dense within-person arm included only five healthy adults (Kay et al., 2025).

SUPPORTED INTERPRETATION

Catecholamine and arousal state can change the gain and stability of task configurations.

107 Sleep, circadian timing, and waking local sleep

Sleep problems are common in children and adults with ADHD, and circadian differences have been documented across systematic reviews (Coogan & McGowan, 2017; Díaz-Román et al., 2018; Becker, 2020; Bondopadhyay et al., 2022; Cortese et al., 2024). Causal direction is complex: ADHD symptoms disrupt routines, delayed schedules restrict sleep, comorbid conditions disturb sleep, and stimulants can affect latency or duration while improved daytime control may help routines.

Sleep pressure can change the same person's network dynamics across the day. Pinggal et al. (2026) linked local sleep-like slow waves during wakefulness to errors, slowing, variability, mind wandering/blanking, and sleepiness in adults with ADHD. This provides one plausible route from bodily state to momentary failure.

ESTABLISHED CLINICAL EVIDENCE. Sleep and circadian problems commonly interact with ADHD and can worsen functioning.

EMERGING NEURAL EVIDENCE. Local waking slow waves may mediate some lapses.

Diagnostic guardrail. Sleep deprivation can cause ADHD-like concentration problems; it does not by itself establish developmental ADHD.

108 Stress and task demand

Stress changes catecholamines, bodily salience, threat monitoring, memory retrieval, and the apparent cost of control. Moderate arousal can sharpen performance in one context; uncontrollable or prolonged stress can destabilize it. Task demand also has multiple dimensions: cognitive load, perceptual load, time pressure, uncertainty, working-memory span, and emotional meaning.

Fisher et al. (2023) found that cognitive and perceptual load had opposing effects on network efficiency and behavioral variability in ADHD. This is an empirical warning against treating "difficulty" as one axis.

SUPPORTED INTERPRETATION

Context can transform performance by changing both the task configuration required and the internal state available to realize it.

Boundary. Stress-related attentional impairment is not diagnostic evidence of ADHD. PTSD, anxiety, depression, sleep loss, and substance effects can produce distinct but overlapping patterns.

109 Incentive-dependent improvement is not proof of voluntary control

Suppose performance improves when incentives are introduced. Three conclusions do **not** follow:

1. baseline impairment was deliberately chosen;
2. the person can reproduce the incentive condition through self-criticism;
3. the improvement generalizes to every task and timescale.

In Liddle et al. (2011), incentive and methylphenidate removed a low-incentive DMN-modulation difference in a small responder-enriched pediatric sample. This demonstrates modifiability, not voluntariness. It also does not prove durable normalization.

The causal chain may involve increased cue salience, reduced delay, stronger expected value, altered catecholamine gain, clearer feedback, or a more stable control configuration. These can be experimentally separated.

CORE SENTENCE State dependence is not evidence of moral choice; it is evidence that performance is conditional.

Figure concept 9A — Same person, different control landscape

Two within-person panels show the same goal under (a) delayed reward, ambiguous steps, sleep loss, and interruption, and (b) proximal feedback, visible steps, adequate sleep, and protected time. Use probability distributions over entry and dwell time, not "bad brain/good brain" cartoons.

110 Hyperfocus as high capture, strong persistence, or impaired release

Hyperfocus lacks a single mature operational definition. Self-report studies find that people with higher ADHD symptoms report more frequent or dispositional hyperfocus, and the Adult Hyperfocus Questionnaire–Dispositional has initial psychometric support (Hupfeld et al., 2019; Groen et al., 2020; Ashinoff & Abu-Akel, 2021; Hupfeld et al., 2024). Convenience samples, self-diagnosis, and retrospective reporting limit causal inference. There is no established neural signature.

Three mechanisms should be distinguished:

- **capture** — unusually high probability of entering a high-salience activity;
- **persistence** — long dwell once engaged;
- **release failure** — difficulty leaving when priorities change.

These need not co-occur. Flow typically includes skill–challenge balance, intrinsic reward, and a sense of effective control. Hyperfocus can be pleasant or costly, productive or maladaptive, and sometimes difficult to interrupt. Perseveration emphasizes inflexibility rather than positive absorption.

PLAUSIBLE REFRAMING. Hyperfocus is consistent with dysregulated allocation and transition of attention rather than absence of capacity.

Not proof. It does not by itself validate a network mechanism or disprove attention deficits measured in other contexts.

Figure concept 9B — Absorption feature space

A triangular or three-dimensional plot uses controllability, value/positive affect, and switching flexibility as axes. Flow, productive deep work, rigid perseveration, and hyperfocus reports occupy overlapping—not categorical—regions. Add a prominent "operational definitions immature" label.

111 Trait liability × state modulation

Let θ represent relatively stable liabilities—development, genetics, learned history, and enduring cognitive traits—and let z_t represent changing states such as arousal, sleep pressure, affect, reward context, and medication. Performance is

$$Y_t = F(\theta, z_t, c_t, u_t) + \epsilon_t,$$

where c_t is task context and u_t the supports or control inputs. The important term may be interaction, not additive deficit:

$$\frac{\partial^2 F}{\partial \theta \, \partial z} \neq 0.$$

The same loss of sleep can have a larger functional effect for one developmental profile; the same incentive can stabilize one task but create overcapture in another. Trait liability shifts probabilities; state and context select among them.

SUPPORTED INTERPRETATION

ADHD is both trait-like and state-dependent. Longitudinal persistence of the syndrome coexists with marked within-person fluctuation.

FLOW HIJACKED SYNTHESIS. A deeper account asks how context deforms the landscape of reachable cognitive configurations: which states become easier to enter, which become more stable, which perturbations gain leverage, and whether adaptive release remains possible.

CORE SENTENCE The contradiction disappears when attention is treated as regulated allocation across time: difficulty entering one state can coexist with excessive persistence in another.

Teaching matrix 9C — Context variables and falsifiable predictions

Context variable	If it mainly affects…	Predicted observation	Evidence status
Proximal reward	entry/value	shorter initiation latency	supported in selected paradigms
Stable feedback	maintenance/learning	longer accurate runs, better policy updating	plausible; task dependent
Novel notifications	unwanted exit	higher capture hazard during weakly anchored tasks	general attention support; ADHD-specific dynamics incomplete
Intrinsic interest	entry plus dwell	rapid engagement and prolonged occupancy	phenomenologically supported; neural evidence sparse
Sleep pressure	state stability	more slow trials, omissions, local slow waves	supported, with recent direct EEG evidence
Emotional threat	salience arbitration	faster reorientation and poorer return	plausible; comorbidity-sensitive
Explicit task chunking	re-entry/goal memory	lower restart cost after interruption	clinically plausible; neural mechanism inferred
Time-of-day alignment	arousal	improved stability at preferred phase	sleep/circadian evidence; individual variation large

The table converts "context matters" from a vague explanation into separable predictions.

112 Cross-part synthesis: from a cast of networks to a conditional trajectory

Parts VI–IX support five conclusions at different evidence levels.

1. **ESTABLISHED EVIDENCE.** Human task performance depends on multiple dissociable large-scale systems. DMN is adaptive; "task positive" is not one anatomical network.
2. **ESTABLISHED SMALL GROUP EFFECTS.** ADHD is associated with small distributed connectivity and activation differences, including DMN–attention coupling, reward anticipation, and systems involved in cognitive control. Effects vary by age, task, medication, and method and do not diagnose individuals.
3. **EMERGING DIRECT EVIDENCE.** Some ADHD samples show altered state occupancy, dwell time, time-varying cross-network interaction, neural flexibility, representational stability, entropy dynamics, or pre-lapse physiology.

4. **SUPPORTED INTERPRETATION.** ADHD can be studied as a disorder of context-appropriate configuration and temporal regulation, not merely lower mean activation.
5. **OPEN / FLOW HIJACKED HYPOTHESIS.** Distinct entry, persistence, unwanted exit, adaptive release, and re-entry hazards may explain heterogeneity and treatment response. This framework requires prospective within-person tests; it is not yet established neuroscience.

Context changes the landscape, not the reality of impairment

Reward, interest, novelty, urgency, emotion, and social consequence can change what is salient, how future value is discounted, and how much effort a task appears to require. These variables reshape the probability of entry and persistence. Their influence is not peculiar to ADHD, but the magnitude, reliability, or cost of the modulation may differ across people and situations.

Hyperfocus is useful only when operationalized. It may describe rapid capture by a highly valued activity, unusually long dwell, reduced awareness of competing needs, difficulty releasing when priorities change, or retrospective loss of time. These components need not covary. A person can be productively absorbed and switch appropriately, or can remain engaged after the activity has ceased to serve the current goal. The clinical question is flexible allocation, not the moral status of intense interest.

This perspective also distinguishes performance from cost. Immediate incentives may normalize accuracy during a brief task while requiring unsustainable arousal, producing rebound fatigue, or failing to generalize to distant goals. Ecological studies should therefore measure not only whether performance improves, but how long the effect lasts, what happens after reward is removed, which competing obligations are displaced, and whether the person gains greater control over both entry and release.

Context changes transition probabilities without abolishing disorder

Motivation does not sit outside cognitive control. Expected value, delay, novelty, social consequence, uncertainty, fatigue, and opportunity cost influence whether a task representation wins access to action and whether it remains worth protecting. Every person is context sensitive. The scientific question is whether particular contexts produce larger, less predictable, or more costly changes in entry and persistence for some people with ADHD.

Immediate reward can improve performance through several routes. It may increase cue salience, reduce the subjective distance to an outcome, increase response vigor, clarify the rule, or supply trial-by-trial feedback. These mechanisms make different predictions after the reward is removed. If performance collapses immediately, the incentive may have stabilized only the current state. If a learned policy persists, reinforcement may have changed the future transition landscape. A brief accuracy improvement cannot distinguish these possibilities.

Urgency is similarly double-edged. An approaching deadline can sharply raise expected cost and compress the action set until entry becomes likely. The resulting performance may be excellent, yet it can depend on stress-level arousal, eliminate opportunities for revision, disrupt sleep, and produce recovery costs afterward. Deadline responsiveness therefore does not show that earlier non-entry was voluntary. It shows that the control landscape changed when the consequences became immediate.

Hyperfocus should be decomposed into capture, dwell, awareness, controllability, and release. Long engagement in a valued task may be productive absorption. It becomes clinically relevant when the person cannot redirect attention after priorities change, loses awareness of bodily or social needs, or repeatedly sacrifices more important delayed goals. These dimensions allow hyperfocus to be studied without romanticizing it or treating every enjoyable period of concentration as pathology.

Sleep and circadian timing alter the same landscape. Insufficient sleep can increase reaction-time variability, weaken inhibition, intensify reward seeking, and reduce prospective memory in people with and without ADHD. Delayed sleep timing and difficulty disengaging from evening activity can then create feedback: impaired regulation worsens sleep behavior, and sleep loss worsens regulation. Assessment and treatment should measure this loop rather than assigning every fluctuation to the diagnosis.

The deeper point is that context dependence and genuine impairment are compatible. A lock that opens only under unusually intense pressure is still unreliable. Treatment can be understood as broadening the range of ordinary conditions under which intended action becomes accessible, while reducing the need for crisis, novelty, or immediate reward. That is a regulation goal, not a demand for constant productivity.

Hyperfocus becomes measurable when release is included

A useful hyperfocus paradigm would offer two engaging activities with changing priority. The first begins with high intrinsic interest and immediate feedback. Later, a cue signals that the second task now carries greater value. The participant can remain, switch, or return. This design separates deep engagement from the capacity to reallocate attention when the goal changes.

Several variables would be recorded. Entry latency measures capture by the preferred task. Dwell time measures persistence. Missed bodily or external cues index perceptual narrowing. Confidence and experience sampling measure awareness. Switch latency after the priority signal measures release, while performance after switching measures whether the task set was reconstructed. A person can score high on one dimension and low on another.

Reward manipulations can test whether the apparent contradiction is really a change in allocation. Immediate incentives for the initially dull task may shorten entry without improving release. Novelty may produce rapid capture that fades with repetition. Social accountability may stabilize dwell. A distant reward may remain weak until its temporal distance is reduced. These patterns implicate different control constraints even when all are described colloquially as motivation.

The experiment must also distinguish flow. Flow usually includes perceived control and an adaptive match between challenge and skill. Hyperfocus reports may include absorption without control, persistence after value has changed, or negative after-cost. The constructs can overlap without being synonymous. Productive creative absorption should not be pathologized merely because it is intense.

An ecological extension could use consented computer activity and brief self-reports over several weeks. The important outcomes would include abandoned obligations, successful switches, sleep displacement, subjective cost, and whether the person endorsed the allocation afterward. Duration alone is insufficient; four hours on a chosen creative project and four hours trapped in an activity after wanting to stop occupy different regions of the outcome space.

Within TSVE, hyperfocus may represent a deep basin for one highly valued configuration combined with high exit cost when priorities change. That is a Flow Hijacked hypothesis, not an established neural finding. It becomes useful only if basin-like parameters predict controllability and functional outcomes better than interest, habit strength, or ordinary task-switch cost.

Reward changes the control problem without abolishing impairment

Suppose a low-interest administrative task becomes urgent, novel, socially consequential, or immediately rewarded. Entry can accelerate because the expected value of acting now rises relative to delay. Salient feedback can reduce uncertainty about progress, while a short deadline compresses an otherwise distant outcome into the present. These changes can stabilize a task representation without implying that the person possessed frictionless voluntary control all along.

The same manipulation may create costs. Urgency can recruit stress, narrow exploration, encourage speed over accuracy, or produce an unsustainable burst followed by exhaustion. Novelty loses value with repetition. External rewards can crowd the environment with competing cues or become impractical to maintain. A mechanism account therefore asks which parameter changed—expected value, effort cost, temporal distance, uncertainty, or arousal—and which outcome improved.

Hyperfocus supplies a complementary test. Long dwell on a highly valued activity shows that persistence is possible under some conditions; it does not show that entry, switching, prioritization, or release are reliable across conditions. The clinically relevant contrast is flexible allocation versus state capture. A strong account must predict both the productive episode and the obligations displaced by it.

In the Flow Hijacked synthesis, reward and salience are candidate deformations of the state landscape, not magic fuel. They may deepen one basin, reduce an entry barrier, amplify a cue, or change transition probabilities. That description is a supported way to formulate experiments, but the particular geometry has not been directly measured in an individual with ADHD. The hypothesis earns status only through prospective prediction.

PART X

DOPAMINE AND NOREPINEPHRINE AS CONTROL PARAMETERS

Give pharmacotherapy a mechanistic substrate without turning a distributed system into a deficiency myth.

Volkow · Arnsten · Aston-Jones · Cools · Bymaster

Purpose and evidentiary boundary

This part builds the molecular and cellular substrate needed to discuss medication without collapsing ADHD into a chemical-deficiency slogan. The central proposition is deliberately narrower than "dopamine causes attention." Dopamine and norepinephrine participate in the regulation of learning, vigor, arousal, value, prefrontal representation, action selection and neural gain. Drugs that alter these systems can reduce ADHD symptoms. Neither fact establishes that ADHD is a unitary state of globally deficient dopamine or norepinephrine.

Throughout this part, five levels must remain separate:

1. **Molecular target engagement:** a drug binds a transporter or receptor.
2. **Cellular or local-circuit effect:** transmitter concentration or membrane dynamics change in a particular tissue.
3. **Large-scale network effect:** distributed coupling, activation, variability or state occupancy changes.
4. **Cognitive effect:** performance changes on a defined operation, under a defined task.
5. **Clinical effect:** symptoms, functioning, safety or quality of life change over a meaningful interval.

An arrow between two levels is an empirical claim only when the study measured both sides under a design capable of linking them. Otherwise it is a translational inference. This rule matters because much of the ADHD story is assembled across species, spatial scales and timescales. The assembly can be scientifically valuable without being mistaken for a single continuous measurement.

Core sentence. Catecholamines are not a fuel gauge for attention. They are context-sensitive control parameters in a distributed, adaptive system.

Evidence labels used in this part

- **Established evidence:** replicated pharmacology, clinical trials or convergent human measurement.
- **Supported interpretation:** a synthesis consistent with multiple evidence streams but not directly measured end-to-end.
- **Plausible mechanism:** usually cross-species or cross-level; useful, but not demonstrated as the explanation of human ADHD.
- **Flow Hijacked hypothesis:** a testable dynamical interpretation introduced by this lecture.
- **Boundary or contradiction:** evidence that constrains the preceding claim.

113 Why "ADHD is low dopamine" is inadequate

The phrase survives because it compresses three true observations into one false certainty. First, dopamine is involved in reward, reinforcement, action and cognitive control. Second, some of the most effective ADHD medications alter dopaminergic signaling. Third, molecular imaging has identified dopamine-related differences in some ADHD samples. The illicit inference is that these observations prove a single, chronic, brain-wide shortage that causes the diagnosis.

They do not. A treatment target is not necessarily a disease lesion. Acetaminophen reducing fever would not show that fever is caused by acetaminophen deficiency. Likewise, blockade of the dopamine transporter can improve performance without demonstrating that pretreatment extracellular dopamine was globally low. A drug may move a nonlinear control system toward a more useful operating regime even when the original perturbation lies elsewhere—in receptor distribution, developmental timing, network topology, arousal, learned policy, sleep, reward contingencies or their interaction.

"Dopamine level" is itself underspecified. Relevant quantities include synthesis capacity, vesicular stores, release probability, tonic extracellular concentration, event-linked transients, transporter density, transporter occupancy, receptor availability, receptor affinity state, downstream signaling, regional innervation, and the sensitivity of the network receiving the signal. A higher concentration in one compartment can coexist with lower effective signaling in another. PET binding potential is not a direct beaker measurement of synaptic transmitter. It depends on ligand kinetics, receptor or transporter availability, competition, blood flow, modeling assumptions and the temporal relation to medication.

ADHD is also heterogeneous and developmental. Group means do not specify every individual, and a childhood phenotype cannot be assumed to share the same molecular operating point as persistent adult ADHD. Sex, prior treatment, genotype, comorbidity, sleep, recent reward and stress can moderate catecholamine response. In healthy adults, methylphenidate-evoked ventral-striatal dopamine increases differed by sex, directly warning against universalizing male-dominated imaging results (Manza et al., 2022; doi:10.1038/s41380-021-01294-9; PMID 34707237).

The scientifically defensible replacement is therefore: **catecholaminergic signaling is one important modulator of ADHD-relevant control, reward and arousal processes; its causal contribution is regional, temporally structured, developmentally contingent and heterogeneous.** That statement is less memorable than "low dopamine," but it can survive contact with the data.

114 Dopamine synthesis, release, reuptake and metabolism

Dopamine synthesis begins with the amino acid tyrosine. Tyrosine hydroxylase converts tyrosine to L-3,4-dihydroxyphenylalanine (L-DOPA), the rate-limiting step under many conditions. Aromatic L-amino-acid decarboxylase converts L-DOPA to dopamine. Vesicular monoamine transporter 2 (VMAT2) packages cytosolic dopamine into vesicles, protecting it from metabolism and positioning it for activity-dependent exocytosis. Following release, dopamine can bind receptors, diffuse beyond a classical synaptic cleft, undergo transporter-mediated uptake, or be metabolized through monoamine oxidase and catechol-O-methyltransferase pathways.

A minimal extracellular mass-balance model is

$$\frac{dD_e}{dt} = R_D(t) - \frac{V_{\max,D} D_e}{K_{m,D} + D_e} - k_{\text{loss}} D_e,$$

where D_e is extracellular dopamine concentration, $R_D(t)$ is release, the Michaelis–Menten term approximates saturable transporter clearance, and k_{loss} collects diffusion and nonsaturable loss. This is a teaching model, not a patient-specific equation. It shows why the same extracellular concentration can result from increased release, reduced uptake, altered transporter capacity, or multiple simultaneous changes. It also shows why transporter blockade has nonlinear effects: the change depends on the baseline relation among D_e, K_m, release and regional transporter abundance.

Release is temporally structured. Midbrain cells may show changes in average firing and event-linked burst firing; terminal release is additionally shaped by local receptors, acetylcholine, glutamate, reuptake and terminal architecture. “A dopamine burst” is therefore not an indivisible broadcast. It is a distributed event whose amplitude and meaning vary across projections and target regions.

No robust body of evidence establishes one globally reduced dopamine synthesis rate as the defining lesion of ADHD. Molecular findings vary by sample, medication history, age and analytic approach. The clinically important conclusion is not agnosticism about dopamine; it is precision about what was measured.

115 DAT and regional transporter differences

The dopamine transporter (DAT) clears extracellular dopamine especially strongly in striatum. Therapeutic oral methylphenidate produces substantial striatal DAT occupancy in humans, and PET work showed increased extracellular dopamine at therapeutic exposure (Volkow et al., 1998, doi:10.1176/ajp.155.10.1325, PMID 9766762; Volkow et al., 2001, doi:10.1523/JNEUROSCI.21-02-J0001.2001, PMID 11160455). These are foundational target-engagement results. They show what methylphenidate can do. They do not show that every untreated person with ADHD has excessive DAT function or low basal dopamine.

In a simple one-site occupancy model,

$$O(C) = \frac{C}{C + K_d},$$

where O is the fraction occupied, C is free drug concentration at the target, and K_d is an equilibrium dissociation constant. The model clarifies two points. First, dose and occupancy are not linearly related. Second, identical oral doses need not produce identical brain concentration or occupancy because absorption, metabolism, formulation, body size, timing and interacting drugs differ. Real transporter pharmacology is more complicated than this equilibrium expression, especially for transporter substrates such as amphetamine.

Regional anatomy changes the meaning of uptake. In prefrontal cortex, DAT density is lower than in striatum, and the norepinephrine transporter contributes materially to dopamine clearance. A selective NET inhibitor can therefore increase prefrontal dopamine while producing much less striatal dopaminergic effect than a DAT-engaging stimulant. The phrase “raises dopamine” does not make two drugs pharmacologically interchangeable.

Long-term exposure may also alter the target. In a small, open, nonrandomized 12-month study, methylphenidate treatment was associated with an approximately 24% increase in striatal DAT availability; the authors proposed compensatory up-regulation (Wang et al., 2013; doi:10.1371/journal.pone.0063023; PMID 23696790). The functional consequence was not established, and binding interpretation after chronic exposure is difficult. Yet the result is a decisive conceptual warning: a molecule’s acute action and the system’s adaptation to repeated exposure are different objects of study.

116 D1-like and D2-like receptor families

Dopamine receptors are commonly grouped into D1-like receptors, principally D1 and D5, and D2-like receptors, including D2, D3 and D4. The families differ in G-protein coupling, cellular location, affinity, distribution and downstream effects. "Dopamine activation" therefore has no single sign. It can stabilize one ensemble, inhibit another, alter plasticity, change the threshold for action or reshape how value affects control.

Moderate D1 receptor stimulation in prefrontal circuits can sharpen persistent representations by reducing irrelevant activity and strengthening task-relevant recurrent organization. Too little D1 signaling may leave representations weak; too much may overconstrain the circuit or suppress information needed for flexible updating. This cellular literature, strongly associated with Arnsten and colleagues, is a mechanistic foundation for the inverted-U principle. Much of its most precise evidence comes from animal neurophysiology and pharmacology, not direct receptor manipulation in humans with ADHD. It is therefore a plausible bridge, not a measured diagnosis-wide cellular lesion.

D2-family signaling is prominent in striatal learning, action selection and motivational processes, but the receptor family spans presynaptic autoreceptors and postsynaptic populations with different roles. D2 availability in molecular imaging is a compound signal, not a direct measure of "motivation." In healthy-human PET-fMRI work, individual response to methylphenidate depended more on baseline D1:D2/3 availability than on the magnitude of evoked dopamine release, and cortical activation changes tracked performance (Manza et al., 2025; doi:10.1073/pnas.2423785122; PMID 40127280). This does not prove the same mechanism in ADHD, but it falsifies the simplest dose-to-dopamine-to-benefit chain.

Receptor-level heterogeneity helps explain why the same drug can improve one person, do little for another, or produce overactivation in a third. It does not authorize receptor genotyping or PET as routine treatment selection tools. The current evidence is mechanistic and group-level, not a validated clinical dosing algorithm.

117 Mesocortical, mesolimbic and nigrostriatal pathways

Three pathway labels organize discussion but should not be mistaken for sealed pipes.

The **mesocortical system**, broadly referring to midbrain projections to prefrontal and association cortex, participates in working memory, rule maintenance, cognitive effort and flexible control. A catecholamine intervention can alter the stability of a task representation without simply increasing mean prefrontal activation. Efficient performance may require either greater recruitment or lower activation, depending on baseline state and strategy.

The **mesolimbic system**, including projections to ventral striatum and related limbic structures, contributes to reward prediction, incentive salience, learning and behavioral vigor. ADHD reward findings are not uniform: anticipation, receipt, omission and delay can differ, and comorbidity or medication history matters. The clinically recognizable phenomenon—attention becoming more available when consequences are immediate, novel or intrinsically meaningful—can be described without accusing the person of choosing not to care. Reward changes the control problem itself.

The **nigrostriatal system**, especially projections from substantia nigra to dorsal striatum, is central to motor and action selection, sequencing and habit-related processes. It matters because ADHD includes not only cognitive reports but altered response timing, motor activity and action regulation. It also matters to stimulant pharmacology because striatal DAT engagement is substantial. Yet ADHD is not a focal nigrostriatal lesion, and motor improvement is not a complete account of therapeutic benefit.

These systems interact with cortex, thalamus, cerebellum, hippocampus and brainstem. A lecture that treats dopamine as "the reward chemical" omits action and learning; one that treats it as "the focus chemical" omits timing, salience and state. The more accurate statement is that dopaminergic projections alter the probability, precision and persistence of distributed computations.

118 Tonic and phasic signaling

The tonic–phasic distinction is useful if handled as a model rather than a literal two-fluid theory. Tonic dopamine refers to a slower background operating condition; phasic signaling refers to event-linked changes, often associated with bursts or pauses. The two interact: tonic state can affect autoreceptors and the relative impact of a transient, while environmental uncertainty and reward history affect event-linked responses.

In reinforcement-learning notation, a temporal-difference prediction error is

$$\delta_t = r_t + \gamma V(s_{t+1}) - V(s_t),$$

where r_t is obtained reward, $V(s_t)$ is expected future value in state s_t, and $\gamma \in [0, 1]$ discounts delayed value. Midbrain dopamine activity has been linked to quantities resembling δ_t in defined paradigms. Dopamine is not identical to this scalar.

Neural responses also reflect movement, novelty, sensory features, motivational state and heterogeneity across cells and projections. The equation is a computational lens, not a biomarker definition.

ADHD-relevant hypotheses include altered encoding of delayed consequences, noisier value updates, reduced vigor for low-immediacy actions, or excessive capture by salient alternatives. Human studies rarely measure tonic and phasic dopamine directly while also estimating large-scale network states and real-world task persistence. Claims that ADHD is a "tonic dopamine deficit with compensatory phasic bursts" should therefore be identified as theory unless directly supported in the population and task at issue.

What the model contributes is temporal precision. A person can have adequate capacity and still show unstable allocation because the value landscape and state transitions change from moment to moment. Medication may alter learning rate, value sensitivity, action vigor or the neural gain through which events influence control. These alternatives make different predictions and should not be merged.

119 Reward prediction, vigor and learning

Reward is not a bribe appended to cognition; it is one of the variables through which organisms allocate effort. Expected benefit, delay, uncertainty, opportunity cost and effort cost contribute to whether a control policy is initiated and sustained. A simplified net action value can be written

$$Q(a,s) = \mathbb{E}\left[\sum_{k=0}^{\infty} \gamma^k r_{t+k} \mid s_t = s, a_t = a\right] - \kappa E(a,s),$$

where $E(a,s)$ is expected effort and κ is its subjective cost. This does not claim that the brain literally subtracts two numbers in one nucleus. It makes explicit why delay, fatigue, uncertainty and task friction can change engagement even when intellectual ability is unchanged.

Dopamine has been implicated in reinforcement learning and vigor, while norepinephrine influences arousal, uncertainty and responsiveness. ADHD research reports altered delay discounting and reward anticipation on average, but neither finding is universal or diagnostically specific. Reward can improve performance in ADHD, sometimes reducing group differences, but incentive-dependent improvement is not proof of voluntary control. It shows that the system is condition-sensitive.

Medication can change reward processing without producing a generic increase in desire. Three-month OROS methylphenidate treatment increased nucleus-accumbens and thalamic activation during low-reward processing toward control levels in one small pediatric study; the effect was selective to low reward (Mizuno et al., 2013; doi:10.1016/j.nicl.2013.03.004; PMID 24179790). In a preliminary adult crossover study, clinical improvement with lisdexamfetamine covaried with increased activation across reinforcement-learning regions rather than with generic cortical suppression (Newcorn et al., 2024; doi:10.1016/j.jpsychires.2023.11.037; PMID 38101205). These findings support a reward-sensitive mechanism while resisting a one-network explanation.

120 Locus coeruleus norepinephrine

Most forebrain norepinephrine arises from the locus coeruleus (LC), a compact brainstem nucleus with broad projections. LC activity has been modeled as operating in modes: lower tonic activity with task-linked phasic responses can support exploitation of a current policy; higher tonic activity with diminished task-linked selectivity may accompany scanning, distractibility or exploration. The Aston-Jones and Cohen framework is influential because it links arousal, utility and behavioral flexibility (2005; doi:10.1146/annurev.neuro.28.061604.135709; PMID 16022602). Human ADHD-specific LC measurement remains limited, so it should be used as a constrained systems hypothesis.

Norepinephrine can change response gain. Let a neural population transform input h through

$$y = \sigma(g(h - \vartheta)),$$

where σ is a saturating nonlinearity, g is gain, and ϑ is threshold. Increasing g makes the response more discriminating around threshold, but it can also amplify irrelevant inputs or saturate the system. If the currently selected representation is task-relevant, higher gain may stabilize control; if salience has already been captured by an irrelevant event, the same gain can deepen the wrong state.

This is why "more norepinephrine improves focus" is no better than the low-dopamine slogan. The relation depends on tonic arousal, receptor recruitment, region and task. LC-norepinephrine may contribute to wakefulness, response to novelty, interruptibility and the decision to remain with or leave a task. A strong test would measure LC-sensitive physiology, time-

varying network configuration, perturbations and behavior in the same experiment. Much current clinical reasoning infers across these levels.

121 Alpha-2A signaling in prefrontal microcircuits

Postsynaptic alpha-2A adrenergic receptors provide one of the clearest cellular mechanisms relevant to ADHD treatment. In primate prefrontal cortex, alpha-2A stimulation can inhibit cyclic-AMP signaling and close hyperpolarization-activated cyclic-nucleotide-gated (HCN) channels near recurrent network synapses. The result can strengthen persistent firing that maintains a goal across delay. Wang and colleagues demonstrated this cAMP–HCN mechanism in prefrontal working-memory networks (Cell, 2007; doi:10.1016/j.cell.2007.03.015; PMID 17448997).

A stylized membrane-current term is

$$I_{\mathrm{HCN}} = \bar{g}_{\mathrm{HCN}}\, m(cAMP, V)(V - E_{\mathrm{HCN}}),$$

where $\bar{g}_{\mathrm{HCN}}$ is maximal conductance, m describes channel opening as a function of cyclic AMP and voltage, and E_{HCN} is the reversal potential. Alpha-2A signaling reduces cAMP-dependent channel opening; in the relevant dendritic microdomains, this can reduce shunting and strengthen network connectivity. The equation is schematic and omits compartmental detail.

Guanfacine is relatively selective for alpha-2A receptors. It does not treat ADHD by "adding norepinephrine." It acts as a receptor agonist while also lowering aspects of sympathetic output. This distinction explains why guanfacine can strengthen some forms of regulation while causing sedation, bradycardia or hypotension. The same person may show improved impulse control and reduced wakeful throughput.

The translation boundary is essential. Strong cellular evidence does not establish that guanfacine repairs a named large-scale network or normalizes state switching in every child. Direct ADHD network evidence remains sparse. The cellular model is a biologically grounded mechanism; the whole-brain claim is still to be tested.

122 Alpha-1 and beta signaling under stress

Receptor affinity creates state dependence. At moderate norepinephrine levels, higher-affinity alpha-2A signaling can support prefrontal representation. Under high stress or arousal, recruitment of lower-affinity alpha-1 and beta receptors can weaken prefrontal control and favor rapid, habitual or salience-driven responding. Dopamine can show a comparable nonlinear relation through D1-dependent effects.

This literature explains why a medication that helps on one day may feel excessive on another, why sleep loss and acute stress can change performance, and why anxiety-related concentration problems cannot be diagnosed as ADHD from concentration alone. It also gives a mechanistic reason to reject dose escalation as a monotonic strategy.

A local quadratic approximation to performance around an optimum is

$$P(z) \approx P(z^*) - \frac{q}{2}(z - z^*)^2, \qquad q > 0,$$

where z is an effective catecholamine–arousal coordinate and z^* is task- and person-dependent. The expression is not a clinical dose curve. Drug dose maps to brain exposure nonlinearly; brain exposure maps differently to dopamine and norepinephrine across regions; performance aggregates multiple operations. The equation says only that deviation on either side of a local optimum can be costly.

Stress may move the operating point before medication is taken. A fixed exposure Δz can improve performance if $z < z^*$ and impair it if $z > z^*$. Baseline dependence is thus not noise around the treatment effect. It is part of the treatment effect.

123 Catecholamines, signal-to-noise and gain control

"Signal-to-noise" is often invoked as though signal and noise were objectively labeled inputs. In a brain, relevance depends on task and context. A spontaneous memory is noise during proofreading, signal during autobiographical planning, and perhaps a warning during danger. Catecholamines can alter the gain, persistence and competition of representations; they do not carry a universal relevance tag.

For a linearized local circuit,

$$\dot{\mathbf{x}} = A\mathbf{x} + B\mathbf{u} + \eta, \qquad \mathbf{y} = C\mathbf{x},$$

where $\mathbf{x}$ is neural state, $\mathbf{u}$ is task input, and η is endogenous and exogenous perturbation. A pharmacological intervention can change effective coupling A, input gain B, noise covariance Σ_η, or readout C. Saying "the drug increases signal-to-noise" fails to identify which of these changed. It also ignores nonlinear saturation and state-dependent network topology.

Supported interpretation: moderate catecholaminergic modulation can improve the fidelity and stability of task-relevant prefrontal representations and the motivational value of completing actions. Direct evidence: stimulants improve average reaction-time consistency and core symptoms, and some imaging studies show changes in activation or connectivity. Remaining gap: few human ADHD studies simultaneously measure molecular engagement, network dynamics and behavior with adequate power.

The slogan "norepinephrine increases signal while dopamine reduces noise" is anatomically too clean. Both transmitters have multiple receptors, interact within prefrontal cortex, and influence distributed systems. The useful concept is dynamic gain, not a one-transmitter/one-function dictionary.

124 Inverted-U and state-dependent effects

The inverted-U is a family of relationships, not one universal curve. Different cognitive operations have different optima. The catecholamine state that supports stable maintenance may impair flexible updating; the state that increases response speed may increase impulsive errors; the state that supports wakefulness may hinder sleep. A person's optimum changes with task load, time of day, sleep debt, stress, menstrual cycle, food, concurrent medication and learned skill. The influential synthesis by Cools and D'Esposito formalized why both depletion and excess can impair prefrontal cognition and why baseline state matters (2011; doi:10.1016/j.biopsych.2011.03.028; PMID 21531388).

If treatment effect on an outcome j is written

$$\Delta Y_j = P_j(z_0 + \Delta z(d,t)) - P_j(z_0),$$

then z_0 is baseline state, d dose, t time since dose, and P_j the operation-specific performance function. Two people with the same diagnosis and plasma exposure can have opposite ΔY_j because z_0, z_j^* or network sensitivity differs. The function may also be asymmetric: overshooting can be more costly than undershooting, or vice versa.

Dose–response meta-analysis estimates average curves across heterogeneous trials. In the 2026 systematic review and dose-effect network meta-analysis, pooled efficacy appeared to plateau at particular dose ranges for several classes, but uncertainty widened at high doses and the result was not an individualized target (Nourredine et al., 2026; doi:10.1016/S2215-0366(26)00091-X; PMID 42134365). A population plateau neither tells a clinician the optimal dose for one patient nor proves the cellular inverted-U mechanism.

125 Molecular mechanism does not establish disorder cause

A causal explanation of a disorder must account for why symptoms develop, persist, vary with context and cluster with other features. A drug mechanism answers a different question: under a defined exposure, what target is engaged and what downstream changes follow? Treatment can act downstream of multiple causal pathways.

The distinction can be formalized with a causal graph. Let G denote developmental liability, E environment and experience, N network organization, S symptoms, D drug exposure and M molecular target engagement. A plausible graph contains $G, E \to N \to S$ and $D \to M \to N \to S$. Observing that changing D changes S through M does not identify whether G or E originally altered M. A downstream control point can be therapeutically powerful without being the etiological origin.

This is especially important for public narratives. If medication helps, that does not prove a congenital shortage. If medication does not help, that does not disprove ADHD. Response is influenced by dose, formulation, adherence, measurement, comorbidity, outcome chosen, baseline state and the possibility that a different intervention target is needed.

126 Molecular-to-network translation: measured versus inferred

The bridge from molecule to network should be drawn with graded line styles.

Bridge	What is measured	What remains inferred	Confidence
Oral methylphenidate → striatal DAT occupancy	Drug exposure and PET transporter binding	Exact synaptic time course in each network	High for target engagement; lower for network translation
Methylphenidate → extracellular dopamine	PET displacement under defined conditions	Regional cellular source and individual clinical mediation	Moderate-to-high for human striatal effect
Atomoxetine → PFC dopamine	Microdialysis in animal PFC	Equivalent magnitude and clinical mediation in human ADHD	Strong preclinical; indirect clinical bridge
Guanfacine → cAMP–HCN closure	Cellular/primate prefrontal physiology	Large-scale state switching in treated ADHD	Strong local mechanism; sparse whole-brain evidence
Medication → DMN/FPN change	fMRI activation/connectivity in small studies	Catecholamine-specific causal path and durability	Limited-to-moderate, heterogeneous

Bridge	What is measured	What remains inferred	Confidence
Medication → symptom reduction	Randomized clinical ratings	Complete recovery or durable real-world function	Strong short-term; incomplete long-term

The most informative future designs will be multilevel: pharmacokinetic sampling, PET or molecular proxies, high-reliability dynamic imaging, computational task measures, ecological behavior and longitudinal function. Until then, mechanistic stories should show where one study ends and another begins.

Part X synthesis. Dopamine and norepinephrine help set the gain, stability, value sensitivity and interruptibility of cognitive states. ADHD is not established as a global deficit of either transmitter. The clinical problem is better framed as heterogeneous catecholamine-sensitive regulation embedded in development, networks and context.

Catecholamines regulate operating conditions

Dopamine and norepinephrine do not carry one psychological meaning. Their effects depend on receptor family, concentration, region, cell type, firing mode, transporter density, baseline state, and task demand. In prefrontal circuits, catecholamines can alter recurrent stability, distractor resistance, gain, and working-memory updating. In striatal and midbrain systems, they contribute to learning, vigor, prediction error, action selection, and sensitivity to delay. These functions overlap but are not reducible to a single quantity.

The inverted-U metaphor is helpful only as a local approximation. The optimum for maintaining a rule may differ from the optimum for flexible updating; the same dose or arousal state can improve one operation while impairing another. A population mean can therefore hide baseline-dependent and task-dependent responses. Tonic and phasic signaling are also conceptual distinctions whose measurement in humans is indirect and method-specific.

“Low dopamine” compresses this complexity into a misleading global deficit. ADHD evidence supports catecholaminergic involvement and the efficacy of drugs that alter dopamine and norepinephrine signaling. It does not establish that every person has uniformly low brain dopamine, that dopamine explains the full phenotype, or that a beneficial drug response proves etiology. Molecular engagement changes control conditions; it does not identify a single cause.

Catecholamines alter operating regimes, not a single fuel gauge

Dopamine and norepinephrine affect cognition through receptor-specific, region-specific, and time-dependent mechanisms. Dopamine synthesis, vesicular storage, release, reuptake, and degradation form one layer; receptor distribution and intracellular signaling form another; circuit state, baseline arousal, and task demand determine what the molecular change does. A drug can raise extracellular catecholamine availability without producing a uniform increase in signaling across every synapse or psychological function.

In prefrontal cortex, moderate catecholamine signaling can strengthen task-relevant recurrent activity and reduce the influence of distractors. Alpha-2A adrenergic actions and D1-family dopamine actions are often used to explain this stabilization, but the relationship is not monotonic. Too little modulation can leave representations weak; too much can reduce flexibility, impair working memory, or favor stress-related response modes. The familiar inverted U is therefore a family of local response surfaces, not one universal curve for an entire person.

The locus coeruleus adds a temporal dimension. Tonic and phasic norepinephrine have been linked to arousal, gain, uncertainty, orienting, and exploration-exploitation balance. Human measures such as pupil diameter are indirect and multiply determined, while fMRI cannot resolve every firing mode. It is useful to ask whether a treatment changes gain or state switching, but those terms must be tied to a measurement rather than inferred from the drug’s known target.

In striatal systems, dopamine contributes to prediction error, learning, action selection, vigor, and the weighting of delayed outcomes. Ventral and dorsal striatal territories participate in different loops, and D1- and D2-family receptors do not simply encode “more” and “less” motivation. Mesocortical, mesolimbic, and nigrostriatal pathways overlap anatomically and functionally; they should not be converted into separate pipes carrying cognition, pleasure, and movement.

Tonic-versus-phasic language is likewise useful but easy to overstate. PET can index aspects of receptor availability, synthesis capacity, transporter binding, or displacement under particular protocols; it does not provide a continuous meter of synaptic dopamine during ordinary life. Peripheral catecholamine values do not report regional brain signaling. Genetic variants and transporter measures can influence hypotheses without assigning a fixed neurotransmitter level to an individual.

This is why “ADHD is low dopamine” fails as a causal statement. The evidence supports catecholaminergic involvement, distributed developmental liability, and clinical benefit from several drugs that alter dopamine and/or norepinephrine signaling. It does not establish a global dopamine deficit shared by every person, a unique molecular lesion, or a diagnostic test. Response to a stimulant shows that changing the system can improve symptoms; it does not prove that the untreated

system lacked one chemical quantity.

The network bridge must be empirical. Catecholamine modulation could plausibly alter signal-to-noise ratio, control-state stability, salience weighting, learning, and perturbation sensitivity. Yet a molecular mechanism does not automatically identify the network mediator, and an imaging change does not automatically mediate improvement. Studies need exposure measures, task timing, behavioral outcomes, and preferably within-person dose or treatment contrasts to connect these levels.

Clinically, the same multilevel view explains heterogeneity without mystification. Baseline state, dose, formulation, metabolism, sleep, comorbidity, and task can shift the balance between stabilization and rigidity, calm and sedation, or improved initiation and excessive persistence. The objective is not maximal catecholamine action. It is a tolerable operating regime that improves meaningful function.

From dose to behavior through a state-dependent response surface

A dose is not a direct coordinate of cognition. It determines a time-varying exposure shaped by formulation, absorption, metabolism, body state, and adherence. Exposure then interacts with baseline catecholamine tone, receptor distribution, arousal, and task. The resulting surface may improve one operation while leaving another unchanged or impairing it. A single “optimal dose” therefore has meaning only relative to defined outcomes and times.

Consider maintenance and updating. Stronger recurrent stability can protect a goal against distraction, yet excessive stability can make it harder to replace an obsolete rule. The preferred operating point for sustained proofreading may differ from that for flexible problem solving. If a trial averages both epochs, a real improvement and a real cost can cancel. Dose-response work should separate the operations before describing a global cognitive benefit.

The same applies across regions. A given plasma exposure does not imply equal catecholamine change in prefrontal cortex and striatum. Transporter density, local clearance, receptor occupancy, and circuit activity differ. Atomoxetine’s cortical dopamine effect through norepinephrine-transporter blockade is not the same mechanism as amphetamine-mediated release; alpha-2A agonism changes signaling without reproducing stimulant pharmacology.

Baseline dependence is more than a statistical nuisance. Sleep deprivation, anxiety, stress, prior medication, and genetic or metabolic variation can move the starting point on the response surface. A group-average improvement may contain strong benefit, no change, and adverse response. Within-person titration with repeated functional measures is therefore more informative clinically than assuming a population mean identifies an individual’s optimum.

Mechanistic studies could estimate exposure rather than nominal dose, sample several task operations, and model nonlinear interaction with baseline state. The result would not be “dopamine rose and attention improved,” but a conditional map: under this exposure and context, this operation changed with this uncertainty. That is the level at which molecular pharmacology can meet network dynamics without reductionism.

The safety surface belongs in the same model. Appetite, sleep, cardiovascular measures, anxiety, irritability, mood activation, and rare psychiatric events may have different dose and time relations from symptom benefit. Optimization is constrained: the preferred regime maximizes meaningful function subject to tolerability and risk, not catecholamine action itself.

Catecholamines tune several operations at once

Regional baseline, receptor engagement, release dynamics, task demand, and arousal jointly determine the effect of a catecholaminergic change. The same exposure can improve resistance to distraction while leaving temporal planning unchanged, or strengthen maintenance while making flexible updating harder. “More dopamine” therefore predicts too little. A mechanistic claim should specify transmitter, receptor or transporter, region, time scale, cognitive operation, and the range over which benefit is expected.

PART XI

PHARMACOLOGICAL TREATMENT —

DISTINCT MOLECULES, DISTINCT TIMESCALES

Present medication as a family of multilevel interventions, not a single stimulant story.

Cortese · Faraone · Volkow · MTA · Moran

127 How to read medication evidence

Medication evidence answers different questions at different levels. A placebo-controlled trial can estimate average short-term symptom change under trial conditions. It cannot, by itself, establish long-term safety, school performance, occupational stability, relationships or neurodevelopmental normalization. A register study can examine rare or long-duration outcomes in large populations, but treatment is not randomly assigned; severity, access, adherence, discontinuation and health behavior can confound the association. A brain-imaging study can identify an acute physiological shift, usually in tens rather than thousands of participants, but cannot automatically explain the clinical effect.

Five coordinates should accompany every efficacy number:

$$\mathcal{E} = (\text{population}, \text{rater}, \text{comparator}, \text{duration}, \text{outcome}).$$

A standardized mean difference in clinician-rated symptoms after 12 weeks in adults is not equivalent to a teacher-rated result in children, a six-month functional outcome, or an individual probability of response. In Cortese and colleagues' landmark network meta-analysis, clinician-rated estimates near 12 weeks favored multiple agents, with age-dependent comparative patterns (Lancet Psychiatry, 2018; doi:10.1016/S2215-0366(18)30269-4; PMID 30097390). Those estimates remain major anchors, but they inherit heterogeneity in trial design, sponsorship, rating and dose.

The 2026 dose-effect network meta-analysis by Nourredine, Cortese and colleagues adds current pooled dose–response information (doi:10.1016/S2215-0366(26)00091-X; PMID 42134365). A pooled plateau is not a prescription. Individual titration seeks the lowest exposure that produces meaningful benefit with tolerable cost, judged across the day and across outcome layers.

The outcome hierarchy is:

Layer	Example	Why symptom response is insufficient
Core symptoms	inattention, hyperactivity, impulsivity	ratings may improve before function changes
Cognitive operations	inhibition, working memory, temporal consistency	laboratory gains are task-specific
Self-management	initiation, planning, persistence, returning after interruption	often requires learned strategies and environmental support
Function	school, work, driving, relationships	affected by opportunity, habits and comorbidity
Well-being	distress, self-esteem, sleep, quality of life	can improve, worsen or remain dissociated from symptom score
Long-term risk	injury, substance-related events, cardiovascular health	requires long observation and causal caution

This lecture is educational, not a prescribing guide. Medication selection, dosing, monitoring, contraindications and discontinuation require an appropriately licensed clinician using the current jurisdiction-specific product information and guideline.

