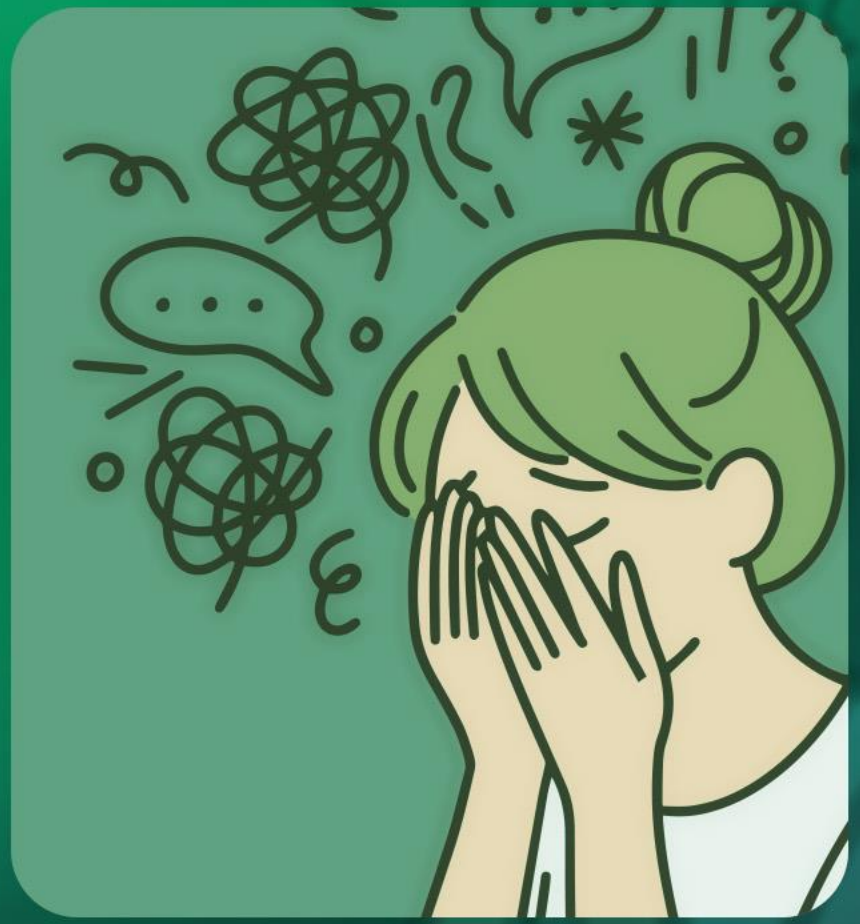
Features Out of Focus: Recognition and Treatment of Emotional Dysregulation and Executive Dysfunction in ADHD



MasterClass

Supported by an educational grant from Otsuka.

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Faculty Disclosures

- **Greg Mattingly, MD:** Consultant – AbbVie, Acadia, Akilli, Alkermes, Angelini, Axsome, Biogen, Boehringer Ingelheim, Cerevel, Colegium, Corium, Eisai, Intracellular, Johnson & Johnson, Liva Nova, Lumos Labs, Lundbeck, Neurocrine, Noven, Otsuka, Redax, Relmada, Revibe, Roche, Sage, Sirona, Sunovion, Supernus, Takeda, Teva, and Tris Pharma; Research – AbbVie, Acadia, Alkermes, Akilli, Alto Therapeutics, Avanir, Axsome, Boehringer Ingelheim, Cingulate, Click Therapeutics, Corium, Emalex, Idorsia, Intracellular, Johnson & Johnson, Lumos Labs, Medgenics, Neurocrine, NLS Pharma, Redax, Relmada, Roche, Sage, Sirtsei, Sumitomo, Sunovion, Supernus, Takeda, and Teva; Speaker's Bureau – AbbVie, Alkermes, Angelini, Axsome, Corium, Intracellular, Ironshore, Johnson & Johnson, Lundbeck, Neurocrine, Noven, Otsuka, Sunovion, Supernus, Takeda, Teva and Tris Pharma
- **Rebecca Barbee, PA-C:** Advisory Board – Alkermes, Axsome Therapeutics, Neurocrine Biosciences; Consultant – AbbVie, Tempus; Speaker's Bureau – Alkermes, Axsome Therapeutics, Neurocrine Biosciences, Johnson and Johnson