Response, remission and number-needed-to-treat

"Response rate" is not a molecule's fixed property. Trials define response using different percentage reductions, absolute rating thresholds, clinician global-improvement scores, informants and time points. If response is defined as at least a proportion q of symptom reduction, participant i is classified by

$$R_i(q) = \mathbf{1}\left(\frac{S_{i0} - S_{i1}}{S_{i0}} \geq q \right),$$

where S_{i0} and S_{i1} are baseline and endpoint scores. A person with severe residual impairment may meet a 30% or 50% reduction criterion, while a person with lower baseline severity can fail the percentage rule despite becoming minimally symptomatic. Dichotomization also discards dose–response information and magnifies measurement error near the threshold.

Remission is stricter but equally definition-dependent: it may require a score below a cutoff, loss of diagnostic criteria, or minimal symptoms plus functioning. Symptomatic remission does not guarantee restored organization, relationships, sleep or self-esteem. Conversely, meaningful functional improvement can occur without full symptom remission when the treatment reduces the most disruptive bottleneck.

The number needed to treat is

$$NNT = \frac{1}{p_{\text{active}} - p_{\text{control}}},$$

for a particular binary outcome and interval. It changes with placebo response, population severity, rater and response definition. It should never be detached from those coordinates. The number needed to harm has the same dependence and becomes unstable for rare events in short trials.

Sequential clinical trials of medication also differ from a one-shot RCT comparison. If estimated response probabilities to two classes are p_M and p_A, and response failures are not perfectly correlated, the probability of responding to at least one is

$$1 - (1 - p_M)(1 - p_A),$$

under the simplifying—and usually false—assumption of independence. The expression nevertheless illustrates why a second supervised class trial can help some people who do not respond to the first. It does not estimate actual individual probability because responses share biological and measurement determinants.

Finally, completer response rates can overstate effectiveness. Let $D_i = 1$ denote remaining in treatment. Reporting $\Pr(R = 1 \mid D = 1)$ answers a selected-tolerator question, not $\Pr(R = 1)$ among all starters. Intention-to-treat analyses, discontinuation, adherence and missing-data assumptions must accompany response claims.

128 Methylphenidate: DAT/NET blockade

Methylphenidate is principally a dopamine- and norepinephrine-transporter blocker. It inhibits reuptake; it is not a classic transporter substrate that drives monoamine release in the manner of amphetamine. Human PET demonstrates substantial DAT occupancy and increased extracellular dopamine at therapeutic oral doses (Volkow et al., 1998, PMID 9766762; Volkow et al., 2001, PMID 11160455). A 2026 longitudinal dual-tracer PET study in adults with ADHD also demonstrated DAT engagement in caudate/putamen and NET engagement in thalamus/pons during extended-release treatment (Oya et al., doi:10.1111/pcn.13911; PMID 41128391). Only twelve participants completed the longitudinal molecular comparison; binding changes did not correlate with cognitive improvement. Target engagement was direct; clinical mediation was not.

On average, methylphenidate reduces core symptoms and improves aspects of sustained attention, response inhibition and reaction-time consistency. In the 2018 network meta-analysis, clinician-rated standardized mean differences versus placebo were approximately -0.78 in children/adolescents and -0.49 in adults near 12 weeks. The sign reflects lower symptom scores. These are group effects, not probabilities that a given person will respond. The 2025 Cochrane update continued to find benefit in children and adolescents while emphasizing limitations in trial certainty and adverse-event evidence (Storebø et al., doi:10.1002/14651858.CD009885.pub4; PMID 41342306).

Immediate- and extended-release formulations produce different concentration–time curves. A useful exposure model is

$$C(t) = \sum_{k=1}^{K} \frac{F_k D_k k_{a,k}}{V(k_{a,k} - k_e)} \left(e^{-k_e(t-t_k)} - e^{-k_{a,k}(t-t_k)}\right) \mathbf{1}_{t \geq t_k},$$

where each release component k has bioavailable dose $F_k D_k$, absorption rate $k_{a,k}$, elimination rate k_e, volume V, and release time t_k. Real formulations can involve osmotic, bead, multilayer or transdermal delivery and need not follow this exact model. The equation demonstrates why equal total milligrams can yield different onset, peak, duration and rebound.

Common adverse effects include decreased appetite, weight loss, insomnia or delayed sleep, headache, abdominal symptoms, irritability and small average increases in pulse or blood pressure. Rare psychotic or manic symptoms and peripheral vasculopathy warnings matter despite low absolute incidence. Pediatric monitoring includes growth, appetite and sleep; adult monitoring includes the same domains plus cardiovascular and psychiatric context.

Long-term evidence is less definitive than acute efficacy. Trial completion over weeks is not real-world persistence over years. Growth findings, discontinuation, cumulative exposure and functional outcomes remain active evidence problems. A treatment may be highly effective when taken and still fail in practice because coverage, adverse effects, stigma, access, forgetting, or the person's priorities make sustained use difficult.

129 Dexmethylphenidate and formulation differences

Dexmethylphenidate is the pharmacologically active d-threo enantiomer of racemic methylphenidate. It inhibits DAT and NET through the methylphenidate-class mechanism. Greater potency per milligram is a statement about stereochemistry and dose conversion, not evidence of superior correctly dosed clinical efficacy.

Immediate- and extended-release dexmethylphenidate products differ in delivery. They are not interchangeable with each other or with racemic methylphenidate milligram-for-milligram. Product-specific age authorization, conversion and administration instructions matter. A 2026 phase 3 formulation trial supports acute symptom efficacy (PMID 42484049), but the class-specific long-term and network literature remains far smaller than for racemic methylphenidate.

The evidentiary error to avoid is inheritance by name: one cannot assign every methylphenidate pharmaco-fMRI result to dexmethylphenidate. The active enantiomer supports class-level mechanistic plausibility; it does not establish a unique

DMN, frontoparietal or salience-network signature. Similarly, an enantiopure formulation does not eliminate stimulant adverse effects or abuse liability.

130 Amphetamine as transporter substrate and monoamine releaser

Amphetamine is not simply "stronger methylphenidate." It is a transporter substrate with release-promoting pharmacology. Amphetamine enters catecholaminergic terminals through DAT and NET, alters vesicular monoamine handling through VMAT2-related processes, increases cytosolic monoamine availability, and promotes reverse transport. TAAR1-linked transporter phosphorylation and trafficking contribute to mechanistic accounts. Recent molecular work continues to refine reverse-transport mechanisms (PMID 37468107).

A schematic transporter-flux expression is

$$J_{\text{DAT}} = J_{\text{uptake}}(D_e, V_m, Na^+, Cl^-) - J_{\text{reverse}}(A_i, D_i, \Phi),$$

where extracellular dopamine D_e, membrane potential V_m, ionic gradients, intracellular amphetamine A_i, intracellular dopamine D_i, and transporter regulatory state Φ influence net flux. Methylphenidate mainly reduces the uptake term; amphetamine can increase the reverse term. This is the molecular reason the two classes cannot be treated as interchangeable versions of one operation.

The pooled amphetamine class shows strong short-term efficacy. Cortese et al. estimated clinician-rated standardized mean differences versus placebo of approximately -1.02 in children/adolescents and -0.79 in adults near 12 weeks, with higher adverse-event discontinuation than placebo. Larger average symptom effect does not mean superior choice for every person or outcome. The same class has important sleep, appetite, cardiovascular, psychiatric and misuse risks, and its direct network evidence is thinner than the clinical symptom evidence.

Route and rate are crucial. Therapeutic oral exposure produces a different concentration–time profile from high-dose, intranasal or intravenous nonmedical use. Faster delivery increases the rate of brain concentration change and can intensify reinforcing and cardiovascular effects. Scientific communication must not use the risks of one exposure regime to stigmatize all prescribed treatment, nor use therapeutic trial data to sanitize nonmedical use.

131 Dextroamphetamine and mixed amphetamine salts

Dextroamphetamine is the dextrorotatory amphetamine enantiomer, with potent dopaminergic and noradrenergic release-promoting effects. Mixed amphetamine salts combine dextro- and levoamphetamine salts; the levo component contributes relatively more peripheral and noradrenergic activity. Immediate-release, extended-release and transdermal products differ in exposure and approved ages. These are clinically consequential differences, not packaging details.

Older head-to-head studies and a small 2026 randomized open-label comparison indicate that response and tolerability can differ between dexamphetamine and methylphenidate (Poulton et al., doi:10.1111/jpc.70487; PMID 42415397). This supports individualized class trials under supervision. It does not establish a universal sequence or dextroamphetamine superiority.

Mixed amphetamine salts have placebo-controlled evidence in adults and youth. Day-course trials show coverage across structured settings, but "works for twelve hours" and "improves long-term life function" are different propositions. Formulation studies often measure repeated classroom or workplace analog tasks; these can be useful yet remain controlled approximations.

Adverse effects include appetite suppression, insomnia, dry mouth, headache, anxiety or irritability and increases in pulse and blood pressure. Rare psychosis and mania require attention. A 2026 acute randomized study in amphetamine/dextroamphetamine-naïve young adults documented marked short-term cardiovascular responses in a small healthy sample (PMID 41770187). It establishes acute physiology under that exposure, not long-term event incidence in treated ADHD.

132 Lisdexamfetamine as a delivery-kinetic transformation

Lisdexamfetamine is an inactive prodrug converted in blood to d-amphetamine. The prodrug changes the rate and shape of active exposure. It does not change d-amphetamine into a different final molecular class. This is a delivery-kinetic transformation: slower conversion can reduce sharp peaks relative to some immediate-release exposures, while once-daily dosing can extend coverage.

Randomized trials and meta-analyses support acute efficacy in children, adolescents and adults. A European pediatric phase 3 trial (PMID 23332456), an adult randomized-withdrawal maintenance study (PMID 22780921) and a pediatric meta-analysis (PMID 25897203) form part of that base. Withdrawal studies answer whether selected prior responders

relapse when switched to placebo; because they enrich for people who already tolerated and benefited, they should not be interpreted as general-population response rates.

The prodrug does not eliminate appetite, sleep, blood-pressure, pulse, psychosis, mania or misuse risk. Manipulating some routes may produce less rapid active exposure than with immediate-release amphetamine, but abuse, dependence, diversion and overdose warnings remain. "Smoother" is pharmacokinetic; "safer for every person," "nonaddictive," and "network normalizing" are unproved extensions.

133 Why methylphenidate and amphetamine are not interchangeable

Dimension	Methylphenidate family	Amphetamine family
Primary transporter action	DAT/NET uptake blockade	DAT/NET substrate; uptake competition plus release/reverse transport
Vesicular/cytosolic action	not the defining therapeutic mechanism	VMAT2-related redistribution and increased cytosolic monoamine availability
Active chemical	methylphenidate stereoisomers	dextro-/levoamphetamine; lisdexamfetamine yields d-amphetamine
Exposure variants	IR, multiparticulate, osmotic, transdermal and others	IR, XR salts, prodrug, transdermal and others
Pooled acute efficacy	strong; pediatric guidelines often favor initial use	strong; adult comparative estimates often larger
Tolerability	appetite, sleep, hemodynamic and psychiatric risks	overlapping risks; higher discontinuation in some syntheses
Comparative psychosis signal	lower in a large matched cohort	higher than methylphenidate in that cohort
Network evidence	MPH-heavy but heterogeneous	less extensive; cannot inherit all MPH findings

In a large matched cohort of adolescents and young adults, new-onset psychosis was uncommon in both groups but more frequent with amphetamine than methylphenidate (Moran et al., New England Journal of Medicine, 2019; doi:10.1056/NEJMoa1813751; PMID 30893533). Observational residual confounding remains possible, yet the finding is clinically and scientifically material. It is one reason "stimulant" is too coarse a pharmacological noun.

Individual response is not predictable from the class-average effect size alone. A person may respond to one class and not the other because of exposure kinetics, transporter biology, baseline state, comorbidity, adverse effects or unmeasured factors. A mechanistic distinction justifies careful comparison; it does not enable a deterministic pre-treatment forecast.

134 Atomoxetine and selective NET inhibition

Atomoxetine primarily inhibits NET and is not a controlled substance. In prefrontal cortex, where NET contributes to dopamine clearance, NET inhibition can increase extracellular norepinephrine and dopamine without strong striatal DAT blockade. The canonical direct demonstration is preclinical microdialysis: atomoxetine increased both transmitters in rat prefrontal cortex (Bymaster et al., 2002; doi:10.1016/S0893-133X(02)00346-9; PMID 12431845). That result supports a regional mechanism; it is not direct measurement of human ADHD cortex.

Clinical benefit usually develops across weeks, with some patients continuing to improve over 6–12 weeks or longer. It should not be judged using a same-day stimulant expectation. In Cortese et al. 2018, clinician-rated standardized mean differences versus placebo were approximately -0.56 in children/adolescents and -0.45 in adults near 12 weeks. Average efficacy was meaningful but lower than the pooled amphetamine estimate. Choice can still favor atomoxetine because duration, misuse risk, tics, anxiety, prior response, sleep and patient preference alter the benefit–cost problem.

Atomoxetine can cause nausea, appetite or weight change, somnolence or fatigue, insomnia, pulse or blood-pressure increases, and sexual or urinary adverse effects in adults. Labeling includes a boxed warning concerning suicidal ideation in children and adolescents and warnings about rare severe liver injury and emergent psychotic or manic symptoms. Nonstimulant does not mean physiologically neutral.

Task-imaging studies suggest changes in inhibitory-control and prefrontal systems. In drug-naïve adults, eight weeks of atomoxetine improved inhibition while right inferior-frontal/ACC activation decreased; pretreatment ACC activity predicted symptom improvement (Fan, Chou & Gau, 2017; doi:10.1002/hbm.23683; PMID 28657141). Efficient improvement can therefore accompany less activation, contradicting an "activation up equals normalization" rule.

135 Guanfacine and extended-release guanfacine

Guanfacine is a relatively selective alpha-2A adrenergic receptor agonist. Extended-release guanfacine is approved for pediatric ADHD in the United States as monotherapy or adjunctive treatment; adult approvals differ internationally. It does not increase synaptic catecholamines like a stimulant. It activates a receptor and reduces aspects of sympathetic outflow.

The cellular account—alpha-2A inhibition of cAMP–HCN signaling strengthening prefrontal recurrent activity—is strong mechanistic evidence (Wang et al., 2007, PMID 17448997). The clinical base supports pediatric symptom benefit and adjunctive use when stimulant response is partial. A systematic review and meta-analysis found alpha-2 agonist efficacy in monotherapy and add-on trials (Hirota, Schwartz & Correll, 2014; doi:10.1016/j.jaac.2013.11.009; PMID 24472251), and a controlled trial supports extended-release guanfacine added to psychostimulants (Wilens et al., 2012; doi:10.1016/j.jaac.2011.10.012; PMID 22176941).

Somnolence, sedation, fatigue, dizziness, hypotension and bradycardia are central tradeoffs. Sedation can reduce daytime performance even while impulse control improves. The drug must generally be tapered; abrupt cessation can produce rebound hypertension and tachycardia. Extended-release and immediate-release guanfacine are not milligram-for-milligram substitutes.

Direct evidence for guanfacine-induced DMN, FPN or salience-state normalization is sparse. Source-localized EEG studies of guanfacine, dexmethylphenidate and combination therapy show that physiological predictors and changes can differ across treatment conditions, but do not establish one canonical network route (Michelini et al., 2023; doi:10.1016/j.jaac.2022.06.017; PMID 35963558).

136 Clonidine and broader alpha-2 effects

Clonidine is a less alpha-2A-selective agonist with broader alpha-2 and imidazoline-related physiology. Extended-release clonidine is approved for pediatric ADHD in the United States; immediate-release ADHD use is off-label. It can reduce hyperactivity, impulsivity, hyperarousal and sleep-related dysregulation, but the clinical evidence base is smaller than for stimulants and atomoxetine.

Sedation, fatigue, dizziness, hypotension, bradycardia, dry mouth and constipation are common concerns. Like guanfacine, clonidine requires gradual discontinuation because abrupt cessation can precipitate rebound hypertension, tachycardia, agitation or headache. Stimulant and alpha-2-agonist cardiovascular effects should not be assumed to cancel when combined; monitoring remains necessary.

Clonidine creates a conceptual lesson: a treatment can improve behavior partly by changing arousal while simultaneously degrading sustained alertness. A lower activity level is not automatically better executive control. Direct clonidine-specific large-scale network evidence in ADHD is insufficient; a claim of restored switching would exceed the data.

137 Viloxazine extended release

Viloxazine extended release is a noncontrolled ADHD medication approved in the United States from age six through adulthood. It inhibits NET and has serotonergic receptor actions; experimental work reports activity at 5-HT2C, 5-HT2B and 5-HT7 receptors, and macaque PET supports in-vivo 5-HT2C occupancy. Receptor breadth is pharmacological evidence, not proof of superior human network regulation.

Phase 3 placebo-controlled trials support pediatric and adult symptom efficacy (Nasser et al., 2020, doi:10.1016/j.clinthera.2020.05.021, PMID 32723670; Nasser et al., 2022, doi:10.1007/s40263-022-00938-w, PMID 35896943). Long-term extensions show continued improvement among retained participants, but open-label retention enriches for tolerators and responders.

Adverse effects include somnolence or fatigue, reduced appetite, nausea or vomiting, headache, insomnia, irritability and increased blood pressure or heart rate. Labeling includes a boxed warning for suicidal thoughts and behaviors and warnings about manic or hypomanic activation. Clinically important CYP1A2 inhibition creates drug-interaction constraints.

Direct ADHD evidence for viloxazine-induced DMN suppression, frontoparietal recruitment, salience switching or dynamic-state normalization is insufficient. Novelty should increase curiosity, not certainty.

138 Bupropion as off-label treatment

Bupropion is approved for depressive disorders and smoking cessation under product-specific labels, not for ADHD. It inhibits norepinephrine and dopamine reuptake through the parent drug and active metabolites and antagonizes nicotinic acetylcholine receptors. Human PET suggests modest striatal DAT occupancy at clinical exposure; shared "dopamine and norepinephrine" language does not make it a stimulant equivalent.

A Cochrane review found a possible adult ADHD benefit but emphasized the small, low-certainty evidence base (Verbeeck et al., 2017; doi:10.1002/14651858.CD009504.pub2; PMID 28965364). Cortese et al. estimated an adult clinician-rated standardized mean difference of about -0.46 versus placebo, with wide uncertainty and few trials. Bupropion may be considered in particular clinical contexts, including co-occurring depression or smoking, but that is a clinician-level individualized decision rather than a general first-line mechanistic conclusion.

Adverse effects include insomnia, anxiety or activation, dry mouth, nausea, headache, appetite/weight reduction and blood-pressure increase. Seizure risk is dose- and formulation-related; mania/hypomania and antidepressant suicidality warnings matter. ADHD-specific long-term and network evidence is sparse. Antidepressant neuroimaging cannot simply be relabeled as an ADHD network mechanism.

139 Modafinil: evidence and regulatory boundary

Modafinil is a wake-promoting drug approved in the United States for narcolepsy, sleepiness associated with obstructive sleep apnea, and shift-work disorder—not ADHD. It is Schedule IV. Its pharmacology includes DAT blockade and distributed arousal-system effects involving orexin, histamine, glutamate and GABA. Human PET demonstrates dopamine and DAT engagement (Volkow et al., JAMA, 2009; doi:10.1001/jama.2009.351; PMID 19293415); it should not be described as dopamine-neutral.

Small ADHD trials report improvements in vigilance or response inhibition, but clinical findings are mixed. A 2017 meta-analysis reported benefit in selected trials (Wang et al.; doi:10.1016/j.jpsychires.2016.09.034; PMID 27810669), whereas the 2018 network meta-analysis found no adult clinician-rated superiority over placebo: SMD 0.16, 95% CI -0.28 to 0.59. Pediatric use is constrained by regulatory history and rare serious rash or hypersensitivity concerns.

The conceptual boundary is valuable: increased wakefulness, DAT engagement and improvement on an attention task are not interchangeable with effective treatment of ADHD as a disorder. Modafinil can cause headache, nausea, insomnia, anxiety or agitation, hemodynamic change and rare psychiatric reactions. ADHD-specific long-term and network evidence is insufficient.

140 Age-stratified comparative efficacy

Age changes both evidence and clinical choice. The 2018 network meta-analysis supported methylphenidate as a favored initial pharmacological choice in children and adolescents when efficacy and tolerability were considered together, while amphetamines had the strongest adult efficacy signal. This is a population-level comparative inference, not a rule that bypasses patient history, licensing, comorbidity or preference.

Development also changes pharmacodynamics. In an acute arterial-spin-labeling study, methylphenidate reduced cortical perfusion in both boys and adult men but more strongly in adults, while thalamic perfusion fell only in children (Schrantee et al., 2017; doi:10.1016/j.nicl.2016.11.021; PMID 27942455). The same nominal intervention therefore did not produce an age-invariant brain response.

Pediatric outcomes place special weight on growth, school-day coverage, sleep, family observation and developmental exposure. Adult outcomes require attention to work, driving, relationships, cardiovascular health, substance use, pregnancy-related context and adherence without parental scaffolding. A symptom scale cannot make these outcome spaces equivalent.

141 Dose–response curves and plateaus

Average benefit typically increases from ineffective low exposure, then plateaus; adverse effects can continue increasing. Let expected utility at dose d be

$$U(d) = w_B B(d) - \sum_{j=1}^{m} w_j H_j(d),$$

where $B(d)$ is benefit, $H_j(d)$ are harms or burdens, and weights reflect clinical importance and patient preference. Optimal dose is not $\arg\max B(d)$; it is the dose that produces the best acceptable multivariate tradeoff under uncertainty. The weights are not fixed across people or developmental periods.

The 2026 dose-effect synthesis suggested pooled pediatric efficacy plateaus around 45 mg/day for methylphenidate and roughly 25 mg/day in amphetamine equivalents, and an adult amphetamine plateau around 50 mg/day, with substantial high-dose uncertainty. These values must never be printed as targets for an individual. Formulations, salt equivalence, body size, metabolism and trial distributions complicate comparison.

The inverted-U adds another complication: some cognitive operations can worsen before symptom ratings reveal a clear problem. Emotional flattening, excessive narrowing, reduced spontaneity or sleep erosion may signal that the overall utility has declined even if a morning task improves.

142 Onset, coverage, titration and discontinuation

Stimulant effects can appear on the first treated day; atomoxetine, alpha-2 agonists, viloxazine and bupropion usually require evaluation over days to weeks. Formulation governs coverage. A long-acting preparation may reduce school-day gaps but extend appetite or sleep effects. A short-acting preparation may permit timing flexibility but produce more pronounced peaks, troughs or adherence burden.

Titration is an experiment with repeated measurement. Useful monitoring separates morning initiation, sustained work, impulsivity, emotional regulation, appetite, evening rebound and sleep. It also records the context: a drug cannot compensate reliably for chronic sleep deprivation, impossible workload or a hostile environment.

Discontinuation differs by class. Alpha-2 agonists require tapering because of rebound hypertension and tachycardia. Stimulant cessation may produce fatigue, dysphoria, altered sleep and appetite or return of symptoms, especially after prolonged/high exposure, but does not share the same rebound-hemodynamic mechanism. Atomoxetine and viloxazine do not have classic stimulant withdrawal, yet stopping can lead to symptom return. Randomized-withdrawal designs estimate relapse among prior responders and tolerators, not the experience of all starters.

Real-world adherence is not a nuisance variable. A 2026 Norwegian register study found discontinuation and low adherence common and increasing through adolescence (Garcia-Argibay et al., doi:10.1136/bmjment-2026-302649; PMID 42331561). A medication that works pharmacologically but is not taken, cannot be afforded or creates unacceptable identity costs has low real-world effectiveness.

143 Appetite, growth, sleep, anxiety and mood

Stimulants commonly suppress appetite and can shift meal timing and weight trajectory. Growth findings are heterogeneous; average effects do not predict a particular child. The proper scientific stance is neither “stimulants stunt growth” as an inevitability nor “growth concerns are a myth.” It is repeated measurement, interpretation of trajectory, nutritional context and individualized benefit–risk review.

Sleep can improve if evening chaos and delayed task completion decrease, or worsen if medication delays sleep onset or extends arousal. Baseline sleep disorders, circadian delay and inconsistent schedules can mimic or amplify ADHD symptoms. Treating daytime ratings without measuring sleep risks a self-reinforcing cycle.

Anxiety and irritability can move in either direction. Better control can reduce secondary anxiety; catecholaminergic activation can worsen somatic arousal, rumination or agitation. Mood elevation, decreased need for sleep, grandiosity or marked activation require a different clinical interpretation than ordinary symptom improvement. Bipolar-spectrum vulnerability and medication context matter.

Alpha-2 agonists can aid sleep initiation yet cause disabling daytime somnolence. Atomoxetine and viloxazine can cause either somnolence or insomnia. Bupropion and modafinil are often activating. “Stimulant versus nonstimulant” therefore does not map cleanly onto “wakeful versus sedating.”

144 Cardiovascular effects and monitoring

Stimulants and atomoxetine commonly produce small mean increases in pulse and blood pressure; viloxazine can also increase them. Guanfacine and clonidine tend to lower pulse and pressure, with risks of hypotension, bradycardia and syncope. Mean changes conceal tails, comorbidity, interactions and individual sensitivity.

The 2025 comparative cardiovascular network meta-analysis across children, adolescents and adults provides the current short-to-medium-term synthesis (Farhat et al., Lancet Psychiatry; doi:10.1016/S2215-0366(25)00062-8; PMID 40203844). Longer-term inference remains less secure. A large 2024 Swedish nested case-control study associated longer cumulative ADHD-medication exposure with increased cardiovascular disease risk, especially hypertension and arterial disease (Zhang et al., JAMA Psychiatry; doi:10.1001/jamapsychiatry.2023.4294; PMID 37991787). Observational confounding and exposure classification constrain causal interpretation, but the duration signal cannot be dismissed by citing only short trials.

The contradiction should remain visible: serious acute events appear uncommon at the population level, yet modest physiological changes and possible cumulative associations justify monitoring. Clinical assessment considers history, symptoms,

pulse, blood pressure, concurrent drugs and indicated further evaluation. This lecture cannot supply an individual screening protocol.

145 Tics and common safety myths

The belief that stimulants invariably cause or worsen tics is not supported by randomized-trial meta-analysis. Tics naturally wax and wane, and ADHD symptoms can change the visibility or burden of tics. Some individuals may still experience clinically relevant change. The correct statement is probabilistic, not absolute.

Another myth is that nonstimulants are risk-free. Atomoxetine has cardiovascular, hepatic, suicidality and psychiatric warnings; alpha-2 agonists can cause hypotension, bradycardia, sedation and rebound hypertension; viloxazine carries suicidality and activation warnings; bupropion has seizure and mood-switch risks; modafinil has rare serious rash and psychiatric concerns.

The opposite myth—that any long-term stimulant exposure is inevitably neurotoxic or addictive—is also unsupported at therapeutic exposure. Risk depends on molecule, dose, route, supervision, comorbidity and outcome. Uncertainty is not evidence of catastrophe, and absence of catastrophe in averages is not proof of zero risk.

146 Psychosis and mania risk

New-onset psychosis during prescribed stimulants is uncommon, but it is not imaginary. The 2019 matched cohort found a higher incidence with amphetamine than methylphenidate among adolescents and young adults (Moran et al., PMID 30893533). Because exposure was not randomized, the estimate may retain confounding; its large scale and active comparison nevertheless make it important.

All major catecholaminergic treatments require attention to emergent psychotic or manic symptoms. Atomoxetine and viloxazine labels include psychiatric activation warnings; bupropion and modafinil can destabilize vulnerable patients. Familial bipolar risk may also moderate network response: a 2026 mixed-design study found that twelve weeks of mixed amphetamine salts produced different topology changes in youth with and without familial bipolar-I risk, including an adverse-direction amygdala-efficiency change in the high-risk group (Qin et al., doi:10.1016/j.jaac.2025.07.421; PMID 40712681).

Clinical phenomenology matters. Transient insomnia or appetite loss is not mania; reduced need for sleep with escalating energy, grandiosity or risky behavior is different. Suspiciousness, hallucinations or disorganization require prompt clinical assessment. Education should reduce both panic and minimization.

147 Therapeutic use, diversion and nonmedical use

Prescribed oral stimulant treatment and nonmedical stimulant use are different exposure regimes. They can involve the same molecule, but route, rate, dose, context, monitoring and intent alter pharmacokinetics and risk. Schedule II status reflects real abuse, dependence, diversion and overdose potential. It does not imply that every appropriately treated patient becomes addicted.

Reinforcing impact is related partly to the speed and magnitude of brain concentration change. Manipulating extended-release products or using non-oral routes can collapse a controlled delivery profile into a rapid exposure. Sharing medication also bypasses cardiovascular and psychiatric screening and makes dose unpredictable.

Longitudinal and within-person studies generally do not support the claim that prescribed ADHD treatment causes later substance-use disorder. Some observational studies associate treatment periods with lower substance-related events, injury or criminality, but confounding by adherence and functioning remains. The defensible public-health message is dual: treatment should not be stigmatized as equivalent to illicit use, and controlled status should not be trivialized.

148 Long-term outcomes and methodological limits

Most randomized medication trials last weeks or months, whereas ADHD and treatment decisions can span years. Long-term randomized withholding is difficult and may be unethical for responders. The resulting evidence gap is filled by open-label extensions, treatment-withdrawal designs, naturalistic cohorts and registries. Each answers a different question and carries a different bias.

Major threats include:

- **confounding by indication:** more severe patients are more likely to receive medication;
- **healthy-adherer bias:** people who sustain treatment may differ in organization, support and health behavior;
- **depletion of susceptibles:** those with early adverse effects discontinue and disappear from long-term exposed groups;

- **time-varying exposure:** dose, class and adherence change;
- **immortal-time and selection bias:** cohort definitions can create artificial protection;
- **outcome substitution:** symptom rating is treated as function or development;
- **informative discontinuation:** stopping reflects both lack of efficacy and adverse effects.

Long-term claims should therefore use calibrated language. There is strong evidence for average short-term symptom reduction with licensed agents. There is meaningful but less definitive evidence for some functional and risk outcomes. There is insufficient evidence that medication alone produces complete recovery or uniform durable brain normalization.

The Multimodal Treatment Study of ADHD illustrates why time changes inference. At 14 months, carefully managed medication and combined treatment produced strong symptom advantages relative to community care and intensive behavioral treatment on several primary outcomes (MTA Cooperative Group, 1999; doi:10.1001/archpsyc.56.12.1073; PMID 10591283). Group differences diminished across uncontrolled follow-up as treatment exposure converged and selection accumulated (24-month PMID 15060224; eight-year PMID 19318991). Sixteen-year follow-up documented substantial adult functional impairment across the childhood-ADHD cohort and did not justify a simple lasting randomized-treatment ranking (Hechtman et al., 2016; doi:10.1016/j.jaac.2016.07.774; PMID 27806862). Growth analyses preserved an association between sustained stimulant exposure patterns and height trajectory (Greenhill et al., 2020; doi:10.1016/j.jaac.2019.06.019; PMID 31421233). The MTA therefore supports acute efficacy, the value of treatment quality, and the inadequacy of treating a 14-month contrast as a 16-year causal effect.

Large observational programs add outcomes that short trials cannot measure. Within-person and register analyses have associated medication periods with lower criminality (Lichtenstein et al., 2012; doi:10.1056/NEJMoa1203241; PMID 23171097), fewer substance-related problems (Quinn et al., 2017; doi:10.1176/appi.ajp.2017.16060686; PMID 28659039), and fewer unintentional injuries in youth (Ghirardi et al., 2020; doi:10.1016/j.jaac.2019.06.010; PMID 31302218). A 2024 registry study associated pharmacotherapy initiation with lower mortality (Li et al.; doi:10.1001/jama.2024.0851; PMID 38470385), and a 2025 target-trial emulation examined suicidal behavior, substance misuse, injuries, transport accidents and criminality across treatment strategies (Zhang et al.; doi:10.1136/bmj-2024-083658; PMID 40803836). These designs use powerful comparison strategies, but residual time-varying confounding, adherence and treatment changes prevent them from becoming randomized lifetime proofs.

Functional-outcome meta-analysis suggests medication benefits extend beyond symptom ratings on average (Boland et al., 2020; doi:10.1016/j.jpsychires.2020.01.006; PMID 32014701). The evidence is uneven across academic achievement, employment, relationships, driving, quality of life and self-concept. “Medication improves function” is therefore more defensible than “medication restores every functional layer,” and each domain requires its own measurement.

The estimand must also match the question. An intention-to-treat contrast estimates the effect of assignment under the adherence, switching and discontinuation that actually occurred in the trial. A per-protocol contrast targets sustained exposure but requires stronger adjustment for time-varying reasons that people remain treated. A within-person register comparison controls stable individual differences yet remains vulnerable when worsening symptoms both trigger treatment and predict the outcome. A target-trial emulation can make eligibility, treatment strategies, follow-up and censoring explicit, but it cannot repair unmeasured confounding by specification alone.

These distinctions matter because the public question is rarely “what was the mean symptom contrast at week eight?” Families and adults ask whether treatment changes learning, accidents, driving, relationships, substance risk, employment or health over years. No single design supplies every answer. Short randomized trials offer strong control of assignment for common near-term outcomes; registries supply scale and rare events; longitudinal cohorts reveal development; withdrawal studies test maintenance among selected responders. Convergence across designs strengthens a conclusion, whereas disagreement should narrow it. A responsible long-term claim therefore names the outcome, exposure strategy, comparison, follow-up and remaining bias instead of borrowing the certainty of acute efficacy.

Treatment	Molecular action	Local/regional implication	Direct network evidence	Clinical evidence	Key burdens and boundaries

149 Molecular → cellular → network → clinical comparative matrix

Treatment	Molecular action	Local/regional implication	Direct network evidence	Clinical evidence	Key burdens and boundaries
Methylphenidate	DAT/NET blockade	striatal DA and PFC catecholamine availability	largest imaging corpus; heterogeneous acute/task effects	strong short-term youth and adult symptom benefit	appetite, sleep, hemodynamic effects; rare psychosis/mania; controlled; long-term uncertainty
Dexmethylphenidate	active d-threo MPH enantiomer; DAT/NET blockade	MPH-class effects at different milligram potency	insufficient unique signature	moderate acute pediatric evidence	do not infer superiority or unique safety
Amphetamine salts / dextroamphetamine	transporter substrate; monoamine release/reverse transport	potent striatal, PFC and arousal effects	thinner than MPH; reward and topology findings are conditional	strong acute symptom benefit	appetite/sleep, hemodynamic and psychiatric risk; high misuse potential
Lisdexamfetamine	prodrug → d-amphetamine	smoother conversion-shaped exposure	preliminary reward-learning evidence; no unique normalization signature	strong acute, selected-responder maintenance evidence	prodrug does not eliminate amphetamine risks
Atomoxetine	NET inhibition	increases NE and PFC DA; little classic striatal DAT blockade	small task/rest studies; drug-specific effects	strong-to-moderate across ages; slower onset	GI, appetite, somnolence/insomnia, hemodynamic, suicidality and rare hepatic/psychiatric risks
Guanfacine ER	alpha-2A agonism	cAMP–HCN mechanism can strengthen PFC recurrent firing; lowers sympathetic tone	sparse fMRI; some EEG combination evidence	moderate pediatric and adjunctive evidence	sedation, hypotension, bradycardia; taper for rebound
Clonidine ER	broader alpha-2 agonism	lowers sympathetic output; sedating	insufficient	moderate-to-limited pediatric evidence	sedation, hypotension/bradycardia; taper essential
Viloxazine ER	NET inhibition plus serotonergic actions	cortical NE with serotonergic modulation	insufficient ADHD network evidence	moderate phase 3 evidence	somnolence/insomnia, BP/HR, suicidality, mania, CYP1A2 interactions
Bupropion	NDRI plus nicotinic antagonism	distributed catecholamine/nicotinic effects; modest DAT occupancy	insufficient ADHD-specific network evidence	moderate-to-limited adult off-label evidence	insomnia/activation, BP, seizure and mania risk
Modafinil	atypical DAT blockade plus arousal systems	wakefulness across hypothalamic/brainstem/-cortical systems	sparse ADHD-specific evidence	conflicting; adult pooled null in 2018 synthesis	not ADHD-approved; insomnia, psychiatric and rare serious-rash risks

From average efficacy to an individual longitudinal experiment

At the individual level, medication evaluation is a repeated-measures problem. Let $\mathbf{y}_t$ be a vector containing symptoms, initiation latency, sustained-task performance, emotional regulation, sleep, appetite, pulse or blood pressure, and functional outcomes at time t. A useful evaluation asks whether a planned exposure changes the vector relative to a credible baseline while keeping cost within acceptable bounds:

$$\Delta\mathbf{y}_t = \mathbf{y}_t(d, f, c) - \mathbf{y}_t(0, c),$$

where d is dose, f formulation and c context. In ordinary clinical care, the untreated counterfactual $\mathbf{y}_t(0, c)$ is unobserved and context changes from day to day. Ratings from more than one setting, repeated vital signs, sleep records and explicit functional goals reduce—but do not remove—this uncertainty.

Three common errors follow from inadequate measurement. First, a morning benefit can conceal evening rebound or sleep cost. Second, improved compliance can be mistaken for improved self-directed functioning. Third, a euphoric or highly activated first exposure can be mistaken for the stable therapeutic optimum. The relevant endpoint is reproducible, sustainable functioning, not the intensity of an immediate subjective effect.

Medication holidays, switching, combination therapy and discontinuation are clinical decisions with different evidence and risks across agents; none can be derived from a generic lecture matrix. What the matrix supplies is a structure for questions: Which outcome is changing? Who observes it? At what time after exposure? What cost appears later? Does the effect persist across contexts? Is another intervention needed for skills, environment, sleep or comorbidity? This makes the person an active source of longitudinal evidence without pretending that self-observation replaces medical oversight.

Part XI synthesis. Pharmacological treatment is not one intervention. Molecules differ in transporter action, receptor action, delivery kinetics, timescale, evidence base and risk. Acute symptom efficacy is strongest; durable function and network reorganization are less certain. The treatment question is not "stimulant or no stimulant?" but "which perturbation, for which person, outcome, context and timescale, at what cost?"

From molecular action to lived outcome

A drug description should follow several links without assuming that one guarantees the next: molecular target, regional transmitter change, cellular and circuit effect, network configuration, cognitive operation, behavior, symptom rating, and daily function. Evidence is strongest at different links for different medications. Target engagement may be well established while the network mediator remains unknown; symptom efficacy may be robust while long-term functional evidence remains incomplete.

Formulation and pharmacokinetics matter because treatment is experienced in time. Immediate- and extended-release preparations differ in onset, coverage, peak-to-trough variation, rebound, adherence demands, and opportunities for diversion. Methylphenidate and amphetamine formulations reach catecholamine systems through different transporter mechanisms. Atomoxetine, alpha-2 agonists, viloxazine, bupropion, and modafinil should not be described as weaker versions of the same intervention.

Clinical comparison must preserve age, outcome, dose optimization, tolerability, and follow-up. A large short-term symptom effect does not answer whether sleep, appetite, growth, cardiovascular measures, mood, tics, substance risk, relationships, school, work, driving, or quality of life improve for a particular person. Good prescribing is therefore an iterative measurement process, not the selection of a molecule from a ranking table.

Drug classes must remain pharmacologically and clinically distinct

Methylphenidate primarily blocks dopamine and norepinephrine transporters, whereas amphetamine formulations are transporter substrates with additional release-related and vesicular actions. Their pharmacokinetics, formulation profiles, and adverse-effect patterns overlap but are not identical. Dexmethylphenidate is the active d-enantiomer of methylphenidate; dextroamphetamine, mixed amphetamine salts, and lisdexamfetamine differ in composition and delivery. Treating all stimulants as one interchangeable mechanism erases clinically relevant variation.

Atomoxetine inhibits the norepinephrine transporter and can indirectly increase cortical dopamine where dopamine clearance relies substantially on that transporter. Guanfacine and clonidine act through alpha-2 adrenergic receptors with different selectivity and sedative profiles. Viloxazine extended release has noradrenergic and broader pharmacological actions whose clinical evidence is newer. Bupropion and modafinil occupy off-label or jurisdiction-dependent positions and carry their own contraindications; evidence for one cannot be borrowed by another.

Efficacy should be stated by age, comparator, duration, and outcome. Short-term symptom reduction is best established for stimulants, with important individual variation and nonresponse. Nonstimulants can be valuable when stimulants are ineffective, poorly tolerated, contraindicated, or clinically unsuitable. Response rate is not cure rate, and a lower symptom score does not guarantee improved grades, employment, relationships, driving, sleep, or quality of life.

Safety monitoring is part of mechanism-informed care. Appetite, growth in children, sleep, blood pressure, pulse, mood, anxiety, tics, and rare psychiatric reactions require attention according to the drug and person. Alpha-2 agonists require caution around hypotension, sedation, and abrupt discontinuation. Misuse and diversion concern formulation, access, and context; they should not be conflated with medically supervised treatment. Population findings about psychosis or cardiovascular events inform risk management but do not predict an individual outcome with certainty.

Long-term evidence is harder than acute efficacy. Treatment continuation is not randomized indefinitely, and people who remain on medication differ from those who stop. Registry studies can address rare outcomes and real-world associations but retain confounding; randomized trials often have shorter horizons and selective samples. The honest conclusion is layered: short-term efficacy is robust for several agents, some functional and safety outcomes are supported, and many long-term causal questions remain less certain than ordinary clinical language implies.

Medication choice is therefore a monitored experiment within guideline-informed care. The clinically relevant endpoint is the best balance of symptoms, function, tolerability, adherence, and risk—not loyalty to a drug class or a neurochemical story. The lecture should explain mechanisms precisely while preserving the fact that treatment decisions are individualized medical judgments.

Comparative treatment evidence is a map, not a winner's podium

Network meta-analyses can compare average symptom effects across multiple drugs, but the ranking depends on age, trial duration, outcome, tolerability, and the geometry of the evidence network. Direct comparisons are often fewer than placebo-controlled trials. A higher mean effect does not establish superiority for every person, a better long-term functional outcome, or an interchangeable risk profile.

Formulation changes the lived pharmacology. Onset, peak, duration, rebound, ability to swallow, food effects, and the possibility of diversion influence whether a molecular mechanism becomes a usable treatment. A prodrug may alter abuse liability and temporal delivery without becoming risk free. An extended-release preparation can reduce repeated dosing while making evening appetite or sleep effects more relevant. The same active class can therefore create different daily trajectories.

Nonstimulants occupy more than a fallback category. Slower onset changes how response should be evaluated; sedating or calming effects may help one clinical profile and burden another. Comorbid anxiety, tic disorder, substance-use risk, cardiovascular status, sleep difficulty, and prior adverse reactions shape the decision. The evidence supports options, not an algorithm detached from clinical judgment.

Functional monitoring should be defined before treatment. A weekly symptom score can be paired with task initiation, missed obligations, driving events, school completion, family conflict, appetite, sleep timing, and the person's own priority outcome. Improvement in a narrow test without improvement in the target life domain may still teach something about mechanism, but it should not be called full success.

Discontinuation is also data. Stopping may reflect lack of efficacy, adverse effects, access, stigma, forgetfulness, or a mismatch between duration and daily need. Trials that report only completers can overstate tolerability and benefit. Longitudinal care requires periodic re-evaluation rather than assuming the first effective prescription remains optimal through every developmental and environmental transition.

The correct comparison is thus multidimensional: molecular action, exposure profile, short-term efficacy, functional benefit, adverse effects, misuse risk, monitoring burden, patient preference, and certainty of long-term evidence. No single row can decide the treatment, but omitting rows creates a false simplicity.

From trial efficacy to an individual treatment decision

Population evidence begins the decision but does not finish it. A large standardized symptom effect describes an average contrast over a trial window. It does not identify the formulation, duration, adverse-effect tradeoff, or functional target that will matter for a particular person. A decision should specify what improvement would count, when it should appear, and which costs would make it unacceptable.

Repeated observation then becomes a small within-person experiment. Ratings from more than one setting, time-stamped functional outcomes, sleep and appetite, cardiovascular measures where indicated, and exposure timing can distinguish insufficient coverage from nonresponse or intolerance. A rebound period is different from persistent evening impairment; missed doses are different from an ineffective molecular target. These distinctions protect against escalating a dose to solve the wrong problem.

Class differences remain real. Methylphenidate blocks catecholamine transporters; amphetamine also promotes release through presynaptic mechanisms. Atomoxetine, alpha-2 agonists, viloxazine, bupropion, and modafinil occupy different mechanistic and regulatory positions. Evidence cannot be transferred simply because all can influence alertness or catecholamines. Comparative choice integrates efficacy, onset, duration, comorbidity, misuse risk, monitoring burden, preference, and prior response.

The outcome hierarchy should remain visible at review. Fewer symptoms can coexist with continued missed deadlines, relationship strain, unsafe driving, or low quality of life. Conversely, scaffolding and skill can improve function even when symptom ratings remain elevated. Continuing treatment is justified by meaningful net benefit, not by allegiance to a pharmacological story.

PART XII

MEDICATION AS NETWORK MODULATION

Test whether the molecular story reaches time-varying coordination, and audit every claim of normalization.

Rubia · Mizuno · Cai · Pan · Shaw

150 The question changes at the network level

The fact that a medication reduces symptoms does not tell us whether it strengthens a frontoparietal state, alters salience arbitration, changes reward weighting, reduces neural noise, modifies arousal, increases default-mode suppression or recruits a compensatory path. Several of these can occur at once, and the dominant mechanism may differ across people and tasks.

The network-level target is not a single region's mean activation. It is the time-varying configuration through which a person enters, sustains, updates and leaves a task. Let $Z_t \in \{1, \dots, K\}$ denote a latent network state and let $P_{ij} = \Pr(Z_{t+1} = j \mid Z_t = i)$ be a transition matrix. Medication could change state occupancy π_i, dwell-time distribution $F_i(\tau)$, transition probability P_{ij}, within-state connectivity, or the relation between state and behavior. An activation contrast averaged across the scan cannot distinguish these possibilities.

This part therefore asks a stricter question: **what network quantity changed, during what task or rest condition, after what exposure, in which age group, and was that change linked to clinical or behavioral benefit?**

151 Acute target engagement versus chronic adaptation

Acute and chronic effects belong to different timescales. An acute dose changes transporter occupancy, receptor stimulation, arousal and performance over minutes to hours. Repeated exposure can produce learning, receptor or transporter adaptation, changes in sleep and appetite, altered strategies, environmental feedback and selection through discontinuation.

A fast–slow pharmacodynamic system can be written

$$\dot{\mathbf{x}} = f(\mathbf{x}, \mathbf{z}, u, c) + G(\mathbf{x})\, C(t),$$
$$\dot{\mathbf{z}} = \varepsilon h(\mathbf{x}, \mathbf{z}, C(t)), \qquad 0 < \varepsilon \ll 1,$$

where $\mathbf{x}$ contains fast neural states, $\mathbf{z}$ slower adaptive parameters, u task input, c context, and $C(t)$ drug exposure. A single-dose experiment estimates part of G, conditional on the current $\mathbf{z}$. It does not identify the long-term solution of the coupled system.

The distinction is empirically necessary. Acute methylphenidate produces DAT blockade and can modify connectivity within hours. After 12 months, DAT availability increased in one small study (Wang et al., 2013, PMID 23696790), a change that could oppose the acute direction. Naturalistic two-year connectivity findings in the ABCD sample did not demonstrate broad symptom-linked normalization and were sensitive to corrected dataset labeling (Kaminski et al., 2024; doi:10.1038/s41398-024-03165-7; PMID 39505862). One cannot infer durable reorganization from a scanner session.

152 Pharmaco-fMRI design and inference limits

Pharmaco-fMRI is powerful because a controlled perturbation can strengthen causal inference relative to cross-sectional case–control imaging. It is fragile because medication changes vascular tone, heart rate, arousal, motion and task performance—each of which can change BOLD signals without representing the proposed neural mechanism.

Key design distinctions include:

Design	Strongest inference	Main unresolved problem
Randomized placebo crossover, acute	within-person drug-state effect	carryover, unblinding, vascular/arousal confounding, no durability
Parallel randomized treatment, weeks	treatment-course causal effect	sample size, attrition, practice and limited follow-up
Open pre–post treatment	temporal association in clinical responders	placebo, maturation, regression to mean, practice
On/off usual medication	current medication-state association	withdrawal/order effects and treatment selection
Treatment-history comparison	association with prior exposure	confounding by indication and developmental timing
Acute imaging predictor of later response	candidate stratification marker	circularity, small nonresponder group, external validation

Motion is particularly important in ADHD. Even submillimeter systematic differences can alter connectivity estimates, and medication may reduce movement. Aggressive motion control can also preferentially remove the most symptomatic participants, changing the sample. Global signal regression can alter apparent anticorrelation. Short rest scans have limited individual reliability. Dynamic analyses introduce choices about windows, state number, priors and clustering. The correct response is not to abandon imaging, but to downgrade claims whose design cannot carry them.

A systematic review of medication effects on intrinsic connectivity found a small, heterogeneous literature divided by age, drug, exposure duration, and analysis, and therefore did not support one normalization signature (Pereira-Sanchez et al., 2021; doi:10.1016/j.jaac.2020.10.013; PMID 33137412). In an adult community-structure study, stimulants altered topology and reduced some group differences without eliminating them (Cary et al., 2017; doi:10.1093/cercor/bhw209; PMID 27422412). Together, these studies sharpen the distinction between network change and normalization.

153 DMN suppression and DMN–control coupling

Early accounts proposed that ADHD involved inadequate suppression or intrusion of default-mode activity during task. Medication findings partly support this picture, but not as a universal off-switch.

In a very small one-month pediatric study, methylphenidate was followed by partial restoration of antiphase organization between broadly defined default-mode and task-positive components, alongside lower reaction-time variability (Querne et al., 2017; doi:10.1177/1087054713517542; PMID 24420764). “Partial” and “broadly defined” are essential. There was no placebo/retest ADHD arm, and the task-positive label combined distinct systems.

A 2023 randomized acute study used a Bayesian latent dynamical-system model and found that methylphenidate reduced behavioral variability, shifted a latent-state process toward the typically developing pattern, reduced state-dependent DMN hyperconnectivity and linked salience–DMN connectivity change to variability improvement (Cai et al.; doi:10.1038/s41386-023-01668-3; PMID 37491674). This is among the most direct dynamic results, yet it remains acute, modest in sample size and model-dependent.

Conversely, a 2024 washout-status study found no significant effect on within-DMN, within-FPN or DMN–FPN connectivity (Harkness, Bray & Murias; doi:10.1016/j.ridd.2024.104691; PMID 38340416). A null can reflect insensitivity, heterogeneous exposure or inadequate washout; it still constrains claims of a robust persistent effect.

154 Beneficial increases in some DMN measures

A mature account must allow adaptive default-mode activity. The DMN supports autobiographical memory, future simulation, internal models, meaning and some forms of planning. Successful task performance may require regulation and coordination, not maximal suppression.

Mizuno and colleagues found that acute methylphenidate increased spontaneous low-frequency activity in nucleus accumbens, salience, frontoparietal and default-mode systems in children with ADHD. Changes in a DMN-related spatial pattern tracked lower response-time variability and aspects replicated across differing protocols (Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 2023; doi:10.1016/j.bpsc.2022.10.001; PMID 36717325). Benefit therefore co-occurred with increased, not uniformly suppressed, default-mode-related activity.

This result does not prove that “more DMN is better.” Low-frequency amplitude is not connectivity, and resting activity is not task intrusion. It proves that a one-dimensional suppression rule is false. The relevant quantity may be context-appropriate configuration: internal-model systems can participate productively when coupled to control or reward processes and disrupt performance when they pull cognition away at the wrong time.

155 Frontoparietal recruitment and state persistence

Task-fMRI studies often report medication-related increases in inferior frontal, dorsolateral prefrontal or parietal recruitment, particularly during inhibition and attention. Rubia and colleagues’ 2014 systematic review and meta-analysis identified a relatively consistent acute increase in right inferior frontal/insula activity, while working-memory effects were null and putamen convergence depended on a more lenient threshold (doi:10.1016/j.biopsych.2013.10.016; PMID 24314347). The accurate claim is task- and locus-specific, not global executive normalization.

An adolescent study reported that methylphenidate and atomoxetine moved frontoparietal underactivation toward controls during sustained attention (Kowalczyk et al., 2019; doi:10.1016/j.euroneuro.2019.07.139; PMID 31358436). Another acute n-back study in boys found that both drugs removed one parieto-insular hyperconnectivity pattern, while methylphenidate uniquely increased wider fronto-temporo-parietal and striato-thalamic connectivity; direct whole-brain within-patient contrasts and task performance were null (Kowalczyk et al., 2023; doi:10.1007/s00213-023-06422-7; PMID 37500785). A control-like contrast and a causal drug effect are not identical tests.

Dynamic evidence adds an important possibility. In healthy adults, methylphenidate increased occupancy and dwell time of a frontoparietal-dominant state and faster low-load performance tracked that change; the result did not extend to higher load and was not an ADHD sample (Yan et al., 2025; doi:10.1523/JNEUROSCI.1693-24.2025; PMID 40101961). In stimulant-naïve children with ADHD, acute methylphenidate reduced whole-brain flexibility during standard and rewarded go/no-go tasks, and greater stabilization tracked performance improvement (Nugiel et al., 2025; doi:10.1038/s41398-025-03694-9; PMID 41271625). Useful control may involve less switching during a task, not maximal flexibility.

156 Dorsal-attention findings and important nulls

The dorsal attention network (DAN) supports top-down orienting and selection, but medication does not reliably act by simply amplifying DAN connectivity. A 2023 adult diffusion study found that smaller pretreatment left dorsal superior longitudinal fasciculus I—a tract associated with the DAN—predicted poorer methylphenidate response (Parlatini et al.; doi:10.1038/s41398-023-02598-w; PMID 37777529). This was a baseline association, not evidence that the drug changed the tract.

A large 2025 multimodal program concluded that prescription-stimulant-associated connectivity mapped more strongly to arousal, reward, salience and parietal-memory systems than to canonical attention networks; acute methylphenidate in a small precision-imaging healthy sample reversed a sleep-deprivation-like pattern (Kay et al., Cell; doi:10.1016/j.cell.2025.11.039; PMID 41448140). The naturalistic pediatric arm cannot prove medication causality, and five healthy adults cannot define ADHD treatment. Nonetheless, the result is a major contradiction to the assumption that stimulants work mainly by directly strengthening DAN.

An acute 2024 adult task-fMRI study likewise found no categorical stimulant effect within or between ADHD and healthy groups. A post hoc division by reactive versus proactive control suggested selective frontoparietal benefit in the reactive subgroup (Thunberg et al.; doi:10.3389/fphar.2024.1412178; PMID 39050752). The categorical null is robust enough to report; the subgroup mechanism needs replication.

157 Salience and cingulo-opercular effects

Anterior insula and dorsal anterior cingulate/midcingulate systems detect behaviorally relevant events, maintain task set and coordinate control. Acute stimulant meta-analysis most consistently identified right inferior frontal/insula effects, and a 2024 comparative neuroimaging meta-analysis mapped convergent stimulant and nonstimulant activation increases to left supplementary motor, middle cingulate and superior frontal regions with strong ventral-attention representation (Pan et al.; doi:10.1017/S003329172400285X; PMID 39806554). Drug-specific effects and age/sex moderation remained.

The 2023 dynamical study linked salience–DMN connectivity change to reduced performance variability (Cai et al., PMID 37491674). The 2025 Cell study also implicated salience-related connectivity and arousal rather than canonical attention-network strengthening (Kay et al., PMID 41448140). Together these support the interpretation that medication may alter arbitration—what becomes behaviorally commanding—rather than merely turning up a task module.

However, “the salience network switches the DMN off” is too strong. fMRI connectivity does not reveal a central switch, and network labels vary across parcellations. Salience, ventral attention and cingulo-opercular systems overlap in some atlases and separate in others. The empirical conclusion is distributed, context-dependent coordination.

158 Striatal reward and reinforcement-learning effects

Striatal effects are central but not uniform. Acute methylphenidate target engagement is clearest in striatal PET. Functional consequences differ by reward phase, genotype, sex, task and comorbidity.

Three months of OROS methylphenidate moved low-reward nucleus-accumbens and thalamic activation toward controls in a small youth study, while high-reward processing was not the same story (Mizuno et al., 2013; PMID 24179790). In a functional-genetic pilot, methylphenidate attenuated exaggerated striatal reward modulation only in a DAT1 9R subgroup; no diagnostic effect appeared among 10R homozygotes (PMID 25485641). In adults, acute post-dose wanting and ventral-striatal connectivity distinguished later stimulant responders from only five nonresponders, an intriguing but unvalidated result (Rode et al., 2023; doi:10.1016/j.jpsychires.2023.05.073; PMID 37269772).

Lisdexamfetamine-related clinical improvement covaried with increased reward-learning activation in a twenty-person crossover study (Newcorn et al., 2024, PMID 38101205). Mixed amphetamine salts produced different reward-network changes in children with versus without externalizing/substance-risk features (PMID 38293912). These results make reward modulation plausible and subgroup-dependent. They do not establish a single deficient reward circuit.

159 Thalamic and cerebellar effects

Thalamus and cerebellum are often omitted from the "DMN versus task network" story even though both contribute to timing, gating, prediction, motor coordination and cognitive state. Acute methylphenidate altered thalamic perfusion in children but not adults in one study (Schrantee et al., 2017, PMID 27942455). Low-reward thalamic activation changed after three months of methylphenidate in youth (Mizuno et al., 2013, PMID 24179790). A 2022 twelve-week nonrandomized comparison found both methylphenidate and atomoxetine shifted widespread fronto-cingulo-parieto-cerebellar degree-centrality patterns, with more limited cerebellar effects under atomoxetine and drug-specific brain–symptom correlations (Fu et al.; doi:10.1093/ijnp/pyac028; PMID 35524732).

In adults, an acute methylphenidate-induced increase in vermis-lobule-VI to precentral connectivity predicted two-month clinical response. Crucially, the useful shift moved away from the neurotypical mean, favoring a compensatory interpretation (Pretzsch et al., 2025; doi:10.1038/s41598-025-87204-3; PMID 39962109). Improvement without convergence is not failure; it is a warning that a control average is not always the therapeutic target.

160 EEG, ERP and neural-noise findings

EEG provides millisecond temporal resolution but has its own inverse problem and analytic variability. Methylphenidate can alter oscillatory power, event-related potentials and trial-to-trial consistency. A 2019 study proposed that modulation of neural noise underlay methylphenidate effectiveness (doi:10.1016/j.bpsc.2019.03.011; PMID 31103546). Such results align with reduced reaction-time variability, but "noise" must be defined—spectral variance, phase consistency, entropy and behavioral variability are not interchangeable.

In a 2017 resting EEG study, the theta/beta ratio decreased after methylphenidate primarily because beta increased, not because theta normalized (PMID 27798290). In a responder-enriched six-month comparison, methylphenidate and dexamphetamine moved broad EEG power toward control patterns despite different baseline responder profiles; selection of good responders and lack of randomization inflate a normalization interpretation (PMID 27552823).

An eight-week source-localized EEG study compared dexmethylphenidate, guanfacine and combination treatment during spatial working memory. Treatment-related beta dynamics and prediction patterns differed by agent and task phase (Michelini et al., 2023; PMID 35963558). Similar symptom improvement can therefore arise through different electrophysiological routes. EEG biomarkers remain research tools; they are not validated universal medication selectors.

161 Dynamic connectivity, flexibility and dwell time

Dynamic analyses are closest to the Flow Hijacked question: does medication change the probability of entering and remaining in a task-favorable state? For a semi-Markov model, state i has a dwell distribution $F_i(\tau)$ rather than the memoryless geometric duration of a standard Markov chain. Medication effect can be expressed as

$$\Delta h_i(\tau) = h_i^{\text{drug}}(\tau) - h_i^{\text{placebo}}(\tau),$$

where $h_i(\tau)$ is the hazard of leaving state i after dwelling for τ. A negative Δh_i for a task-favorable state would mean longer stability, but only if the state has been independently linked to useful performance.

The 2022 randomized NeuroImage study reported remediation of aberrant brain-network dynamics in children under methylphenidate (Mizuno et al.; doi:10.1016/j.neuroimage.2022.119332; PMID 35640787). The 2023 Bayesian work linked state-dependent DMN and salience coupling to variability (Cai et al., PMID 37491674). The 2025 task study found reduced network flexibility associated with better performance (Nugiel et al., PMID 41271625). Together, these support the hypothesis that medication can stabilize some task-relevant configurations acutely.

They do not establish that ADHD always entails excessive flexibility or short dwell time. Hyperfocus may involve overly stable engagement and costly release. An optimal treatment might reduce unwanted departures without making all states rigid. Dynamic benefit is directional and task-specific.

162 Children and adults can show opposite effects

Development changes receptor expression, network segregation, myelination, task strategy, metabolism and prior medication exposure. Pooling ages can erase or reverse meaningful effects. The acute perfusion study's child-specific thalamic response and larger adult cortical perfusion reduction is one direct example (Schrantee et al., 2017, PMID 27942455). The 2018 clinical network meta-analysis also found different comparative treatment rankings by age.

Age interactions can be mistaken for replication failure if the samples differ developmentally. Conversely, a nominal interaction in a small study can be unstable. Strong conclusions require adequately powered age-stratified longitudinal designs, not separate underpowered child and adult literatures narrated as one.

The lecture should never state "medication does X to the ADHD brain" without naming the developmental population. At minimum: children, adolescents and adults must remain separate evidence rows.

163 Responder-specific changes

Group-average effects combine responders, nonresponders and people who discontinue. A biomarker can be predictive, prognostic, mediating or merely correlated; these roles are different.

- A **prognostic marker** predicts improvement regardless of treatment.
- A **predictive marker** interacts with treatment choice.
- A **mediator** changes because of treatment and carries part of the effect to outcome.
- A **correlate** covaries with response without establishing direction.

Baseline caudate activation predicted differential methylphenidate versus atomoxetine response in one youth study, while motor-cortex activation related to atomoxetine response (Schulz/Rubia program; doi:10.1016/j.jaac.2017.04.005; PMID 28647012). A 2026 replicated cognitive-profile study found that an inhibitory-control profile responded strongly to atomoxetine whereas a sustained-attention profile responded well only to methylphenidate; prospective biomarker-guided replication is still needed (Leikauf et al.; doi:10.1016/j.jaac.2025.07.007; PMID 40681145). Baseline DAN tract size, acute reward salience and acute cerebellar–motor connectivity have each predicted later response in small studies.

These findings oppose diagnosis-wide pharmacological interchangeability. They do not yet justify routine imaging-based assignment. A treatment predictor must survive independent prospective validation, add value beyond clinical variables, and change outcomes when used to allocate treatment.

164 Treatment prediction versus induced change

Suppose X_0 is a baseline network measure, $M_1 - M_0$ an induced change, and Y clinical outcome. A regression

$$Y = \beta_0 + \beta_1 X_0 + \beta_2 T + \beta_3 (X_0 \times T) + \epsilon$$

tests whether baseline X_0 predicts differential response to treatment T. It does not show that treatment changes X. A mediation model instead asks whether $T \to \Delta M \to Y$, requiring temporal ordering, treatment randomization and strong assumptions about mediator–outcome confounding.

Many medication-imaging papers are called mechanistic when they are predictive. Others show induced change without linking it to behavior. Still others correlate acute brain change with later symptoms in small samples. Each can be valuable if named correctly.

The 2026 dual-tracer PET study is a model boundary: methylphenidate altered apparent DAT/NET binding and cognition improved, but binding changes did not correlate with cognitive change (Oya et al., PMID 41128391). Parallel change is not mediation.

165 The "normalization" audit

Normalization requires a defined normative target and a design capable of showing movement toward it. Let μ_C be a control mean, and x_0, x_1 patient measures before and after treatment. A scalar convergence index is

$$N = |x_0 - \mu_C| - |x_1 - \mu_C|.$$

Positive N indicates movement toward the control mean. Even then, five questions remain:

1. Is the measure reliable within individuals?
2. Was the pre-treatment difference replicated and clinically meaningful?

3. Was change caused by treatment rather than practice, motion or maturation?
4. Did convergence mediate functional benefit?
5. Is the control mean optimal for this person and task?

The term is justified only locally: for example, a specific activation contrast, during a specific task, after a specified exposure. It is not justified when controls were not rescanned, when the treatment group was selected cross-sectionally, when improvement moved away from the control mean, or when no behavioral link exists.

The 2024 structural MRI paper used normalization language because treated low-symptom children did not differ from controls in right insula thickness and left nucleus-accumbens volume, whereas untreated high-symptom children did (Wu et al.; doi:10.1038/s41386-024-01831-4; PMID 38409281). Without pretreatment scans or random assignment, this equivalence cannot identify a medication effect. Selection and severity are alternative explanations.

166 Convergence, compensation and improvement without measurable network change

Three distinct therapeutic architectures should be kept visible.

Convergence: a reliable abnormal metric moves toward a normative range and the change relates to benefit. Some task-activation and latent-state findings fit this category locally.

Compensation: the system recruits an alternative configuration that improves behavior without becoming more control-like. The adult vermis–precentral connectivity predictor moved away from controls yet predicted benefit (Pretzsch et al., 2025, PMID 39962109).

Behavioral improvement without detected network change: symptoms or performance improve while the chosen imaging measure is null. This can mean the measure missed the mechanism, statistical power was inadequate, or benefit arose at another level. Acute n-back comparisons and washout connectivity studies provide examples of bounded neural nulls.

A fourth possibility is **network change without behavioral improvement**. Acute methylphenidate has moved some network patterns toward controls without improving already-normal task performance. Neural convergence is not automatically clinically useful.

The mapping can be represented as a 2×2 table:

	Behavioral benefit detected	No behavioral benefit detected
Network change detected	possible mediation, compensation or parallel effect	physiological action without demonstrated functional value
No network change detected	mechanism elsewhere or insensitive measure	null under tested conditions

Only the upper-left cell invites a mechanistic claim, and even there mediation must be tested.

167 Acute benefit cannot establish durable neural reorganization

An acute drug can transiently increase the probability of a useful state. Durable reorganization would mean that the system remains changed after the acute drug state, or that repeated treatment produces learned or developmental effects beyond momentary exposure. Evidence for that stronger claim is limited and mixed.

Longitudinal imaging studies are often open-label, small and confounded by treatment selection. A corrected two-year ABCD analysis did not show broad symptom-linked striatal normalization (Kaminski et al., 2024, PMID 39505862). Twelve-month PET suggested DAT adaptation rather than a simple maintained acute state (Wang et al., 2013, PMID 23696790). A 2024 review of stimulant pharmacodynamics concluded that acute circuit effects are better supported than prolonged normalization and emphasized small, heterogeneous samples (Parlatini et al.; doi:10.1016/j.neubiorev.2024.105841; PMID 39098738).

The strongest current formulation is modest: medication can acutely and sometimes over weeks alter activity, coupling, variability and state dynamics in ADHD-relevant systems. Some changes track symptom or performance improvement. The direction, network, timescale and developmental pattern are heterogeneous. Evidence does not support one universal normalized brain state.

168 Flow Hijacked interpretation: medication as a parameter perturbation

Supported interpretation, not established unitary mechanism. In the Task-State Viability Envelope developed later in the lecture, medication may change several separable parameters:

- increase the gain of task-relevant representations;
- raise the expected value or vigor of low-immediacy actions;
- reduce unwanted transition hazard during task;
- increase dwell time in a useful configuration;
- alter salience arbitration so distractors produce smaller displacement;
- reduce reaction-time or neural variability;
- lower control energy required to enter a task state;
- change arousal so that wakefulness becomes adequate for control.

These are alternative fingerprints, not synonyms. Guanfacine may influence recurrent prefrontal stability and sympathetic arousal differently from methylphenidate. Atomoxetine may alter prefrontal catecholamine regulation without amphetamine-like striatal release. A stimulant may increase reward salience in one responder and stabilize network configuration in another.

The Flow Hijacked prediction is therefore multivariate: two patients with equal symptom improvement can show different changes in entry latency, dwell time, perturbation susceptibility and adaptive release. A treatment that lengthens dwell but worsens release could help ordinary sustained work while intensifying hyperfocus costs. A treatment that improves arousal but not learned task policy could make capacity available without deciding where it is directed.

169 Contradiction ledger for medication–network claims

Preferred story	Resisting evidence	Consequence
medication suppresses DMN	methylphenidate increased beneficially associated DMN-pattern activity (PMID 36717325)	regulation and coupling matter more than global suppression
medication strengthens attention networks	large 2025 study mapped effects to arousal/reward, not DAN (PMID 41448140)	canonical DAN is not the only or primary route
more flexibility is better	acute MPH reduced flexibility and better performance tracked stabilization (PMID 41271625)	optimal flexibility is state- and task-dependent
benefit means convergence to controls	beneficial vermis–motor shift moved away from controls (PMID 39962109)	compensation can be therapeutic
a drug class has one network effect	age, sex, genotype, familial bipolar risk and cognitive profile moderate response	subgroup and state are part of the mechanism
acute effect implies chronic repair	DAT adaptation and weak two-year causal evidence	timescale must be explicit
target occupancy mediates benefit	PET binding change did not correlate with cognitive improvement (PMID 41128391)	molecular action and clinical mediation are separate
frontoparietal activation must increase	atomoxetine improved inhibition with lower IFG/ACC activation (PMID 28657141)	efficiency may appear as less activation
network change guarantees function	some convergence occurred without performance gain	neural endpoints need behavioral validation

170 What is established, supported and still hypothetical

Established evidence

- Several medications reduce core ADHD symptoms over weeks in randomized trials.
- Methylphenidate engages DAT and NET; amphetamine-class drugs have release-promoting transporter-substrate pharmacology; atomoxetine inhibits NET; alpha-2 agonists act at adrenergic receptors.
- Medication can change task activation, resting connectivity, oscillations and dynamic-state measures under specific conditions.
- Effects vary by molecule, age, task, exposure and individual.

Supported interpretation

- Medication can improve control partly by altering catecholamine-dependent gain, arousal, reward weighting, network stability and the relation between internally and externally oriented systems.
- Some useful effects are better described as stabilization or compensation than uniform activation or normalization.
- Molecular target engagement is necessary for drug action but does not alone explain clinical response.

Plausible synthesis

- Different drug classes may widen the Task-State Viability Envelope through different combinations of lower entry cost, reduced unwanted-exit hazard, increased useful dwell time and altered reward sensitivity.
- Medication may create a more learnable cognitive state in which strategies and environmental scaffolds can be acquired, although direct mediation evidence is limited and belongs in the combined-treatment part.

Flow Hijacked hypothesis

- The most informative medication biomarker may prove to be an individualized transition fingerprint—change in state-entry probability, perturbation amplification, dwell-time hazard, adaptive-release capacity and return latency—rather than a static regional mean. This is a research prediction, not a validated biomarker.

Open questions

- Which dynamic metrics replicate across scanners and tasks?
- Do acute state changes predict years-long function?
- Are responders characterized by convergence, compensation, or distinct mechanistic subtypes?
- Can medication improve unwanted departure without impairing adaptive switching or creative internal cognition?
- Which network changes are pharmacological, and which arise because successful performance changes experience and learning?

Part XII synthesis. Medication does not turn a single task network on or the default-mode network off. It perturbs a multiscale system. Under some conditions that perturbation changes arousal, reward, gain, coupling, variability or state stability in ways that support control. The scientifically defensible object is a treatment-, person-, task- and timescale-specific network fingerprint—not a universal image of normalization.

What would neural normalization actually require?

"Normalization" is meaningful only when a measure that differed from a specified comparison group shifts toward that group under a defined treatment, task, dose, and time interval. Even then, the word does not establish mediation or recovery. A measure can move toward the group mean without causing clinical improvement; a person can improve through compensation while the measure remains atypical; and a group mean can conceal several trajectories.

Acute pharmaco-fMRI is especially easy to overread. A single dose can change vascular tone, arousal, motion, task performance, and neural activity simultaneously. Chronic treatment introduces adaptation, learning, exposure, selection of responders, and discontinuation. Cross-sectional comparisons of medicated and unmedicated participants cannot separate treatment effects from the reasons treatment was initiated or continued.

The stronger design combines randomization where feasible, repeated measurement, a credible control condition, pharmacokinetic timing, behavioral mediation, and follow-up after sustained exposure. It asks whether a neural change predicts later function beyond baseline severity and whether the same relationship replicates. Until those conditions are met, medication should be described as modulating measured network behavior in particular paradigms, not repairing a universal ADHD network.

A brain change after medication is not yet a mechanism of recovery

Pharmaco-neuroimaging studies occupy a demanding inferential position. They must establish that a drug changed a measured signal, that the signal relates to a defined cognitive operation, and ideally that this change explains clinical or functional benefit. Many studies establish only the first link. Target engagement is important, but it is not mediation.

Acute and chronic designs answer different questions. A single dose can reveal immediate modulation during a task, often near peak exposure. Repeated treatment introduces learning, adaptation, sleep and appetite changes, expectancy, adherence, and altered task familiarity. An acute shift toward a comparison-group mean cannot justify a claim of durable neural normalization. Conversely, absence of an acute change does not show that longer-term treatment lacks a mechanism.

The word normalization should be replaced by a vector of explicit observations. Did activation increase or decrease in a specified region and epoch? Did within-network coherence or between-network segregation change? Did the change occur only during successful trials? Was it associated with symptom improvement, accuracy, variability, or no behavioral endpoint? Did untreated participants, placebo recipients, and healthy comparison participants show stable reference values? Without these details, normalization compresses several possible results into one flattering label.

Age matters because the reference system is developing. A medication-related pattern in children cannot automatically be projected onto adults, and a control-group mean is not a timeless optimum. Prior treatment history also matters: washout does not erase developmental exposure, and medication-naive samples may differ systematically from previously treated

samples. Motion, arousal, vascular effects, and task performance can all change the imaging signal independently of the proposed network mechanism.

The strongest design would combine randomized treatment, pharmacokinetic sampling, repeated imaging, ecological outcomes, and preregistered mediation. It would measure entry, stable performance, lapse, re-entry, and adaptive release rather than averaging an entire block. Dynamic models would be trained on one subset and tested on held-out sessions, with motion and physiological alternatives carried through the uncertainty analysis.

Several treatment fingerprints are possible. One drug might shorten entry latency without changing dwell. Another might reduce unwanted-exit hazard but make adaptive switching harder. A behavioral intervention might leave local neural measures unchanged while making cues and routines more effective. Two treatments can yield similar symptom improvement through different state-space routes. That possibility is a reason to measure multiple layers, not to infer the route from the clinical endpoint.

Negative results are especially valuable here. Null or inconsistent network findings limit claims of a common neural pathway and can expose dependence on task, age, preprocessing, or responder status. A mechanistic lecture should preserve these nulls because they define what medication imaging has not yet established.

The disciplined conclusion is narrower and more useful than "medication normalizes the ADHD brain." Medication can alter catecholamine signaling, behavior, and some task- or rest-related neural measures. Which neural changes mediate sustained, ecologically meaningful improvement—and for whom—remains an active empirical question.

A causal chain can fail at every arrow

Write the proposed mechanism as a sequence: drug exposure changes catecholamine signaling; signaling changes a network parameter; the parameter changes a cognitive operation; the operation changes daily function. Evidence for one arrow does not validate the rest. A PET finding may support target engagement without identifying the network route. An fMRI change may correlate with improved accuracy without mediating symptom change. A symptom response may occur without the measured network effect.

Mediation is strongest when exposure precedes mediator change, mediator change precedes outcome, treatment is randomized, relevant post-treatment confounders are addressed, and alternative mediators are measured. Most small imaging studies cannot satisfy all conditions. Their value is often hypothesis generation and constraint rather than a complete causal explanation.

Responder-only analyses are especially treacherous. Defining response after treatment and then searching for the neural pattern that responders show can produce selection artifacts. Baseline prediction, target engagement, and mediation are different analyses and require separate validation samples. A biomarker should be tested against clinical information already available; added value matters more than classification accuracy reported in isolation.

The network claim should also survive behavioral matching. If treated participants perform better, their different neural signal may reflect a different task state rather than a direct drug effect. Designs can compare trials matched on accuracy or model performance jointly, while acknowledging that matching on a post-treatment variable can introduce its own bias. There is no purely mechanical correction for a poorly specified causal question.

The Flow Hijacked treatment map remains useful if it is kept conditional. A wider viability envelope, longer task-state dwell, or lower perturbation gain are candidate mediators. Each requires an operational measure and a falsification test. Until then they organize research questions; they do not certify neural normalization.

Acute modulation is not developmental normalization

A single dose can demonstrate target engagement or an immediate change in performance-linked activity. It cannot show that the same network configuration persists after drug clearance, that repeated exposure produced learning, or that development followed a different trajectory. Those claims require repeated randomized measurement, credible untreated or alternative-treatment comparisons, and outcomes beyond the scanner.

PART XIII

PSYCHOTHERAPY, BEHAVIOR AND THE ARCHITECTURE AROUND ATTENTION

Show how interventions can change cues, policies, habits, feedback loops and function without inventing neural repair.

Safren · Solanto · MTA · Sonuga-Barke · Westwood

Part proposition

Psychological and behavioral treatment does not need to "repair a defective attention circuit" to matter. It can change the task, the cue, the sequence, the reinforcement schedule, the interpretation of failure, the probability of beginning, and the route back after a lapse. Those are not decorative effects around a supposedly biological core. They are changes in the coupled person–environment system through which disability or participation is expressed.

This part therefore asks a more exact question than "Does therapy work?" For every intervention we ask: **which outcome layer changes, according to whom, against what comparator, for how long, and with what direct evidence about mechanism?** A reduction in self-rated symptoms, a teacher-observed increase in on-task behavior, a completed tax return, less family conflict, and a change in an fMRI signal are all legitimate observations. They are not interchangeable observations.

Evidence boundary. Clinical benefit can be established without a scan. Conversely, a changed EEG or BOLD signal does not by itself establish meaningful clinical benefit, mediation, far transfer, or durable neural reorganization.

Treatment map: what is trained and what is actually known

Intervention family	Principal target	Best-supported outcome layer	Important resistance in the evidence	Direct ADHD neural-mechanism evidence
ADHD-adapted CBT	planning, task execution, maladaptive appraisals, relapse recovery	adult symptoms and selected functional outcomes	effects shrink against credible active comparators; packages are heterogeneous	generally absent
Metacognitive / executive self-management therapy	monitoring, organization, time use	adult ratings and targeted organization	narrower replication base than CBT	absent
Organizational-skills treatment	materials, calendars, homework, routines	targeted organization and homework	parent effects often exceed teacher effects; broad transfer is not guaranteed	absent
Behavioral parent training	antecedents, contingencies, instructions, reinforcement	parenting, disruptive behavior, family function	probably blinded core-symptom effects are smaller	absent at network level
Classroom behavioral treatment	immediate feedback and classroom contingencies	on-task behavior and proximal school function	implementation and rater dependence; attainment data are thinner	absent
Mindfulness-based intervention	meta-awareness and reorientation	small-to-moderate clinical effects in heterogeneous studies	a key active-comparator RCT found no superiority over psychoeducation	sparse, small studies
DBT-informed / emotion-regulation work	affective escalation, response delay, interpersonal behavior	emerging symptom and emotional-function evidence	adaptations differ; no clear core-symptom superiority to CBT	absent
Digital therapeutics	product-specific cognitive practice or treatment delivery	selected objective-attention or access outcomes	digital is not one mechanism; durability and real-world transfer uncertain	sparse exploratory EEG
Computerized cognitive training	trained cognitive process	near transfer and selected task measures	far transfer and daily function are inconsistent	limited target engagement, mediation unproven
Neurofeedback	learned regulation of a selected signal	protocol-specific cognitive measures	recent probably blinded synthesis finds essentially null average core-symptom benefit	training signal is not proof of therapeutic neural mediation
Coaching	accountability and implementation	possible self-management benefit	small pilot/observational base, heterogeneous providers	absent

How to read a psychosocial-treatment effect

Psychological and behavioral trials cannot blind participants and therapists to the intervention in the way a matched pill trial can sometimes blind drug identity. This does not invalidate them. It changes what must be controlled and how outcomes should be interpreted. A parent who receives training knows that treatment occurred and also observes the child most closely. Their rating can capture a real context-specific improvement, altered expectations, changed tolerance, or all three. A teacher or independent observer may be less exposed to expectancy but may miss change at home.

The recurring **rater gradient**—larger effects from people closest to treatment, smaller effects from probably blinded raters—is therefore substantive evidence. It can mean reporter bias, proximal context-specific benefit, or limited cross-setting transfer. The solution is not to select the preferred rater. Report each layer and ask whether objective or independently observed function changed.

Comparators also define the question. Waitlist controls estimate the combined effect of treatment content, hope, attention, structure, and natural change relative to delayed care. A credible active comparator estimates whether the specific package adds value beyond time, support, monitoring, and expectation. Both questions matter, but effect sizes cannot be placed on one scale without noting the contrast.

For outcome Y, an intent-to-treat mean contrast is

$$\widehat{\Delta}_{\text{ITT}} = \bar{Y}_{T=1} - \bar{Y}_{T=0}.$$

Its standardized version depends on the chosen standard deviation and can conceal clinically different baseline variance. Attrition makes complete-case contrasts vulnerable when dropout depends on response, burden, or adverse effects. Multiple reporters, time points, and outcomes create multiplicity. Treatment allegiance and fidelity affect transportability.

A strong lecture statement therefore carries its design with it: "In medication-treated adults, manualized CBT outperformed relaxation plus educational support on specified symptom outcomes" is more informative than "CBT rewires attention." "Parent training improves parenting and disruptive behavior more consistently than independently rated core symptoms" is more honest than either "it fixes ADHD" or "it only changes perception."

Persistence is not a single property

Follow-up after psychotherapy can test at least four different things: retention of knowledge, continued use of a strategy, persistence of functional benefit, and persistence of benefit after the support is removed. These are not equivalent. An organizational routine may remain effective only while the calendar and weekly review remain in place; that is sustained treatment use, not necessarily a failure of learning. A parent-training effect may decline when school, household, or developmental demands change. A cognitive-training effect may persist on the practiced task without transferring to daily life.

Long-term comparisons also lose their original meaning as subsequent care diverges. Participants seek medication, therapy, coaching, or accommodations outside the protocol; people doing poorly may intensify care; people doing well may stop. Attrition is rarely random. The lecture should therefore specify whether "maintained" means a within-group change from baseline, a continued advantage over the original comparator, or an outcome associated with naturalistic treatment exposure. Durability is a causal question with its own design, not a decorative follow-up p-value.

The time horizon belongs inside every treatment claim, never outside it.

171 Why psychotherapy is not secondary decoration

The phrase "core disorder" can create a false hierarchy. Medication appears to act on the core; psychotherapy is then described as supportive decoration. That hierarchy confuses a causal story with an outcome map. ADHD is diagnosed through persistent symptoms and impairment in real environments. A treatment that changes whether a student submits work, whether a parent–child interaction escalates, whether an adult can re-enter a task after interruption, or whether shame turns one missed deadline into a week of avoidance has changed the disorder's lived expression, even if no study has demonstrated a change in intrinsic network topology.

The correct comparison is not biological versus psychological. A reminder is physically instantiated; a medication is behaviorally expressed; reinforcement history alters what becomes salient; sleep changes both neural and behavioral control. The useful distinction is instead between **intervention targets and evidence levels**. Pharmacotherapy can modify catecholaminergic signaling and reduce symptoms during exposure. Skills treatment can install explicit action policies. Parent training can alter reinforcement latency and conflict. An accommodation can reduce the unsupported control required by a task. Each acts at a different coordinate of the coupled system.

This also prevents two equal and opposite errors. The first is biologic reductionism: if an intervention has not altered a scan, it has not treated anything real. The second is psychotherapeutic neuro-mythology: because learning necessarily involves the brain, a clinical improvement may be narrated as demonstrated normalization of the DMN, salience network, or frontoparietal control. The first denies function; the second invents mechanism.

Established evidence: several psychosocial interventions improve specific symptoms or functions. **Supported interpretation:** external structures and learned strategies can compensate for unreliable endogenous control. **Flow Hijacked synthesis:** such interventions may change entry routes, boundary conditions, and recovery policies in task-state space. **Not established:** that standard ADHD psychotherapy normalizes large-scale network switching.

172 ADHD-adapted adult cognitive behavioral therapy

ADHD-adapted CBT differs from generic cognitive restructuring. Its active vocabulary is concrete: calendar use, prioritization, breaking assignments into observable actions, estimating time, reducing distractors, using reminders, rehearsing problem solving, examining all-or-nothing interpretations, and planning for recurrence. The model assumes that knowing what to do is not equivalent to reliably executing it at the needed moment. Treatment therefore repeatedly couples an intention to a cue and a small action.

Randomized trials and syntheses support a moderate adult evidence base, especially for persistent symptoms and functional problems among people already receiving medication. In the Safren trial, medication-treated adults with residual symptoms were randomized to a manualized CBT program or relaxation with educational support; CBT improved symptoms more strongly (Safren et al., 2010; PMID 20736471). Meta-analytic work, including a Cochrane review, supports benefit while emphasizing heterogeneity, self-report, imperfect blinding, and limited certainty for some outcomes (López et al., 2018; PMID 29566425). Later component-level synthesis suggests that organizational and problem-solving elements contribute to benefit, but a component network meta-analysis cannot make each ingredient independently randomized (Ostinelli et al., 2025; PMID 39732478).

The active comparator matters. In the large COMPAS factorial study, structured group psychotherapy did not outperform individual clinical management on the observer-masked primary outcome, although both psychological conditions could be clinically useful; methylphenidate had an independent acute effect (Philipsen et al., 2015; PMID 26536057). This is not a verdict that CBT is ineffective. It shows that time, expertise, expectation, monitoring, and structured clinical contact are potent comparators, and that between-treatment superiority is a harder question than improvement from baseline.

The most defensible lecture claim is therefore specific: adult ADHD-adapted CBT has meaningful evidence for symptoms and selected functional outcomes, including organization and coping, with larger and more secure effects against waitlist or weak controls than against high-quality active care. It teaches procedures rather than proving restoration of a generic executive capacity. Direct evidence that these clinical gains are mediated by DMN suppression, frontoparietal recruitment, or altered network dwell time is not established.

173 Metacognitive therapy

"Metacognitive" in this literature usually means explicit monitoring and executive self-management rather than an abstract claim about consciousness. The patient learns to notice recurrent failure points—misestimated duration, unrecorded intention, task switching without closure, materials lost during a transition—and then to deploy a preselected routine. A foundational randomized trial found greater improvement with metacognitive therapy than with supportive psychotherapy in adults, with medication status incorporated into the design (Solanto et al., 2010; PMID 20231319).

The distinction between capacity and policy is useful. A person may be capable of planning when prompted in a quiet clinic but fail to evoke that plan at 08:10 while locating keys, answering a message, and remembering a child's school form. Metacognitive treatment attempts to make the policy callable: pause, externalize, sequence, execute, check. It reduces reliance on an unprompted realization arriving at precisely the right time.

Evidence is promising but narrower than the general adult CBT corpus. The intervention overlaps substantially with organization, problem solving, and cognitive restructuring; long-term independent replications are fewer. Subjective improvement in executive functioning does not prove a change in laboratory executive capacity. Nor does increased awareness prove a specific frontoparietal or cingulo-opercular mechanism.

Within the Flow Hijacked lens, metacognitive training can be represented as learning an observation policy π_{monitor} that detects departure from a task-favorable state and calls a recovery routine. This is a **modeling interpretation**, not a measured neural result. Its value is that it generates an empirical question: after treatment, are departures detected earlier, are re-entry latencies shorter, and is ecological performance improved even if lapse frequency itself changes little?

174 Organizational and planning strategies

Organizational-skills treatment makes the future perceptible in the present. Calendars, launch pads, checklists, visible clocks, single capture systems, color-coded materials, planned review times, and standardized transitions are often caricatured as tips. In treatment they are repeatedly installed, rehearsed, audited, and repaired. Their function is to reduce working-memory load, the number of branching decisions, and the delay between an intention and the cue that retrieves it.

A meta-analysis of organizational-skills interventions in young people supports moderate-to-strong effects on targeted organization and homework outcomes, with less secure effects on core symptoms and meaningful differences between parent and teacher reports (Bikic et al., 2017; PMID 28088557). Randomized school-based programs have reported immediate and maintained gains, but generalization is conditional on continued use and environmental support (PMIDs 22889336,

29172596). Recent trials continue to test central-executive and organizational packages, but a change in school organization should not be redescribed as a normalized executive network (PMID 37439737).

The intervention's success can be real even when scaffolding remains necessary. Glasses do not fail because vision worsens when they are removed. Likewise, an external planning system may be a durable component of functioning rather than temporary evidence of an unhealed mind. The relevant outcome is not independence from every aid; it is reliable participation at acceptable cost.

Flow Hijacked interpretation: external organization may enlarge the set of states from which task entry is feasible and reduce the control effort required to remain viable. **Empirical requirement:** demonstrate lower initiation latency, fewer unplanned transitions, or improved task completion under ecological measurement. No claim about intrinsic network normalization is required.

175 Problem solving and task decomposition

"Write the report" is not one action. It is an unresolved tree containing topic selection, retrieval, reading, drafting, citation, editing, formatting, and submission. Each branch adds uncertainty. For a person whose task engagement is strongly shaped by delay, ambiguity, and competing salience, the global instruction can remain motivationally distant even when the deadline is understood.

Problem-solving modules convert an opaque goal into a finite sequence with visible stopping rules: open the file; name the question; list three claims; retrieve one source; draft one paragraph; mark the next action. Component network meta-analysis associates problem-solving elements with modest inattention reduction in adult psychological treatment (Ostinelli et al., 2025; PMID 39732478), and the technique is embedded in established CBT packages (Safren et al., 2010; PMID 20736471). Yet components are seldom randomized alone. Therapist structure, expectancy, organizational tools, and behavioral rehearsal travel together.

The mechanistic statement should remain modest. Decomposition reduces decision branching and makes feedback more immediate. It may lower task-entry cost, but no study has isolated a corresponding reduction in neural control energy. The intervention can be evaluated directly without speculative imaging: time to first observable action, probability of returning after interruption, proportion of subgoals completed, and calibration between predicted and actual duration.

176 Avoidance, shame, and recovery after failure

Repeated inconsistency can become a learning history. A missed task evokes criticism; criticism becomes anticipatory shame; shame makes the task aversive; avoidance produces urgent consequences; urgency finally creates enough salience for action; last-minute completion then teaches both that crisis "works" and that calm initiation does not. This loop cannot be reduced to inattention. It contains reinforcement, emotion, self-prediction, and relationship history.

CBT addresses catastrophic and global appraisals—"I missed this, therefore I am incapable"—while behavioral planning specifies the smallest recoverable action. The target is not positive thinking. It is preventing a local failure from causing a long excursion away from the task and from care. Relapse planning makes expected variability explicit: the system will sometimes depart; success includes shortening the return.

Evidence for adult CBT includes improvement in emotional symptoms, self-esteem, and global functioning, although outcome coverage varies and self-report is common (Safren et al., 2010; López et al., 2018; PMID 29566425). Shame-specific mediation is not established. Emotional relief may follow improved performance; improved performance may follow reduced avoidance; both may be driven by therapeutic contact or expectation.

The lecture should therefore present this as a clinically grounded feedback model rather than an etiological claim. Early relational adversity is neither necessary nor sufficient to generate ADHD. But once failure–shame–avoidance dynamics exist, they are legitimate treatment targets regardless of how ADHD began.

177 DBT-informed emotion-regulation approaches

Emotional dysregulation is common and impairing in ADHD, but it is not uniquely diagnostic and must not be made universal. DBT-informed adaptations teach attention to escalating cues, response delay, distress tolerance, behavioral alternatives, and interpersonal repair. They target what happens when affective salience displaces the current goal and narrows the available response repertoire.

Recent randomized and meta-analytic evidence is emerging. A 2025 meta-analysis of adult ADHD DBT trials reported benefit, while a 2026 direct comparison of DBT skills and CBT did not establish clear superiority for core symptoms (PMIDs 40513141, 42106651). Programs vary: some are full DBT-derived protocols, others are skills groups containing mindfulness and emotion-regulation components. This heterogeneity limits the meaning of a single pooled label.

The most secure claim is that emotion-focused skills may benefit selected people with prominent lability, impulsive reactions, shame, or interpersonal conflict. It is not established that they correct a unitary ADHD mechanism. No replicated treatment-neuroscience evidence links DBT-informed benefit to salience, limbic, or control-network change.

Flow Hijacked hypothesis: emotion-regulation practice could reduce the hazard that an affectively salient perturbation ejects the system from a task-viable region and could accelerate repair after displacement. A study could test this with ecological momentary assessment, wearables, task logging, and preregistered dynamic imaging. Until then, "salience-network regulation" is an inference, not a result.

178 Behavioral parent training

Behavioral parent training changes the learning environment; it does not diagnose the parent as the cause. This distinction is ethically and scientifically indispensable. Caregivers learn to make instructions brief and observable, establish predictable routines, use immediate and proportionate reinforcement, reduce inadvertent reinforcement of escalation, and respond consistently across repeated episodes. The child's behavior changes because antecedents and consequences change—not because the treatment has proved an attachment-based origin.

Meta-analyses show a consistent rater gradient. Parent-rated ADHD symptoms often improve by small-to-moderate amounts, whereas independently rated or probably blinded core-symptom effects are smaller and can be nonsignificant. Effects on parenting behavior, disruptive behavior, family conflict, and global child or family function are generally stronger (PMIDs 27179355, 34224837). Follow-up syntheses suggest some maintenance over months, but continuation depends on implementation and context (PMID 37720584).

The MAPPA preschool factorial study clarifies layer-specific effects: methylphenidate produced clearer symptom reduction, while parent training contributed to functional outcomes; the two approaches were not interchangeable (PMID 36306807). In families where a caregiver also has ADHD, instructions and monitoring may need to be simplified and externalized for both generations. Treating parental ADHD, however, has not reliably magnified the child's response across analyses.

The Flow Hijacked formulation is environmental, not blaming: parent training changes feedback latency, cue reliability, and perturbation intensity. These are boundary conditions of the child's regulatory system. There is no direct evidence that standard parent training normalizes the child's large-scale neural networks.

179 Reinforcement, antecedents, and family contingencies

Behavior is shaped not merely by reward magnitude but by timing, predictability, effort, and the availability of competing rewards. "You will benefit at the end of the semester" has low temporal proximity. A small, immediate, credible consequence can exert greater control over behavior than a large distant one. This does not mean a child values the future less as a moral matter; it means the implemented contingency has different effective weight.

Behavioral treatment begins upstream. An antecedent can specify the action, reduce distracting options, and signal when reinforcement becomes available. Consequences are then delivered consistently and rapidly enough to be learnable. Families are helped to distinguish planned ignoring from emotional withdrawal, proportionate consequences from punitive escalation, and reinforcement from bribery after refusal. The target is a stable contingency system rather than permanent surveillance.