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration)
- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity
- This activity has been independently reviewed for balance
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Learning Objectives

- Describe the prevalence and burdens of ADHD symptoms/features beyond current diagnostic criteria, such as executive dysfunction, emotional dysregulation, and common psychiatric comorbidities
- Implement strategies to improve recognition and assessment of executive dysfunction, emotional dysregulation, and psychiatric comorbidities in patients with ADHD
- Explain how the serotonin system interacts with dopamine and norepinephrine in the regulation of emotion and cognition in ADHD
- Assess the pharmacologic and clinical safety and efficacy profiles of conventional, novel, and investigational agents for ADHD, including consideration of their potential to address often under-addressed symptoms/features of the disorder

ADHD Beyond the Core Symptoms

ADHD Is More Than What We See on the Surface

Inattention

Distractibility

Executive Dysfunction

Relationship Strain

Emotional Dysregulation

Self Esteem Erosion

Functional Impairment

Rejection Sensitivity

Barkley, R. A. (2010). Deficient Emotional Self-Regulation: A Core Component of Attention-Deficit/Hyperactivity Disorder. *Journal of ADHD and Related Disorders* 1, 5-37. Graziano, P. A. & Garcia, A. (2016). Attention-deficit hyperactivity disorder and children's emotion dysregulation: A meta-analysis. *Clin Psychol Rev* 46, 106-23

Reactive Reba

Reba is a 12 year old female presenting for psychiatric evaluation after escalating emotional outbursts, school refusals, worsening family conflict

- “always on edge”
- Intensely reactive to minor frustrations
- Easily overwhelmed by transitions or perceived criticism
- Frequently tearful, explosive, or irritable
- Interrupts peers
- Difficulty tolerating mistakes
- Emotional ‘meltdowns’ when redirected
- Abandons assignments when frustrated
- Social conflict due to impulsive comments and rejection sensitivity

Reactive Reba

Despite these concerns, Reba is a ‘star student’ and excels academically.

Parents are concerned about anxiety, depression, and even have wondered if she is bipolar.

What is your differential diagnosis? Next steps?

ADHD Is Prevalent in All Age Groups

Historically, ADHD has been thought of as a childhood disorder, but it has been demonstrated to persist into adulthood

8%
of children are diagnosed with ADHD

6%
of adolescents are diagnosed with ADHD

4.4%
of adults are diagnosed with ADHD

2.8%
of seniors are diagnosed with ADHD

Up to 65% of children with ADHD continue to experience the disorder into adulthood

Faraone SV, et al. *Psychol Med*. 2006;36(2):159-165. American Academy of Pediatrics. *Pediatrics*. 2000;105:1158-1170. Pastor PN, et al. *Vital Health Stat*. 10(237). 2008. Kessler RC, et al. *Am J Psychiatry*. 2006;163(4):716-723. Michelsen M et al. Br J Psychiatry. 2012;210:298-305.

Stressed Sara

- 32 yo single commercial media consultant
- Presents stressed and overwhelmed
- Reports a history of being diagnosed with “ADD” in college
- Tried lisdexamphetamine
  - but I totally lost my appetite and got “really snappy”
- Tried a SSRI and it helped some with anxiety, but I still felt overwhelmed
- “I’ve read about ADHD, but it seems like more than that”
- Reports running late, being disorganized, difficulty stopping and starting things and keeping up with deadlines