Reward language must not be collapsed into dopamine language. Behavioral reinforcement is an observed relation between context, action, and future action probability. Dopaminergic signaling participates in reinforcement learning, but a token system's efficacy does not prove that it "raises dopamine to normal." The clinically testable variables are delay, consistency, response cost, generalization, and maintenance.

180 Organizational-skills treatment for young people

Youth organizational treatment addresses a developmental mismatch: the environment expects increasingly independent planning before the student can reliably supply it. Treatment often combines materials management, assignment recording, time estimation, homework routines, and parent or school check-ins. The scaffolding is gradually adjusted rather than removed by ideology.

Evidence supports targeted improvements in organization and homework, often with larger parent- than teacher-rated effects (Bikic et al., 2017; PMID 28088557). That discrepancy may reflect context-specific change, differential observation, allegiance, or weak generalization. It should be inspected, not averaged away. Grades and standardized attainment are also more distal than assignment recording or binder organization; a proximal gain need not immediately move a cumulative academic endpoint.

The intervention is best evaluated against its declared target. If the target is "record every assignment accurately and submit a higher proportion," a symptom scale alone is insufficient. If the target is broad independence, continued reliance on adult

prompts matters. Treatment fidelity, school resources, developmental stage, learning disorders, and medication status can all modify outcome.

181 School–home coordination

A plan that exists only in one setting creates a transition failure. School–home coordination aligns task definitions, communication channels, reinforcement, and responsibility. Daily report cards, shared assignment systems, brief teacher feedback, and scheduled caregiver review can reduce the information loss that occurs between classroom intention and home execution.

Collaborative school–home randomized studies support improvements in proximal school and family outcomes (PMIDs 27566117, 29588050). Digital implementation systems can support fidelity, but implementation success is not the same as efficacy and may depend on staffing, training, and local infrastructure (PMID 39650565).

Coordination should not become continuous moral accounting. A child who receives only deficit signals across settings can experience the system as surveillance. Good design keeps measures few, observable, time-limited, and linked to teachable actions. It also includes successes and reduces the burden of carrying information through the very working-memory channel most likely to fail.

182 Academic and classroom interventions

Classroom interventions include altered seating, reduced distraction, shorter task units, movement opportunities, explicit transition cues, immediate feedback, daily report cards, and contingency management. Their common operation is to change the ratio between task signal, delay, effort, and competing input. Teacher training aims to make these contingencies consistent enough to learn.

A 2025 systematic review and meta-analysis of school-based randomized trials reported small improvements in inattention and combined symptoms, with no significant pooled hyperactivity/impulsivity effect, alongside small-to-moderate effects in selected academic, externalizing, and social domains (PMID 40761448). Outcomes are sensitive to rater blinding and implementation; teachers both deliver and often rate the intervention.

On-task behavior is not the same as learning. A child can face the page more often without mastering the concept; conversely, a modest behavioral change can compound into meaningful attainment over time. The lecture should show the causal distance: intervention → classroom behavior → completed practice → learning → accumulated attainment. Evidence weakens as the horizon lengthens and other determinants enter.

183 Workplace accommodations and the evidence gap

Adult occupational impairment is central to ADHD, yet workplace intervention trials are sparse compared with symptom trials. Common accommodations—written priorities, fewer simultaneous channels, protected focus blocks, reduced notification load, flexible scheduling, quieter workspace, structured check-ins, explicit deadlines, and task chunking—are mechanistically plausible because they reduce interruption, ambiguity, and unsupported prospective memory. Plausibility is not an RCT.

The evidence base allows a restrained conclusion: school environmental modifications have moderate support for proximal outcomes, while controlled ADHD-specific workplace evidence is insufficient. Employment context also matters. An accommodation that aids a software developer may be impossible for an emergency clinician; a quiet room may help one person and reduce essential stimulation for another. The unit of fit is person × role × environment.

Workplace function should be measured directly: lateness, error rate, project completion, job retention, supervisor-rated performance, burnout, and accommodation sustainability. Symptom reduction cannot stand in for these outcomes. Nor should disclosure be assumed safe or necessary; legal and organizational contexts vary.

184 Psychoeducation

Psychoeducation gives a shared model of symptoms, impairment, treatment options, monitoring, and realistic expectations. Its humane function is often underestimated. Replacing “lazy” with a precise account of initiation difficulty can reduce shame while preserving agency. Replacing “medication fixes everything” with an outcome-specific model can improve monitoring and help the patient notice what remains to be learned.

Pragmatic trials such as PEGASUS support gains in knowledge, satisfaction, and selected quality-of-life or engagement outcomes (PMID 28641216). Digital and app-supported programs may improve homework adherence or access, though format effects can reflect novelty and engagement rather than informational content (PMID 36041353). Core-symptom reduction is not the primary or most secure effect.

Psychoeducation often forms part of an active comparator. In the adult mindfulness trial, psychoeducation itself produced improvement, helping explain why mindfulness did not demonstrate clear superiority (PMID 29356899). That result illustrates why "control" does not mean inert.

No isolated neural mechanism has been established. Psychoeducation may change prediction, self-observation, care-seeking, and treatment use. It does not follow that it directly changes network topology.

185 Motivational approaches and engagement

Motivational interviewing does not attempt to manufacture motivation by lecture. It elicits the person's own goals, makes ambivalence discussable, and reduces coercive conflict. In adolescents, it is frequently embedded within parent–teen skills programs or used to improve medication engagement. Its proximal outcome may be attendance or willingness to practice, not core symptom reduction.

Trials show mixed clinical results. Parent–teen behavior therapy enhanced with motivational interviewing has produced acute benefits in some studies (PMID 27077693), while the community STAND trial did not outperform usual care on its principal outcome trajectory despite engagement-related promise (PMID 32861773). Longer follow-up is emerging (PMID 39442667), but subsequent care and developmental change complicate causal inference.

Within a dynamical account, motivation changes the value of entering and remaining in an effortful state. That statement can remain psychological. It is not evidence that motivational interviewing reweights ventral-striatal prediction errors or salience-network gain. A direct test would require concurrent changes in valuation behavior, treatment adherence, and prespecified neural measures mediating clinical outcome.

186 Mindfulness-based interventions

Mindfulness training asks the participant to notice that attention has moved, recognize the current object of thought or sensation, and return without converting every departure into failure. For ADHD, this maps naturally onto meta-awareness and reorientation. Yet conceptual fit should not be mistaken for decisive efficacy.

Meta-analyses suggest small-to-moderate potential benefit with substantial heterogeneity across age, protocol, comparator, and rater (youth: PMID 36429915; adults: PMID 40958241). A key adult randomized trial found mindfulness-based treatment no better than active psychoeducation, although both groups improved (PMID 29356899). Expectancy, instructor contact, home practice, and self-report are difficult to blind.

Direct neural evidence is sparse. A 40-participant complete-case fMRI study reported treatment-related working-memory activation associations after mindfulness versus psychoeducation (PMID 29758392). A 2026 EEG/LORETA study of 30 participants reported electrocortical changes including beta-power and precuneus-related measures (PMID 42350829). These studies are too small and method-dependent to establish replicated DMN regulation, network switching, or mediation.

The defensible claim is that mindfulness may train detection of attentional drift and deliberate reorientation for some people. It is not established as a replacement for indicated medication, nor as a method that normalizes DMN–task anticorrelation. Creative spontaneous thought should not be pathologized; the target is flexible regulation of when internal cognition serves or displaces the current goal.

187 Acceptance-based approaches

Acceptance-based work targets the struggle with internal experience: the urge to wait until a task feels easy, the attempt to suppress every distracting thought, or the conclusion that discomfort means action is impossible. Values-guided action can be clinically meaningful when shame and avoidance dominate.

However, a mature standalone ADHD evidence base for acceptance and commitment therapy was not identified in the acquired corpus. Acceptance elements occur inside third-wave packages and mindfulness programs, making their independent contribution difficult to estimate. Component network meta-analysis does not turn co-occurrence into isolated causality (Ostinelli et al., 2025; PMID 39732478).

Any claim that acceptance reduces salience capture or transition volatility is therefore a **Flow Hijacked hypothesis**. The clinical rationale may justify careful use; it does not justify presenting core-symptom efficacy or neural mechanism as established.

188 ADHD coaching and evidential immaturity

Coaching commonly supplies regular accountability, collaborative goal selection, planning, and external monitoring. In the Flow Hijacked vocabulary, it resembles an external control loop: intention is sampled at short intervals, deviation is detected, and a corrective action is selected. That description explains face validity; it does not establish treatment efficacy.

The verified research base contains small pilot evidence rather than a mature set of adequately powered, independently replicated randomized trials (for one complementary coaching pilot, PMID 26383058). Provider training, boundaries, dose, and intervention content vary widely. Selection effects are strong: people able to purchase and sustain coaching may differ systematically; expectancy and concurrent medication or psychotherapy confound observational gains.

Coaching should therefore be presented as promising and potentially useful for implementation, with indeterminate core-symptom efficacy and no direct neural evidence. Popularity is not a negative finding—but neither is it evidence.

189 Internet-delivered CBT and telehealth

Digital delivery can reduce geographic, scheduling, and service-access barriers. Internet CBT may deliver the same planning and cognitive modules as in-person treatment, while telehealth parent training preserves live relational work. Yet "digital" names a channel, not a mechanism. A reminder application, therapist-guided CBT, an attention game, and an AI chatbot should never be pooled as one intervention.

Randomized evidence supports feasibility and possible clinical benefit for internet-delivered adult CBT (PMID 37483263). Smartphone-assisted psychoeducation can improve engagement relative to a brochure, but novelty and homework adherence may explain part of the difference (PMID 36041353). Digital parent-training evidence is encouraging but often small and brief.

Critical variables include therapist guidance, adherence, dropout, data privacy, accessibility, comparator intensity, and whether effects persist after access ends. A scalable intervention with a small individual effect can have population value; a technically sophisticated product can also generate no far transfer.

190 Game-based digital therapeutics

Game-based therapeutics use adaptive cognitive demands and immediate reinforcement to train selected attention operations. The STARS-ADHD randomized digital-control trial reported improvement in an objective attention measure in children, supporting product-specific target engagement (PMID 33334505). Objective performance is valuable, but it is not equivalent to broad symptom control, school function, or durable developmental change.

A review of reviews through 2025 judged the overall digital-intervention evidence heterogeneous and often low in certainty (PMID 40264083). Short follow-up, proprietary outcome selection, sponsor involvement, and product heterogeneity complicate synthesis. Medication may remain more effective for core symptoms even when a game improves a trained or related attention measure.

Small electrophysiological studies add biological observations but not definitive mediation. An uncontrolled 25-child study reported increased midline frontal theta power after four weeks of digital training (PMID 34972140); an 18-child adjunctive qEEG study reported altered prefrontal theta–gamma coupling (PMID 42036744). Without adequate controls, preregistration, replication, and outcome mediation, these are exploratory signals.

191 Cognitive training and the near-transfer/far-transfer boundary

Cognitive training repeats an operation—working-memory updating, inhibition, sustained attention—with the expectation that practice improves that process. The most common interpretive error is to move silently from better performance on the trained task to better executive control in life.

Near transfer refers to improvement on similar tasks; far transfer refers to improvement in dissimilar cognitive operations, symptoms, academic or occupational behavior, and daily function. A recent synthesis restricted to blinded or objective outcomes found small and setting-specific effects, with more convincing trained-process change than broad clinical transformation (PMID 36977764). Strategy-based interventions often show clearer impairment benefit than process training.

The correct causal ladder is: exposure to training → learning on trained task → transfer to an untrained process → use in an uncontrolled environment → improvement in patient-valued function. Evidence at one rung cannot be assumed at the next. A neural change can sit between rungs but does not bridge them automatically.

192 Neurofeedback and the probably blinded null result

Neurofeedback trains a participant to alter an EEG or fMRI-derived signal. This makes it uniquely tempting to describe the treatment as direct brain repair. Three questions must remain separate: can the participant change the target signal; does the target signal change after training; and does that change cause blinded clinical improvement?

The 2025 meta-analysis by Westwood and colleagues included 38 randomized trials and 2,472 participants aged approximately 5–40. On probably blinded ratings, the pooled average effect on total ADHD symptoms was essentially null, although protocol-specific and cognitive effects remained possible (PMID 39661381). A 25-month double-blind follow-up attributed much within-group improvement to nonspecific elements of the treatment package (PMID 36521694). Add-on EEG neurofeedback synthesis reported small short-term parent-rated effects that did not persist clearly and found no evidence connecting physiological change to symptom change (PMID 36437272).

An active-versus-sham fMRI neurofeedback trial in 88 boys targeted right inferior frontal cortex. It failed to show an advantage on the primary inhibition-performance or successful-stop activation outcomes; exploratory error-monitoring effects were observed (PMID 39428885). This is informative target-engagement failure, not an embarrassment to erase.

The lecture decision is firm: neurofeedback remains scientifically interesting, but current probably blinded evidence does not support a meaningful average core-symptom effect. Learned signal control must not be equated with improved DMN–FPN switching, everyday self-regulation, or durable remission.

193 Part XIII synthesis — treatment can change the route

Psychosocial treatment can operate through at least six nonexclusive levers:

1. **Task definition:** reduce ambiguity and specify the next observable action.
2. **Cue structure:** externalize goals, time, transitions, and prospective memory.
3. **Learned policy:** select, monitor, persist, stop, and re-enter after a lapse.
4. **Contingency:** change the timing and reliability of feedback.
5. **Emotion and meaning:** reduce shame, avoidance, and escalation loops.
6. **Environment:** reduce perturbation load and unsupported control demand.

These are legitimate treatment mechanisms at behavioral and systems levels. Whether any particular lever changes large-scale neural dynamics remains a separate empirical question.

Compensation is not a lesser endpoint

Three treatment outcomes are often collapsed. **Restoration** means an impaired process itself becomes more reliable across contexts. **Compensation** means another process or external support achieves the goal despite persistent vulnerability. **Accommodation** changes the demand so the vulnerable process is invoked less intensely. A calendar can compensate for prospective-memory failures; a quiet workspace can accommodate distractibility; practiced monitoring might partly restore detection of attentional drift. The same intervention can contain all three.

These categories are not moral rankings. A durable compensatory system may create more participation than a small change in a laboratory process. Conversely, apparent accommodation can become exclusion if it removes challenge or opportunity. Evaluation must ask whether the arrangement improves autonomy, learning, well-being, and access at an acceptable burden.

For a repeated task (j), let successful completion be (Y_j=1), intrinsic control capacity be (C_j), learned skill support (L_j), and environmental support (E_j). A conceptual model is

$$\Pr(Y_j = 1) = \sigma\big(\beta_0 + \beta_C C_j + \beta_L L_j + \beta_E E_j + \beta_{CL} C_j L_j + \beta_{CE} C_j E_j\big)\,,$$

with logistic link $\sigma(z) = 1/(1 + e^{-z})$. An improvement in Y_j can occur through L_j or E_j even if C_j is unchanged. The equation is an explanatory decomposition, not a validated ADHD prediction model. It prevents the mistaken inference that real-world improvement proves intrinsic neural normalization.

Changing the architecture around attention

Psychotherapy and behavioral treatment often work by changing the policy and environment through which cognition is deployed. A calendar externalizes prospective memory. A visible timer converts an abstract future into present information. A launch ritual reduces the number of decisions required for entry. Problem solving converts an ambiguous project into executable actions. Emotion-regulation work reduces the secondary avoidance created by shame, threat, or repeated failure.

These changes are not merely cosmetic compensation. Human cognition normally depends on tools, routines, other people, and environmental structure. At the same time, functional usefulness does not prove that a specific brain network has

normalized. Direct neural evidence after ADHD psychotherapy remains small relative to the clinical literature, and cognitive training often shows stronger improvement on practiced tasks than on distant outcomes.

Mechanism studies should specify the target. Does treatment reduce initiation latency, increase use of external cues, improve recovery after interruption, alter reinforcement contingencies, or reduce avoidance? Does the effect persist when therapist contact ends and generalize across settings? Symptom scores, strategy use, objective performance, family burden, school or occupational function, and quality of life belong on separate outcome layers.

Psychotherapy changes the architecture in which attention must operate

Psychological treatment does not need to erase a neurodevelopmental difference to matter. It can change what happens before a task begins, how the next action is represented, which cues are visible, how interruptions are handled, and what the person predicts after a setback. These are changes in policy, learning, environment, and meaning. They can improve function even when symptom vulnerability remains.

ADHD-adapted CBT typically makes executive demands explicit. Large goals are converted into observable next actions; time is externalized; planning is practiced rather than merely recommended; distractors are anticipated; and beliefs formed through repeated failure are examined. The mechanism is not simply "thinking positively." It is the construction and rehearsal of procedures that are more likely to survive delay, ambiguity, and emotional activation.

Behavioral parent training changes antecedents, consequences, prompt structure, and reinforcement in the child's environment. Its strongest effects may appear in parenting practices and proximal behavior, with smaller effects under probably blinded assessment. That gradient does not make the intervention unreal; it specifies where evidence is strongest and warns against claiming a context-free cure. School interventions and organizational-skills training operate similarly by redesigning the task ecology.

Mindfulness-based approaches may train detection of attentional departure, decentering from internal content, and return without extended self-criticism. Evidence is heterogeneous, and the neural corpus is much smaller than the clinical literature. Coaching can supply accountability, sequencing, and feedback, but controlled evidence remains less mature. Digital tools can deliver cues at the correct moment yet also create distraction, dependence, privacy concerns, and engagement attrition.

The outcome hierarchy is crucial. A therapy may produce modest change in core symptom ratings while meaningfully improving completion, relationships, emotional recovery, or self-efficacy. Another may improve performance only while prompts remain present. Compensation, skill acquisition, generalization, and symptom change should therefore be measured separately. The question is not whether a strategy is "just a workaround," but whether it reliably expands functioning at an acceptable cost.

Claims about brain change require restraint. Cognitive training and neurofeedback studies sometimes report neural effects, but small samples, variable controls, target-engagement uncertainty, and limited far transfer constrain interpretation. For psychotherapy broadly, direct evidence of altered DMN regulation, salience switching, or frontoparietal dynamics is not yet commensurate with the confidence of many mechanistic diagrams. A plausible neural account must be labeled as inference until measured.

Under the Flow Hijacked lens, psychotherapy can modify the effective control policy π, lower the complexity of the task boundary, increase the salience of useful cues, and shorten recovery after departure. Environmental support can reduce perturbation load; rehearsal can make a response more reachable; self-compassion can prevent one error from becoming a prolonged avoidance state. These are testable mappings, not established neural mechanisms.

The practical synthesis is layered. Medication may improve the conditions under which learning and control occur. Psychotherapy and behavioral treatment can supply the learned procedures, external structures, and relational contingencies that medication does not teach. Neither layer should be devalued because it acts differently.

Mechanism evidence begins by naming the trained operation

A psychotherapy study should state whether it trains cue use, task decomposition, prospective memory, lapse detection, reentry, emotion regulation, or belief revision. "Executive function" is too broad to serve as a mediator. The trained operation should improve before it is invoked to explain distal function, and far transfer should be tested rather than assumed.

This standard allows an honest result: treatment may improve organization and quality of life through learned scaffolding while direct evidence of altered large-scale network dynamics remains absent. That is a clinically important mechanism at the behavioral level, not a lesser outcome.

PART XIV

PSYCHOTHERAPY AND MEDICATION

TOGETHER — DIFFERENT LAYERS OF CONTROL

Establish outcome-specific complementarity while refusing to manufacture a neural synergy mechanism.

MTA · Safren · Philipsen · COMPAS · Emilsson

Part proposition

Medication can reduce symptoms during pharmacological exposure; psychotherapy can install strategies; behavioral treatment can alter contingencies; environmental design can lower task demand. These effects can be complementary without being identical, additive on every outcome, or neurally synergistic. "Combined treatment" is therefore not one verdict. It is a family of comparisons indexed by age, intervention intensity, outcome, time, and subsequent care.

194 The direct psychotherapy-neuroscience corpus is small

The psychological-treatment literature is clinically much larger than its treatment-neuroscience subset. In the acquired evidence system, only a small set of studies directly measured neural change around mindfulness, digital training, or neurofeedback. The core adult CBT, parent-training, school, organization, and coaching trials generally did not include pre/post fMRI, EEG, dynamic functional connectivity, or formal neural mediation.

This matters for both skepticism and enthusiasm. The absence of a scan does not weaken a well-designed trial of homework completion or family functioning. But the phrase "therapy rewires the brain" is too nonspecific to count as mechanism. Every learning event has a physical substrate; the scientific question is whether a defined neural variable changed relative to a credible control, temporally preceded outcome, statistically mediated that outcome under defensible assumptions, replicated, and generalized.

A useful evidential ladder is:

1. clinical outcome changes;
2. a neural measure changes;
3. neural change differs from an active control;
4. neural change precedes and predicts outcome change;
5. perturbing the neural target changes outcome;
6. the mediation result replicates and generalizes.

Most ADHD psychotherapy studies establish level 1. A few exploratory studies reach levels 2–3. Very little establishes 4, and the corpus does not support a general claim at levels 5–6.

195 Mindfulness and working-memory fMRI

The 2018 randomized fMRI study of mindfulness and psychoeducation in adults with ADHD analyzed 40 complete cases. It reported associations between reduced self-rated inattention/memory problems and stronger activation in portions of the left putamen and globus pallidus during working-memory processing (PMID 29758392). The design is important because it included an active comparator and a neural task.

Its interpretation must remain narrow. The sample was small; complete-case analysis raises attrition questions; multiple regions and behavioral outcomes increase multiplicity; BOLD activation is not a direct neurotransmitter measure; and an association between symptom change and activation does not demonstrate that activation change caused the clinical effect. The study did not establish global DMN normalization or corrected salience switching.

The lecture can use the result as proof that treatment-neuroscience measurement is possible, while also demonstrating how much stronger the evidence must become before a mechanistic claim is secure.

196 EEG changes after mindfulness or digital intervention

Electrophysiology offers millisecond resolution and can measure training-linked oscillatory changes, but frequency labels are not transparent psychological states. Midline theta can index different processes depending on task and decomposition; scalp power contains oscillatory and aperiodic components; source localization from limited electrodes is model-dependent.

A 25-child uncontrolled digital-training study reported increased midline frontal theta power and improved objective attention after four weeks (PMID 34972140). A 2026 adjunctive qEEG study in 18 young participants reported increased prefrontal theta–gamma coupling (PMID 42036744). A 30-participant 2026 mindfulness/LORETA study reported beta-power and precuneus-related changes (PMID 42350829). Each is a candidate signal, not a replicated mechanism. Small samples, absence or weakness of controls, analytic flexibility, and uncertain behavioral mediation make confirmation essential.

The safe sentence is: *some small studies report electrophysiological changes after behavioral or digital intervention.* The unsafe sentence is: *psychotherapy restores ADHD network dynamics.*

197 fMRI neurofeedback target-engagement failures

Neurofeedback is a particularly strong test of mechanistic reasoning because the intervention names a neural target. The active-versus-sham study of right inferior frontal cortex in 88 boys found no advantage on its primary inhibition-performance or successful-stop activation outcomes (PMID 39428885). Exploratory error-monitoring effects did not rescue the prespecified primary hypothesis.

Null target engagement can mean the signal was difficult to learn, the target was not causally decisive, the dose was insufficient, the feedback mapping was noisy, or the task outcome was insensitive. It does not prove that all neurofeedback is impossible. It does show why mechanistic plausibility and a sophisticated apparatus cannot substitute for a successful controlled test.

198 Neural association is not treatment mediation

Let $T \in \{0, 1\}$ denote randomized treatment, M a post-treatment neural variable, and Y a clinical outcome. A common analysis finds that T changes Y, and that change in M correlates with change in Y. This does not identify mediation. Both changes may be caused by expectation, engagement, arousal, task practice, motion, or an unmeasured variable U.

In potential-outcome notation, the average causal mediation effect at treatment level t is

$$\text{ACME}(t) = \mathbb{E}\big[Y(t, M(1)) - Y(t, M(0))\big] .$$

Identification generally requires assumptions stronger than treatment randomization: no unmeasured mediator–outcome confounding conditional on observed covariates, well-defined interventions and mediators, appropriate temporal order, and no problematic treatment-induced confounder of the mediator–outcome relation. A small pre/post correlation does not meet these requirements.

Even successful mediation would be measure-specific. If a working-memory activation contrast mediates a rating change, it does not follow that a resting-state network was normalized, that the effect is durable, or that the same mediator operates in children.

199 MTA at 14 months

The Multimodal Treatment Study of Children with ADHD randomized 579 children with combined-type ADHD to carefully managed medication, intensive behavioral treatment, their combination, or community care for 14 months (MTA Cooperative Group, 1999; PMID 10591283). It remains a landmark because it compared treatment strategies at scale rather than testing only one drug against placebo.

Carefully managed medication and combined treatment led on core symptom outcomes. Combined treatment was not uniformly superior to medication management on every core symptom measure, but it produced advantages in selected non-ADHD and functional domains and achieved benefit with a lower average stimulant dose. Intensive behavioral treatment changed parenting, classroom, and family contingencies that medication did not teach.

The accurate summary is outcome-specific: medication management produced the strongest acute core-symptom signal; combination extended benefit to some broader domains and could be dose-sparing. The slogan “combined always wins” is false, as is the opposite slogan that behavior added nothing.

200 MTA at 24 months, eight years, and 16 years

After the randomized treatment phase ended, families selected care in the community. Treatment exposure converged, adherence varied, and indication affected who continued medication. At 24–36 months, initial group differences attenuated (24-month report: PMID 15060224).

At six to eight years, original treatment assignment no longer predicted major symptom or functional outcomes; baseline severity and contextual factors were more informative (Molina et al.; PMID 19318991). The finding is frequently recruited into opposing narratives. One says medication has no lasting value; another dismisses the follow-up because randomization ended. Both are incomplete.

Long-horizon analyses extending to roughly 16 years associated sustained stimulant-exposure trajectories with altered height/weight patterns in some models. These are observational exposure classes after the randomized phase; confounding by indication, adherence, and selection remains. Growth monitoring is warranted without presenting a single deterministic trajectory.

201 Why the randomized comparison does not survive unchanged over decades

The transition out of the protocol changes the causal question. The 14-month trial estimates the effect of assigned, protocolized strategies under intensive management. Later follow-up describes trajectories after assignment no longer controlled treatment. It cannot simply extend the randomized ranking into a decade. Nor does convergence prove that the acute randomized effect was illusory. It shows that treatment implementation, self-selection, developmental change, and environment become part of the long-horizon system.

The follow-up does not estimate continuous protocolized treatment versus no treatment. It documents that an acute assignment did not create separable long-term groups after years of naturalistic, changing exposure. This is directly relevant to claims of disease modification: the trial does not demonstrate a durable "teaching the brain to focus" effect that persists independently of subsequent care.

202 Combined treatment by outcome domain

Treatment effects should be represented as a vector, not a single number. Let

$$\Delta \mathbf{y} = (\Delta S, \Delta E, \Delta A, \Delta O, \Delta R, \Delta Q, \Delta B),$$

where S is core symptom burden, E ecological executive function, A academic function, O occupational function, R relationships, Q quality of life, and B treatment burden or adverse effects. Medication and psychotherapy can have different signatures across these coordinates.

A scalar "best treatment" score $J = \mathbf{w}^\top \Delta \mathbf{y}$ requires weights $\mathbf{w}$. Those weights are not discovered by neuroimaging; they express patient values, age, context, risk, and clinical priorities. For one family, preventing classroom exclusion may dominate. For an adult, restoring reliable work while preserving sleep may be decisive. For another, emotional regulation or driving safety may be the urgent endpoint.

Adult trials support adjunctive CBT for residual symptoms and skills among medication-treated participants (Safren et al., 2010; PMID 20736471), and a recent meta-analysis found short-term combined benefit that could narrow by six to nine months (PMID 38084075). Parent training plus medication can improve parenting and oppositional or family outcomes beyond what medication teaches. School and organizational treatment can improve routines even when core symptoms remain.

203 Dose-sparing behavioral complementarity

A behavioral intervention can be complementary by allowing a lower medication intensity to achieve an acceptable functional target. Factorial home-setting and adaptive-treatment studies provide support for behavior-by-dose tradeoffs in selected pediatric contexts (e.g., PMID 37382748). The MTA similarly found lower average stimulant dosing in combined care than in medication management alone during the acute phase.

Dose-sparing is not automatically superior. Lower dose may reduce appetite or sleep burden, but greater behavioral-treatment intensity costs time, expertise, family capacity, and money. Some patients require medication at an effective dose regardless of scaffolding. The relevant outcome is the joint benefit–burden surface, not dose minimization as a virtue in itself.

204 Medication as a possible learning corridor

The **learning-corridor hypothesis** asks whether medication-induced symptom stabilization makes it easier to attend therapy, encode a routine, practice it repeatedly, and receive corrective feedback. It is clinically plausible: a strategy cannot be learned or enacted if the learner repeatedly leaves the training situation or never initiates practice.

But plausibility is not proof. A decisive test would require a factorial design with medication and structured skills treatment, repeated measurement of treatment attendance and skill acquisition, ecological assessment of implementation, a post-discontinuation or carefully controlled maintenance phase, and prespecified neural dynamics. The key interaction would be not merely whether combined care changes symptoms, but whether medication increases the *rate or durability of learning from psychotherapy*.

Formally, if L_k is acquired skill after session k, a simple learning model is

$$L_{k+1} = L_k + \alpha(M_k)\, e_k - \beta L_k + \varepsilon_k,$$

where e_k is usable practice/error information, $\alpha(M_k)$ is a learning-rate function under medication state M_k, β is forgetting, and ε_k is noise. The hypothesis is $\partial\alpha/\partial M > 0$ in a therapeutically responsive range—not that medication directly supplies the skill. This equation is a research scaffold, not an established biological law.

205 Demonstrated complementarity versus unproven neural synergy

Clinical complementarity is demonstrated when two treatments improve different outcomes or their combination improves a prespecified outcome beyond either alone. Neural synergy is a stronger claim: the combination produces an interaction in a neural mechanism that mediates clinical benefit.

In a factorial model,

$$Y = \beta_0 + \beta_M M + \beta_P P + \beta_{MP}(M \times P) + \epsilon,$$

β_M and β_P estimate main effects of medication and psychotherapy under the model; β_{MP} estimates statistical interaction on the chosen scale. Even a nonzero clinical β_{MP} is not neural synergy. To establish the latter, an analogous interaction on a prespecified neural mediator plus credible mediation evidence is needed.

The acquired corpus supports acute medication efficacy, psychosocial skill and functional effects, outcome-specific combined benefits, and possible dose-sparing. It does **not** establish that medication opens a neural learning corridor, that psychotherapy consolidates medication-induced network normalization, or that combined treatment permanently reorganizes ADHD brain dynamics.

Outcome hierarchy — what counts as recovery?

Layer	Representative measures	Typical evidence pattern	Guardrail
Core symptoms	clinician, parent, teacher, self ratings	strongest short-term medication evidence; psychosocial effects depend on rater and control	symptom change is necessary for many, never sufficient for all
Executive function	tasks and ecological ratings	laboratory and daily executive measures often diverge	do not infer daily organization from one cognitive task
Academic function	completed work, grades, attainment	proximal classroom behavior changes exceed evidence for long-term attainment	looking on-task is not identical to learning
Occupational function	attendance, errors, output, retention	thinner evidence than adult symptom trials	measure work directly
Relationships	conflict, parenting, partner/peer function	behavioral and combined care may add value beyond medication	relational change can occur without symptom normalization
Emotion regulation	lability, irritability, distress tolerance	important, heterogeneous, transdiagnostic	outcome and moderator, not universal criterion
Quality of life	participation and patient-rated well-being	improves on average but not in lockstep with symptoms	a patient-valued endpoint
Injury and driving	records, crashes, violations, simulators	clinically important, often observational	causal caution and exposure timing
Substance outcomes	initiation, disorder, acute events	therapeutic use differs from nonmedical use	never merge route, dose, supervision, and indication
Self-esteem and identity	shame, efficacy, qualitative accounts	psychotherapy may benefit this layer despite persistent symptoms	humane outcome, not cosmetic
Sleep, appetite, growth	sleep measures, weight/height, adverse-event reports	benefits must be balanced against burden	monitor across development
Cardiovascular outcomes	pulse/BP and rare events	small short-term mean changes and long-term events are different questions	duration-sensitive monitoring
Life-course participation	education, employment, mortality	predominantly observational	acute response is not lifetime recovery

The outcome hierarchy prevents a quiet substitution: a statistically significant symptom score cannot be used as proof of restored education, work, relationships, health, or identity. Different treatments may improve different layers, and complete care often means selecting a portfolio rather than declaring one winner.

A decisive test of the learning-corridor hypothesis

A strong study would randomize medication-responsive participants in a 2×2 factorial design: optimized medication versus matched pharmacological control, and manualized skills treatment versus structurally equivalent clinical management. Medication allocation would begin before skills acquisition, and treatment exposure, expectancy, therapist contact, sleep, and adverse effects would be measured. The design would sample five levels:

1. **state readiness:** momentary arousal, task initiation, and within-session attention;
2. **skill learning:** trial-by-trial acquisition and retention of explicit routines;
3. **implementation:** passive or ecological measurement of routine use outside sessions;
4. **function:** work, school, household, relationship, and patient-valued outcomes;
5. **neural dynamics:** preregistered task-state dwell, transition, or representational-stability measures.

Let L_{ik} be participant i's skill at session k, M_i medication assignment, and P_i psychotherapy assignment. A hierarchical learning curve could be written

$$L_{ik} = L_{\infty,i} - (L_{\infty,i} - L_{0,i}) \exp\{-k(\alpha_0 + \alpha_M M_i + \alpha_P P_i + \alpha_{MP} M_i P_i)\} + \epsilon_{ik}.$$

The key learning-corridor parameter is α_{MP}: does medication increase the rate at which psychotherapy-specific skill is acquired, beyond generic practice and main effects? A post-training probe under a carefully defined medication condition would test retention rather than same-day performance. Ecological implementation would test whether learned skill exits the clinic.

The neural hypothesis should be narrower still. If D_{ik} is task-favorable dwell time, demonstrate that randomized combination changes D, that change temporally precedes improved learning, and that it predicts retention under sensitivity analyses for mediator confounding. A null interaction with positive main effects would support complementarity without synergy. A neural interaction without better learning would show target engagement without the proposed behavioral mechanism. This design makes failure informative.

Ethically, a "pharmacological control" cannot mean depriving participants of indicated care without justification. Pragmatic alternatives include add-on designs among stable treated patients, randomized timing of skills treatment, micro-randomized medication-state comparisons under clinical oversight, or within-person N-of-1 components. Every design trades causal identification against feasibility and participant welfare.

Complementarity is not automatically synergy

Medication and psychotherapy can be complementary because they address different constraints. Medication may improve the probability that a cue is detected or a task rule is maintained during a treatment session. Psychotherapy may supply the rule, routine, environmental redesign, or recovery sequence that the medicine does not teach. Behavioral work may alter contingencies around the person. These layers can add value without interacting at a neural level.

Synergy is a stronger causal claim. It requires the combined outcome to exceed what would be expected from the components under an explicit model, ideally with factorial randomization, adequate power, treatment fidelity, and temporal measurement of learning. The attractive "learning corridor" hypothesis further predicts that medication changes a state variable that enables greater acquisition or consolidation of therapeutic skills. Clinical improvement alone does not identify that mediator.

The hypothesis remains worth testing. Trials could vary medication timing relative to skills training, measure within-session engagement and later strategy use, and test whether early changes in task stability mediate durable functional gains. Until then, the practical case for combined care should rest on demonstrated outcomes and individual needs, not on an unmeasured claim of neural optimization.

Complementarity must be demonstrated outcome by outcome

Combined treatment is often discussed as though two effective components must automatically create synergy. That conclusion does not follow. Additive benefit, complementary benefit, sequential benefit, and true statistical interaction are different patterns. The answer can also change across core symptoms, family behavior, organizational skill, academic performance, emotional regulation, and quality of life.

The Multimodal Treatment Study of ADHD remains foundational because it compared carefully managed medication, intensive behavioral treatment, their combination, and community care. Its acute findings, later follow-ups, changing treatments, and naturalistic trajectories should be read together. Initial group differences did not translate into a simple lifelong ranking of assigned conditions. Long-term interpretation is complicated because randomized treatment ended, subsequent care changed, and developmental and family factors continued to operate.

A learning-corridor hypothesis is nevertheless plausible. If medication reduces distractibility, improves response consistency, or lowers the cost of remaining with a task, a person may be better able to notice cues, rehearse organizational procedures, tolerate corrective feedback, and experience successful completion. Psychotherapy can then convert a temporarily more stable state into routines and skills that remain useful across contexts. This sequence is clinically intelligible, but the specific mediation from drug to neural stability to learning has not been established as a general mechanism.

The reverse direction is also possible. Behavioral structure can make medication effects easier to observe by defining tasks and outcomes. Psychoeducation can improve adherence and interpretation of adverse effects. Sleep routines can reduce variability that otherwise obscures dose response. Family work can prevent the treatment from being framed as the child's sole responsibility. Complementarity is therefore systemic, not merely pharmacological.

To test synergy, a study needs more than a combined arm with the largest mean improvement. A factorial or sequential design should estimate component effects, their interaction, treatment fidelity, exposure, and mediators. Repeated measures

should ask whether one component changes acquisition rate, generalization, durability, or context sensitivity of the other. Outcomes should include function and burden, not only symptom ratings from people who know the assigned treatment.

Timing may matter as much as package. Some people may first need symptom stabilization to participate in therapy; others may need environmental structure or treatment of sleep, trauma, anxiety, or substance use before stimulant response can be interpreted safely. Booster sessions, medication adjustments, developmental transitions, and changing demands turn combined care into an adaptive process rather than a one-time comparison.

The defensible message is neither "medication teaches no skills" nor "therapy corrects the cause." Medication, learning, relationships, and environment can act on different constraints within the same task lifecycle. Their combination is justified when the person's outcome profile and preferences indicate that multiple layers require support. Neural synergy remains a hypothesis until directly shown.

The learning-corridor hypothesis has a clear failure test

If medication creates a wider learning corridor, participants receiving effective pharmacological stabilization should acquire and generalize a trained strategy more rapidly than equally engaged participants without that stabilization. The prediction concerns learning rate or transfer, not merely a larger final symptom reduction. It should remain after differences in attendance, expectancy, and baseline severity are addressed.

A sequential randomized design could begin with medication or placebo stabilization, then introduce the same manualized skills program. Repeated probes would measure strategy use, task entry, lapse recovery, and function. A factorial alternative could test medication, psychotherapy, both, and neither while estimating interaction. In either design, exposure and treatment fidelity matter; assignment alone is not the received intervention.

The hypothesis would be weakened if medication improved symptoms but did not alter skill acquisition, if combined treatment benefit were fully additive, or if learning persisted equally without pharmacological stabilization. It would also be weakened if apparent synergy existed only in unblinded ratings. These are informative outcomes, not failures of treatment.

Several competing mechanisms remain. Medication may improve attendance rather than learning. Reduced family conflict may create practice opportunities. Successful early performance may change expectancy and avoidance. Psychotherapy may improve adherence and make the medication effect more consistent. The study must measure these routes before selecting the preferred one.

The Flow Hijacked interpretation is therefore modest: a more stable state may create opportunity for learning, while learning can change the future policy landscape. The two directions are plausible and clinically useful. Their neural implementation and generality remain open.

Complementarity can occur without neural synergy

Medication may reduce the volatility that makes practice difficult, while psychotherapy supplies explicit procedures for planning, cueing, monitoring, re-entry, and emotion regulation. That division of labor is clinically coherent. Yet a larger benefit from receiving both interventions can be additive, sequential, expectancy-mediated, or produced by better attendance; it is not automatically evidence that one treatment potentiated the neural mechanism of the other.

The strongest test distinguishes outcome layers. Symptom ratings, acquired strategy use, transfer to an untrained setting, persistence after treatment, and family or occupational function should be measured separately. If medication changes acute state control and therapy changes learned policy, their signatures should differ in timing and retention. A factorial or sequential design can test that prediction.

The Flow Hijacked "learning corridor" is therefore a hypothesis with a concrete burden: demonstrate that stabilization changes the rate, generalization, or durability of learning, not merely the final score. Until such evidence exists, the concept is best used to explain why combined care may be rational while keeping its proposed neural synergy explicitly unestablished.

PART XV

PUBLIC NARRATIVES AND CLINICAL

AUTHORITIES UNDER AUDIT

Teach the difference between a compelling explanatory story, a supported claim and a guideline recommendation.

Maté audit · Huberman claim map · AAP · NICE · EAGG

Part proposition

A compelling explanation can be humane, memorable, and partly right while exceeding its evidence. This part does not ask whether a public figure is "good" or "bad." It asks whether each consequential statement survives a transparent chain:

The Huberman audit covers the substantive ADHD/focus material located on the official site through the evidence cutoff: *ADHD & How Anyone Can Improve Their Focus* (13 September 2021); *Controlling Your Dopamine for Motivation, Focus & Satisfaction* (27 September 2021); *Time Perception & Entrainment by Dopamine, Serotonin & Hormones* (15 November 2021); *Focus Toolkit: Tools to Improve Your Focus & Concentration* (5 September 2022); *Adderall, Stimulants & Modafinil for ADHD: Short- & Long-Term Effects* (29 May 2023); *Tools to Enhance Working Memory & Attention* (29 January 2024); the John Kruse guest episode *Improve Focus with Behavioral Tools & Medication for ADHD* (10 March 2025); and *Essentials: ADHD & How Anyone Can Improve Their Focus* (31 July 2025). The audit uses legally accessible official episode pages, show notes, and public transcript text where available. The 2024 working-memory and 2025 Kruse pages expose official summaries and chapter navigation, while their complete transcripts are member-gated; those entries therefore audit the official **segment framing**, not a purported verbatim claim. In a guest interview, a chapter topic is not automatically attributed to either speaker. A timestamp is retained only when it appears in the official navigation or public transcript; it locates material and is not scientific evidence.

public claim → proposed mechanism → primary evidence → replication / newer evidence → lecture decision.

Authority cannot terminate the chain. Neither can popularity, clinical experience, an impressive mechanistic vocabulary, or a single citation.

206 How charismatic explanations acquire scientific authority

Public explanations gain power by compressing complexity. "Low dopamine," "the trauma response," "the default network," or "the prefrontal cortex" turns a distributed, heterogeneous, developmental phenomenon into a story with an agent and a remedy. Compression is necessary for teaching; the danger is concealed compression loss.

Several rhetorical moves deserve explicit detection:

- **Phenomenology-to-etiology:** an experience feels defensive, therefore defense caused the disorder.
- **Mechanism-to-efficacy:** an intervention could affect a pathway, therefore it treats ADHD.
- **Group-to-person:** a small mean imaging difference becomes an individual explanation or test.
- **Acute-to-durable:** a drug changes performance today, therefore it permanently trains attention.
- **Association-to-causation:** adversity or smartphone use precedes symptoms in some studies, therefore it creates ADHD.
- **Citation laundering:** a paper is cited near a claim stronger or different from what the paper tested.
- **Evidence flattening:** a first-line medication, a small adjunctive nutritional effect, and an unvalidated supplement appear in one list.

The audit does not require contempt. The better pedagogical move is to preserve what is experientially true while correcting causal confidence.

207 Maté's humane developmental and relational insights

Gabor Maté's account in *Scattered Minds* and related public material speaks to experiences often omitted from mechanistic accounts: the shame of inconsistency, the developmental importance of attuned relationships, the effects of chronic stress, the limits of medication as a complete life solution, and the need to understand a person's history rather than reduce them to a checklist. Several propositions align with contemporary evidence when stated carefully.

First, a diagnosis describes a recurring symptom-and-impairment pattern; it is not a complete etiological explanation. Second, no blood test or brain scan currently makes a validated standalone ADHD diagnosis. Third, genes influence probability rather than imposing a single predetermined life. Fourth, social and emotional environments shape development and can worsen or buffer impairment. Fifth, medication can be helpful without teaching every skill or repairing every relationship. These claims can belong in the lecture.

The clinical stance also has value independent of causal certainty. Listening for stress, family conflict, trauma, sleep, poverty, and relational strain is good assessment. Parent support can improve a child's life without implying parental causation. A person may find healing in self-understanding even if inherited liability remains.

Verification boundary. The current Maté audit is based on legally accessible public author material, publisher/preview material, and timestamped public transcripts listed in the evidence workbook. A complete legally supplied edition of *Scattered Minds* was not available for page-by-page inspection. Therefore book-level passage attribution remains provisional; the lecture must not present unverified quotations or exact chapter locators as if directly audited.

208 Maté's heredity, trauma, attachment, and reversibility claims

The central scientific tension is not whether environment matters. It does. It is whether early stress or relational disruption should replace inherited liability as the primary general cause of ADHD.

Twin and family designs show substantial heritability across the lifespan (Larsson et al., 2014; PMID 24107258). Molecular-genetic studies identify a highly polygenic architecture rather than one "ADHD gene" (Faraone & Larsson, 2019; PMID 29892054; Demontis et al., 2023; PMID 36702997). A 2025 genome-wide meta-analysis of childhood symptoms and diagnosis adds loci and plausible effector pathways (van der Laan et al., 2025; PMID 40962958). These findings do not imply determinism, immutability, or a purely biological essence. They do directly contradict the broad claim that ADHD is not inherited or that familial clustering merely transmits family conditions.

Adverse childhood experiences, prenatal stress, postpartum depression, poverty, and racialized stress are associated with ADHD symptoms or diagnosis in observational research (e.g., Zhang et al., 2022; PMID 36068993; Christaki et al., 2022; PMID 36096371; Manzari et al., 2019; PMID 31324962). Yet association can reflect causal exposure, inherited liability, gene–environment correlation, reciprocal effects, measurement, healthcare access, and residual confounding in different proportions. Genetically informed work has qualified simple maternal-stress interpretations (Eilertsen et al., 2021; PMID 32338109).

Trauma can produce distractibility, hyperarousal, sleep disruption, dissociation, avoidance, and executive impairment. These can coexist with ADHD or mimic aspects of it. It does not follow that tuning out is generally an emotional defense that becomes ADHD. That account may fit some biographies; it is unsupported as a general etiology.

Reversibility also requires precision. ADHD symptoms can remit, recur, or become less impairing; environment and treatment matter. The MTA longitudinal analysis found fluctuating trajectories and relatively uncommon sustained recovery, not universal fixed persistence and not universal reversibility (Sibley et al., 2022; PMID 34384227). Neuroplasticity means systems can change; it does not guarantee eradication of polygenic liability or permanent recovery after relational repair.

Maté claim audit

Consequential proposition	Contemporary assessment	Evidence that supports part of it	Evidence that resists it	Lecture use
A life history is essential; DNA alone is insufficient	well supported with qualification	biopsychosocial assessment; adversity and developmental context	strong inherited liability makes an either/or frame misleading	keep
ADHD is not inherited	substantially contradicted	none adequate for categorical denial	twin, family, GWAS, rare-variant and consensus evidence	replace with probabilistic polygenic account
ADHD is a reversible developmental delay, not a disorder	partly supported but overgeneralized	developmental change and episodic remission	fluctuating persistence; sustained recovery uncommon in long follow-up	present as contested hopeful framing
ADHD originates in infancy	plausible but underspecified	prenatal and early developmental liability	no single origin or developmental mechanism	qualify
Multigenerational stress and social conditions are the root	associations supported; causal exclusivity contradicted	adversity, prenatal stress, postpartum depression, socioeconomic gradients	genetic transmission, gene–environment correlation, bidirectionality	preserve context, reject singular root
No scan or blood test diagnoses ADHD	well supported	current diagnostic and biomarker literature	no validated routine standalone biomarker	keep
Genes predispose rather than predetermine	well supported	polygenic-probabilistic model	becomes misleading only if used to minimize inherited effect	keep
Rising diagnoses disprove genetics	invalid inference	diagnosis rates can change	recognition, criteria, access, ascertainment and service use can change faster than genes	omit/correct
Social experience shapes the developing brain	broadly supported	experience-dependent development	"social product" erases endogenous biology and nonsocial exposures	keep with bidirectional framing
Animal stress/dopamine findings establish human ADHD causation	mechanistically overextended	animal studies can show plausible pathways	translation, construct validity, and human dopamine evidence do not support a unitary chain	omit as proof
Familial clustering reflects repeated conditions, not transmission	contradicted	families transmit environment too	genetically informative and molecular evidence	correct explicitly
Distractibility begins as emotional defense	primarily clinical interpretation; unsupported generally	trauma-related attention disruption exists	not necessary or sufficient for ADHD	use only as individual formulation, never general cause

Consequential proposition	Contemporary assessment	Evidence that supports part of it	Evidence that resists it	Lecture use
Optimal conditions would prevent ADHD in sensitive children	untestable counterfactual certainty	support can reduce impairment	persistent liability occurs in supportive settings; "never" cannot be established	retain hope, remove certainty
Medication can help but is not the complete answer	clinically reasonable	guideline-based multimodal care	medication may appropriately be first-line by age/severity	keep
Family stress should always be addressed before child medication	too categorical	first-line parent/classroom treatment in preschool; nonblaming family assessment	sequencing differs by age and severity; family dysfunction must not be presumed	qualify by guideline and individual need

209 Phenomenological value versus causal overreach

Phenomenology answers *what an experience is like and how it is organized*. Etiology asks *what generated the disorder across people*. A causal model can be wrong while a phenomenological observation remains useful. A person may indeed "tune out" during conflict, experience work only when urgency becomes overwhelming, or carry shame from repeated misunderstanding. Therapy can address those patterns even if they did not cause ADHD.

This distinction protects compassion from becoming blame. If attachment rupture is presented as the general cause, parents can hear accusation and adults can feel required to discover hidden trauma. If genetics is presented as destiny, people can hear that learning and environment are irrelevant. The contemporary model is neither: inherited and developmental liability is substantial; environmental exposures, relationships, sleep, opportunity, and treatment modify expression and outcome; causal proportions cannot be inferred for one person from population estimates.

210 Huberman's DMN and task-network anatomy

The September 2021 Huberman Lab episode and July 2025 "Essentials" reprise offer an intuitively strong story: the default-mode and task networks should alternate, dopamine acts as a conductor, and ADHD reflects inappropriate coordination. The problem is not that network coordination is irrelevant. The problem is anatomical and evidential overprecision.

At approximately 00:26:40 in the 2021 episode, the account presents healthy anticorrelation and ADHD coupling with dopamine as conductor. The transcript also assigns dorsolateral prefrontal cortex to the DMN and medial prefrontal cortex to the task network, reversing standard network anatomy. Moreover, "task-positive network" collapses FPN, DAN, VAN, salience, cingulo-opercular, motor, and context-specific configurations.

Large-sample evidence supports a small average alteration in DMN–task/attention segregation in ADHD (Norman et al., 2023; PMID 36100657), building on earlier cingulate–precuneus work (Castellanos et al., 2008; PMID 17888409). It does not validate a binary switch, an individual biomarker, maximal DMN suppression as the goal, or dopamine as a directly demonstrated master conductor. The 2025 Essentials reprise at approximately 00:05:22 retains the simplified causal framing.

Lecture decision: replace the public network model with a coordination account involving multiple systems, state, development, task context, and small group effects. Preserve the intuition that transitions matter; remove the false anatomy and causal certainty.

211 Huberman on dopamine and stimulants

At approximately 00:32:57 in the 2021 episode, a 2015 Spencer paper is described as formalizing a low-dopamine ADHD hypothesis and explaining irrelevant neuronal firing. Spencer and colleagues reviewed direct prefrontal actions of psychostimulants; the paper did not originate or validate a unitary low-dopamine cause (PMID 25499957). A 2024 critical review finds robust dopamine involvement but limited evidence for a global hypodopaminergic state (MacDonald et al.; PMID 39619336).

The May 2023 episode is more reliable when distinguishing drug classes: methylphenidate primarily blocks catecholamine transporters; amphetamine is a transporter substrate and promotes release/reverse transport; lisdexamfetamine is a prodrug with delayed conversion. These distinctions belong in the lecture. The phrase "dopamine reduces noise and norepinephrine amplifies signal" (approximately 00:40:10) can be retained only as a pedagogical metaphor for some prefrontal models, not a literal clean division across the brain.

The episodes correctly distinguish supervised therapeutic use from rapid, high-dose, or nonmedical exposure and discuss rare psychosis risk, growth, and cardiovascular monitoring. Population studies do not support the general claim that prescribed treatment causes later substance use disorder, while diversion and nonmedical use remain real. Comparative cohort evidence found new-onset psychosis rare but more frequent with amphetamine than methylphenidate (Moran et al., 2019; PMID 30893533).

The recurrent statement that stimulants "teach the brain how to focus" is stronger than the evidence. Acute efficacy is well established (Cortese et al., 2018; PMID 30097390), and medication may make practice easier. But neither efficacy trials

nor observational safety studies demonstrate a durable attention-circuit training effect after discontinuation. This is exactly the learning-corridor hypothesis identified in Part XIV: testable, clinically plausible, not established.

212 Attentional blinks, visual-focus exercises, and the “17-minute” claim

The 2021 episode links spontaneous blinking, dopamine, time perception, attentional gaps, visual focus, and a single approximately 17-minute interoceptive practice. The evidential chain does not support the strongest public conclusion.

Terhune and colleagues reported time-estimation changes around spontaneous blinks in a laboratory paradigm (2016; PMID 27269720). That does not validate blink rate as a specific dopamine biomarker, show that manipulating blinks treats ADHD, or establish durable clinical change. A small school-based fixation-focus activity study reported attention improvement in elementary students (Lai et al., 2020; PMID 32635159). It did not show that one 17-minute meditation permanently rewires attention, generalize to diagnosed ADHD across ages, or test the same intervention described in the podcast.

The 2025 Essentials reprise again combines attentional blinks, open monitoring, panoramic vision, and visual-focus training. Lecture decision: these may be presented as interesting experimental or self-regulation practices, but not as established ADHD treatments and not with permanent-effect language.

213 Omega-3, modafinil, meditation, and smartphones

Evidence tiers must remain visible.

Omega-3 fatty acids. A meta-analysis supports at most a small average symptom effect, substantially below established stimulant effects; formulation and EPA dose vary (Bloch et al., 2011; PMID 21961774). It may be discussed as an adjunct with modest expectations, not a medication substitute.

Modafinil. Pediatric trials produced efficacy signals, but an adult nine-week dose-finding trial was negative (Arnold et al., 2014; PMID 22617860), and modafinil is not a standard first-line ADHD treatment. Healthy-volunteer cognitive-enhancement findings cannot be used as ADHD efficacy evidence. Safety and regulatory status must be explicit.

Meditation. ADHD-specific mindfulness evidence is heterogeneous and active-comparator results are not clearly superior; the single-session “permanent” claim is unsupported. A reasonable attention practice is not automatically a validated treatment.

Smartphones. Longitudinal evidence supports small, complex, sometimes bidirectional associations between problematic digital-media use and ADHD symptoms (Thorell et al., 2024; PMID 36562860). A 2026 within-person adolescent study reported small and time-limited bidirectional associations rather than proof that smartphones create ADHD (Nagata et al., 2026; DOI 10.1001/jamanetworkopen.2026.23748). Reducing problematic use may improve sleep, distraction, and functioning. It should not be sold as reversal of an adult-onset disorder caused by the phone.

15.8A Additional Huberman episodes: dopamine, time, focus tools, working memory, and clinical management

The broader episode stream changes the audit in two useful ways. First, it shows that the public model is not confined to one ADHD episode: the same dopamine, timing, focus-training, and circuit-plasticity propositions recur across years. Second, later episodes sometimes introduce better distinctions—especially therapeutic versus nonmedical stimulant exposure and treatment pluralism—while still placing interventions with radically different evidence bases in one practical-tool vocabulary.

Dopamine peaks, baselines, and stimulant context. The 27 September 2021 dopamine episode describes “dopamine peaks” and “baseline dopamine” as an accessible regulatory system and labels stimulant-driven dopamine elevation at 01:19:45 as potentially counterproductive for work, exercise, and attention. At 01:27:57 it explicitly separates ADHD prescriptions from non-prescription use. The separation is scientifically essential; the generic counterproductive claim is not. Randomized evidence establishes average short-term therapeutic efficacy of licensed stimulants in ADHD (Cortese et al., 2018; PMID 30097390), while PET work shows that oral therapeutic methylphenidate occupies DAT and changes extracellular dopamine without implying a global “dopamine tank” (Volkow et al., 1998, PMID 9766762; Volkow et al., 2001, PMID 11160455). Rapid, high-dose, and nonmedical exposure differs in pharmacokinetics, risk, and purpose. “Peak” and “baseline” can be teaching labels, but they are not single brain-wide quantities a listener can reliably feel, reset, or optimize.

Time as a transmitter-controlled frame rate. The 15 November 2021 episode links approximately 90-minute work bouts to ultradian chemistry at 00:25:00 and, at 00:34:40, presents dopamine and norepinephrine as producing time overestimation through a higher internal “frame rate.” ADHD research does support average timing differences, with task, age, interval, and modality heterogeneity (2022 child/adolescent meta-analysis, PMID 33302769; 2023 adult review, PMID 36833791).

It does not establish a one-transmitter clock, a universal ninety-minute ceiling on waking focus, or a fixed catecholamine-depletion schedule. The frame-rate account should therefore be identified as a metaphor and broader mechanistic proposal, not used to diagnose ADHD or prescribe a universal work cycle. The spontaneous-blink finding remains a narrow laboratory result, not a dopamine meter (Terhune et al., 2016; PMID 27269720).

The 2022 focus toolkit. At 00:09:37 the episode offers an "arrow" model in which epinephrine supplies alertness, acetylcholine supplies direction, and dopamine supplies persistence. This is memorable but anatomically and pharmacologically nonexclusive: all three systems have receptor-, region-, dose-, and state-dependent actions, and attention emerges from interacting cortical, subcortical, sensory, and motor systems. At 00:18:11 and 00:20:54, binaural beats and colored noise are proposed as focus or transition tools; at 01:01:19, brief daily meditation is proposed as refocusing practice; and at 01:36:50, prescriptions are again linked to training attention circuits and possibly reducing later dosage. A healthy-volunteer study, an acute laboratory effect, and a clinical ADHD treatment trial answer different questions. ADHD-specific mindfulness findings are heterogeneous and an active-comparator RCT did not establish superiority over psychoeducation (Janssen et al., 2019; PMID 29356899). The general cognitive-training literature shows clearer near transfer than durable far transfer (Westwood et al., 2023; PMID 36977764). No cited evidence establishes that binaural beats, colored noise, gaze practice, or brief meditation treats core ADHD, nor that stimulant exposure durably trains attention circuitry so medication can later be reduced. Reasonable self-regulation experiments should not be relabeled as validated disorder treatment.

Working memory as a dopamine assay. The 29 January 2024 episode pairs a working-memory test at 00:20:04 with striatal dopamine mechanisms at 00:27:02, and its official summary says memory tasks can be used to determine "baseline dopamine levels" in certain circuits. A group-level association between working-memory capacity and dopamine synthesis is not an individual biochemical assay. Working memory is affected by strategy, sleep, anxiety, practice, age, task design, and multiple transmitter systems; dopamine effects are often nonlinear and baseline-dependent. A 2022 meta-analysis supports an inverted-U relation between prefrontal dopamine/D1 signaling and working memory across experimental evidence (PMID 35389678), but it does not allow a person's latent dopamine concentration to be inferred from one score. Lecture decision: retain the inverted-U principle; reject "test your dopamine" as a clinical or self-measurement claim.

The 2025 John Kruse ADHD episode. This guest episode is clinically broader than the earlier solo accounts. Its official chapters cover genetic and environmental contributions (00:05:37), interest and hyperfocus (00:14:26–00:27:39), regular sleep timing (00:42:21), stimulant and psychiatric risk (01:04:32–01:26:06), fish oil (01:43:28), CBT (01:52:56), neurofeedback and video games (01:57:52), alpha-2 agonists (02:02:26), modafinil (02:10:13), and drug holidays/formulations (02:19:02). The lecture should preserve that plurality but reimpose the evidence hierarchy. Sleep is a clinically important state modifier, not a singular cause or cure (PMID 33402013; PMID 38738544). ADHD-adapted CBT has replicated adult symptom and selected functional benefit (PMID 20736471; PMID 29566425). Omega-3 has a small average adjunctive signal, not stimulant-equivalent efficacy (PMID 21961774). Probably blinded neurofeedback evidence is substantially weaker and recent synthesis finds essentially null average core-symptom benefit (PMID 39661381); a video-game study in older adults is not ADHD treatment evidence. Hyperfocus remains an emerging, non-diagnostic construct without a demonstrated dopamine signature (PMID 30267329). Long-duration cardiovascular associations require monitoring and cautious causal language rather than either alarm or reassurance without horizon (PMID 37991787; 2025 network meta-analysis PMID 40203844).

Huberman claim-to-primary-source map

Episode anchor	Public claim	Primary/newer evidence	Audit	Lecture decision
2021, 00:07:56	strong genetics plus roughly half "age out"	Faraone 2019; Sibley 2022; van der Laan 2025	genetic point strong; sustained recovery is less common and trajectories fluctuate	revise
2021, 00:14:57–00:20:00	hyperfocus, time, and working-memory difficulty characterize ADHD	consensus and emerging hyperfocus work	recognizable, heterogeneous; hyperfocus is not diagnostic	keep with qualification
2021, 00:24:10	dopamine is the neurochemical identity of focus	Spencer 2015; MacDonald 2024	dopamine modulates several relevant processes; attention has no single transmitter identity	revise
2021, 00:26:40	dopamine alternates DMN and task network; ADHD loses anticorrelation	Castellanos 2008; Norman 2023	small group effect; anatomy and binary-switch account oversimplified	replace with multi-network evidence
2021, 00:32:57	Spencer 2015 formalized low dopamine	Spencer 2015; MacDonald 2024	citation attribution inaccurate; global deficiency not established	correct explicitly
2021, 00:37:10	sugar/stimulant preference is dopamine self-medication	critical dopamine review	post hoc, nonspecific, not a diagnostic probe	omit
2021, 00:49:18; Essentials 00:14:33	stimulants teach children's brains to focus	medication efficacy and longitudinal literature	possible learning facilitation; durable disease modification not shown	hypothesis only
2021, 00:56:35	elimination diets help responsive subgroup	INCA and nonpharmacological review	some evidence, but burden, blinding, nutrition, and generalizability limit use	qualify and require supervision

Episode anchor	Public claim	Primary/newer evidence	Audit	Lecture decision
2021, 01:04:46	omega-3 improves focus/reduces medication need	Bloch 2011	small average adjunctive effect; replacement claim unsupported	qualify
2021, 01:16:56	one 17-minute practice produces near-permanent focus change	Lai 2020	study design and effect duration do not support claim	omit
2021, 01:22:50–01:33:40	blink manipulation trains dopamine-linked attention	Terhune 2016	association, proxy, and treatment efficacy conflated	omit as treatment
2021, 01:41:15–01:51:45	modafinil is an ADHD focus alternative	pediatric signals; negative adult trial	nonstandard, mixed evidence, regulatory context	contextual note only
2021, 01:56:19–02:01:23	precursors/nootropics improve focus	no adequate ADHD clinical base	biochemical plausibility is not efficacy	omit
2021, 02:09:14; Essentials 00:35:18	smartphones induce ADHD	Thorell 2024; Nagata 2026	small/bidirectional symptom associations; causation and diagnosis overstated	general digital hygiene only
Dopamine 2021, 00:09:58–00:15:30	dopamine level is framed as the primary determinant of motivation and drive, organized through two main circuits	direct ADHD PET (PMID 20856250); critical review (PMID 39619336)	some regional dopamine measures associate with motivation at group level; no global level or two-circuit account explains motivation across people	revise to regional, receptor-, state-, and task-dependent modulation
Dopamine 2021, 00:36:58; 01:19:45–01:27:57	repeated “peaks” lower a dopamine baseline; stimulant-induced spikes may be counterproductive or produce harmful rewiring	oral-MPH PET (PMIDs 9766762, 11160455); efficacy NMA (PMID 30097390); 12-month DAT study (PMID 23696790)	“peak/baseline depletion” is not a validated quantitative law for treated ADHD; route, dose, formulation, and supervision matter	split high-dose/nonmedical risk from therapeutic oral treatment; do not infer permanent rewiring
Time 2021, 00:25:00	waking focus follows universal approximately 90-minute bouts because acetylcholine/dopamine availability falls	sleep/circadian syntheses (PMIDs 28064405, 29477617, 31629217)	the syntheses support sleep/circadian interaction, not an exact waking clock or transmitter-depletion mechanism	present, if at all, as a flexible pacing heuristic
Time 2021, 00:34:40–00:39:10	dopamine/NE causes time overestimation, serotonin underestimation, through a “frame-rate” mechanism	timing EEG and meta/reviews (PMIDs 29391481, 22922163, 33302769, 36833791)	ADHD timing differences are heterogeneous; the clean transmitter-direction rule is not established	omit as ADHD mechanism; at most label an illustrative hypothesis
Toolkit 2022, 00:09:37	“arrow model”: LC epinephrine supplies alertness, acetylcholine target selection, and dopamine persistence	LC-NE and catecholamine syntheses (PMIDs 16022602, 17448997, 21531388)	LC is primarily noradrenergic; one-transmitter/one-function mapping is a mnemonic, not established anatomy	keep only as an explicitly corrected metaphor
Toolkit 2022, 01:01:19; 01:16:46–01:20:42; 01:36:50–01:39:19	meditation/refocusing, visual gaze, and medication train focus circuits, ideally allowing later dose reduction	active-comparator mindfulness RCT (PMID 29356899); fixation study (PMID 32635159); treatment-imaging review (PMID 39098738)	practices may aid reorientation; ADHD efficacy and mediation remain limited; medication efficacy does not show durable circuit training or expected dose reduction	separate self-regulation practice from validated treatment; learning-corridor claim remains a hypothesis
2023, 00:21:29–00:36:36	amphetamine, lisdexamfetamine, and methylphenidate mechanisms differ	pharmacology and comparative trials	high-level distinction sound	keep
2023, 00:40:10	dopamine removes noise; norepinephrine amplifies signal	prefrontal catecholamine models	useful metaphor, not transmitter law	label metaphor
2023, 00:54:48–00:58:06	childhood treatment does not raise addiction risk and shapes circuits	within-person substance-outcome studies	safety inference broadly supported; circuit-shaping claim stronger	split claim
2023, 01:13:28	growth and cardiovascular risks are monitorable	MTA growth; Farhat 2025	generally small averages do not remove individual risk	keep with monitoring
2023, 01:27:45–01:38:20	therapeutic and nonmedical exposure differ	Moran 2019; Chang 2014; Quinn 2017	important and supported distinction	keep
Working Memory 2024, 00:20:04; 00:27:02; 00:36:13	working-memory tasks can determine a person’s baseline dopamine in selected circuits	inverted-U review/meta-analysis (PMIDs 21531388, 35389678); healthy PET-fMRI (PMID 40127280)	group associations and baseline moderation do not validate an individual behavioral dopamine assay	reject self-assessment inference; retain baseline-dependence concept
Kruse 2025, 00:05:37; 00:20:40	genetics/environment, diagnostic trends, and social-media distractibility are discussed together	ADHD GWAS/heritability (PMIDs 30478444, 36702997, 29892054); digital-media review (PMID 36562860)	polygenic liability and environmental modulation coexist; diagnosis rates and digital exposure do not adjudicate etiology	keep only with incidence/ascertainment/causation separated
Kruse 2025, 00:27:39	hyperfocus and flow are treated as ADHD phenomenology	hyperfocus studies (PMIDs 30267329, 39169147, 37878578)	self-report and emerging measurement support a phenomenon, but definitions vary and no neural signature is established	keep as emerging, non-diagnostic phenotype; FH allocation/release account is synthesis
Kruse 2025, 00:42:21–00:48:06	regular sleep timing is an essential tool; stimulants affect sleep	stimulant/sleep meta-analysis and reviews (PMIDs 26598454, 29477617, 38738544)	sleep is bidirectionally related and medication effects vary by person and formulation	keep; do not imply sleep hygiene universally treats core ADHD
Kruse 2025, 00:56:35–01:04:32; 01:18:03–01:26:06	childhood medication, addiction, psychosis, and adult cardiovascular risk form one medication-risk arc	substance outcomes (PMIDs 25158998, 28659039); psychosis comparison (PMID 30893533); cardiovascular studies (PMIDs 37991787, 40203844)	prescribed treatment, diversion, class-specific rare psychosis, mean short-term changes, and cumulative risk are distinct questions	split into three claims; report absolute risk, class, monitoring, and timescale

Episode anchor	Public claim	Primary/newer evidence	Audit	Lecture decision
Kruse 2025, 01:52:56–02:02:26	CBT/task lists, video games, and neurofeedback are behavioral or technology options	adult-CBT RCT (PMID 20736471); WM-training RCT (PMID 24117656); neurofeedback meta-analysis (PMID 39661381)	adult ADHD-CBT has meaningful evidence; far transfer is limited; probably blinded neurofeedback core-symptom effects are essentially null on average	do not flatten these into equivalent "brain-training" tools
Essentials, 00:27:43–00:34:21	medication, omega-3, modafinil, and supplements form one focus-tool sequence	unequal evidence bases	visual/rhetorical flattening obscures clinical hierarchy	separate by evidence tier

Timestamps in this table are retained only where they were verified in the acquired public transcript/episode source map. They are episode locators, not independent evidence.

214 The reusable audit chain

For every public claim, the lecture should display five questions:

1. **What exactly was said?** Preserve scope, population, endpoint, and certainty.
2. **What mechanism is proposed?** Do not infer a mechanism the speaker did not state.
3. **What did the cited study actually test?** Inspect population, intervention, comparator, outcome, and time horizon.
4. **What happened afterward?** Search replication, larger studies, meta-analysis, contradiction, and methodological criticism.
5. **What is the lecture decision?** Keep, qualify, replace, omit, or use only as a labeled hypothesis.

This process is not unique to Maté or Huberman. It is how the lecture should audit its own Flow Hijacked concepts.

215 What guidelines recommend—and what mechanistic neuroscience does not decide

Clinical guidelines integrate efficacy, harm, feasibility, developmental stage, patient preference, and healthcare context. A network model cannot determine first-line care by itself. Even if a drug reliably shifted a network measure, that would not settle benefit–harm balance or patient values.

Authority and status at 8 September 2026	Age scope and first medication sequence	Psychosocial and combined care	Monitoring and cardiovascular safeguards	Substance use, comorbidity, and long-horizon boundary
American Academy of Pediatrics: 2019 CPG, 2020 erratum; no superseding AAP CPG located	ages 4–6: evidence-based parent/teacher behavior management first; methylphenidate may follow if serious impairment persists. Ages 6–18: an approved medication is recommended within behavioral, classroom, and school support	combined care is recommended when outcomes span symptoms and functioning	titrate to maximum benefit with tolerable adverse effects; monitor vital signs, growth where relevant, adverse effects, and comorbidity	assess adolescent substance use and diversion; pediatric only, and the evidence search predates recent syntheses (Wolraich et al., 2019; PMID 31570648)
NICE NG87: published 2018, last updated 2019; live at cutoff	children: methylphenidate is generally first medication after persistent significant impairment despite environmental modification; adults: methylphenidate or lisdexamfetamine first-line, with age-specific switching	environmental modification and condition-specific support; parent training or ADHD-focused psychological treatment according to need and preference	baseline physical and cardiovascular assessment; monitor pulse, blood pressure, weight/height where relevant, benefit, adverse effects, and ongoing need	assess diversion and coexisting conditions; unchanged publication status is not a 2026 evidence update; reconfirm revision history before publication
Australian AADPA: first edition 2022; current major national guideline located	lifespan approach; medication and nonpharmacological treatment selected by age, needs, impairment, preference, and regulation rather than one universal sequence	CBT, parent, organizational, educational, workplace, and environmental supports within individualized multimodal care	shared decisions plus continuing physical, mental-health, adherence, and adverse-effect monitoring	addresses co-occurring substance-use disorders and specific populations; certainty varies across recommendations (overview PMID 37254562)
CADDRA 4.1: January 2020 remained the available full guideline; the July 2026 medication chart is not a new edition	across the lifespan; long-acting stimulants are commonly first-line, with nonstimulants and alternatives individualized	psychoeducation, functional supports, and psychosocial care accompany medication as needed	routine blood pressure/pulse, growth where relevant, sleep, adverse-effect, adherence, and functional review	diversion, substance-use disorder, and comorbidity require explicit planning; the older evidence base needs supplementation
European adult consensus: influential 2019 statement, not a binding pan-European CPG	adults; stimulant or nonstimulant medication is a major component after developmental and differential assessment, selected by clinical context	psychoeducation and disorder-focused CBT/skills treatment within multimodal care	cardiovascular and psychiatric review, treatment-response monitoring, and service continuity	childhood history, common comorbidity, substance use, and transition failures are central; national rules differ (Kooij et al., 2019; PMID 30453134)

Authority and status at 8 September 2026	Age scope and first medication sequence	Psychosocial and combined care	Monitoring and cardiovascular safeguards	Substance use, comorbidity, and long-horizon boundary
European ADHD Guidelines Group: active synthesis program, not one 2026 guideline	informs medication and nonpharmacological decisions by age and outcome rather than issuing a single national sequence	emphasizes probably blinded outcomes when judging nonpharmacological care and supports individualized multimodality	evaluates adverse effects and evidence quality across topic-specific reviews	diversion/substance use and comorbidity are handled in relevant reviews; a living research portfolio is not a comprehensive current CPG (PMID 34677682)
Scottish CR235: 2023 adult good-practice guidance	adults; provides assessment, medication selection, and titration pathways in Scottish practice	practical and psychological supports; individualized combined care	physical monitoring, shared care, and local prescribing arrangements	addresses adult comorbidity, substance use, and services; read with NICE and local formularies; good-practice report rather than a separately evidence-graded national CPG
German AWMF S3 ADHD guideline: previous version expired in 2022; revision still in progress at cutoff	across the lifespan historically; the expired sequence must not be presented as a current recommendation	historical psychotherapy and combined-care recommendations only pending the revision	current monitoring language must be checked against the eventual revision	status row prevents silent use of an outdated guideline; no 2026 recommendation is inferred from the registry entry
NHS England Independent ADHD Taskforce, Part 1: 2025 service report, not a treatment CPG	across the lifespan at service-system level; addresses access and pathways rather than replacing NICE medication recommendations	system-level support, not a comparative psychotherapy or combined-treatment recommendation	service monitoring and pathway quality rather than a drug-monitoring protocol	equity, access, and system pressure are central; keep service reform separate from clinical-efficacy and mechanistic evidence

Guidelines converge on structured assessment, developmental and differential diagnosis, monitoring, shared decisions, and multimodal support. They differ in sequencing by age, severity, availability, and regulatory context. Long-term follow-up means repeated review of benefit, burden, functioning, physical health, comorbidity, adherence, diversion risk, and continuing need—not a presumption of indefinite continuation or routine discontinuation. The lecture must distinguish a guideline recommendation from a claim about neural mechanism—and must state that educational material is not individualized medical advice.

How to audit an explanatory authority

Public explanations are valuable because they organize experience, provide language, and motivate inquiry. Their persuasive force, however, can exceed the evidence behind individual claims. A responsible audit separates phenomenological accuracy, mechanistic plausibility, causal evidence, treatment recommendation, and philosophical framing. A speaker can be insightful about lived experience while overstating a biological mechanism; a scientifically correct mechanism can still be irrelevant to the practical advice attached to it.

For Maté, the key distinction is between the clinical importance of stress, attachment, and emotional environment and the stronger claim that those factors primarily cause ADHD relative to inherited liability. For Huberman, the task is to trace claims about dopamine, networks, stimulants, visual focus, supplements, meditation, or smartphone use to the actual population, intervention, and outcome studied. Absence of a recoverable primary source lowers confidence; it does not justify ridicule.

Guidelines occupy another authority layer. They integrate efficacy, safety, feasibility, values, and health-system constraints. They tell clinicians what is recommended under specified conditions, not which neural theory has been proven. The lecture therefore preserves three maps: what public narratives say, what primary studies show, and what clinical guidance recommends.

Public explanation, scientific evidence, and clinical guidance carry different authority

Public educators and clinicians can identify experiences that formal research has neglected. A vivid description of interest-based attention, shame after inconsistency, or the role of family stress may help people recognize patterns and ask better questions. Phenomenological usefulness does not, however, establish a developmental cause, molecular mechanism, or treatment effect. The lecture must preserve the insight while auditing the inference.

For Gabor Maté, the central distinction is between a compassionate developmental interpretation and contemporary causal evidence. Attachment, stress, attunement, and emotional environment matter for regulation and wellbeing. Current genetics and developmental research does not support replacing substantial heritable liability with a primarily attachment-based origin story for ADHD. A proposition can therefore be clinically resonant, partially supported at one level, and in tension with evidence at another.

For Andrew Huberman, the task is claim-to-source reconstruction. Mechanistic explanations about dopamine, visual focus, attentional blinks, meditation, omega-3 fatty acids, smartphones, stimulants, or modafinil should be traced to the exact study population, design, endpoint, and dose. Animal work, healthy-volunteer experiments, correlational technology studies, and ADHD treatment trials answer different questions. A plausible protocol does not become an ADHD therapy because it shares a neurotransmitter vocabulary.

Guidelines carry another form of authority. They integrate efficacy, safety, feasibility, values, age, monitoring, and health-system constraints. A first-line recommendation is not proof of a singular neural mechanism, and a mechanistically interesting intervention may remain absent from guidelines because evidence is preliminary or implementation is uncertain. The lecture should state whether it is describing a guideline recommendation, an empirical effect, or a Flow Hijacked interpretation.

Recency matters. A canonical model can remain useful while newer meta-analysis reduces its effect size, identifies heterogeneity, or exposes dependence on method. Citation count signals influence, not reliability. Highly cited work should anchor historical development, while preregistered, larger, longitudinal, and better-controlled research tests what survived. Null findings deserve the same narrative visibility when they change the claim boundary.

The decision rule is simple but demanding. Keep a public claim when it is accurate, useful, and properly scoped. Qualify it when the underlying evidence supports only part of the mechanism. Remove it when the effect is unreplicated, clinically irrelevant, or dependent on a category error. When the phenomenology remains valuable but causation is uncertain, say exactly that.

This audit is not an exercise in dismissal. It is a way to respect both the audience and the source. A humane story becomes stronger when it does not need to impersonate settled neuroscience, and scientific evidence becomes more usable when it remains connected to the experiences that made the question matter.

A claim audit worked from sentence to lecture decision

Begin with a public sentence such as “stimulants train the brain to focus.” The phrase contains at least four claims: medication improves performance; the improvement reflects learning rather than acute state change; the learning changes the brain; and the change persists beyond exposure. Each requires different evidence. Acute randomized efficacy cannot by itself establish durable training.

The audit then retrieves the closest primary studies and identifies population, treatment, duration, comparator, and endpoint. Evidence in healthy adults cannot automatically answer a pediatric ADHD treatment question. A rodent synaptic mechanism can motivate a hypothesis but not establish functional development in children. An observational association between treatment history and later outcome remains vulnerable to treatment selection and confounding by severity.

Newer evidence is used to update, not merely decorate, the anchor. A later meta-analysis may support short-term efficacy while finding limited evidence for a proposed mechanism. A large cohort may constrain a rare safety risk without resolving individual causality. A null imaging trial may show that clinical improvement does not require the expected network signature. The conclusion should reflect the joint pattern.

The final lecture decision has several options: retain the claim, narrow it, present it as a hypothesis, use only its phenomenological insight, or omit it. “Medication may create conditions in which practice is easier” is a plausible, testable formulation. “Medication permanently teaches the developing attention system” is stronger and requires direct longitudinal evidence.

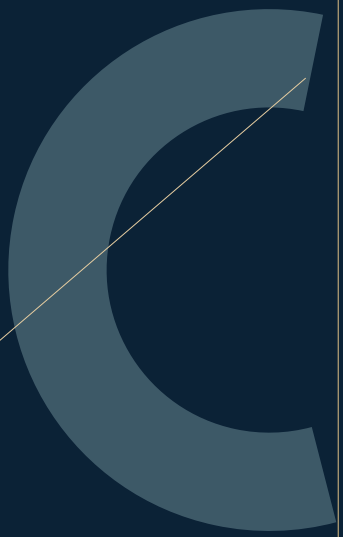
The same procedure applies to claims about attachment, visual focus exercises, omega-3 supplementation, smartphone fragmentation, or the DMN. The goal is not to strip the lecture of intelligible language. It is to ensure that every accessible sentence has an evidence boundary strong enough to survive scrutiny.

Public translation needs a chain of custody

For every memorable statement, retain the population, intervention or exposure, comparator, outcome, time horizon, and uncertainty of the underlying study. A plausible mechanism is not a clinical effect, an association is not a cause, and a recommendation is not proof of one neural pathway. This chain lets the lecture preserve useful phenomenology from Maté and useful explanatory prompts from Huberman while allowing primary and updated evidence to determine the scientific wording.

PART XVI

THE CONTRADICTION CHAMBER



Prevent the Flow Hijacked synthesis from becoming another totalizing story.

Cortese · Norman · Power · Sidlauskaite · independent nulls

Part proposition

A synthesis earns trust by surviving evidence that could make it smaller. The contradiction chamber is not a ceremonial limitations slide. It is where the lecture asks whether its preferred network-dynamics story is identifiable, replicated, clinically meaningful, and more explanatory than alternative accounts.

216 No single diagnostic neural biomarker

ADHD remains a clinical diagnosis. Structural MRI, task fMRI, resting connectivity, EEG, PET, cognitive tasks, and polygenic scores reveal group-level information and research mechanisms. None currently supplies sufficiently accurate, reliable, generalizable, and externally validated standalone diagnosis for routine practice.

This should not be misheard as "there is no biology." A distributed developmental condition can have robust population-level biological associations while retaining large overlap between diagnosed and non-diagnosed individuals. Heterogeneity, measurement noise, developmental change, comorbidity, and multiple causal routes make a single marker unlikely.

Machine-learning classification must be evaluated out of sample, across scanners, sites, demographic groups, and realistic clinical differentials—not only case–control extremes. Leakage, site confounding, and flexible feature selection can make internal accuracy look clinically mature when it is not. Biomarker reviews and consensus statements preserve the diagnostic boundary (Faraone et al., 2021; PMID 33549739; Chen et al., 2023; PMID 36970271).

217 Small distributed effects and large individual overlap

Suppose one network metric is Gaussian in ADHD and controls with equal variance and standardized mean difference d. Under that idealized model, the probability that a randomly selected ADHD observation exceeds a randomly selected control observation is

$$\mathrm{AUC} = \Phi\left(\frac{d}{\sqrt{2}}\right),$$

where Φ is the standard normal cumulative distribution. If $d = 0.20$, then $\mathrm{AUC} \approx 0.556$: a real group difference with poor person-level discrimination. This illustrates why statistical significance in a mega-analysis does not yield an individual explanation.

Large samples can recover subtle distributed effects that small studies miss. That is scientific progress. But the language must shrink with the effect size. Norman and colleagues' mega-analysis supports small average alterations compatible with the default-mode interference hypothesis (2023; PMID 36100657); it does not show that every person with ADHD has an intrusive DMN or that the metric diagnoses an individual.

218 Resting-state spatial nonconvergence

The resting-state literature reports differences involving default-mode, frontoparietal, attention, salience, striatal, thalamic, cerebellar, and sensorimotor systems. Yet preregistered meta-analytic work has found limited spatial convergence across studies (Cortese et al., 2021; PMID 32946973). This resists a story in which ADHD has one reproducible resting dysconnectivity lesion.

Nonconvergence can arise from small samples, different atlases, seed selection, preprocessing, medication history, age, motion handling, comorbidity, scanner effects, and genuine biological heterogeneity. It can also mean the hypothesized effect is weaker or less spatially fixed than expected. One may not invoke heterogeneity only when a favored result fails.

The lecture should show both findings: standardized mega-analysis can recover subtle distributed group effects, while coordinate/seed-level synthesis does not yield a stable singular locus. The joint conclusion is not "nothing" and not "biomarker"; it is a small, distributed, method-sensitive signal.

219 Task findings can differ from resting state

Rest is an unconstrained condition, not a neutral baseline. Participants differ in thought content, arousal, fatigue, eye state, recent experience, and motion. A task constrains some processes while adding performance, error, reward, and strategy differences. The distributions are conditional on context:

$$P(X \mid D) = \sum_{c} P(X \mid D, C = c) P(C = c \mid D),$$

where X is a neural metric, D diagnostic group, and C context. A marginal group effect can change or disappear when context differs; opposite conditional effects can be obscured by averaging.

Reports of reduced DMN suppression in low-engagement tasks coexist with preserved suppression or reduced group differences under high incentive or medication. Naturalistic engagement can reveal effects absent at rest. The contradiction is therefore discriminating: a static trait-lesion model predicts consistency; a context-sensitive coordination model predicts interactions. But interaction predictions must be preregistered rather than retrofitted to every inconsistency.

220 Head motion as nuisance, phenotype-adjacent behavior, and selection bias

Small movements create structured changes in fMRI time series and can generate distance-dependent connectivity artifacts (Power et al., 2012; PMID 22019881). ADHD studies face an unusually difficult version of this problem because motion may correlate with age, hyperactivity, medication, discomfort, and task engagement.

Regressing motion parameters is not always sufficient. Scrubbing high-motion volumes, global-signal choices, ICA denoising, and minimum-data thresholds can materially change results. Yet aggressive exclusion can select a subgroup of participants with ADHD who can remain still, producing a different bias. Motion is thus both artifact and phenotype-adjacent behavior; imaging inference must separate them without pretending the separation is perfect.

Every network claim should report framewise displacement, group differences, retained data, censoring rules, sensitivity analyses, and whether state occupancy changes survive matched-motion analyses. Dynamic connectivity is especially vulnerable because transient motion can resemble state transitions.

221 Medication history, washout, and vascular confounds

"Medication-free at scan" is not one condition. It can mean never treated, untreated for months, or withheld that morning. Prior chronic exposure may alter physiology or select responders; short washout can preserve pharmacodynamic or behavioral effects; withdrawal, sleep, and expectation can also matter.

Pharmaco-fMRI adds vascular complexity. BOLD reflects neurovascular coupling, not neural firing directly. A drug can change heart rate, blood pressure, respiration, vascular tone, or motion, influencing the signal even when neuronal action is the scientific target. Acute crossover designs improve within-person control but cannot establish chronic reorganization; longitudinal observational comparisons introduce indication and adherence confounding.

Therefore "normalization" must be indexed to one measure, task, dose, age, and exposure duration. A clinically useful effect can occur with no measured network change, a move toward controls, or a move away from control means that represents compensation.

222 Age, sex, comorbidity, and ascertainment

The developing brain changes its baseline organization. DMN segregation, control-network integration, corticostriatal function, myelination, and catecholamine systems do not stand still while ADHD is studied. Pediatric effects can be larger, smaller, or opposite to adult effects because both the disorder and the comparator are developing. Pooling ages can create an uninterpretable average.

Girls and women have historically been underrepresented, particularly in imaging cohorts. Referral pathways select more externalizing presentations; masking, internalizing symptoms, hormonal transitions, and diagnostic delay can alter the observed sample. Most studies are underpowered for sex-by-diagnosis interactions, so absence of evidence is not equivalence.

Anxiety, depression, autism, learning disorders, sleep problems, trauma exposure, tics, and substance use can affect the same tasks and networks. Excluding all comorbidity increases internal homogeneity while reducing clinical representativeness. Including it without modeling creates confounding. The lecture should distinguish mechanism studies of selected samples from estimates intended to generalize to clinics.

223 Different variability measures are not interchangeable

ADHD research uses "variability" for several mathematically distinct objects:

$$\mathrm{CV} = \frac{\sigma}{\mu}$$

is the coefficient of variation. It is not equivalent to the ex-Gaussian tail parameter τ, and neither quantity is a dwell time.

- reaction-time standard deviation;
- coefficient of variation $\mathrm{CV} = \sigma/\mu$;
- ex-Gaussian tail parameter τ;
- trial-to-trial representational similarity;
- BOLD amplitude variability;

- dynamic connectivity variance;
- state occupancy and dwell time;
- transition entropy;
- EEG power variability;
- aperiodic spectral slope;
- sample entropy or multiscale entropy.

Greater reaction-time variability does not imply greater BOLD variability. A system may show short dwell in one state but reduced repertoire diversity overall. Stronger early visual connectivity can coexist with unstable control representations. The metric, timescale, preprocessing, and behavioral relation must be named.

Dynamic-state studies report altered occupancy or shorter task-favorable dwell in some samples (Cai et al., 2018, PMID 29486868; Shappell et al., 2021, PMID 33454408; Cai et al., 2021, PMID 33589738). Results depend on atlas, window or hidden-state model, number of states, and motion. A 2025 study of trial-wise cognitive-control representations adds direct evidence for instability in a specific paradigm (PMID 40057478), not a universal state-space law.

224 Publication bias, reverse inference, and analytic flexibility

Small neuroimaging studies historically combined low power with many analytic choices. Positive results were more publishable; region labels could be selected after observing a cluster; the same dataset might support several contrasts. Contemporary consortia and preregistration improve this landscape but do not erase it.

Reverse inference confuses $P(\text{activation} \mid \text{process})$ with $P(\text{process} \mid \text{activation})$. Bayes' rule makes the missing terms explicit:

$$P(P \mid A) = \frac{P(A \mid P)P(P)}{P(A)}.$$

If anterior insula activation occurs in many processes, observing it does not uniquely identify salience switching. If striatal activation changes, the result is not automatically "dopamine." If precuneus connectivity changes, the participant was not necessarily mind wandering.

Analytic flexibility affects dynamic studies acutely: filter range, parcellation, global-signal regression, state number, distance metric, temporal resolution, and clustering initialization can all alter output. Robust work reports multiverse or sensitivity analysis, out-of-sample validation, and convergent behavior.

225 What the deeper model can—and cannot—claim

The accumulated evidence supports a deeper description than a chronically weak attention faculty: in at least some people and paradigms, ADHD involves altered coordination, stability, and context sensitivity among systems supporting internal cognition, task control, attention, salience, reward, timing, and action. Performance is modulated by incentive, arousal, development, sleep, and treatment. Dynamic measures are promising because they address moment-to-moment inconsistency.

The evidence does not establish one dynamical phenotype shared by all people with ADHD. It does not show that the salience network is a broken master switch, that the DMN is an invader, that hyperfocus has a known neural signature, or that high non-normality causes attentional capture. It does not authorize diagnosis from network states. The Task-State Viability Envelope is a synthesis and hypothesis-generating formalism, not a discovered anatomical object.

Contradiction ledger

Domain	Supporting signal	Resisting or null signal	Boundary condition	Lecture consequence
Default-mode interference	large samples find small weaker anticorrelation	preregistered resting meta-analysis finds little spatial convergence	standardized scale can recover diffuse effects without a lesion	teach small group effect, not individual cause
DMN suppression	reduced suppression in some low-engagement tasks	incentive or medication can remove difference; suppression can be intact	task, motivation, direction, and age matter	never equate attention with maximal DMN "off"
Neural variability	elevated variability in several measures	some sensory signals are less variable or null	metrics and systems differ	define the quantity every time
Dynamic states	altered dwell, occupancy, flexibility, or representation stability	state solutions depend on model and motion	promising, method-dependent	emerging direct evidence only
Salience switching	salience-centered interactions differ in some studies	anterior-insula switch activation can be preserved	arbitration is distributed	reject broken-switch cartoon

Domain	Supporting signal	Resisting or null signal	Boundary condition	Lecture consequence
Reward anticipation	mean ventral-striatal hypoactivation in some syntheses	reward phase, type, and sample yield mixed findings	reward phenotype heterogeneous	specify phase and task
Medication normalization	selected acute measures move toward controls	other useful effects diverge or canonical measures remain	normalization is endpoint-specific	ban blanket term
Acute versus chronic medication	single-dose crossover changes network metrics	chronic transporter regulation and longitudinal effects can differ	exposure duration changes question	label dose and timescale
Age	pediatric effects often stronger	adult effects can be absent or reversed	developmental baselines differ	never merge child/adult neuroscience silently
Sex/gender	some sex-specific findings	samples often underpowered and male-skewed	representation gap	do not overinterpret absence
Head motion	findings survive some controls	motion changes connectivity and state occupancy; censoring selects	artifact and phenotype-adjacent behavior coexist	show sensitivity analyses
Rest versus task	resting dysconnectivity reported	effects may appear only during engagement	rest is not task control	use context-dependent models
Theta/beta ratio	canonical literature and clinical use	recent multiverse work finds no robust standalone group marker	age, analysis, aperiodic activity	exclude diagnostic claim
Stimulant efficacy	strong acute symptom effects	rater, age, dose, and endpoint alter ranking	efficacy is not one number	report layer and comparator
Cardiovascular safety	short trials and cohorts reassuring for rare events	duration-sensitive cohorts raise cumulative questions	endpoint and horizon differ	preserve monitoring and uncertainty
Psychosis risk	absolute incidence is low	comparative risk higher with amphetamine than methylphenidate	rare, class-specific, person-specific	avoid alarmism and dismissal
Tics	common fear of worsening	randomized syntheses do not show inevitable causal exacerbation	individual responses remain	monitor, do not impose categorical ban
Substance use	diversion and nonmedical exposure can harm	therapeutic treatment does not generally increase later SUD and may associate with fewer events	route, dose, supervision, indication	separate phenomena
Psychotherapy symptoms	positive self/parent ratings	blinded and objective outcomes are smaller	reporter and comparator matter	emphasize function and compensation
Neurofeedback	unblinded and protocol-specific positives	probably blinded average core-symptom effect essentially null	target engagement is not mediation	classify as contested
Combined treatment	selected acute and functional advantages	long-term MTA groups converged	randomized phase ended; care self-selected	outcome- and time-specific claim
Genetics and environment	high heritability and polygenicity	adversity, sleep, prematurity, and context influence expression	both operate; no individual destiny	reject false dichotomy
Attachment	relational associations and clinical importance	direction, shared liability, and confounding unresolved	benefit does not prove origin	retain humane insight, qualify causation
Hyperfocus	recurrent self-report and emerging measurement	no universal definition or established neural signature	emerging phenotype	clue, not diagnostic proof
Non-normality	mathematics permits large transient growth in stable systems	no direct ADHD pseudospectral/resolvent evidence located	Flow Hijacked mathematical hypothesis	isolate from established evidence

Contradiction-handling protocol

When two studies appear to disagree, the first question is not which one to believe. Construct a comparison vector

$$\mathbf{q} = (N, A, S, C, M, T, X, P, R),$$

where (N) is sample size, (A) age/development, (S) sex/gender composition, (C) comorbidity and ascertainment, (M) medication history/state, (T) task or rest condition, (X) measurement modality, (P) preprocessing/model pipeline, and (R) outcome/rater. A contradiction is interpretable only after comparing these coordinates.

Then classify the disagreement:

- **direct contradiction:** materially similar **q**, opposite estimate with adequate precision;
- **boundary-condition difference:** the effect changes under incentive, age, task, or treatment as predicted;
- **measurement non-equivalence:** studies use different definitions of suppression, variability, or network membership;
- **precision difference:** a small study's estimate is compatible with the confidence interval of a larger null or small effect;
- **analytic dependence:** pipeline choices or motion handling explain the divergence;
- **heterogeneity signal:** subgroups or individual trajectories differ in a reproducible way;
- **unresolved:** no current evidence adjudicates.

The protocol forbids three conveniences. A favored positive study cannot be protected by invoking heterogeneity after the fact. A null cannot be called proof of absence when its interval includes clinically relevant effects. And two directionally different measures cannot be averaged under the word "dysregulation" without specifying what direction the theory

predicted.

Falsification ledger for the Flow Hijacked treatment story

The treatment synthesis should retreat if preregistered studies repeatedly find any of the following:

1. task-state dwell or transition measures have poor within-person reliability and no ecological predictive value;
2. momentary lapses are better explained entirely by peripheral factors such as sleep and motion than by proposed network variables;
3. medication improves behavior without reproducible change in any hypothesized stability, gain, or transition measure, across sensitive modalities;
4. behavioral scaffolding changes reported function but not independently measured completion or re-entry;
5. the same dynamic signature fails to distinguish unwanted departure from adaptive exploration or deliberate release;
6. person-specific models do not generalize across sessions better than static symptom and context measures;
7. the Task-State Viability Envelope adds no predictive value beyond ordinary task difficulty, reward, and baseline performance.

Failure would not negate the clinical usefulness of medication, psychotherapy, or accommodation. It would negate or restrict the proposed dynamical explanation. That separation is the standard the lecture applies to every external authority and must apply to itself.

226 The evidential landing

After the contradiction chamber, five statements remain defensible:

1. **Established evidence:** ADHD is a heterogeneous developmental disorder with robust inherited liability, context-sensitive impairment, effective treatments, and no single diagnostic biomarker.
2. **Supported interpretation:** altered coordination and temporal stability among multiple neural systems contribute to group-level ADHD phenomena in some tasks and samples.
3. **Plausible synthesis:** difficulty assembling, stabilizing, and appropriately releasing task-favorable configurations can unify initiation difficulty, lapses, variability, reward dependence, and some forms of hyperfocus better than a pure capacity deficit.
4. **Flow Hijacked hypothesis:** interventions may alter different coordinates of a task-state viability landscape—pharmacology may change gain and immediate stability; psychotherapy may change learned policies; environmental treatment may change boundary conditions; combined care may widen a learning corridor.
5. **Open question:** which person-specific dynamical measurements predict unwanted departure, adaptive release, re-entry, functional outcome, and differential treatment response with enough reliability to matter clinically?

The deeper model is worthwhile only if it stays falsifiable. It must predict when the task configuration will fail, what kind of intervention should change that failure, and what observations would make the model retreat.

What survives the contradiction chamber

A strong synthesis should become narrower when it meets disconfirming evidence. Spatial nonconvergence across imaging studies weakens claims about one defective region. Small effects and overlapping distributions weaken individual prediction. Motion and physiological artifacts threaten resting-state results. Medication history, comorbidity, age, sex, recruitment, task design, preprocessing, and analytic flexibility can change both direction and magnitude.

These limitations do not imply that nothing is known. They change the level at which conclusions are defensible. ADHD is reliably associated with impairment and heterogeneous cognitive differences; several treatments have reproducible short-term clinical efficacy; distributed neural and developmental differences occur at the group level. What remains unsettled is the existence of one mechanism that explains all presentations or one network signature that can diagnose an individual.

The coordination account survives only as a constrained interpretation: timing, stability, and context-dependent recruitment offer useful questions that integrate several literatures, but no single dynamical parameter is yet established as the core lesion. A robust model must outperform simpler symptom and performance measures, generalize across sites, survive motion and preprocessing controls, and predict ecologically meaningful outcomes. The contradiction ledger is therefore part of the theory, not an appendix designed to protect it.

The model earns credibility by surviving its strongest alternatives

ADHD neuroimaging has repeatedly faced small samples, flexible analysis, inconsistent task definitions, head motion, medication-history differences, and comorbidity. Multisite datasets improve power but introduce scanner and protocol heterogeneity. Meta-analysis can reveal a small average effect while concealing opposite subgroup effects or publication bias. A sophisticated network vocabulary does not neutralize these problems.

Motion is especially consequential because ADHD groups can differ in movement, and motion can generate patterned changes in functional connectivity. Aggressive correction can also remove neural signal or select a less representative sample. Studies should report exclusion, censoring, residual motion, group differences after correction, and sensitivity across pipelines. A result that survives only one preprocessing choice should not carry a mechanistic lecture.

Medication history creates another ambiguity. Current washout may reduce acute drug action but cannot erase long-term exposure, treatment selection, or the clinical differences that led to medication. Medication-naive samples reduce one confound while often being younger or otherwise selective. Both designs contribute information; neither is a universal solution.

Diagnostic heterogeneity is not statistical inconvenience. People meeting ADHD criteria can differ in symptom profile, cognitive performance, sleep, emotional regulation, autism traits, learning disorder, substance use, and developmental trajectory. A group mean may therefore describe no typical individual. Subtyping after inspecting the same data risks overfitting, so proposed biotypes require preregistration, stability, and external validation.

Alternative explanations should be made explicit. Apparent network instability may reflect arousal fluctuation, strategy change, task disengagement, vascular variation, or classifier uncertainty. Reward-related normalization may reflect better performance rather than a corrected valuation system. Greater activation may indicate compensation or inefficiency. Reduced activation may indicate failure to recruit or more efficient processing. Direction is not mechanism.

The TSVE framework must face simpler competitors. Perhaps symptom severity and reaction-time variability predict function just as well. Perhaps entry and dwell are useful behavioral descriptors but do not require a latent viability envelope. Perhaps non-normality adds no prediction beyond ordinary perturbation sensitivity. These possibilities define the tests the framework must pass.

A contradiction ledger is therefore part of the model, not an appendix to it. For every favored conclusion it should retain null studies, opposite directions, age differences, methodological critiques, and outcomes that fail to generalize. The lecture becomes original by organizing uncertainty into better questions, not by claiming that one new metaphor has solved ADHD.

The minimum credible test of the dynamical story

A useful test would follow participants repeatedly across low- and high-reward tasks, controlled interruptions, sleep variation, and treatment conditions. It would preregister entry latency, dwell, unwanted exit, adaptive release, and recovery, then compare TSVE with simpler behavioral and static-connectivity models on held-out sessions.

Success would require reliable parameters, prediction beyond symptoms and reaction-time variance, sensitivity to experimentally manipulated context, and replication in an independent cohort. Failure to outperform simpler models would count against the added state-space machinery. A direct non-normality claim would require estimated operators and perturbation responses, not behavioral volatility alone.

This standard keeps the synthesis ambitious and corrigible. It proposes measurements that could reveal a deeper architecture of cognitive regulation while preserving the possibility that a simpler account will win.

A contradiction changes the sentence

Null findings, reversed directions, developmental differences, motion-sensitive estimates, and weak out-of-sample prediction do more than populate a limitations slide. They determine whether a statement remains established evidence, becomes a conditional interpretation, or moves into the hypothesis layer. A synthesis is credible only when encountering contrary data changes its precision.

PART XVII

FLOW HIJACKED SYNTHESIS — THE TASK-STATE VIABILITY ENVELOPE

Integrate entry, stability, perturbation, recovery and adaptive release into a testable dynamical research architecture.

227 Mathematical status, scope, and epistemic contract

This part proposes a mathematical research architecture for a particular question: what must happen for a brain to enter, sustain, leave, and later recover a configuration that supports a task? It is not a replacement definition of attention-deficit/hyperactivity disorder, not a diagnostic instrument, and not a claim that one equation explains a heterogeneous developmental condition. Its purpose is narrower and more demanding: to convert the lecture's central dynamical interpretation into quantities that can be estimated, compared, contradicted, and, if necessary, rejected.

Five labels are used without interchange:

- **ESTABLISHED EVIDENCE** — supported by convergent clinical or neuroscientific evidence and stated within the limits of that evidence.
- **SUPPORTED INTERPRETATION** — a defensible synthesis across established findings, but not itself a directly measured biological entity.
- **PLAUSIBLE SYNTHESIS** — a mechanistically coherent bridge whose components have support, while the complete bridge has not been directly demonstrated.
- **FLOW HIJACKED HYPOTHESIS** — an original, testable proposal introduced here.
- **OPEN QUESTION** — a matter for which current evidence cannot adjudicate the alternatives.

Every appearance of the Task-State Viability Envelope, the Dual-Exit Principle, lifecycle fingerprints, or ADHD-specific non-normal gain belongs to one of the final three categories. These constructs must never be silently upgraded to established ADHD neuroscience.

ESTABLISHED EVIDENCE

ADHD is a clinically diagnosed, heterogeneous developmental disorder. Across some samples, investigators have found differences in network segregation, time-varying connectivity, latent-state occupancy, dwell time, transition structure, response variability, and trial-wise stability of cognitive-control representations. These measurements are not interchangeable, their effects are generally distributed rather than lesion-like, and their direction can depend on task, age, incentive, medication exposure, physiology, movement, and analytical choices. Cai and colleagues' time-varying network studies, Shappell and colleagues' state-occupancy work, and Gao and colleagues' trial-wise representational results make dynamics scientifically relevant; they do not establish one universal ADHD attractor geometry (Cai et al., 2018, PMID 29486868; Shappell et al., 2021, PMID 33454408; Cai et al., 2021, PMID 33589738; Gao et al., 2025, PMID 40057478).

SUPPORTED INTERPRETATION

A useful cross-study description is that ADHD can involve altered regulation of the allocation, stabilization, and transition of cognition across distributed configurations. This description is deeper than "too little attention," yet remains compatible with multiple causal routes and substantial individual overlap.

FLOW HIJACKED HYPOTHESIS

The probability of successful performance is governed not by proximity to a single ideal brain state but by whether the system occupies, reaches, and remains inside a context-dependent set of viable configurations. This set is called the **Task-State Viability Envelope**, abbreviated **TSVE**.

The phrase "state" will be used carefully. Sometimes it denotes a continuous vector of latent neural, cognitive, and bodily variables. Sometimes it denotes a discrete state inferred by a hidden Markov model. Those are different mathematical objects. A network "state" inferred from fMRI is also not automatically an attractor in the dynamical-systems sense. The text will identify the object each time.

228 Return to the opening task: capacity is not reliability

Imagine a familiar, low-drama demand: open a document, locate the relevant paragraph, revise it, and send it before a deadline. The person knows how to perform every constituent act. On one occasion the sequence begins almost effortlessly. On another, initiation consumes an hour. On a third, the person starts, is displaced by a notification, and cannot reconstruct the task context. On a fourth, the same person becomes absorbed in an intrinsically compelling problem and continues beyond the time when stopping would have been adaptive.

A scalar capacity model has difficulty representing this pattern. Let C denote a hypothetical quantity called "amount of attention." If performance failure were a monotone consequence of low C, then high performance under a highly engaging condition would be puzzling, and extreme persistence would appear to disprove impairment. One might add motivation as a second scalar, but this still compresses several distinct events: entering the task configuration, stabilizing it, resisting irrelevant displacement, recovering after displacement, and releasing it when the goal changes.

The conceptual error is a failure of state and time. A person can possess the component skills required for a task while having low reliability in assembling and maintaining the configuration in which those skills are usable. In control language, **reachability** is not the same as **capacity**, **residence** is not the same as **reachability**, and **selective exit** is not the inverse of residence.

Let $Y_T(t)$ be a task-specific performance process. It may include accuracy, response-time distribution, omissions, rule fidelity, work produced, or a composite functional outcome. A capacity-only account tries to explain Y_T with a mostly time-invariant latent trait. A dynamical account instead asks for the conditional law

$$\mathbb{P}(Y_T(t:t+\Delta) \in \mathcal{A}_T \mid \mathcal{F}_t, T, c_t), \tag{17.1}$$

where $\mathcal{A}_T$ is an acceptable-performance set, $\mathcal{F}_t$ is the information available up to time t, T identifies the task, c_t describes context, and Δ is a future horizon. This probability can vary sharply even when knowledge and general ability do not.

This reformulation does not deny stable traits. It places traits among the parameters that constrain a trajectory rather than treating them as the trajectory itself. It also leaves room for the fact that a clinically meaningful diagnosis requires developmental history and impairment across contexts; a momentary transition failure is not equivalent to ADHD.

CORE SENTENCE — The central mathematical object is not "how much attention exists," but the conditional probability that the whole system can enter and remain in one of several task-supporting configurations for long enough to accomplish the goal—and can later leave that configuration when leaving is appropriate.

229 Notation: task, context, state, policy, and outcome

We begin with a partially observed stochastic system. The notation is intentionally more general than any single imaging modality.

Symbol	Meaning	Possible operationalization
$T \in \mathcal{T}$	current task or task family	continuous performance, writing, working memory, conversation, driving
$x_t \in \mathbb{R}^n$	fast latent state	network amplitudes, directed interactions, oscillatory phase, control representation, motor readiness
$c_t \in \mathcal{C}$	observable context	instructions, interruptions, reward, social setting, time pressure, task difficulty
$m_t \in \mathcal{M}$	medication/exposure state	concentration or pharmacodynamic proxy; acute versus chronic history
$a_t \in \mathcal{A}$	arousal and bodily state	pupil-linked arousal, autonomic state, fatigue, local-sleep proxy
$r_t \in \mathcal{R}$	reward/value state	expected value, delay, uncertainty, intrinsic interest, loss salience
$h_t \in \mathcal{H}$	sleep/circadian state	sleep debt, phase, time of day, chronotype mismatch
$\theta_d(t)$	slowly changing developmental parameters	maturation, accumulated adaptation, developmental constraints
ϕ_t	learned policy parameters	routines, metacognitive rules, therapy-acquired strategies, habits
u_t	endogenous or externally scaffolded control input	self-cue, timer, task decomposition, clinician-taught policy, environmental prompt
p_t	perturbation input	notification, intrusive thought, emotional cue, novelty, competing reward
o_t	measured observation	fMRI, EEG/MEG, behavior, eye tracking, physiology, experience sample
$Y_T(t:t+\Delta)$	task outcome trajectory	accuracy, latency, omissions, goal progress, functional completion

The latent state x_t is not defined as "the connectome." It may contain fast neural coordinates, but a useful model may also require short-memory cognitive variables such as the currently active rule or the precision of a working representation. The purpose of a state variable is the Markov idealization

$$\mathbb{P}(x_{t+dt} \mid x_{0:t}, u_{0:t}, c_{0:t}) = \mathbb{P}(x_{t+dt} \mid x_t, u_t, c_t), \tag{17.2}$$

not anatomical literalism. If this property fails, the state must be augmented or modeled with memory. In empirical work, a recurrent state-space model, delay embedding, switching autoregression, or non-Markov semi-Markov process may be more defensible than Equation 17.2.

We assume an observation model

$$o_t = H(x_t, c_t) + \nu_t, \qquad \nu_t \sim \mathcal{P}_\nu, \tag{17.3}$$

and an outcome model

$$Y_T(t : t + \Delta) = \mathcal{G}_T(x_{t:t+\Delta}, c_{t:t+\Delta}, \zeta_{t:t+\Delta}), \tag{17.4}$$

where H maps latent state into measurements, ν_t is measurement noise, $\mathcal{G}_T$ maps the trajectory into task performance, and ζ_t contains outcome noise not captured elsewhere. Measurement noise, latent process noise, and genuine within-person variability must not be conflated.

The learned policy is written

$$u_t = \pi_{\phi_t}(\hat{x}_t, c_t, T), \tag{17.5}$$

where $\hat{x}_t$ is the person's or model's estimate of the state. The policy may be implicit. "When I notice I have left the document, close all other windows and read the last two sentences aloud" is a policy. So is an environmental rule that places the phone outside the room. A policy can alter trajectories without changing the diagnostic liability that made the policy necessary.

230 The nonlinear stochastic state equation

The fast dynamics are represented provisionally by the controlled stochastic differential equation

$$dx_t = f_T(x_t, c_t, \theta_d, m_t, a_t, r_t, h_t)\, dt + B_T(x_t, c_t)\, u_t\, dt + E_T(x_t, c_t)\, p_t\, dt + \Sigma_T(x_t, c_t)\, dW_t. \tag{17.6}$$

Here:

- f_T is the endogenous drift—the direction and rate in which the system tends to evolve in the absence of the explicitly modeled inputs;
- B_T maps control or scaffolding inputs into state change;
- E_T maps perturbations into state change;
- W_t is a multivariate Wiener process under the diffusion approximation;
- $Q_T(x, c) = \Sigma_T \Sigma_T^{\mathsf{T}}$ is the process-noise covariance;
- the subscript T allows the vector field and input maps to be task dependent.

Equation 17.6 is a **Flow Hijacked synthesis**, not a fitted ADHD model. Its value is organizational. It prevents five different mechanisms from being hidden inside the word "attention." A treatment might change the drift f_T, the effective gain in B_T, the perturbation map E_T, the stochastic covariance Q_T, or the policy π_ϕ. These changes need not produce the same neural fingerprint.

The equation also makes state dependence explicit. The same notification p_t can have a small effect when the system is deeply engaged, a large effect near a viability boundary, and a paradoxically useful effect when it cues return to the intended goal. Likewise, the same stimulant dose can have different consequences under sleep deprivation, high anxiety, low task demand, or a different developmental baseline. None of this requires a claim that response is arbitrary. It requires conditional models.

For discrete observations $t_k = k\delta$, an estimable approximation is

$$x_{k+1} = F_T(x_k, c_k; \Theta_i) + B_T u_k + E_T p_k + w_k, \qquad w_k \sim \mathcal{N}(0, Q_k), \tag{17.7}$$

with participant-specific parameter vector Θ_i. A hierarchical model can decompose

$$\Theta_i = \bar{\Theta} + Z_i \beta + b_i, \qquad b_i \sim \mathcal{N}(0, \Omega), \tag{17.8}$$

where Z_i contains age, sex, diagnosis, presentation, medication history, sleep, and other covariates; β gives population-level associations; and b_i represents residual person-specific structure. The group label is one covariate among several, not the definition of the individual dynamical system.

Assumptions that must be tested rather than smuggled in

1. **State sufficiency.** The chosen coordinates retain enough history to predict near-future behavior.
2. **Timescale adequacy.** The sampling rate resolves the transitions of interest. A conventional fMRI repetition time cannot identify millisecond switching without strong modeling assumptions.
3. **Observation invariance.** Changes in o_t reflect latent neural change rather than medication-related vascular effects, head motion, respiration, or scanner drift.
4. **Task validity.** Laboratory success is meaningfully related to the functional task the model is intended to explain.
5. **Policy consistency.** The same observed action does not necessarily imply the same internal policy across people.
6. **Intervention consistency.** "On medication" is not a single condition; molecule, dose, timing, prior exposure, adherence, and acute versus chronic state matter.
7. **No diagnostic essentialism.** Parameters may overlap extensively across diagnosed and non-diagnosed populations.

These assumptions are part of the model. They are not footnotes.

231 Defining the Task-State Viability Envelope

Let $\mathcal{A}_T$ be the set of acceptable outcome trajectories for task T over a horizon Δ. A simple threshold representation is

$$\mathcal{A}_T = \{Y_T(t : t+\Delta) : g_T(Y_T(t : t+\Delta), c_{t:t+\Delta}) \geq y_{\min}\}, \tag{17.9}$$

where g_T is a task-valid performance functional and $y_{\min}$ is a clinically or functionally meaningful floor. The performance functional can penalize omissions, dangerous variability, or failure to make real progress rather than rewarding only mean speed.

For a fixed policy π, define the **Task-State Viability Envelope**

$$\boxed{\mathcal{V}_T^{\pi}(c, t; \Delta, y_{\min}, q) = \{x \in \mathcal{X} : \mathbb{P}^{\pi}[Y_T(t : t+\Delta) \in \mathcal{A}_T \mid x_t = x, c_t = c] \geq q\}.} \tag{17.10}$$

The confidence threshold $q \in (0, 1)$ specifies how reliable performance must be. The horizon Δ matters: a configuration that supports ten seconds of correct responding may not support forty minutes of writing. The context c matters: quiet work, social evaluation, monetary incentive, and repeated notifications produce different envelopes. The policy π matters: learned strategies can enlarge the set of states from which adequate performance is likely.

Equation 17.10 is a **chance-constrained viable set**. It is not a single coordinate, anatomical region, network, or "normal" connectome. Two people can meet the same task criterion through different configurations. The same person can do so through different configurations on different days. This many-to-one mapping is a form of degeneracy in the constructive biological sense: multiple realizations support the same function.

For a pointwise performance margin $s_T(x, c)$, a simpler instantaneous envelope is

$$\mathcal{V}_{T,0}(c) = \{x : s_T(x, c) \geq 0\}. \tag{17.11}$$

But Equation 17.11 ignores future drift and noise. A point can lie inside the instantaneous set while being almost certain to leave it a moment later. Equation 17.10 therefore places trajectory probability at the center.

Viable set versus viability kernel

The term **viability kernel** is reserved for a stricter control question. Let $\mathcal{U}$ be the set of admissible policies or inputs. Define

$$\mathrm{Viab}_T(\mathcal{A}_T) = \{x : \exists \pi \in \Pi_{\mathrm{adm}} \text{ such that } \mathbb{P}^{\pi}[Y_T(t : t+\Delta) \in \mathcal{A}_T \mid x_t = x] \geq q\}. \tag{17.12}$$

The TSVE in Equation 17.10 asks whether performance is viable under a particular policy and context. The kernel in Equation 17.12 asks whether any admissible policy can make it viable. The difference is clinically meaningful. A state may be outside the envelope under the person's present strategy yet inside the kernel under an available scaffold. Conversely, a task demand may place the state outside the kernel given the current environment and resources. In that case, exhorting the person to "try harder" is not a control solution.

We can define an **envelope margin** as the signed distance

$$d_T(x, c) = \begin{cases} +\inf_{z \notin \mathcal{V}_T} \|x - z\|_M, & x \in \mathcal{V}_T, \\ -\inf_{z \in \mathcal{V}_T} \|x - z\|_M, & x \notin \mathcal{V}_T, \end{cases} \tag{17.13}$$

where $\|v\|_M = (v^\top M v)^{1/2}$ and $M \succ 0$ weights directions by behavioral relevance and measurement scale. The margin is not invariant to the coordinate system unless M is chosen accordingly. A Euclidean distance in an arbitrary fMRI embedding is not a biological depth measure.

A probability field rather than a hard border

In practice the more honest object is the **viability field**

$$v_T^\pi(x, c, t) = \mathbb{P}^\pi[Y_T(t : t + \Delta) \in \mathcal{A}_T \mid x_t = x, c_t = c], \tag{17.14}$$

with envelope $\mathcal{V}_T^\pi = \{x : v_T^\pi(x, c, t) \geq q\}$. The hard boundary is a chosen contour of a continuous probability landscape. This makes uncertainty visible and prevents a binary "attentive/unattentive" label from being mistaken for an intrinsic boundary in the brain.

FLOW HIJACKED HYPOTHESIS

For some people and tasks, ADHD-related difficulty may appear as a smaller, more anisotropic, more context-sensitive, or more weakly retained high-v_T region—not as globally reduced capacity. None of these geometric descriptors has yet been validated as an ADHD biomarker.

Stochastic reach–stay formulation

The TSVE can be connected to stochastic reachability without pretending that the complete neural state is observed. Let $K_T(c) \subset \mathcal{X}$ be an instantaneous task-compatible region and let $G_T(c) \subseteq K_T(c)$ be a target region corresponding to stabilized task engagement. For a policy π, define the reach–stay probability

$$V_{\text{RS}}^\pi(x, t) = \mathbb{P}_x^\pi[\exists \tau \in [t, t + \Delta] \text{ such that } x_\tau \in G_T \text{ and } x_s \in K_T \ \forall s \in [\tau, t + \Delta]]. \tag{17.14a}$$

This probability simultaneously represents entry and subsequent residence. The corresponding optimal probability is

$$V_{\text{RS}}^*(x, t) = \sup_{\pi \in \Pi_{\text{adm}}} V_{\text{RS}}^\pi(x, t). \tag{17.14b}$$

An optimal-policy viability kernel at reliability q is $\{x : V_{\text{RS}}^*(x, t) \geq q\}$. A person-policy envelope is $\{x : V_{\text{RS}}^{\pi_\phi}(x, t) \geq q\}$. Their difference identifies a theoretical **policy gap**:

$$\mathcal{G}_{\text{policy}} = \text{Vol}\{x : V_{\text{RS}}^*(x, t) \geq q\} - \text{Vol}\{x : V_{\text{RS}}^{\pi_\phi}(x, t) \geq q\}. \tag{17.14c}$$

Volume depends on coordinates and is included only to illustrate the idea; a probability-weighted measure under an empirically relevant state distribution is preferable:

$$\mathcal{G}_{\text{policy}}^\mu = \int_{\mathcal{X}} \left[\mathbf{1}\{V_{\text{RS}}^*(x, t) \geq q\} - \mathbf{1}\{V_{\text{RS}}^{\pi_\phi}(x, t) \geq q\}\right] \mu(dx). \tag{17.14d}$$

The policy gap is not a clinical blame score. A large gap could arise because an effective policy has never been taught, because the environment makes it unavailable, because the model's admissible-policy class is unrealistic, or because the supposedly optimal strategy imposes intolerable burden. Admissibility must include safety, effort, values, access, and side effects.

For a diffusion started at (x, t) and killed when it exits K_T, define the post-t exit time $\tau_{K_T}^{(t)} = \inf\{s \geq t : x_s \notin K_T\}$. The survival probability

$$s(x, t) = \mathbb{P}_{x,t}(\tau_{K_T}^{(t)} > t + \Delta) \tag{17.14e}$$

satisfies a backward Kolmogorov boundary-value problem under suitable regularity:

$$\partial_t s + \mathcal{L}^\pi s = 0 \quad \text{in } K_T, \qquad s = 0 \text{ on } \partial K_T, \qquad s(x, t + \Delta) = 1 \text{ in } K_T. \tag{17.14f}$$

The controlled version replaces $\mathcal{L}^\pi$ by a supremum over admissible u, yielding an HJB-type reachability equation. In discrete time, the recursion is more transparent. If $v_N(x) = \mathbf{1}_{K_T}(x)$, then

$$v_k^\pi(x) = \mathbf{1}_{K_T}(x) \int v_{k+1}^\pi(x') p(dx' \mid x, \pi(x), c_k), \tag{17.14g}$$

and

$$v_k^*(x) = \mathbf{1}_{K_T}(x) \sup_{u \in \mathcal{U}(x)} \int v_{k+1}^*(x') p(dx' \mid x, u, c_k). \tag{17.14h}$$

These recursions expose a central distinction. Increasing immediate task performance need not increase reach–stay probability over a longer horizon. A high-gain strategy might improve the next response while increasing fatigue or later exit hazard. Conversely, a brief adaptive pause can reduce immediate output while increasing the probability of successful completion.

Robustness to contextual uncertainty

If context is not known exactly, let $c \in \mathcal{C}_\delta$ be an uncertainty set. A robust envelope is

$$\mathcal{V}_{T,\text{rob}}^\pi = \left\{ x : \inf_{c \in \mathcal{C}_\delta} v_T^\pi(x, c, t) \geq q \right\}. \tag{17.14i}$$

The robust set may be far smaller than the context-specific set. That difference formalizes one possible meaning of "reliable across settings." Yet worst-case robustness can be excessively conservative. A distributionally robust alternative takes the infimum over plausible context distributions P in an ambiguity set $\mathfrak{P}$:

$$\inf_{P \in \mathfrak{P}} \mathbb{E}_{c \sim P}[v_T^\pi(x, c, t)] \geq q. \tag{17.14j}$$

Clinical cross-situational impairment should not be translated mechanically into Equation 17.14i or 17.14j, but the mathematics clarifies why success in one high-interest setting does not prove reliability in other necessary settings.

Coordinate dependence and invariant claims

Let $z = \varphi(x)$ be a smooth one-to-one reparameterization. The physical set transforms as $\varphi(\mathcal{V}_T)$, but its Euclidean volume, shape, and distance-to-boundary generally change. Therefore claims such as "the envelope is smaller" or "the basin is shallower" require a metric or reference measure that has scientific meaning. Transition probabilities, first-passage distributions, held-out performance probability, and cause-specific hazards are more defensible invariants than a picture's apparent width.

For this reason the strongest version of the TSVE is probabilistic and behavioral: $v_T^\pi(x, c, t)$ and lifecycle events. Geometric language is a visualization of those estimands, not a license to read physiology from the shape of a low-dimensional embedding.

232 Entry: reachability, latency, and the cost of beginning

Suppose the task becomes active at cue time t_0. Entry is not defined by a button press alone; it is the first time at which the latent state reaches a viable set and performance evidence supports that inference. Define the first-entry time

$$\tau_{\text{entry}} = \inf\{t \geq t_0 : x_t \in \mathcal{V}_T^\pi(c_t, t)\}. \tag{17.15}$$

If entry does not occur before a deadline $t_0 + H$, the observation is right-censored rather than assigned an arbitrary long latency. Across repeated episodes, the entry distribution

$$F_{\text{entry}}(t \mid z) = \mathbb{P}(\tau_{\text{entry}} - t_0 \leq t \mid z) \tag{17.16}$$

can depend on $z = (T, c, m, a, r, h, \theta_d, \phi)$.

The **entry committor** offers a richer quantity. For an unviable region $\mathcal{B}$ and viable target $\mathcal{V}_T$, define

$$q_{\text{in}}(x) = \mathbb{P}_x(\tau_{\mathcal{V}_T} < \tau_{\mathcal{B}}), \tag{17.17}$$

the probability of reaching the viable envelope before returning to a specified disengaged region. In a diffusion with infinitesimal generator

$$\mathcal{L}\psi = f^\mathsf{T} \nabla \psi + \tfrac{1}{2} \operatorname{tr}(Q \nabla^2 \psi), \tag{17.18}$$

the committor satisfies the backward equation

$$\mathcal{L}q_{\text{in}} = 0 \quad \text{outside the target sets,} \qquad q_{\text{in}}|_{\mathcal{V}_T} = 1, \quad q_{\text{in}}|_{\mathcal{B}} = 0. \tag{17.19}$$

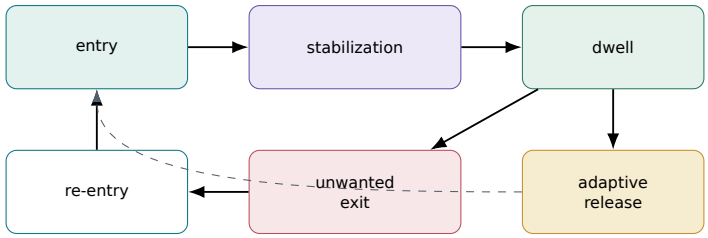
Equation 17.19 is a mathematical idealization. It clarifies what "almost engaged" could mean: not visual similarity to an average activation map, but a high probability of completing the transition under the current dynamics.

Entry failure can arise in at least four ways:

1. the viable region is unreachable under available inputs;
2. it is reachable, but the minimum transition time exceeds the practical deadline;
3. it is reachable only through a narrow channel easily disrupted by noise;
4. the person's current policy does not select the required input even though another policy could.

The four cases suggest different interventions. Medication might change the drift or gain; psychotherapy might teach a policy; environmental design might move the initial condition closer to the target or remove perturbations; changing the task might enlarge the acceptable set. Treating all four as "low motivation" discards causal information.

The task-state lifecycle



233 Stabilization, dwell, unwanted departure, and recovery

Entry does not guarantee persistence. Conditional on entry at τ_{entry}, define the first unwanted exit

$$\tau_U = \inf\left\{t > \tau_{\text{entry}} : x_t \notin \mathcal{V}_T(c_t, t),\ \chi_T(t) = 1\right\}, \tag{17.20}$$

where $\chi_T(t) = 1$ means that continued task engagement remains goal appropriate. The indicator prevents a planned task completion from being mislabeled as a lapse. The symbol χ_T is deliberately distinct from the target set $G_T(c)$ in Equation 17.14a.

The task-state dwell time is

$$D_T = \tau_U - \tau_{\text{entry}}, \tag{17.21}$$

if the first exit is unwanted. Its survival function is

$$S_U(t \mid z) = \mathbb{P}(D_T > t \mid z) = \exp\left[-\int_0^t \lambda_U(s \mid z)ds\right], \tag{17.22}$$

where $\lambda_U(t \mid z)$ is the unwanted-exit hazard. A constant hazard produces an exponential dwell distribution. Real task engagement will often show duration dependence, suggesting fatigue, learning, satiety, deadline proximity, or non-Markov memory. A Weibull, spline hazard, frailty model, or hidden semi-Markov model may therefore be preferable.

Suppose exit occurs at τ_U. Recovery begins with detecting the departure, reconstructing the task model, and returning to the viable set. Define

$$\tau_{\text{return}} = \inf\{t > \tau_U : x_t \in \mathcal{V}_T(c_t, t)\} - \tau_U. \tag{17.23}$$

Recovery has at least three latent components:

$$\tau_{\text{return}} = \tau_{\text{detect}} + \tau_{\text{reconstruct}} + \tau_{\text{reenter}}, \tag{17.24}$$

although these may not be separately identifiable from ordinary behavioral data. Experience sampling, eye tracking, interruption probes, and task-context reconstruction measures can help.

The lecture's lifecycle vector becomes

$$L_T = \left(\tau_{\text{entry}}, \lambda_U(t), \tau_{\text{return}}, \tau_{\text{switch}}\right). \tag{17.25}$$

Strictly, L_T is not a four-number vector because one component is a function and all components have distributions. A practical summary might use median entry time, an integrated unwanted-exit hazard over a fixed interval, median return time, and median valid-switch latency. The full distributions should be retained in the research model.

SUPPORTED INTERPRETATION

Behavioral response variability is compatible with unstable task engagement, but it is not a direct measure of the hazard in Equation 17.22. Motor timing, speed–accuracy strategy, arousal, local sleep, and measurement artifacts can also broaden response distributions. The proposed hazards must be estimated with task events that distinguish genuine departure and return.

234 Adaptive release and the Dual-Exit Principle

Persistence is not unconditionally desirable. A system that remains locked to yesterday's goal after the environment has changed is not demonstrating ideal control. Let $C_A(t) = 1$ denote the arrival of a valid release or switch cue: the task is complete, safety requires reorientation, or a higher-priority goal has become active. Define adaptive exit

$$\tau_A = \inf\left\{t > t_{\text{cue}} : x_t \notin \mathcal{V}_T \text{ and } x_t \in \mathcal{V}_{T'}\right\}, \tag{17.26}$$

where T' is the newly valid task. The adaptive switch cost is

$$\tau_{\text{switch}} = \tau_A - t_{\text{cue}}. \tag{17.27}$$

The **Dual-Exit Principle** distinguishes two cause-specific hazards. Let $\tau = \min(\tau_U, \tau_A)$ denote the first exit time and $J \in \{U, A\}$ its cause:

$$\lambda_U(t \mid \mathcal{F}_t) = \lim_{dt \downarrow 0} \frac{\mathbb{P}(t \le \tau < t + dt, J = U \mid \tau \ge t, \mathcal{F}_t)}{dt}, \tag{17.28}$$

$$\lambda_A(t \mid \mathcal{F}_t, C_A = 1) = \lim_{dt \downarrow 0} \frac{\mathbb{P}(t \le \tau < t + dt, J = A \mid \tau \ge t, \mathcal{F}_t, C_A = 1)}{dt}. \tag{17.29}$$

For a fixed covariate/history path, with no additional exit causes, the cumulative incidence of cause j is

$$F_j(t) = \int_0^t S(s)\lambda_j(s)ds, \qquad S(t) = \exp\left[-\int_0^t (\lambda_U(s) + \lambda_A(s))ds\right]. \tag{17.30}$$

The distinction is not semantic. A low unwanted-exit hazard is good while the task remains valid; a high adaptive-exit hazard is good after a valid cue. A selectively controlled system therefore has

$$\lambda_U \text{ small when } \chi_T = 1, \qquad \lambda_A \text{ large when } C_A = 1. \tag{17.31}$$

Define a cue-selectivity index over matched windows,

$$\mathcal{S}_{\text{exit}} = \log \frac{\lambda_A^{\text{postcue}} + \epsilon}{\lambda_U^{\text{nocue}} + \epsilon}, \tag{17.32}$$

with small regularizer $\epsilon > 0$ expressed in the same inverse-time units as the two hazards. A high index indicates persistence that is selectively releasable. A low index can arise from excessive unwanted departure, inadequate adaptive release, or both; the raw hazards must accompany the ratio.

Hyperfocus as a lifecycle profile, not an opposite diagnosis

Empirical work on hyperfocus remains limited and operational definitions vary (Hupfeld et al., 2019, PMID 30267329). The TSVE therefore does not claim to have discovered its neural mechanism. It offers a falsifiable decomposition.

One candidate profile is:

$$\tau_{\text{entry}} \text{ short under high interest}, \qquad \lambda_U \text{ low}, \qquad \lambda_A \text{ low after a valid cue}, \qquad \tau_{\text{switch}} \text{ long}. \tag{17.33}$$

This profile describes stable engagement with impaired release. It differs from healthy flow if the persistence is poorly aligned with goals, insensitive to time, or costly to other obligations. A second person could report "hyperfocus" while actually showing rapid re-entry after repeated micro-disruptions. A third might show perseveration without high-quality performance. The same self-report label can therefore conceal different dynamics.

FLOW HIJACKED HYPOTHESIS

Distractibility and hyperfocus can coexist because the hazard of leaving without a valid cue and the hazard of leaving after a valid cue are distinct control variables. This hypothesis is rejected if reliable measurement shows that one latent persistence parameter accounts for both phenomena without loss of prediction.

235 Hidden states, dwell distributions, and the danger of naming clusters

Many dynamic-connectivity studies infer a finite collection of recurring configurations. Let $S_k \in \{1, \dots, K\}$ be a latent state at observation k. A hidden Markov model specifies

$$\mathbb{P}(S_{k+1} = j \mid S_k = i) = P_{ij}, \qquad o_k \mid S_k = j \sim p_j(o; \eta_j). \tag{17.34}$$

The likelihood is

$$p(o_{1:N}) = \sum_{s_{1:N}} p(s_1) \prod_{k=1}^{N-1} P_{s_k s_{k+1}} \prod_{k=1}^{N} p_{s_k}(o_k; \eta_{s_k}). \tag{17.35}$$

State occupancy is the estimated fraction

$$\hat{\pi}_j = \frac{1}{N} \sum_{k=1}^{N} \mathbb{P}(S_k = j \mid o_{1:N}). \tag{17.36}$$

In a standard time-homogeneous HMM, the dwell time in state j is geometrically distributed:

$$\mathbb{P}(D_j = d) = (P_{jj})^{d-1}(1 - P_{jj}), \qquad d \in \{1, 2, \dots\}. \tag{17.37}$$

This memoryless form may be implausible for cognitive engagement. A hidden semi-Markov model replaces it with an explicit duration distribution $p(D_j = d \mid \psi_j)$, allowing increasing fatigue or a minimum stabilization time. Context-dependent transitions can be written

$$P_{ij}(k) = \frac{\exp\{\alpha_{ij} + z_k^{\mathsf{T}} \beta_{ij}\}}{\sum_{\ell \in \mathcal{J}_i} \exp\{\alpha_{i\ell} + z_k^{\mathsf{T}} \beta_{i\ell}\}}, \qquad j \in \mathcal{J}_i, \tag{17.38}$$

where z_k includes reward, cue, medication, difficulty, time-on-task, arousal, and person-level covariates. For an HMM, $\mathcal{J}_i$ can include every state; for an HSMM whose duration law already encodes persistence, segment-to-segment transitions conventionally use $\mathcal{J}_i = \{1, \dots, K\} \setminus \{i\}$.

The crucial validation step is external to the clustering algorithm. A state becomes "task-favorable" only if its posterior probability predicts task success out of sample, beyond motion, physiology, and obvious task events. It is not task-favorable because its spatial map resembles a preferred theory. Label switching, choice of K, scan duration, windowing, atlas, regularization, and initialization can all alter inferred states. A robust analysis should compare multiple state families and report whether the behavioral conclusion survives.

A hierarchical semi-Markov model can estimate individual differences while pooling information:

$$P_{ij}^{(r)}(k) = \frac{\exp\{\alpha_{ij} + b_{ij}^{(r)} + z_{rk}^{\mathsf{T}} \beta_{ij}\}}{\sum_{\ell \in \mathcal{J}_i} \exp\{\alpha_{i\ell} + b_{i\ell}^{(r)} + z_{rk}^{\mathsf{T}} \beta_{i\ell}\}}, \qquad \mathbf{b}_i^{(r)} \sim \mathcal{N}(\mathbf{0}, \Omega_i), \tag{17.39}$$

for participant r, with a reference-category or sum-to-zero constraint imposed for identifiability. The model should allow the possibility that the same state label is not topographically identical across all people. Otherwise, group averaging can manufacture apparent transition differences by forcing heterogeneous configurations into a shared dictionary.

ESTABLISHED EVIDENCE

Some ADHD studies report altered occupancy, dwell, transitions, flexibility, or dynamic connectivity, and acute medication studies report metric-specific changes. **Boundary:** an HMM dwell time is not automatically an attractor depth, a switching rate is not automatically cognitive flexibility, and a cluster centroid is not a neural mechanism.

236 Metastability: temporary coordination without permanent locking

Metastability describes transient coordination: components remain partially autonomous yet form temporarily coherent configurations before reconfiguring. It is not a synonym for "connectivity changes over time." Different operationalizations quantify different properties.

For phases $\theta_j(t)$ of N_θ oscillatory components, a global Kuramoto order parameter is

$$\rho_{\text{sync}}(t)e^{i\bar{\theta}(t)} = \frac{1}{N_\theta}\sum_{j=1}^{N_\theta} e^{i\theta_j(t)}, \qquad 0 \le \rho_{\text{sync}}(t) \le 1. \tag{17.40}$$

One phase-based metastability statistic is

$$M_{\text{sync}} = \text{Var}_t[\rho_{\text{sync}}(t)]. \tag{17.41}$$

High M_{sync} means the system visits different degrees of global phase coordination. It does not tell us whether the visited configurations support a task. It is possible to have high metastability with poor performance, or low metastability during a task that properly demands stable locking.

At the level of a stochastic landscape, suppose temporarily that the dynamics are approximately gradient driven:

$$dx_t = -\nabla U_T(x_t)dt + \sigma dW_t. \tag{17.42}$$

For a local well separated by barrier ΔU, a small-noise approximation gives a Kramers-like mean escape time

$$\mathbb{E}[\tau_{\text{exit}}] \asymp C\exp\left(\frac{2\Delta U}{\sigma^2}\right). \tag{17.43}$$

Equation 17.43 explains why modest changes in effective barrier or noise can produce large changes in dwell time. But the assumptions are severe: neural systems are driven, non-equilibrium, high dimensional, and generally not gradients of a scalar potential. When $f \neq -\nabla U$, the relevant object is a Freidlin–Wentzell action or quasipotential, not a literal energy landscape.

For a path $\varphi : [0, T_a] \to \mathbb{R}^n$ under diffusion covariance Q, the action is schematically

$$I_{0T_a}(\varphi) = \frac{1}{2}\int_0^{T_a} (\dot{\varphi} - f(\varphi))^{\mathsf{T}} Q^{-1} (\dot{\varphi} - f(\varphi))\, dt. \tag{17.44}$$

The most probable rare transition minimizes this action subject to boundary conditions. The quasipotential between a stable set and boundary point is the infimum of I_{0T_a} over admissible paths and durations. This is closer to what "basin depth" would mean in a non-equilibrium stochastic model.

Even then, inferring a quasipotential from short fMRI series is difficult and potentially non-identifiable. Therefore:

- "shallower task attractor" is a **Flow Hijacked hypothesis**;
- "shorter estimated dwell in a task-favorable latent state in a particular study" is an empirical result;
- the first cannot be treated as a direct restatement of the second.

Finite-time stability can also be characterized by a maximal finite-time Lyapunov exponent

$$\lambda_{\max}^{(H_L)}(x_0) = \frac{1}{H_L}\log \sigma_{\max}\left(D\Phi_{H_L}(x_0)\right), \tag{17.45}$$

where $H_L > 0$ is the finite-time window, Φ_{H_L} is the flow map, and $D\Phi_{H_L}$ its tangent map. A positive value over a finite interval indicates local separation of trajectories during that interval. It does not establish chaos, and estimating it from noisy, partially observed human data requires much longer and denser recordings than many clinical studies provide.

OPEN QUESTION

Does ADHD involve too much flexibility, too little flexibility, or context-inappropriate flexibility? The answer may differ by state and task. “More switching” is not inherently pathological; healthy cognition requires both residence and release.

237 Control energy: reachability without moralizing effort

The phrase “control energy” has a precise meaning in control theory and must not be used as a metaphor for subjective effort unless the distinction is stated. Begin with a linear time-invariant approximation

$$\dot{x}(t) = Ax(t) + Bu(t). \tag{17.46}$$

For a control horizon $T_f > 0$, the solution is

$$x(T_f) = e^{AT_f}x(0) + \int_0^{T_f} e^{A(T_f - s)}Bu(s)ds. \tag{17.47}$$

Define the finite-horizon controllability Gramian

$$W_c(T_f) = \int_0^{T_f} e^{As}BB^{\mathsf{T}}e^{A^{\mathsf{T}}s}ds. \tag{17.48}$$

If $W_c(T_f)$ is nonsingular, the minimum of $\int_0^{T_f} u(t)^{\mathsf{T}}u(t)\,dt$ over inputs that reach target x_f is

$$E_{\min}(x_0 \to x_f; T_f) = \left(x_f - e^{AT_f}x_0\right)^{\mathsf{T}} W_c(T_f)^{-1}\left(x_f - e^{AT_f}x_0\right). \tag{17.49}$$

For a target set rather than point, define

$$E_{\min}(x_0 \to \mathcal{V}_T; T_f) = \inf_{x_f \in \mathcal{V}_T} E_{\min}(x_0 \to x_f; T_f). \tag{17.50}$$

The set formulation matters because no single “normal” target is required. A treatment may improve function by making a nearer configuration viable, not by forcing a trajectory toward the control-group mean.

For the nonlinear stochastic system, a more realistic finite-horizon objective is

$$J^{\pi}(x_0) = \mathbb{E}\left[\int_0^{T_f}\left(q_T(x_t, c_t) + u_t^{\mathsf{T}}R_u u_t\right)dt + \varphi_T^{\text{term}}(x_{T_f})\right], \tag{17.51}$$

where q_T penalizes task-incompatible states, $R_u \succ 0$ penalizes modeled input magnitude, and φ_T^{term} is a terminal cost. The weights and cost terms must be scaled to a common utility unit. The value function

$$V(x,t) = \inf_{\pi \in \Pi_{\text{adm}}} J^{\pi}(x,t) \tag{17.52}$$

obeys, under standard assumptions, the Hamilton–Jacobi–Bellman equation

$$-\partial_t V = \inf_u \left\{q_T + u^{\mathsf{T}}R_u u + \nabla V^{\mathsf{T}}(f + Bu) + \tfrac{1}{2}\operatorname{tr}(Q\nabla^2 V)\right\}. \tag{17.53}$$

Equations 17.49–17.53 are not evidence that a brain computes a matrix inverse or solves an HJB equation. They define quantities an investigator can use to compare models.

How scaffolding can reduce modeled transition cost

An external checklist, visible timer, protected workspace, or task decomposition can act in at least three mathematically distinct ways:

1. change the initial condition x_0 by preloading the task rule;
2. change B by making a small self-generated action more effective;
3. change the target set $\mathcal{V}_T$ by reducing memory or sequencing demands.

Thus the plausible statement "behavioral scaffolding lowers control energy" should be unpacked. Unless A, B, the target set, and the cost metric are estimated, **control energy remains a model-based hypothesis**. Functional improvement does not require a scan, but the specific control-theoretic mechanism does require direct testing.

Functional connectivity matrices are usually symmetric correlations. Plugging them into Equation 17.46 does not identify directed causal dynamics. "Average controllability" computed from such a matrix is a graph-model quantity, not a direct measurement of physiological energy. Preliminary ADHD work using network-control metrics can motivate experiments; it does not settle the mechanism.

238 Gain, signal, noise, and why "more activation" is not a theory

The state equation allows a local analysis around a task-dependent trajectory $x_T^*(t)$. Let $\delta x_t = x_t - x_T^*(t)$. Linearization gives

$$d\delta x_t = A_T(t)\delta x_t\,dt + B_T(t)\delta u_t\,dt + E_T(t)p_t\,dt + \Sigma_T(t)dW_t, \tag{17.54}$$

where $F_T^{\mathrm{cl}}(x,t)$ denotes the full closed-loop drift after substituting the nominal context, policy, and input trajectories, so that state dependence in B_T, E_T, and the feedback policy is not omitted:

$$A_T(t) = \left.\frac{\partial F_T^{\mathrm{cl}}(x,t)}{\partial x}\right|_{x=x_T^*(t)}. \tag{17.55}$$

The matrix $A_T(t)$ is a local directed operator. Its diagonal elements describe local self-decay or self-excitation in the chosen coordinates; its off-diagonal elements describe how perturbations in one coordinate influence the rate of another. It is neither a static correlation matrix nor a universal anatomical wiring diagram.

Suppose a task-relevant signal s_t enters through B_s and a distractor d_t enters through B_d. For readout $y_t = Cx_t + \epsilon_t$, a frequency-specific signal-to-distractor ratio can be written

$$\mathrm{SDR}(\omega) = \frac{\|C(i\omega I - A)^{-1}B_s\hat{s}(\omega)\|_2^2}{\|C(i\omega I - A)^{-1}B_d\hat{d}(\omega)\|_2^2 + \mathrm{tr}[C(i\omega I - A)^{-1}Q(-i\omega I - A^{\mathsf{T}})^{-1}C^{\mathsf{T}}]}. \tag{17.56}$$

This formula makes "signal-to-noise" more specific. It depends on the input direction, frequency, system operator, readout, and endogenous covariance—not only the absolute amplitude of a region. A treatment could improve readout by amplifying relevant input, attenuating distractor input, reducing internally generated variance, changing the readout geometry, or moving the state into an operating regime in which the same inputs are separated more reliably.

For a binary decision with scalar readout distributions $y \mid H_1 \sim \mathcal{N}(\mu_1, \sigma_1^2)$ and $y \mid H_0 \sim \mathcal{N}(\mu_0, \sigma_0^2)$, discriminability is

$$d' = \frac{\mu_1 - \mu_0}{\sqrt{(\sigma_1^2 + \sigma_0^2)/2}}. \tag{17.57}$$

Equation 17.57 shows why a gain increase is not automatically beneficial. If signal and nuisance are amplified equally, d' may not improve. If gain pushes a recurrent circuit into saturation or instability, performance can worsen.

Catecholamine-dependent gain as a non-monotone parameter

Let z_t summarize effective catecholaminergic operating state in a particular circuit—not "brain dopamine." A generic inverted-U gain function can be represented as

$$\gamma(z) = \gamma_0 + \gamma_1 \exp\left[-\frac{(z - z^*)^2}{2\sigma_z^2}\right], \qquad \gamma_1 > 0, \tag{17.58}$$

or, locally, by

$$\gamma(z) = \gamma_{\max} - \kappa(z - z^*)^2, \qquad \kappa > 0. \tag{17.59}$$

These are phenomenological functions. They capture the idea that too little or too much catecholaminergic drive can impair prefrontal computation, while the optimum depends on receptor balance, region, baseline state, task demand, stress, arousal, and dose. They do not prove that ADHD is a global low-z condition.

One parameterization of Equation 17.54 is

$$A_T = A_0 + \gamma(z)A_g, \qquad B_T = B_0 + \gamma(z)B_g, \qquad Q_T = Q_0 + Q_z(z), \tag{17.60}$$

where medication could alter all three terms. A clinically effective drug response therefore need not correspond to monotonically increased activation. It may reflect a more favorable gain profile, lower task-irrelevant variability, different state occupancy, or a change in the coupling through which value and salience influence control.

ESTABLISHED EVIDENCE

Catecholamine effects are regional, receptor-, dose-, and state-dependent; stimulant and nonstimulant drugs have distinct mechanisms. **Plausible synthesis.** Some therapeutic effects can be represented as changes in dynamic gain and noise. **Boundary.** No single parameter z adequately represents dopamine and norepinephrine across the brain, and the full mapping in Equation 17.60 has not been estimated in ADHD.

239 Non-normal transient amplification: the explicit mathematical hypothesis

This section introduces the most speculative component of the Flow Hijacked model. The evidentiary boundary must remain visible:

No direct ADHD study in the acquired corpus estimated a non-normal dynamical operator, an ADHD pseudospectrum, a resolvent norm, or an ADHD transient-growth bound.

The following mathematics is established in linear systems and computational neuroscience. Its application to ADHD is a **Flow Hijacked hypothesis**.

Normality and why eigenvalues can be insufficient

A matrix $A \in \mathbb{C}^{n\times n}$ is **normal** if

$$AA^* = A^*A, \tag{17.61}$$

where A^* is the conjugate transpose. Normal matrices possess an orthonormal eigenbasis. If all eigenvalues have negative real parts, perturbations decay monotonically in the Euclidean norm up to oscillation among orthogonal modes.

A non-normal matrix has non-orthogonal eigenvectors. Even when every eigenvalue lies in the open left half-plane, a perturbation can grow temporarily because decaying modes interfere constructively before their asymptotic decay dominates. Asymptotic stability and finite-time susceptibility are therefore different properties.

For the unforced system

$$\delta\dot{x} = A\delta x, \qquad \delta x(t) = e^{At}\delta x(0), \tag{17.62}$$

the maximum amplification at time t is

$$G(t) = \sup_{\delta x(0)\neq 0} \frac{\|\delta x(t)\|_2}{\|\delta x(0)\|_2} = \|e^{At}\|_2 = \sigma_{\max}(e^{At}), \tag{17.63}$$

and the maximal transient gain is

$$G_{\max} = \sup_{t\geq 0} G(t). \tag{17.64}$$

The right singular vector associated with $\sigma_{\max}(e^{At})$ is the perturbation direction that produces the largest finite-time growth; the left singular vector is the state direction in which that growth appears. This directionality is central to the hypothesis. A salient cue is not predicted to be powerful merely because it is large. It is predicted to be powerful when its input pattern aligns with a high-gain direction of the current operator.

A two-dimensional derivation

Consider

$$A = \begin{bmatrix} -a & k \\ 0 & -b \end{bmatrix}, \qquad a > 0,\ b > 0,\ k \neq 0. \tag{17.65}$$

The eigenvalues are $-a$ and $-b$, so the origin is asymptotically stable. Yet for $a \neq b$,

$$e^{At} = \begin{bmatrix} e^{-at} & k\dfrac{e^{-bt} - e^{-at}}{a - b} \\ 0 & e^{-bt} \end{bmatrix}. \tag{17.66}$$

Start with perturbation $\delta x(0) = (0, 1)^{\mathsf{T}}$. Then

$$\delta x_1(t) = k\frac{e^{-bt} - e^{-at}}{a - b}, \qquad \delta x_2(t) = e^{-bt}. \tag{17.67}$$

Both eigenmodes decay, but the second coordinate feeds the first through k. For sufficiently large $|k|$, the norm initially grows and can become much larger than its initial value before eventually decaying. If $a = b$, the limit is

$$e^{At} = e^{-at}\begin{bmatrix} 1 & kt \\ 0 & 1 \end{bmatrix}, \tag{17.68}$$

so the off-diagonal response kte^{-at} peaks at $t = 1/a$, with magnitude $|k|/(ae)$. Stability of eigenvalues alone misses this transient.

The **numerical abscissa**

$$\omega(A) = \lambda_{\max}\left(\frac{A + A^*}{2}\right) \tag{17.69}$$

is the maximum instantaneous logarithmic growth rate of the Euclidean norm. Equivalently, $2\omega(A)$ is the maximum instantaneous growth rate of the squared norm over unit vectors, because

$$\frac{d}{dt}\|e^{At}x\|_2^2\Big|_{t=0} = 2x^*\left(\frac{A + A^*}{2}\right)x. \tag{17.70}$$

Thus $\omega(A) > 0$ guarantees an initial direction of transient growth even if the spectral abscissa

$$\alpha(A) = \max_j \operatorname{Re}\lambda_j(A) \tag{17.71}$$

is negative. The gap $\omega(A) - \alpha(A)$ is one simple warning that finite-time behavior cannot be read from eigenvalues alone.

Forced amplification and the resolvent

For harmonic forcing $p(t) = \operatorname{Re}\{\hat{p}e^{i\omega t}\}$ in

$$\delta\dot{x} = A\delta x + B_p p(t), \tag{17.72}$$

the steady-state response is governed by the resolvent

$$\mathcal{R}(i\omega; A) = (i\omega I - A)^{-1}. \tag{17.73}$$

The largest input-output gain at frequency ω is

$$\mathcal{G}(\omega) = \|C(i\omega I - A)^{-1}B_p\|_2. \tag{17.74}$$

The leading right singular vector of $C\mathcal{R}B_p$ identifies the maximally amplified input pattern; the leading left singular vector identifies the dominant output pattern. A non-normal operator can exhibit a large resolvent norm even when $i\omega$ is far from all eigenvalues.

This leads to a precise ADHD hypothesis: a notification, internal thought, reward cue, or emotional signal may cause disproportionate task-state displacement when its input direction and timing align with a high-gain resolvent mode of the current task configuration. The hypothesis is not "ADHD brains amplify everything." It is anisotropic, frequency dependent, state dependent, and input-channel specific.

Pseudospectra and perturbation sensitivity

The ε-pseudospectrum of A is

$$\Lambda_\varepsilon(A) = \{z \in \mathbb{C} : \|(zI - A)^{-1}\|_2 > \varepsilon^{-1}\}, \tag{17.75}$$

equivalently,

$$\Lambda_\varepsilon(A) = \bigcup_{\|E\|_2 < \varepsilon} \Lambda(A + E). \tag{17.76}$$

Equation 17.76 means that a small change in the operator can move an eigenvalue anywhere inside the pseudospectrum. If $\Lambda_\varepsilon(A)$ extends into the right half-plane for small ε, the system is sensitive to model perturbations even if the estimated eigenvalues themselves are stable.

The pseudospectral abscissa is

$$\alpha_\varepsilon(A) = \sup_{z \in \Lambda_\varepsilon(A)} \operatorname{Re} z. \tag{17.77}$$

A related lower bound on transient growth is

$$\sup_{t \geq 0} \|e^{At}\|_2 \geq \frac{\alpha_\varepsilon(A)}{\varepsilon} \quad \text{for suitable } \varepsilon \text{ with } \alpha_\varepsilon(A) > 0. \tag{17.78}$$

The exact constants and norm matter. In high-dimensional noisy estimates, pseudospectra can be extremely unstable. Regularization, uncertainty propagation, and held-out prediction are indispensable.

State-dependent non-normality

For a nonlinear trajectory, the tangent operator varies:

$$\delta\dot{x} = A_T(t)\delta x, \qquad \delta x(t_1) = \Phi(t_1, t_0)\delta x(t_0), \tag{17.79}$$

where Φ is the state-transition matrix satisfying

$$\frac{d}{dt}\Phi(t, t_0) = A_T(t)\Phi(t, t_0), \qquad \Phi(t_0, t_0) = I. \tag{17.80}$$

The finite-time gain is

$$G(t_1, t_0) = \sigma_{\max}(\Phi(t_1, t_0)). \tag{17.81}$$

This quantity can change as the person approaches a lapse. A system could become vulnerable before mean activation changes appreciably. The most informative precursor may therefore be a change in the tangent geometry or input-output gain rather than the absolute level of DMN or FPN activity.

What would count as direct evidence?

A credible test would require:

1. a task with controlled, randomized perturbations of known timing and content;
2. dense neural measurement sufficient to fit a directed local dynamical model;
3. an independently defined task-favorable state or performance envelope;
4. preregistered estimates of $G(t)$, $\omega(A)$, resolvent gain, or pseudospectral sensitivity;
5. out-of-sample prediction of perturbation-induced displacement and recovery;
6. comparison against spectral abscissa, static connectivity, conventional dynamic connectivity, motion, arousal, sleep, symptoms, and baseline performance;
7. replication in an independent cohort and within-person replication across days;
8. explicit uncertainty for the estimated operator.

If non-normal quantities add no reliable predictive information, the ADHD-specific non-normality hypothesis should be rejected. General mathematical elegance is not evidence.

240 Fast neural dynamics inside slower policy learning and development

The complete architecture is multiscale. Fast state change unfolds within slowly changing policies, medication adaptation, sleep cycles, development, and environment. A compact system is

$$\begin{aligned} dx_t &= f_T(x_t; c_t, \theta_d, \phi_t, m_t, a_t, r_t, h_t)dt + B_T\pi_{\phi_t}(\hat{x}_t, c_t)dt + E_T p_t dt + \Sigma_T dW_t, \\ \dot{\phi}_t &= \varepsilon_\phi L(\phi_t; x_t, Y_t, \text{practice}, \text{feedback}, \text{therapy}), \\ \dot{\theta}_d &= \varepsilon_d D(\theta_d, t, \text{developmental context}), \\ \dot{\eta}_t &= K_{\text{PK}}(\eta_t, \text{dose}, t), \qquad m_t = M(\eta_t), \end{aligned} \tag{17.82}$$

with

$$0 < \varepsilon_d \ll \varepsilon_\phi \ll 1 \tag{17.83}$$

relative to fast task dynamics. The additional variable η_t represents pharmacokinetics, while m_t represents pharmacodynamic effects. Acute concentration change, repeated treatment, compensatory adaptation, and developmental change therefore occupy different equations and timescales.

In singular-perturbation language, the fast subsystem treats ϕ and θ_d as approximately fixed over a short trial:

$$dx_t = f_T(x_t; \phi, \theta_d, ...)dt + \cdots. \tag{17.84}$$

The slow subsystem averages learning over fast-state occupancy:

$$\dot{\phi} = \varepsilon_\phi \bar{L}(\phi, \theta_d) = \varepsilon_\phi \int L(\phi, x)\, \mu_{\phi,\theta_d}(dx), \tag{17.85}$$

where μ_{ϕ,θ_d} is the occupancy distribution of the fast process under the present policy and context. This equation makes a possible treatment interaction mathematically visible: if medication changes μ, it may change which experiences are available for learning even if it does not directly change L.

The "learning corridor" as a testable, unproven hypothesis

Suppose therapy updates policy parameters by a noisy learning rule

$$\phi_{k+1} = \phi_k + \alpha_k \widehat{\nabla}_\phi \mathcal{R}(\phi_k; x_k, c_k), \tag{17.86}$$

where $\mathcal{R}$ is a functional reward and x_k is the state occupied during practice. If pharmacological treatment increases the probability of entering a learning-competent set $\mathcal{L}$, then

$$\mathbb{E}[\Delta\phi\, \mathbf{1}\{x \in \mathcal{L}\} \mid m] = \int_{\mathcal{L}} \alpha\, \mathbb{E}[\widehat{\nabla}\mathcal{R} \mid x, m]\, \mu_m(dx) \tag{17.87}$$

is the learning update contributed by visits to $\mathcal{L}$ and could exceed its no-medication counterpart even if medication does not encode the learned strategy. Without the indicator on the left, the integral over $\mathcal{L}$ would equal the full conditional expectation only under the additional assumption that updates vanish outside $\mathcal{L}$.

This is the **Flow Hijacked learning-corridor hypothesis**: pharmacological stabilization may increase exposure to states in which feedback, rehearsal, and therapy can be used, while psychotherapy changes the policy applied in those states. The components are plausible; decisive neural mediation evidence is absent. Combined-treatment trials show outcome-specific complementarity, not proof of Equation 17.87.

The hypothesis has a clear test. Randomize medication and skills training factorially; repeatedly measure task-state occupancy and trial-level learning; demonstrate that early medication-induced occupancy changes mediate later skill acquisition and that the acquired policy persists when acute drug state is absent. Without temporal mediation and persistence, "medication opens a learning corridor" remains a useful clinical intuition rather than an established mechanism.

Why acute normalization cannot establish developmental normalization

Let $\Theta^{(0)}$ be pretreatment parameters, $\Theta^{(a)}$ the acute on-drug parameters, and $\Theta^{(c)}$ chronic parameters after adaptation. In general,

$$\Theta^{(c)} \neq \Theta^{(a)} \neq \Theta^{(0)}. \tag{17.88}$$

An acute imaging study estimates a contrast conditional on transient exposure. It cannot identify the slow law D, durable off-drug reorganization, or developmental compensation. Molecular evidence of chronic transporter adaptation and imaging studies with age-reversed directions reinforce this caution. "Normalization" must name the metric, age, task, exposure duration, and comparison condition.

241 Intervention fingerprints in the lifecycle parameter space

Let the model-derived fingerprint for person i, task T, context c, and condition z be

$$\Psi_{iTcz} = \left(\tilde{\tau}_{\text{entry}}, \Lambda_U(H), \tilde{\tau}_{\text{return}}, \tilde{\tau}_{\text{switch}}, \mathcal{S}_{\text{exit}}, \pi_{\text{viable}}, G_{\max}, E_{\min}\right), \tag{17.89}$$

where tildes denote robust location summaries, $\Lambda_U(H) = \int_0^H \lambda_U(t)dt$ is cumulative unwanted-exit hazard over a declared horizon H, π_{viable} is viable-state occupancy, and the last two quantities are included only when a directed dynamical model is identifiable.

An intervention effect is not one arrow marked "better." It is the contrast

$$\Delta\Psi^{(I)} = \mathbb{E}[\Psi \mid \text{do}(I = 1)] - \mathbb{E}[\Psi \mid \text{do}(I = 0)]. \tag{17.90}$$

The do-operator emphasizes that observational on/off comparisons generally do not identify the causal contrast. Randomization, within-person crossover, instrumental designs, target-trial emulation, or explicit causal assumptions are needed.

Intervention lever	Primary model location	Candidate fingerprint	Current evidentiary boundary
Stimulant medication	f, B, E, Q, γ, r and state occupancy	shorter entry; lower unwanted-exit hazard; possibly faster return	acute, metric-specific evidence is strongest for methylphenidate; no universal dynamic signature
Atomoxetine	catecholamine-dependent drift/gain over slower onset	improved entry and stability through a different parameter path	comparative dynamic-network evidence sparse
α_{2A} agonist	prefrontal recurrent stability/arousal parameters	lower perturbation susceptibility or better maintenance	direct whole-network lifecycle evidence sparse
ADHD-adapted CBT	policy ϕ, meta-detection, reconstruction rules	shorter entry and return; more valid release	clinical evidence; direct neural mediation very sparse
Organizational skills	context c, policy ϕ, target demand	lower entry cost; reduced prospective-memory loss	neural change not necessary for efficacy
Parent training/school contingency	environmental transition and value structure	improved cue validity, entry, reinforcement, and persistence	child outcomes depend on rater and setting
Reward or intrinsic interest	r_t, drift, target valuation	faster entry, longer dwell; possibly slower adaptive release	heterogeneous and task-phase dependent
Sleep/circadian intervention	h_t, a_t, Q_t	broad changes, especially unwanted exit and recovery	sleep loss can mimic or amplify symptoms; causal ADHD-specific dynamics incomplete
Reduced interruptions	perturbation rate and map p_t, E_T	lower unwanted-exit hazard without neural "normalization"	ecologically meaningful; scanner evidence not required
Combined treatment	fast-state distribution plus learned policy	complementary fingerprint rather than uniform synergy	superiority is outcome- and comparison-specific; neural learning corridor unproven

The table contains predictions, not established parameter estimates. It also shows why different treatments can improve the same symptom score through different mechanisms. A medication may alter the probability distribution of fast states. Therapy may improve recognition and recovery policies. Environmental design may reduce the rate and alignment of perturbations. A symptom scale can decline in all three cases while the latent fingerprints differ.

Normalization is not the objective function

Let μ_C be the control-group mean state and $\mathcal{V}_T$ the viable set. A normalization objective is

$$J_{\text{norm}} = \|x - \mu_C\|^2, \tag{17.91}$$

whereas a functional objective is

$$J_{\text{func}} = \mathbb{E}[\ell_T(Y)] + \rho\ \text{Risk}(Y) + \kappa\ \text{Burden}(u, I). \tag{17.92}$$

Minimizing Equation 17.91 need not minimize Equation 17.92. A compensatory configuration can be farther from the group mean yet function better. Pharmaco-imaging findings in which symptom improvement is associated with a non-normalizing connectivity shift are therefore not paradoxes; they expose the weakness of a normative-point objective.

Mediation, moderation, and mechanism

If treatment I changes candidate mediator M and outcome Y, a causal mediation claim requires more than correlations among change scores. In potential-outcome notation, the natural indirect effect is

$$\text{NIE} = \mathbb{E}\left[Y(1, M(1)) - Y(1, M(0))\right]. \tag{17.93}$$

Identifying Equation 17.93 requires assumptions about mediator–outcome confounding that randomizing treatment alone does not solve. Therefore a finding that connectivity change correlates with symptom improvement is a treatment-associated brain–behavior link, not automatically a mechanism.

Moderation asks a different question:

$$\mathbb{E}[Y \mid I, Z] = \beta_0 + \beta_I I + \beta_Z Z + \beta_{IZ} IZ. \tag{17.94}$$

Here Z may be baseline dynamics, reward sensitivity, age, or sleep. A significant β_{IZ} predicts differential response; it does not show that treatment changes Z. Prediction and mediation must remain separate.

242 Identifiability: when the equations outrun the data

A rich model can explain anything after the fact if its parameters are not identifiable. Let Θ collect the drift, input maps, noise, policy, and observation parameters. Structural identifiability asks whether

$$p(o_{1:N}, Y_{1:N} \mid \Theta_1) = p(o_{1:N}, Y_{1:N} \mid \Theta_2) \quad \forall (o, Y) \implies \Theta_1 = \Theta_2. \tag{17.95}$$

If two parameter settings generate the same observable distribution, no estimator can distinguish them without new measurements or interventions. Practical identifiability asks whether finite, noisy data constrain the parameters tightly enough for useful inference.

Observability and partial measurement

For the linear system $\dot{x} = Ax$, $y = Cx$, the observability matrix is

$$\mathcal{O} = \begin{bmatrix} C \\ CA \\ CA^2 \\ \vdots \\ CA^{n-1} \end{bmatrix}. \tag{17.96}$$

Full state observability requires $\operatorname{rank}(\mathcal{O}) = n$. Human neuroimaging almost never offers direct full-state observation. fMRI is temporally filtered and vascular; EEG/MEG has an ill-posed inverse problem; behavior is low dimensional; subjective reports are intermittent. Multimodal fusion can improve constraints but adds cross-modal alignment assumptions.

For stochastic state-space models, observability is probabilistic. Posterior uncertainty

$$p(x_{1:N}, \Theta \mid o_{1:N}, Y_{1:N}) \tag{17.97}$$

must be propagated into the TSVE and hazard estimates. Reporting a single decoded trajectory as if it were known is inappropriate.

Equifinality and degeneracy

The TSVE deliberately permits multiple configurations to support the same outcome. This functional degeneracy also produces an inverse problem: observing adequate performance does not identify which internal configuration caused it. Conversely, similar performance failures can arise from different routes—weak task representation, low arousal, strong spontaneous thought, motor variability, sensory capture, or unfavorable reward weighting. This is equifinality.

The model therefore needs perturbations. Randomized cues, reward changes, interruption types, time-on-task manipulations, and medication challenges provide inputs whose responses help distinguish mechanisms. Passive resting-state data alone cannot identify a task-state transition model.

Individual parameters versus group averages

Suppose participant-specific hazard follows

$$\lambda_{Ui}(t) = \lambda_0(t) \exp\left(\beta^{\mathsf{T}} z_{it} + b_i\right), \qquad b_i \sim \mathcal{N}(0, \sigma_b^2). \tag{17.98}$$

A mean diagnosis coefficient β_D can coexist with extensive overlap in b_i. It does not permit classification of an individual from the group average. A clinically useful model should establish calibration and decision value at the individual level rather than merely a significant group contrast.

Intensive longitudinal designs can estimate within-person relationships:

$$Y_{it} = \alpha_i + \beta_i X_{it} + \epsilon_{it}, \qquad \beta_i \sim \mathcal{N}(\bar{\beta}, \sigma_\beta^2). \tag{17.99}$$

If σ_β^2 is large or signs differ, a population-average mechanism is misleading. ADHD heterogeneity makes this possibility central rather than peripheral.

Measurement invariance across age and treatment

If the observation map changes with age or medication,

$$o_t = H_{g,m}(x_t) + \nu_t, \tag{17.100}$$

then an observed group contrast can reflect $H_{g,m}$ rather than latent dynamics. Development changes neurovascular coupling, anatomy, motion, and task strategy. Medication can alter vascular and physiological signals. Longitudinal models should test measurement invariance or include modality-specific nuisance pathways.

State-label and model-class uncertainty

An HMM with $K = 5$, a sliding-window clustering with $K = 7$, and a recurrent neural state-space model may partition the same data differently. Inference should average or compare model classes:

$$p(\Delta\Psi \mid D) = \sum_{m \in \mathfrak{M}} p(\Delta\Psi \mid D, m) p(m \mid D). \tag{17.101}$$

Here $\mathfrak{M}$ denotes the candidate model classes and is distinct from the medication-state space $\mathcal{M}$. At minimum, conclusions should survive reasonable choices of parcellation, preprocessing, state number, window, censoring, and regularization. A multiverse that produces sign reversals is evidence that the claim is not yet stable.

243 An estimation program capable of testing the model

The TSVE should be tested with a staged program rather than one heroic scan.

Stage 1 — Define a real functional target

Choose a task with a defensible outcome set $\mathcal{A}_T$. The criterion should distinguish mean performance from catastrophic lapses, account for speed–accuracy tradeoffs, and connect to a meaningful function. For a sustained task, one example is

$$g_T(Y) = w_1\,\text{Accuracy} - w_2\,\text{OmissionRate} - w_3 Q_{0.95}(RT) - w_4\,\text{RuleBreaks}, \tag{17.102}$$

with weights fixed before analysis and scaled so that every term contributes in a common utility unit. For writing, progress and task-context reconstruction may matter more than reaction time.

Stage 2 — Sample within-person dynamics densely

Collect repeated sessions across medication state, sleep, time of day, reward, and interruption context. Use synchronized behavior, eye tracking, physiology, and a neural modality with appropriate temporal resolution. Sparse between-person snapshots cannot separate trait-like parameters from day-specific state.

For person i, decompose unwanted-exit hazard as

$$\lambda_{Ui}(t) = \lambda_0(t) \exp\left[\alpha_i + \gamma_{d(i,t)} + \beta_m m_{it} + \beta_h h_{it} + \beta_r r_{it} + \beta_c c_{it}\right], \tag{17.103}$$

where $\lambda_0(t)$ is a common baseline hazard, α_i is trait-like, γ_d is day-level, and the remaining terms are state/context dependent. Covariates and coefficients must make the exponential predictor dimensionless. Reliability requires enough observations at every level.

Stage 3 — Randomize perturbations

Present internal-capture analogues, reward cues, visual distractors, notifications, and valid switch cues in randomized sequences. Perturbation amplitude, onset, modality, and goal relevance should be independently manipulated. This enables an impulse-response estimate

$$h_{yp}(\tau) = \frac{\delta\, \mathbb{E}[y(t+\tau)]}{\delta p(t)}, \tag{17.104}$$

and tests whether identical inputs have larger consequences near inferred envelope boundaries.

Stage 4 — Fit competing model families

Compare at least:

1. a static trait model;
2. a mean-activation/connectivity model;
3. a discrete HMM or HSMM;
4. a switching linear dynamical system;
5. a nonlinear stochastic state-space model;
6. a model with and without separate adaptive and unwanted exit hazards;
7. for the non-normal hypothesis, models constrained to normal versus unconstrained directed operators.

Evaluation must be out of sample. For predictive density,

$$\text{elpd} = \sum_{i=1}^{N} \log p(y_i \mid y_{-i}), \tag{17.105}$$

or a held-out log score can compare models. Report calibration, discrimination, uncertainty, and practical value—not only likelihood-ratio significance.

Stage 5 — Validate lifecycle events

An algorithmically decoded "departure" should precede behaviorally defined lapses, subjective off-task reports, gaze displacement, or loss of task representation. A decoded "return" should predict recovered task context, not merely a cluster change. Convergent validity is mandatory because state transitions can be produced by motion or physiology.

Stage 6 — Test causal intervention fingerprints

Use randomized crossover for acute medication where appropriate, parallel-group longitudinal designs for learning, factorial designs for combined treatment, and repeated post-treatment assessments with and without acute medication. Separate:

- target engagement;
- state-dynamic change;
- cognitive change;
- core symptom change;
- functional outcome;
- persistence after treatment.

Stage 7 — Replicate across development without pooling it away

Fit age-varying effects

$$\beta(a) = \sum_{j=1}^{J} \gamma_j B_j(a), \tag{17.106}$$

with spline basis B_j, rather than imposing a single child-to-adult coefficient. Test whether measurement, state dictionary, and treatment fingerprint are invariant. Developmental reversals in medication connectivity effects make this more than a statistical refinement.

Stage 8 — External ecological validation

The final test is not whether a latent-state figure is attractive. It is whether the model predicts real episodes of beginning, persisting, resuming, and switching in daily life. Passive sensing should be consented, minimal, and privacy preserving. Ecological momentary assessment can sample task identity, goal relevance, mind wandering, affect, context, and perceived return without turning a person's life into continuous surveillance.

244 Pre-lapse dynamics: what happens immediately before attention departs?

The scientific question "what happens before a lapse?" is sharper than "which region is underactive in ADHD?" Let t_L be a behaviorally validated lapse time. Align trials to $t_L = 0$ and estimate a precursor process $z(t)$ for $t < 0$. Candidate predictors include:

- increasing uncertainty of the task-rule representation;
- changing salience–control–default coupling;
- pupil-linked arousal drift;
- local sleep or oscillatory markers;
- rising model residual variance;
- approach to a viability boundary $d_T(x_t, c_t) \downarrow 0$;
- increasing non-normal finite-time gain;
- a value reversal in which a competing target becomes more attractive.

A time-dependent hazard model is

$$\lambda_U(t \mid \mathcal{F}_t) = \lambda_0(t) \exp\left[\beta_d d_T(x_t, c_t) + \beta_g \log G_H(t) + \beta_a a_t + \beta_r \Delta r_t + \beta_s s_t\right], \tag{17.107}$$

where $G_H(t) = \sup_{0<\tau\le H} \|\Phi(t+\tau, t)\|_2$, Δr_t is competing-value advantage, and s_t is a spontaneous-thought or sleep-related measure. The signs should be preregistered when theory justifies them; flexible feature discovery should be followed by independent confirmation.

In the absence of censoring, predictive performance can be evaluated with the time-dependent Brier score

$$\mathrm{BS}(t) = \frac{1}{N} \sum_{i=1}^{N} \left(\mathbf{1}\{\tau_{Ui} \le t\} - \widehat{F}_{Ui}(t)\right)^2, \tag{17.108}$$

Under censoring, Equation 17.108 must be replaced by an inverse-probability-of-censoring-weighted or otherwise consistent estimator. Calibration curves should accompany the score.

The key alternative explanations must enter the model. If head motion precedes apparent state change, does it represent artifact, behavior adjacent to the lapse, or both? If arousal accounts for the effect, a network-specific interpretation should contract. If reward changes performance without changing the decoded state, the envelope may be misdefined. A strong model learns from these failures.

OPEN QUESTION

Is there a reproducible, person-general pre-lapse signature, or are there multiple routes with person-specific precursors? The heterogeneity literature makes the second possibility serious.

245 Discriminating predictions

The TSVE has scientific value only if it makes predictions that simpler models do not.

Prediction 1 — Lifecycle decomposition will outperform one attention score

A model containing entry, unwanted exit, recovery, and adaptive release should predict functional outcomes better than mean accuracy, total symptom score, or reaction-time variability alone:

$$\Delta R^2_{\text{life}} = R^2(Y_{\text{functional}} \mid L_T, Z) - R^2(Y_{\text{functional}} \mid S_{\text{ADHD}}, \bar{Y}, \mathrm{Var}(RT), Z) > 0. \tag{17.109}$$

This gain should replicate out of sample. If it vanishes after correction for complexity, the lifecycle decomposition has not earned its place.

Prediction 2 — Similar symptom severity will conceal distinct dynamical profiles

Among people matched on symptom score, mixture or hierarchical models should identify reproducible differences such as high entry cost, high unwanted-exit hazard, slow recovery, or low adaptive-release hazard. These profiles should predict different everyday impairments and differential response to interventions.

Prediction 3 — Reward will alter more than mean activation

Incentive or intrinsic interest should change the entry committor, viable occupancy, or unwanted-exit hazard in at least some participants. The magnitude may depend on reward phase and baseline value sensitivity. For a hyperfocus-like profile, reward may improve entry and dwell while worsening valid release. A uniformly beneficial scalar "motivation" effect would argue against the dual-exit model.

Prediction 4 — Medication effects will be metric-, context-, and timescale-specific

Acute medication should alter some components of Ψ without universally moving all neural measures toward a control mean. The sign may differ with age, task, dose, and baseline state. Durable off-drug policy or developmental change should not be inferred from acute fingerprints.

Prediction 5 — Psychotherapy and organizational treatment will preferentially affect policy-linked variables

Skills-based treatment should reduce entry and recovery latency, improve cue-triggered switching, or reduce the functional cost of departures even when acute neural gain estimates remain unchanged. If direct neural changes occur, they should be tested as mediators rather than assumed.

Prediction 6 — Combined treatment may produce complementary, not simply additive, fingerprints

In a factorial design, medication may change early state occupancy while skills treatment changes return policies and long-term cue use. Complementarity is supported if the joint condition covers more lifecycle dimensions or produces persistent strategy use—not merely if a total score shows an interaction.

Prediction 7 — Pre-lapse predictors will be state dependent

The same perturbation will have larger effects near a viability boundary or under high estimated transient gain. Models using perturbation-by-state interactions should outperform models using perturbation magnitude alone:

$$\lambda_U \propto \exp\{\beta_1 \|p\| + \beta_2 d_T + \beta_3 \|p\| d_T\}. \tag{17.110}$$

Prediction 8 — Resting state will not substitute for task dynamics

Rest-derived parameters may constrain priors, but task-evoked transitions and performance-validated states should add predictive information. If rest alone predicts all lifecycle quantities equally well, the emphasis on assembled task configurations requires revision.

Prediction 9 — There are multiple viable configurations, including compensatory ones

Successful performance should occupy a set rather than a single cluster, and some clinically favorable treatment shifts should be non-normalizing. A model that forces all successful trajectories toward the control mean should predict worse than a set-valued model.

Prediction 10 — Hyperfocus and distractibility will dissociate under valid switch cues

Unwanted-exit and adaptive-release hazards should be statistically separable and differentially associated with self-reported hyperfocus, time loss, and functional cost. If they collapse onto one persistence factor across tasks and contexts, the Dual-Exit Principle is unsupported.

Prediction 11 — Development changes the envelope and observation map

Age should moderate state dictionaries, transition dynamics, and treatment fingerprints. Apparent symptom remission may reflect enlarged viability sets, altered policies, compensatory routes, or better environmental fit rather than complete convergence to a normative connectome.

Prediction 12 — Non-normal measures must add specific predictive value or be abandoned

After controlling for spectral stability, static and dynamic connectivity, task state, motion, physiology, arousal, sleep, symptoms, and perturbation amplitude, non-normal gain should predict displacement magnitude or recovery time:

$$\Delta\,\mathrm{elpd}_{\mathrm{NN}} = \mathrm{elpd}(M_{\mathrm{base+NN}}) - \mathrm{elpd}(M_{\mathrm{base}}) > 0. \tag{17.111}$$

No replicable increment means no empirical reason to retain the ADHD-specific non-normality hypothesis.

Proposed component	Result that resists or falsifies it	Required response

246 Falsification conditions

The framework should be weakened, revised, or rejected under the following results.

Proposed component	Result that resists or falsifies it	Required response
Lifecycle decomposition	Entry, departure, return, and release are not reliably separable; a single factor predicts equally well	abandon the multidimensional lifecycle claim
Task-state viability set	Successful trials occupy one stable point-like state and a set-valued model adds no prediction	replace the envelope with the simpler model
Context-sensitive envelope	Reward, sleep, cueing, and task demand do not alter state–performance mapping	remove or narrow context dependence
Dynamic account	Static traits and mean activation explain held-out performance as well as dynamic models	do not claim dynamics add explanatory value
Dual-Exit Principle	Unwanted and adaptive exits share one invariant hazard and do not dissociate behaviorally	reject the principle
Hyperfocus profile	Hyperfocus measures do not associate with adaptive-release cost or show no reproducible task signature	keep hyperfocus phenomenological; remove the mechanism
Treatment fingerprints	Different interventions yield indistinguishable lifecycle changes after adequate power	abandon claims of parameter-specific complementarity
Learning corridor	Medication-related state change does not precede or mediate skill acquisition; no persistent policy effect	reject the corridor mechanism
Metastable/attractor language	HMM dwell changes fail to correspond to perturbation recovery or transition barriers	stop translating dwell into attractor geometry
Non-normal amplification	Directed operators are not reliable, non-normal metrics do not replicate, or add no prediction	delete the ADHD-specific non-normal hypothesis
Developmental model	Parameters and observation maps prove invariant across age	simplify the multiscale developmental account
Person-specific claim	Within-person parameters are unreliable across days and add no ecological prediction	restrict the model to group-level research, not individual use

A framework that reinterprets every null result as "hidden complexity" is not falsifiable. Complexity is justified only when it improves calibrated prediction, causal explanation, or intervention selection under external validation.

Negative controls

Strong tests should include:

- tasks unrelated to the hypothesized configuration;
- irrelevant perturbation channels not expected to align with high-gain directions;
- sham or expectancy-matched conditions where possible;
- non-ADHD clinical comparison groups with anxiety, depression, sleep deprivation, PTSD, autism, or substance-related attentional impairment;
- simulated data with known operators to verify recovery of non-normal quantities;
- phase-randomized or temporally permuted neural controls;
- alternate preprocessing pipelines and motion thresholds;
- predictive baselines using symptoms and behavior alone.

Specificity matters. If the same signature appears across every form of fatigue or distress, it may index general state regulation rather than ADHD. That can still be scientifically valuable, but the diagnostic claim must contract.

247 Ethical and clinical limits

The TSVE is not a diagnostic replacement

ADHD diagnosis rests on a developmental clinical syndrome, impairment, cross-context evidence, and differential diagnosis. The TSVE does not decide whether concentration difficulty arises from ADHD, sleep deprivation, depression, anxiety, PTSD, bipolar disorder, substance effects, autism, medical illness, environmental overload, or another cause. A dynamical transition problem may be transdiagnostic.

Viability is task- and value-dependent

The acceptable set $\mathcal{A}_T$ contains normative choices. Who defines success? A workplace can impose fragmented demands that make nearly everyone's viable set smaller. A school can reward stillness rather than learning. A family can label intense creative engagement pathological because it violates convenience. Every use of $y_{\min}$ and q must therefore state whose goal is being optimized and what burden is imposed.

Difference is not defect at every coordinate

A point farther from the control-group mean is not automatically worse. DMN activity supports memory, simulation, planning, self-related cognition, and creativity. Flexibility can rescue a failing strategy; stability can become perseveration. A humane model evaluates goal alignment, safety, function, and subjective cost—not conformity to a mean connectome.

Model-derived risk can stigmatize

Predicted lapse risk in education, employment, insurance, or driving could be misused. Before any individual application, the model would require external validation, fairness analysis, uncertainty communication, governance, and strict limits on secondary use. A state estimate should not become a new biological moral score.

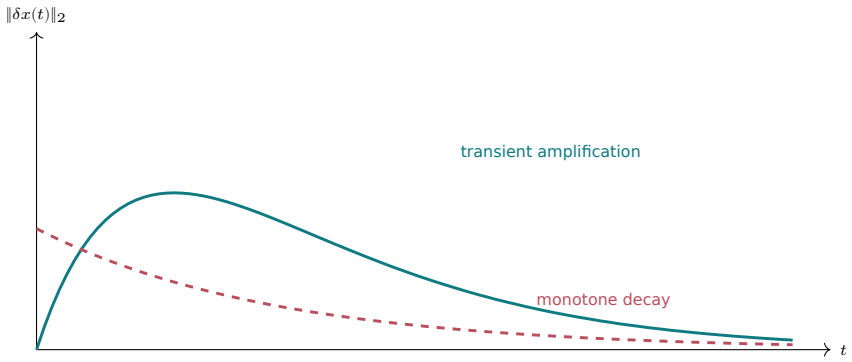
Treatment choice remains clinical and individual

The equations do not prescribe medication, psychotherapy, or environmental change. Treatments differ in evidence, onset, adverse effects, contraindications, monitoring, accessibility, and personal preference. Acute symptom efficacy is not full recovery; functional support can matter even when core symptoms persist. Any clinical decision belongs with a qualified professional and the person affected.

Compassion is not mathematically optional

The model's moral contribution is modest but important. Inconsistent performance need not imply indifference, laziness, or lack of intelligence. If the probability of entering and retaining a useful configuration changes with context, reward, sleep, perturbation, development, and treatment, then behavior cannot be read as a transparent measure of character. The correct response is neither blame nor romanticization. It is precise curiosity about conditions, costs, and supports.

Stable eigenvalues can coexist with transient growth



Conceptual mathematics only—no direct ADHD operator estimate currently establishes this mechanism.

248 The five-layer conclusion

ESTABLISHED EVIDENCE

ADHD is a heterogeneous developmental disorder defined clinically, with substantial genetic contribution and meaningful environmental modulation. Network neuroscience does not identify one broken region or one "task-positive network." The DMN is adaptive. Goal-directed behavior recruits changing configurations involving frontoparietal, dorsal and ventral attention, salience, cingulo-opercular, corticostriatal, thalamic, cerebellar, sensory, motor, and memory systems. In some ADHD samples, studies report differences in segregation, dynamic connectivity, state occupancy, dwell, transitions, response variability, or the stability of task representations. Effects are often small, method dependent, and not diagnostically specific. Reward can alter performance and recruitment. Medication can alter some network measures acutely and over selected longer intervals, without justifying a blanket claim of "brain normalization." Psychosocial interventions can improve symptoms and function even though direct neural mediation evidence remains sparse.

SUPPORTED INTERPRETATION

A deeper description than "attention deficit" is scientifically defensible: ADHD can involve difficulty regulating the allocation, stabilization, and transition of cognition across distributed configurations. This interpretation accommodates variable performance, sensitivity to reward and salience, mind wandering, altered timing, task-initiation difficulty, and some forms of intense persistence without reducing any one of them to willpower. It is a cross-study description, not a singular pathophysiology.

PLAUSIBLE SYNTHESIS

Medication, psychotherapy, sleep, reward, and environment may operate on different layers of the same coupled system. Medication may alter catecholamine-dependent gain, noise, value weighting, and state occupancy. Psychotherapy and organizational treatment may alter policies for entry, monitoring, recovery, and release. Environmental modification may change initial conditions, perturbation rates, and task demands. Combined treatment may be complementary because state availability and learned strategy are different variables. These bridges are plausible, but most have not been jointly estimated.

FLOW HIJACKED HYPOTHESIS

The Task-State Viability Envelope proposes that a task can be supported by many configurations, and that impairment can arise through distinct failures of entry, residence, recovery, or adaptive release. The Dual-Exit Principle predicts that vulnerability to unwanted departure and ability to leave after a valid cue are separable. A further hypothesis proposes that non-normal directed dynamics could transiently amplify selected salient perturbations despite stable eigenmodes. No direct ADHD evidence currently establishes the non-normal component.

OPEN QUESTION

Do these lifecycle parameters replicate within people across days? Do they improve ecological prediction beyond symptoms and ordinary behavior? Which neural precursors reliably precede a lapse? Which changes mediate acute medication effects, durable psychotherapy learning, or their combination? Does hyperfocus reflect low adaptive-release hazard, another mechanism, or several mechanisms? Are apparent developmental improvements normalization, compensation, environmental fit, or mixtures? Do directed non-normal measures add anything after rigorous controls?

249 Final answer to the central question

Is ADHD best understood as a deficit of attention? That phrase captures one visible layer: people can have persistent difficulty sustaining attention where a task requires it. But it is not the deepest available description.

A more complete account asks whether cognition can be allocated to the relevant goal, whether a task-supporting configuration can be assembled, how reliably that configuration can be stabilized, what perturbations displace it, how quickly it can be reconstructed, and whether it can be released when the goal changes. Reward, salience, catecholamines, sleep, development, learning, and environment reshape each of these operations. No single network is simply "on" while another is "off." The problem is coordinated configuration across time.

The Task-State Viability Envelope turns that account into a research program. It does not say that every person with ADHD has a narrow envelope, a shallow attractor, high neural noise, or a non-normal operator. It says that those are distinguishable hypotheses. It demands measurements of entry, dwell, perturbation response, return, and valid release. It allows multiple viable neural solutions. It makes treatment a question of which parameter changed, at which timescale, for which outcome, in which person and context.

The clinically humane answer is therefore neither "the person lacks attention" nor "the person can focus, so nothing is wrong." Capacity can be present while reliable control over its deployment is costly and unstable. Intense engagement can coexist with difficulty disengaging. Medication may change the probability landscape without teaching a life strategy. Psychotherapy may teach a strategy without erasing developmental vulnerability. Environmental design may improve function without normalizing a brain.

The scientific answer remains conditional: **ADHD is defensibly described as involving altered regulation of the allocation, stabilization, transition, recovery, and release of cognition across competing neural configurations—but the TSVE is an original, unvalidated formalization of that description.** Its value will be determined not by elegance, but by whether it predicts better, guides discriminating experiments, survives contradictions, and can be proven wrong.

250 Equation and symbol register

Object	Definition	Status
x_t	continuous latent task-relevant state	modeling choice
$\mathcal{A}_T$	acceptable outcome trajectories	task/normative definition
$v_T^\pi(x, c, t)$	conditional probability of acceptable near-future performance	proposed estimand
$\mathcal{V}_T^\pi$	superlevel set $\{x : v_T^\pi \geq q\}$	Flow Hijacked TSVE
Viab_T	states viable under at least one admissible policy	control-theoretic extension
τ_{entry}	first hitting time of the viable set after task cue	proposed lifecycle variable
λ_U	cause-specific hazard of unwanted exit	proposed lifecycle variable
τ_{return}	first return time after unwanted exit	proposed lifecycle variable
λ_A	cause-specific hazard of valid exit after switch cue	proposed lifecycle variable

Object	Definition	Status
τ_{switch}	delay from valid cue to viable state for next task	proposed lifecycle variable
$\mathcal{S}_{\text{exit}}$	cue-selectivity contrast of adaptive and unwanted exits	Flow Hijacked hypothesis
S_k	discrete latent state in HMM/HSMM	established statistical object
M_{sync}	variance of phase-synchrony order parameter	one metastability operationalization
$W_c(T_f)$	finite-horizon controllability Gramian	established control-theory object
E_{min}	minimum model input to a target point or set	model-derived, not subjective effort
$A_T(t)$	local directed tangent operator	must be estimated; not static FC
$G(t)$	maximum finite-time perturbation amplification	established linear-systems object
G_{max}	supremal transient gain	ADHD application untested
$\mathcal{R}(i\omega; A)$	resolvent operator	established systems object
$\Lambda_\varepsilon(A)$	ε-pseudospectrum	established mathematical object
ϕ_t	learned policy parameters	proposed mechanistic layer
θ_d	slow developmental parameters	proposed mechanistic layer
Ψ	intervention lifecycle fingerprint	Flow Hijacked hypothesis

A worked interpretation of the Task-State Viability Envelope

Imagine a concrete task: preparing and sending an accurate report by a fixed deadline while messages, internal thoughts, fatigue, and a second obligation compete for control. The acceptable outcome set must specify more than "worked on report." It may require a correct document, no critical omission, submission before the deadline, and a tolerable cost. The horizon includes initiation, sustained work, interruption, recovery, and final release. The perturbation law describes when notifications or internally generated events occur; the admissible policy describes controls that are realistically available, such as silencing alerts, using a checklist, taking a planned break, or receiving medication.

The TSVE is then the set of latent states from which criterion performance remains sufficiently probable under those conditions. A treatment need not move every neural variable toward a population mean. It might enlarge the viable set, shorten first-passage time into it, lower unwanted-exit hazard, reduce control energy, or accelerate re-entry. A strategy can act by changing the policy; an environmental modification can weaken the perturbation; reward can reshape the boundary; learning can alter slower parameters. These are distinct intervention fingerprints.

The Dual-Exit Principle prevents hyperfocus from being mistaken for perfect control. Remaining in the report state when the report is relevant and leaving it when the deadline has been met are different achievements. A system can resist irrelevant exits yet release poorly, or switch easily yet fail to protect the task from distraction. The model therefore predicts at least two exit hazards rather than one generic flexibility score.

This worked example remains a Flow Hijacked synthesis. The latent state is not directly observed, and fMRI connectivity is not the envelope itself. Empirical tests require operational proxies, preregistered thresholds, repeated within-person sampling, competing baseline models, and outcomes outside the laboratory. If TSVE-derived metrics fail to add reliable prediction or cannot distinguish adaptive from unwanted transitions, the framework must be revised or rejected.

Evidence anchors: influence is not reliability · 1/2

Citation counts are a dated discovery aid, not a quality score. Each claim in the lecture is still graded by design, directness, replication, recency, and contradiction.

1. **Maurizio Corbetta (2002)** — Control of goal-directed and stimulus-driven attention in the brain. DOI 10.1038/nrn755; 13,157 citations
2. **Marcus E. Raichle (2001)** — A default mode of brain function. DOI 10.1073/pnas.98.2.676; 12,505 citations
3. **B.T. Thomas Yeo (2011)** — The organization of the human cerebral cortex estimated by intrinsic functional connectivity. DOI 10.1152/jn.00338.2011; 10,055 citations
4. **Randy L. Buckner (2008)** — The Brain's Default Network. DOI 10.1196/annals.1440.011; 9,983 citations
5. **Michael Fox (2005)** — The human brain is intrinsically organized into dynamic, anticorrelated functional networks. DOI 10.1073/pnas.0504136102; 8,923 citations
6. **Jonathan D. Power (2011)** — Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. DOI 10.1016/j.neuroimage.2011.10.018; 7,963 citations
7. **William W. Seeley (2007)** — Dissociable Intrinsic Connectivity Networks for Salience Processing and Executive Control. DOI 10.1523/jneurosci.5587-06.2007; 7,645 citations
8. **Russell A. Barkley (1997)** — Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD.. DOI 10.1037/0033-2909.121.1.65; 7,355 citations
9. **Vinod Menon (2010)** — Saliency, switching, attention and control: a network model of insula function. DOI 10.1007/s00429-010-0262-0; 5,767 citations
10. **Jonathan D. Power (2011)** — Functional Network Organization of the Human Brain. DOI 10.1016/j.neuron.2011.09.006; 4,480 citations
11. **Steven E. Petersen (2012)** — The Attention System of the Human Brain: 20 Years After. DOI 10.1146/annurev-neuro-062111-150525; 3,499 citations
12. **The MTA Cooperative Group (1999)** — A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD.. DOI 10.1001/archpsyc.56.12.1073; 3,393 citations
13. **Nico U.F. Dosenbach (2007)** — Distinct brain networks for adaptive and stable task control in humans. DOI 10.1073/pnas.0704320104; 2,769 citations
14. **Ditte Demontis (2018)** — Discovery of the first genome-wide significant risk loci for attention deficit/hyperactivity disorder. DOI 10.1038/s41588-018-0269-7; 2,354 citations
15. **Philip Shaw (2007)** — Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. DOI 10.1073/pnas.0707741104; 1,855 citations
16. **Stephen V. Faraone (2021)** — The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder. DOI 10.1016/j.neubiorev.2021.01.022; 1,519 citations
17. **Samuele Cortese (2018)** — Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis.. DOI 10.1016/s2215-0366(18)30269-4; 1,401 citations

Evidence anchors: influence is not reliability · 2/2

Citation counts are a dated discovery aid, not a quality score. Each claim in the lecture is still graded by design, directness, replication, recency, and contradiction.

1. **Stephen V. Faraone (2015)** — Attention-deficit/hyperactivity disorder. DOI 10.1038/nrdp.2015.20; 1,386 citations
2. **Stephen V. Faraone (2018)** — Genetics of attention deficit hyperactivity disorder. DOI 10.1038/s41380-018-0070-0; 1,346 citations
3. **Brooke S. G. Molina (2009)** — The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study.. DOI 10.1097/chi.0b013e31819c23d0; 1,182 citations
4. **Frank P. Bymaster (2002)** — Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in attention deficit/hyperactivity disorder.. DOI 10.1016/s0893-133x(02)00346-9; 1,143 citations
5. **Samuele Cortese (2012)** — Toward Systems Neuroscience of ADHD: A Meta-Analysis of 55 fMRI Studies. DOI 10.1176/appi.ajp.2012.11101521; 1,080 citations
6. **Martine Hoogman (2017)** — Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis. DOI 10.1016/s2215-0366(17)30049-4; 912 citations
7. **Edmund Sonuga-Barke (2007)** — Spontaneous attentional fluctuations in impaired states and pathological conditions: a neurobiological hypothesis.. DOI 10.1016/j.neubiorev.2007.02.005; 900 citations
8. **Edmund Sonuga-Barke (2002)** — Psychological heterogeneity in AD/HD—a dual pathway model of behaviour and cognition. DOI 10.1016/s0166-4328(01)00432-6; 900 citations
9. **Nora D. Volkow (1998)** — Dopamine transporter occupancies in the human brain induced by therapeutic doses of oral methylphenidate.. DOI 10.1176/ajp.155.10.1325; 893 citations
10. **Timothy E. Wilens (2003)** — Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature.. DOI 10.1542/peds.111.1.179; 875 citations
11. **F. Xavier Castellanos (2008)** — Cingulate-precuneus interactions: a new locus of dysfunction in adult attention-deficit/hyperactivity disorder.. DOI 10.1016/j.biopsych.2007.06.025; 871 citations
12. **Ditte Demontis (2023)** — Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains. DOI 10.1038/s41588-022-01285-8; 804 citations
13. **Nora D. Volkow (2001)** — Therapeutic doses of oral methylphenidate significantly increase extracellular dopamine in the human brain.. DOI 10.1523/jneurosci.21-02-j0001.2001; 769 citations
14. **Min Wang (2007)** — Alpha2A-adrenoceptors strengthen working memory networks by inhibiting cAMP-HCN channel signaling in prefrontal cortex.. DOI 10.1016/j.cell.2007.03.015; 683 citations
15. **Paul Lichtenstein (2012)** — Medication for attention deficit-hyperactivity disorder and criminality.. DOI 10.1056/nejmoa1203241; 621 citations
16. **James M. Shine (2019)** — Human cognition involves the dynamic integration of neural activity and neuromodulatory systems. DOI 10.1038/s41593-018-0312-0; 593 citations
17. **MTA Cooperative Group (2004)** — National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder.. DOI 10.1542/peds.113.4.754; 593 citations

How these anchors are used. Influence and reliability occupy different axes. Citation count accumulates with age, field size, accessibility, controversy, and repeated use as a conventional reference. It can identify the papers that shaped scientific language, but it does not reveal whether an effect is large, a design is unbiased, or a result has survived modern preprocessing and replication. A highly cited theory may remain historically indispensable after some of its empirical predictions have been qualified.

The lecture therefore assigns each anchor at least four companions: the strongest direct test, a recent synthesis, a serious contradiction or limitation, and—where relevant—a developmental or treatment-specific update. Foundational network papers define objects such as the default, control, attention, and salience systems; they do not by themselves establish an ADHD abnormality. Landmark treatment trials establish contrasts under their own protocols and follow-up windows; they do not automatically answer lifetime causality or neural mediation.

Recent frontier papers face the opposite problem. They may use stronger samples, dynamic methods, or randomized pharmacological designs while having little time to accumulate citations. They are retained when they alter a live inference, but labeled for citation lag and read alongside preregistration, sample size, multiplicity, motion control, and independent replication. This two-axis policy prevents prestige from substituting for design and prevents recency from substituting for confirmation.

In the spoken lecture, an anchor earns emphasis only when it clarifies the claim currently being made. The audience should be able to hear whether a paper is historical, directly evidential, synthesizing, contradictory, or hypothesis-generating. That explicit role is more informative than a long name-drop and makes later scientific correction possible without dismantling the entire narrative.

The operational consequence is a claim ledger rather than a prestige ladder. Each consequential sentence is linked to the best available source, the reason that source is fit for purpose, the main uncertainty, and the evidence that would change the wording. Citation counts remain visible because intellectual history matters, but they never determine the confidence label. A low-citation randomized study may carry more causal weight for a narrow treatment question than a famous review; a highly cited atlas may define a network while saying nothing about diagnosis. Keeping both facts visible is the point of the anchor pages.

A practical checkpoint asks whether removing the famous citation would change the claim's evidential strength. If it would, the claim needs a direct source or narrower wording. If it would not, the classic paper can remain as history while the inferential burden is carried by the better-matched evidence.

MATHEMATICAL APPENDIX 1/7 · Notation and dimensional discipline

Notation and dimensional discipline

Every symbol is indexed by task T, person i, and time t whenever invariance cannot be defended. The fast state is $x_t \in \mathbb{R}^n$; observable context is c_t; control is u_t; perturbation is p_t; slow developmental and learned parameters are θ_d and ϕ_t. A model is dimensionally valid only when both sides of every equation share units. Control energy is a mathematical functional, not literal metabolic expenditure.

Interpretation and estimation. The indexing rule prevents an easy but consequential category error. A parameter estimated during one laboratory condition should not silently become a property of the person across all tasks. For example, an entry cost inferred during a delayed, low-reward task may change under immediate feedback, sleep loss, medication, or external cueing. The units also force measurement choices into the open: a behavioral latency is measured in time, a probability is dimensionless, a questionnaire score is ordinal unless stronger assumptions are defended, and a BOLD-derived coordinate is not itself a neurotransmitter concentration. In an empirical implementation, each coordinate of x_t should therefore be accompanied by its measurement scale, temporal resolution, uncertainty model, and expected invariances. Nondimensionalization may be useful for numerical work, but the scale factors must be retained so that a change in model energy is not narrated as a known change in subjective effort or cerebral metabolism. The mathematics earns explanatory value only when the map from symbols to observations remains explicit.

Worked implication. A practical scaling step begins by selecting characteristic magnitudes t_0, x_0, u_0, and p_0, then defining $\tilde{t} = t/t_0$, $\tilde{x} = S_x^{-1}x$, $\tilde{u} = u/u_0$, and $\tilde{p} = p/p_0$. Dimensionless groups reveal which effects can actually be compared across tasks. If a modeled recovery constant is κ with units s^{-1}, then κt_0—not κ alone—governs recovery relative to the task timescale. Scaling choices should be learned on training data and frozen before validation. Otherwise normalization can leak group information, exaggerate separation, or make a person-specific deviation appear like a universal ADHD coordinate.

Formal checks and failure cases. An audit begins with a symbol table containing domain, units, sampling interval, transformation, and the level at which variation is allowed. If x_{iTt} is standardized separately within every task, between-task differences have been removed by construction; if it is standardized globally, site and age composition may dominate. Scale parameters must therefore be learned inside each training fold. Dimensionless coordinates do not remove interpretation: the inverse map must be retained. A second audit checks reparameterization. If multiplying one latent coordinate by a and dividing its loading by a leaves the observation law unchanged, the coordinate scale is unidentified without a constraint. Likewise, a "control-energy" difference can result from B_T, the state metric, the target set, or the time horizon. Reporting only the scalar minimum conceals those dependencies. Sensitivity analyses should vary plausible scales and metrics, then ask whether rankings, treatment contrasts, and failure predictions survive. If they do not, the result belongs to the chosen representation rather than to a stable property of cognitive regulation.

A compact dimensional check is to write $[x_j] = X_j$, $[t] = T$, and demand $[f_j] = X_j T^{-1}$, $[B_{jk}u_k] = X_j T^{-1}$, and $[E_{j\ell}p_\ell] = X_j T^{-1}$. For stochastic terms, $[dW_t] = T^{1/2}$, so $[\Sigma_{jk}] = X_j T^{-1/2}$. Violating this rule can be hidden by standardized data yet reappear when sampling intervals or tasks change. Unit-consistent code should be tested by rescaling seconds to milliseconds and verifying that physical predictions remain invariant after parameter conversion.

Index discipline supplies a parallel test. Dropping i, T, or session s asserts exchangeability at that level. The assertion should be defended by invariance checks or represented hierarchically, for example $\theta_{iT} = \mu + \alpha_i + \beta_T + \gamma_{iT}$. A compact symbol is not permission to pool incompatible contexts. The index set is part of the model and should be included in every estimand definition.

SUPPORTED INTERPRETATION

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

MATHEMATICAL APPENDIX 2/7 · State and observation models

State and observation models

The provisional controlled process is

$$dx_t = f_T(x_t, c_t, \theta_d, m_t, a_t, r_t, h_t)dt + B_T u_t dt + E_T p_t dt + \Sigma_T dW_t.$$

Measurements satisfy $o_t = H(x_t, c_t) + \nu_t$. Neither x_t nor H is identified by an fMRI parcellation alone. State sufficiency, sampling adequacy, vascular invariance, task validity, and measurement error are explicit assumptions.

Interpretation and estimation. The state equation separates four roles that ordinary verbal explanations often mix. The drift f_T describes how the system would evolve under its present task and context; $B_T u_t$ represents modeled control inputs; $E_T p_t$ represents perturbations; and $\Sigma_T dW_t$ represents stochastic variation at the chosen scale. This partition is provisional, because the same event may be controllable at one level and exogenous at another. A phone notification can be an external perturbation, while leaving the phone visible is a slower policy choice. The observation map H is equally important: reaction time, gaze, EEG, fMRI, and experience sampling reveal different projections of the latent process and operate at different sampling rates. A defensible study would fit several observation models, test whether conclusions survive plausible hemodynamic and measurement assumptions, and validate latent coordinates against behavior not used to construct them. Without that discipline, a visually compelling trajectory may describe the analyst's embedding more than the participant's cognitive dynamics.

Worked implication. With observations at discrete and possibly unequal times, one may write $x_{k+1} = F_k(x_k, u_k, p_k) + w_k$ and $o_k = H_k(x_k) + \nu_k$. Linear-Gaussian assumptions permit Kalman filtering; nonlinear or multimodal observations may require extended filters, particle methods, or variational inference. Each method returns uncertainty as well as a trajectory, and that uncertainty should propagate into dwell and transition estimates. Missingness is rarely ignorable in demanding tasks: gaze loss, movement, skipped probes, and session dropout can all depend on the latent state. Jointly modeling the missingness mechanism is therefore preferable to deleting the most unstable epochs.

Formal checks and failure cases. Observability is not guaranteed by collecting many channels. For a linear approximation, the finite-horizon observability Gramian $W_o = \int_0^T \Phi(t,0)^\top C(t)^\top C(t)\Phi(t,0)\,dt$ reveals directions that produce distinguishable observations; small singular values mark combinations that data cannot resolve. Nonlinear models require local rank checks, simulation-based recovery, or information measures, but the principle is unchanged. Sampling rates must also be reconciled: millisecond electrophysiology, second-scale hemodynamics, intermittent thought probes, and daily functioning cannot be concatenated as synchronous features. Their delays and integration kernels belong in H. Missingness is potentially state dependent, because movement, gaze loss, skipped probes, or dropout may occur during the very instability being modeled. A joint missingness model, explicit censoring analysis, and negative controls are preferable to deletion. Finally, latent coordinates are defined only up to transformations permitted by the likelihood. Claims should attach to invariant predictions—future error, recovery, or response to perturbation—rather than to a visually appealing axis orientation.

Observability and controllability should not be conflated. A direction can be strongly affected by an input yet poorly visible in the chosen sensors, or well observed but difficult to move with the modeled control. Their Gramians answer dual-looking but distinct questions. Sensor placement, task design, and perturbation design should therefore be optimized together. A proposed treatment mechanism is especially weak when the mediating direction is both weakly observable and identified only through the same outcome it is meant to explain.

SUPPORTED INTERPRETATION

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

MATHEMATICAL APPENDIX 3/7 · Viability and reach-stay probability

Viability and reach-stay probability

For acceptable outcome set $\mathcal{A}_T$ and horizon Δ, define

$$V_T^{\pi}(x, c) = \Pr^{\pi}\{Y_T(t : t + \Delta) \in \mathcal{A}_T \mid x_t = x, c_t = c\}.$$

The Task-State Viability Envelope at reliability q is $\mathcal{V}_T^{\pi}(c; q) = \{x : V_T^{\pi}(x, c) \geq q\}$. The viability kernel additionally requires an admissible policy that can retain the trajectory within constraints. Empirical estimation must specify task, horizon, threshold, perturbation law, and control budget.

Interpretation and estimation. Viability differs from momentary success. A state belongs to the envelope only if it supports an acceptable trajectory over the declared horizon with at least probability q under the declared policy and perturbation distribution. Increasing q or lengthening Δ generally makes the envelope smaller; adding useful external cues or a more effective policy may enlarge it. This gives treatment claims a sharper form. A stimulant might change local stability or perturbation sensitivity, a planning routine might change the admissible policy set, and a quieter work environment might change the perturbation law. These routes can produce the same observed completion rate while making different predictions under challenge. Estimation could use repeated tasks with experimentally varied delay, reward, interruption, and cue support, followed by hierarchical survival or state-space modeling. Cross-validation must occur across sessions or contexts, not merely across adjacent time points. The envelope should also be outcome-specific: remaining seated is not equivalent to learning, accurate completion, or adaptive disengagement when the task no longer serves the goal.

Worked implication. In a discretized state space, reach-stay probability can be computed by backward recursion. For terminal value $V_K(x) = \mathbf{1}\{x \in \mathcal{A}_T\}$, a finite-horizon policy satisfies $V_k^{\pi}(x) = \int V_{k+1}^{\pi}(x')P(dx' \mid x, \pi(x), c_k)$. Optimization replaces the fixed action with a supremum over admissible controls. This distinction separates performance under the person's current policy from performance under a hypothetical best policy. Clinically, the gap may represent learnable strategy, unavailable support, or a model misspecification; it cannot be interpreted as unused willpower. Robust envelopes should also be recomputed under shifted perturbation laws rather than trusted only in the training environment.

Formal checks and failure cases. The envelope depends monotonically on some commitments but not all. Raising reliability threshold q or lengthening the required horizon generally shrinks a fixed-policy reach-stay set; enlarging the admissible control set cannot shrink the corresponding viability kernel. Changing the acceptable outcome set, disturbance law, or policy class can reverse apparent group rankings. These properties are diagnostic checks for code and interpretation. Estimation from finite trials also creates boundary uncertainty: a state with estimated success probability 0.81 is not securely inside a $q = 0.80$ envelope if its interval spans the threshold. Bootstrap, posterior, or conformal uncertainty should therefore accompany the boundary, and performance should be assessed on new perturbation schedules. Robust analysis replaces one fitted disturbance distribution with an uncertainty set and asks which states remain viable in the least favorable admissible case. That may be clinically more meaningful than an optimistic average. Yet robustness has a price: an overbroad uncertainty set can make every policy fail. The set must be justified by observed environments, and its coverage audited prospectively.

For continuous state spaces, the boundary may be characterized through dynamic programming or a Hamilton–Jacobi reachability equation; for discretized models, backward recursion approximates the same logic. Numerical resolution matters. A coarse grid can merge a narrow viable corridor with a failing region, while an adaptive grid can overfit sampled trajectories. Convergence should be shown across mesh size, horizon step, and interpolation rule. The empirical object is never "the" envelope without these declared choices; it is an estimated envelope indexed by task, outcome, policy, disturbance class, horizon, reliability, and numerical scheme.

SUPPORTED INTERPRETATION

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

MATHEMATICAL APPENDIX 4/7 · Dwell, exit and competing risks

Dwell, exit and competing risks

Entry and exit are stopping times. Let $\tau_{\text{in}} = \inf\{t : x_t \in \mathcal{V}_T\}$ and $\tau_{\text{out}} = \inf\{t > \tau_{\text{in}} : x_t \notin \mathcal{V}_T\}$. For a fixed covariate/history path and no additional exit causes, with cause-specific hazards λ_U for unwanted departure and λ_A for adaptive release,

$$S(t) = \exp\left[-\int_0^t (\lambda_U(s) + \lambda_A(s))ds\right].$$

Low unwanted-exit hazard and high valid-release hazard are distinct achievements: the Dual-Exit Principle.

Interpretation and estimation. Competing-risk notation prevents persistence from being treated as an unconditional good. The cumulative incidence of unwanted exit is not $1 - S(t)$ when adaptive completion or justified stopping can occur first; each exit type must be observed or modeled separately. Censoring also requires care. The end of a scanner block may truncate a successful dwell interval, while an experimenter's instruction to stop is neither a lapse nor a self-initiated release. Time-varying covariates can include fatigue, error history, reward proximity, arousal, and interruption exposure, but coefficients should not be read causally unless the design supports that interpretation. A useful experiment would distinguish first entry, stable engagement, micro-lapses, recovery, completion, and abandonment, then test whether medication or behavioral scaffolding shifts the cause-specific hazards differently. The model predicts that two interventions may yield the same average time on task while one reduces unwanted exits and the other merely delays valid completion. This is why dwell time alone cannot define healthy control.

Worked implication. For cause $k \in \{U, A\}$, the cumulative incidence is $F_k(t) = \int_0^t S(s)\lambda_k(s)\,ds$. Because the two incidences share S, changing one hazard alters the observed probability of the other even without changing its cause-specific mechanism. Recurrent-task data further require frailty or random effects so stable person-level differences do not masquerade as duration dependence. Calendar time, time since entry, and progress toward completion may each define a different clock. Selecting the clock after seeing the effect risks turning task structure into a convenient narrative; it should be specified from the cognitive theory and tested against alternatives.

Formal checks and failure cases. Cause-specific hazards answer what instantaneously produces each exit among trajectories still at risk; cumulative incidence answers how often each exit is observed in the presence of competitors. Neither should be replaced casually by a single "persistence" score. Adaptive completion, an externally required switch, an impulsive departure, and abandonment after accumulating errors can end the same interval while carrying opposite meanings. Coding rules should be preregistered and, where possible, validated by cues, performance, self-report, and subsequent behavior. Recurrent intervals violate independence, so person-level frailty, task random effects, and time-varying covariates may be needed. Informative censoring occurs when a block ends, a participant moves excessively, or medication wears off in a way related to latent risk. Inverse-probability or joint models help only under stated assumptions. Proportional-hazard assumptions should be checked; stabilization may lower unwanted-exit hazard early while fatigue raises it later. A flexible baseline or discrete-time model can reveal that shape. Treatment interpretation then compares the whole cause-specific profile rather than declaring longer dwell universally beneficial.

A multi-state formulation can represent task entry, stable dwell, micro-lapse, recovered dwell, adaptive completion, and abandonment directly. The generator matrix then contains only transitions permitted by the theory, while transition intensities can depend on reward, fatigue, interruption, and treatment. This makes impossible paths explicit and exposes whether an apparent treatment benefit operates by preventing lapses, accelerating recovery, or increasing valid completion. The extra resolution is justified only when states can be measured reliably and the enlarged model improves held-out prediction.

SUPPORTED INTERPRETATION

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

MATHEMATICAL APPENDIX 5/7 · Semi-Markov state inference

Semi-Markov state inference

A hidden semi-Markov model separates segment-to-segment transition probabilities from dwell distributions:

$$\Pr(z_{\ell+1} = j \mid z_\ell = i) = P_{ij}\ (j \neq i), \qquad D_\ell \mid z_\ell = i \sim F_i(\cdot; \eta_i).$$

The model must distinguish latent dynamics from classifier instability. State labels require cross-session alignment, posterior uncertainty, measurement-invariance tests, and out-of-sample behavioral prediction. A state cluster is not automatically an attractor.

Interpretation and estimation. The semi-Markov extension matters because ordinary Markov models imply that exit probability depends only on the present state, not on how long the system has occupied it. Cognitive states often violate that memoryless assumption: early stabilization may reduce near-term exit risk, whereas fatigue may increase risk after prolonged dwell. Choosing F_i therefore encodes a substantive hypothesis, not a technical afterthought. Duration distributions, transition matrices, and emissions should be estimated hierarchically so person-level differences are not confused with noisy state assignment. The number of states should be selected using held-out likelihood, predictive utility, stability across initializations, and interpretability constraints rather than a single information criterion. Sensitivity analyses should vary parcellation, preprocessing, motion thresholds, temporal resolution, and state count. Most importantly, the latent sequence must predict something outside the fitted signal, such as imminent error, self-reported mind wandering, successful re-entry, or real-world task completion. Otherwise the inferred states remain a compact description rather than a demonstrated cognitive mechanism.

Worked implication. For an observed segment sequence, a semi-Markov likelihood sums over unknown states and durations: $p(o_{1:K}) = \sum_{z,D} \prod_\ell P_{z_\ell z_{\ell+1}} f_{z_\ell}(D_\ell) \prod_{k \in \ell} p(o_k \mid z_\ell)$. Forward-backward recursions make the sum tractable under finite-duration assumptions. Posterior state probabilities should be used instead of treating the maximum-probability label as certain. Covariate-dependent $P_{ij}(c)$ can test whether reward, interruption, medication, or fatigue changes a specific transition, while duration regression tests whether the same variables change dwell once the state has been entered. Those are different mechanistic claims.

Formal checks and failure cases. An HSMM is useful only when duration adds information beyond a conventional hidden Markov model. Candidate dwell families—geometric, negative binomial, log-normal, or nonparametric—encode different tails and should be compared on held-out sequences. State-number selection must combine predictive likelihood, stability across initializations, posterior occupancy, and external validity; an information criterion alone often rewards partitions that have no reproducible cognitive meaning. Label switching requires alignment across people and sessions, but forced alignment can erase genuine individual solutions. Hierarchical emissions and partially shared transition structures offer a compromise. Posterior state probabilities should propagate into transition and dwell estimates instead of hard-decoding one path. Online prediction supplies a strong test: using observations only through time t, can the model improve forecasts of an error, report of mind wandering, or failed re-entry in the next interval? Retrospective segmentation is easier and can exploit information from the future. A mechanistic interpretation requires the harder prospective result and sensitivity to preprocessing, parcellation, motion thresholds, and temporal resolution.

Duration dependence can be inspected through the state-specific hazard $h_i(d) = f_i(d)/S_i(d)$. A declining early hazard represents stabilization with continued residence; a rising late hazard can represent fatigue; a nonmonotone hazard can encode both. Those shapes should be inferred with uncertainty rather than read from a fitted family name. Posterior predictive plots should compare observed and replicated run lengths, transition counts, error timing, and missing-data bursts. If the model reproduces average occupancy while missing these temporal features, it has not captured the dynamics the lecture seeks to explain.

SUPPORTED INTERPRETATION

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

MATHEMATICAL APPENDIX 6/7 · Linearization, non-normality and resolvent gain

Linearization, non-normality and resolvent gain

Linearizing near a task-supporting trajectory gives $\delta\dot{x} = A(t)\delta x + B(t)\delta u + E(t)\delta p$. Even when every eigenvalue of constant A has negative real part, a non-normal operator can yield

$$G_{\max} = \sup_{t\geq 0} \|e^{At}\|_2 > 1, \qquad \mathcal{R}(i\omega) = (i\omega I - A)^{-1}.$$

Large transient or resolvent gain is mathematically possible without asymptotic instability. Its ADHD application is a new hypothesis; no acquired ADHD study directly estimated these operators.

Interpretation and estimation. Non-normality concerns the geometry of interacting modes, not simply whether an eigenvalue is positive. When eigenvectors are non-orthogonal, decaying modes can align temporarily and produce large amplification before eventual decay. The resolvent asks how strongly a system responds to sustained or frequency-specific forcing; pseudospectra ask how much the apparent stability could change under small operator perturbations. These tools could, in principle, formalize a system that looks stable in average measures yet is strongly displaced by particular salient inputs. That possibility is not currently an ADHD result. A direct test would require estimating a time-resolved effective operator from sufficiently sampled, perturbation-rich data, quantifying uncertainty, and comparing transient gain with matched normal or low-dimensional alternatives. It would then need to predict attentional capture, lapse probability, or recovery beyond simpler features such as variance, arousal, and baseline performance. Until those steps are completed, non-normal amplification belongs in the Flow Hijacked hypothesis layer: mathematically coherent, experimentally generative, and explicitly unverified.

Worked implication. A two-dimensional example makes transient growth concrete. Let $A = \left(\begin{smallmatrix} -1 & K \\ 0 & -2 \end{smallmatrix}\right)$. Its eigenvalues are -1 and -2 for every K, yet $e^{At} = \left(\begin{smallmatrix} e^{-t} & K(e^{-t}-e^{-2t}) \\ 0 & e^{-2t} \end{smallmatrix}\right)$. As K grows, a perturbation initially placed in the second coordinate can generate a large first-coordinate excursion before both coordinates decay. Eigenvalues alone therefore miss finite-time sensitivity. An ADHD test would need an estimated operator, controlled perturbations, and uncertainty on $G_{\max}$; merely observing variable behavior or salience capture does not identify K, non-normality, or any specific neural mode.

Formal checks and failure cases. Non-normality should be measured, not inferred from volatility. For constant A, candidates include the numerical abscissa $\omega(A) = \lambda_{\max}[(A + A^*)/2]$, eigenvector condition number, Henrici departure, transient gain $\|e^{At}\|_2$, and resolvent norm $\|(i\omega I - A)^{-1}\|_2$. They answer different questions and can disagree. Pseudospectra add perturbation sensitivity but depend on norm and scaling, so nondimensionalization is essential. In a time-varying system the propagator $\Phi(t, s)$ replaces $e^{A(t-s)}$; fitting one stationary matrix may manufacture transient gain from unmodeled switching. Measurement filtering can also create apparent directionality. A credible ADHD experiment would perturb a specified sensory, reward, or control channel, estimate the operator with uncertainty, and predict the amplitude and time course of displacement on held-out perturbations. It would compare matched normal, diagonalizable, and nonlinear alternatives. Group differences in reaction-time variance, salience capture, or static effective connectivity are not sufficient. The hypothesis survives only if operator-based gain adds reliable prediction and changes coherently under intervention.

The optimizing perturbation is given by the leading right singular vector of the propagator at the chosen horizon; the amplified response follows the corresponding left singular vector. This is not generally an eigenmode. Resolvent singular vectors play an analogous input–response role for sustained forcing at frequency ω. A strong experiment would compare these predicted directions with measured responses rather than merely reporting a scalar norm. Confidence intervals must incorporate operator-estimation error, because non-normal metrics can be highly sensitive to small coefficient perturbations—the very property they are intended to quantify.

FLOW HIJACKED HYPOTHESIS

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

MATHEMATICAL APPENDIX 7/7 · Identifiability, estimation and falsification

Identifiability, estimation and falsification

Structural identifiability asks whether distinct parameters can generate the same observation law; practical identifiability asks whether finite noisy data can separate them. Candidate models must be preregistered, compared out of sample, and tested against simpler baselines. TSVE fails if it adds no reliable ecological prediction, cannot distinguish unwanted from adaptive exit, or yields intervention fingerprints that are neither replicable nor treatment-specific.

Interpretation and estimation. Identifiability is the gate between an evocative model and an estimable one. If an increase in perturbation amplitude, a reduction in control effectiveness, and a noisier observation map all produce the same distribution of behavior, the data cannot decide among those narratives without additional manipulations or measurements. Parameter-recovery studies should therefore precede substantive interpretation. Synthetic data generated across realistic sampling rates, missingness, motion, and task lengths can reveal whether entry cost, dwell stability, switching hazard, and observation noise are separable. Prospective falsification also requires predeclared alternatives: a static symptom model, a simple reaction-time-variability model, and a conventional hidden-state model may predict just as well. Evidence for TSVE would require reliable added prediction, intervention-sensitive parameters with plausible specificity, and generalization from laboratory trajectories to meaningful function. Failure is informative: if the model collapses across tasks, cannot distinguish treatment routes, or depends on arbitrary thresholds, its conceptual vocabulary should not be mistaken for an established latent structure.

Worked implication. A hierarchical implementation might posit person parameters $\psi_i \sim \mathcal{N}(Z_i\beta, \Omega)$ and estimate $p(\psi_{1:N}, \beta, \Omega \mid o)$, but a narrow posterior is not proof of truth. Simulation-based calibration tests whether the inference procedure recovers known generative values; posterior predictive checks test whether it reproduces lapse timing, transition counts, and context effects not explicitly fit. Model comparison should be nested within a locked validation design. For intervention claims, randomization can identify a treatment effect on an estimable parameter, while mediation requires additional assumptions about post-randomization confounding. A parameter with a mechanistic name does not inherit causal status from its label.

Formal checks and failure cases. Identifiability should be tested before parameters are given psychological names. Structural analysis asks whether an infinite noiseless observation record would distinguish parameter values; practical analysis asks whether the actual sample can do so. Profile likelihoods, posterior correlations, Fisher-information spectra, and simulation-based recovery expose different failures. Priors can regularize a weak direction but cannot create information; a narrow posterior driven by the prior should be reported as such. Model comparison must be nested inside the validation scheme so that state count, preprocessing, thresholds, and hyperparameters are not selected using the test set. Calibration asks whether predictive intervals contain outcomes at their advertised rates, while discrimination asks whether people or moments are ranked correctly. Clinical utility adds another layer: does the model improve a decision relative to symptoms, history, and simple behavioral variability? Prespecified falsifiers include unstable person parameters, no cross-context generalization, no incremental prediction, or indistinguishable intervention fingerprints. Meeting a goodness-of-fit threshold is not enough; the model must survive recovery, calibration, competition, and consequential use.

Parameter recovery should span the regimes expected in real data, including short sessions, unequal sampling, head-motion censoring, weak treatment effects, and correlated disturbances. Recovery at one convenient synthetic setting is not enough. The confusion matrix between generative mechanisms is especially useful: can low control effectiveness be distinguished from high perturbation variance, or long dwell from a sticky classifier? If two mechanisms remain observationally equivalent, the lecture must not assign them separate causal stories until a new manipulation or sensor breaks the equivalence.

SUPPORTED INTERPRETATION

Definitions are modeling commitments; every empirical use must report operationalization and failure conditions.

Network neuroscience reference matrix · 1/4

System/treatment	Finding or target	Evidence	State/context	Boundary
DMN	Adaptive internal cognition; mixed within-network findings	Rest + task	Small/heterogeneous	Do not equate attention with maximal suppression
FPN	Altered recruitment/coupling in some tasks	Task	Moderate	Control representation and stability are separable
DAN	Small activation/connectivity differences; nulls matter	Task + rest	Mixed	Not a unitary task-positive system
VAN/SN	Altered reorienting/arbitration reported	Switching + distraction	Moderate	No replicated master-switch lesion
CON	Sustained-set/error-monitoring differences	Task	Emerging	Definitions overlap across atlases
Striatum	Reward anticipation and corticostriatal differences	Reward tasks	Moderate	Value and action loops are heterogeneous
Thalamus/cerebellum	Distributed timing/gating findings	Rest + task	Emerging	Direction depends on age and method

The matrix is a navigation layer; the qualified claims and sources remain in the body and companion evidence system.

Pharmacology: distinct mechanisms and evidence · 2/4

System/treatment	Finding or target	Evidence	State/context	Boundary
Methylphenidate	DAT/NET blockade	Strong short-term symptom evidence	Acute imaging ≠ durable normalization	Appetite, sleep, BP/pulse, rare psychiatric risk
Amphetamines	Transporter substrate/release mechanisms	Strong short-term evidence; larger adult estimate	Not methylphenidate at higher strength	Misuse/diversion; psychosis risk higher than MPH in one cohort
Atomoxetine	NET inhibition; cortical DA indirectly	Moderate	Slower onset; network evidence limited	GI, sleep, BP/pulse, mood monitoring
Guanfacine ER	alpha-2A agonism	Moderate pediatric evidence	Sedating/arousal pathway; sparse dynamics	Somnolence, hypotension; taper
Clonidine	broader alpha-2 agonism	More limited	No unique network signature established	Sedation, hypotension; taper
Viloxazine ER	multimodal noradrenergic action	Growing trial evidence	Long-term/network evidence immature	Somnolence, appetite/GI, suicidality warning
Bupropion/modafinil	off-label / regulatory boundaries	Limited or context-specific	Do not generalize cognitive enhancement	Drug-specific contraindications and risks

The matrix is a navigation layer; the qualified claims and sources remain in the body and companion evidence system.

Psychotherapy and behavioral treatment matrix · 3/4

System/treatment	Finding or target	Evidence	State/context	Boundary
Adult ADHD-CBT	Organization, planning, beliefs, recovery	Moderate symptoms/function	Often adjunctive	Direct neural mechanism not established
Behavioral parent training	Antecedents and contingencies	Strong parenting/function; rater gradient	May combine	Changes environment; no network-normalization claim
Organizational skills	External systems and routines	Moderate functional evidence	Sometimes adjunctive	Far transfer varies
Mindfulness	Meta-awareness and response policy	Small/heterogeneous	Mixed	Imaging corpus small
Coaching	Accountability and task structure	Preliminary	Common in practice	Controlled evidence immature
Digital/cognitive training	Practice or cue delivery	Near transfer > far transfer	Variable	Blinding and engagement confounds
Neurofeedback	Self-regulation of selected signal	Probably-blinded effects weak/null	Variable	Target engagement and specificity problems

The matrix is a navigation layer; the qualified claims and sources remain in the body and companion evidence system.

Treatment by network: what is direct and what is inferred · 4/4

System/treatment	Finding or target	Evidence	State/context	Boundary
Stimulant · DMN	Some acute task modulation/coupling changes	Direct but heterogeneous	No global normalization	
Stimulant · FPN/DAN	Activation/connectivity changes in some paradigms	Direct	Nulls and age effects preserved	
Stimulant · striatum	Reward/response effects	Direct	Target engagement not mediation	
Nonstimulants	Sparse network-specific corpus	Limited	Mechanism cannot substitute for imaging	
CBT	Task-entry/recovery policy	Flow Hijacked inference	Clinical benefit without direct neural proof	
Parent/school	Boundary conditions and perturbation load	Systems inference	Not an internal-brain repair claim	
Combined care	Possible wider learning corridor	Plausible hypothesis	Neural synergy unproven	

The matrix is a navigation layer; the qualified claims and sources remain in the body and companion evidence system.

Bilingual scientific termbase · 1/3

English	עברית
Default Mode Network (DMN)	רשת ברירת המחדל
Frontoparietal Control Network (FPN)	רשת הבקרה הקודקודית-המצחית
Dorsal / Ventral Attention Network	רשת הקשב הגבית / הגחונית
Salience Network (SN)	רשת הבולטות
cingulo-opercular network (CON)	רשת הצינגולו-אופרקולרית
functional / effective connectivity	קישוריות תפקודית / אפקטיבית
network segregation / integration	היפרדות / אינטגרציה בין רשתות
state occupancy	מצב תפוסת
dwell time	זמן שהייה
metastability	מטא-יציבות
working memory	זיכרון עבודה
task initiation / persistence	התחלת משימה / התמדה במשימה
delay discounting / delay aversion	תלוי-דיחוי היוון / רתיעה מדיחוי

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Bilingual scientific termbase · 2/3

English	עברית
mind wandering	מחשבות נדידת
hyperfocus	יתר מיקוד
emotional dysregulation	רגשי בוויסות קשיים
heritability / polygenic risk	פוליגני סיכון / תורשתיות
dopamine / norepinephrine	נוראדרנלין / דופמין
DAT / NET	הנוראדרנלין נשא / הדופמין נשא
gain control / inverted U	הפוכה U יחס / הגבר בקרת
Task-State Viability Envelope (TSVE)	המשימה מצב של הקיימות מעטפת
viability kernel	הקיימות גרעין
state space / trajectory	מצב מסלול / המצבים מרחב
entry latency / first-passage time	ראשון מעבר זמן / כניסה חביון
unwanted departure / adaptive release	מסתגל שחרור / רצויה בלתי יציאה
Dual-Exit Principle	היציאות שתי עקרון

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Bilingual scientific termbase · 3/3

English	עברית
survival function / hazard rate	רגעי סיכון קצב / הישרדות פונקציית
control energy / reachable set	השגה בת קבוצה / בקרה אנרגיית
Hidden semi-Markov Model (HSMM)	חבוי חצי-מרקובי מודל
non-normal operator	נורמלי לא אופרטור
transient amplification	חולפת הגברה
resolvent / pseudospectrum	פסאודו-ספקטרום / רזולבנט
identifiability / falsifier	אפשרי מפריך ממצא / זיהוי יכולת
intervention fingerprint	התערבות חתימת
empirical result	אמפירי ממצא
authors' interpretation	המחברים פרשנות
Flow Hijacked synthesis	של סינתזה Flow Hijacked
new hypothesis / open question	פתוחה שאלה / חדשה השערה

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Figure methods, source policy and accessibility

All diagrams in this lecture are original explanatory reconstructions. They do not reproduce copyrighted scientific figures and they do not present simulated curves as measured ADHD data. Network nodes are conceptual labels; line placement does not encode anatomical distance or a quantified edge unless the caption explicitly says so.

The evidence substrate contains 531 deduplicated peer-reviewed records. The 281 references printed here comprise the 266-paper impact-and-notability-gated core plus 15 explicitly labeled records outside that core: 13 citation-lag frontier papers and two direct-citation-integrity exceptions. The companion workbook retains the complete acquisition metadata, contradiction ledger, and treatment matrices. Citation counts are an OpenAlex snapshot dated 8 September 2026 where available and are used only to identify influence.

Color never carries evidence status alone. Every box is labeled in words. Reading order, extractable text, embedded fonts, table headers, mathematical direction, and contrast are checked in both editions. The Hebrew book mirrors layout hierarchy but never mirrors equations, time axes, matrices, chemical notation, or brain laterality.

The diagrams and equations are educational abstractions. Nothing in a state-space figure identifies an individual person’s brain state, prognosis, diagnosis, or treatment response.

The production audit distinguishes textual fullness from decorative occupancy. Ordinary explanatory pages are allowed to break naturally and are inspected for orphaned headings, short end-of-part remnants, clipped boxes, and unexplained blank regions. Full-page part dividers remain intentionally sparse because they perform navigation, while matrices retain their compact geometry to protect row alignment. Mathematical pages are evaluated both for visual balance and for dimensional, inferential, and falsification discipline; additional notation is included only when its empirical mapping can be stated.

Every scientific statement is routed through a claim role. Primary empirical results retain population, design, comparator, measurement, and time scale. Authors’ interpretations are not silently promoted to findings. Cross-study synthesis records heterogeneity and serious null results. Flow Hijacked interpretations are marked as supported, plausible, hypothetical, or open. The original Task-State Viability Envelope and non-normality proposal therefore remain separable from established ADHD neuroscience and can be revised without changing the underlying evidence record.

The bilingual audit is semantic rather than mechanical. English and Hebrew preserve the same claims, equations, uncertainty, safety boundaries, and source roles while permitting native syntax and different line lengths. Bidirectional text is tested around acronyms, receptor labels, DOI and PMID strings, equations, punctuation, and numbered lists. Page-for-page identity is not required; evidential identity is. If one language requires more words to preserve a qualification, pagination yields to the qualification.

The update protocol is date-bounded. New studies enter first as frontier evidence, are checked against the deduplicated corpus, and are promoted only after their design and relevance are assessed. Citation corrections, retractions, guideline changes, and failed replications trigger claim-level review rather than automatic addition. Figures are regenerated from the revised conceptual specification, and both PDFs are rendered page by page before release. This makes the lecture an auditable scientific edition rather than a static collection of persuasive slides.

Accessibility is treated as part of scientific precision. Color is redundant with labels; diagrams have explicit reading order and captions; mathematical symbols are introduced in prose; clinical language avoids blame and deterministic prediction; and treatment discussion never substitutes a population estimate for individualized medical care. These constraints make the material usable without weakening its uncertainty.

Release requires three independent gates. The scientific gate checks that every central claim has an appropriate source class, that highly influential work is not confused with highly reliable work, and that recent evidence has been used to support, qualify, replace, or contest the canonical account. The bilingual gate compares section purposes, evidence status, mathematical commitments, clinical cautions, and conclusions across editions. The visual gate renders every page and inspects density, hierarchy, line endings, table integrity, figure labels, bidirectional text, clipping, and contrast at ordinary reading scale.

Automated checks supplement rather than replace inspection. They count pages and evidence records, verify expected section and equation markers, search for unresolved production tokens, inspect embedded fonts and extractable text, and flag pages whose content bounding boxes end unusually early. A low-density alert is then classified: an intentional divider, a protected table, a figure-led explanation, or a genuine prose defect. Genuine defects are corrected through substantive exposition or reflow and the entire paired build is rerun.

The final artifact also preserves limits that a live speaker can easily lose. Acute and chronic treatment effects remain separate; child and adult findings are not merged; neural correlates are not diagnostic tests; symptom benefit is not complete recovery; and a mathematical analogy is not an empirical mechanism. Those boundaries are repeated because scientific communication fails most often at the transition from a qualified source to an elegant spoken sentence. The methods page records the constraints under which that sentence may be used.

Reproducibility is versioned at the level of inputs and decisions. The build records the dated evidence export, architecture, bilingual manuscripts, matrices, equation register, and rendering rules. A later edition should be able to identify which record entered or left the corpus, which claim changed status, and which page changed as a result. Silent replacement would defeat the contradiction ledger. The same discipline applies to visual reconstruction: data-bearing charts require traceable values and units, while conceptual diagrams are labeled as conceptual and never styled to resemble a measured group effect.

This provenance also governs reuse. A slide, handout, site excerpt, or spoken segment inherits the evidence boundary of the parent passage. Removing a qualification for space requires rewriting the claim, not merely deleting the caution. The durable unit is therefore the claim plus source role, population, time scale, uncertainty, and visual status. That bundle is what allows a long lecture to become shorter assets without becoming less true.

Before release, links and identifiers are sampled back to the source record, page labels are regenerated after pagination changes, and the English and Hebrew closing claims are compared once more in extracted text. The artifact is complete only when scientific, linguistic, mathematical, and visual checks all refer to the same build.

Precision includes saying what a figure does not show.

FLOW HIJACKED · ADHD

ATTENTION IS NOT ABSENT. ITS ALLOCATION, STABILITY, RECOVERY AND RELEASE CAN BE UNRELIABLE.

The aim is not permanent focus. It is greater freedom to enter, remain, return, and leave when life requires it.