Stressed Sara

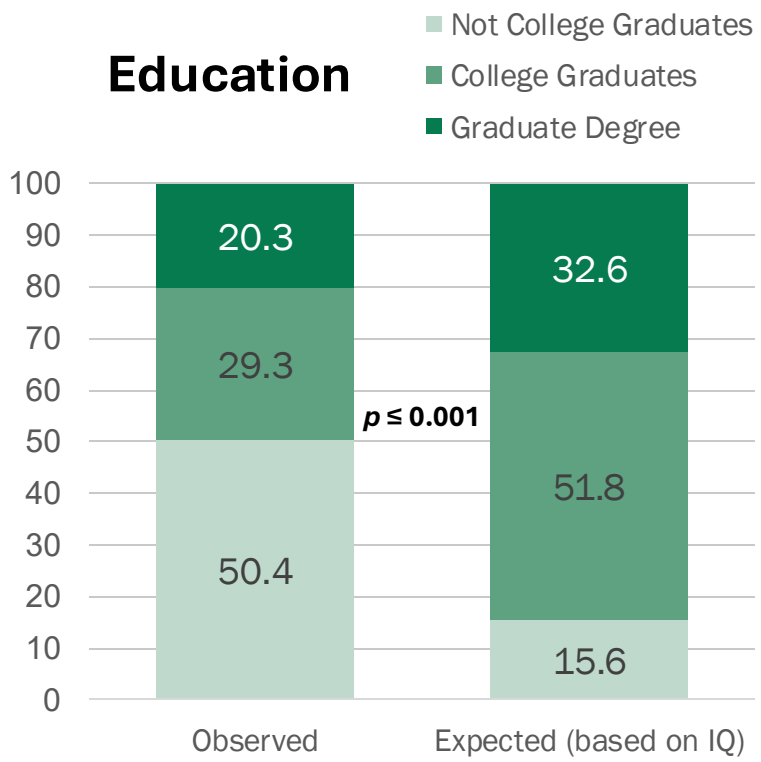
ADHD and Executive Function

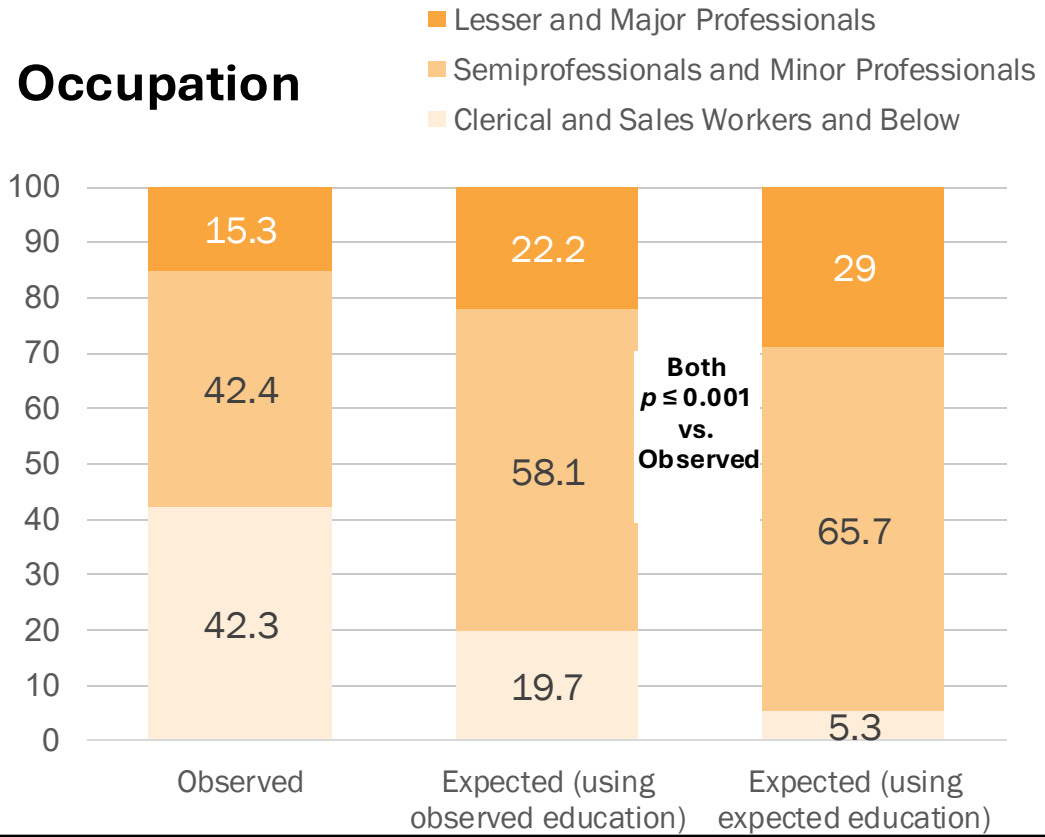
"What Is Executive Function?" November 2025 by Russ Barkley

Clinical scale	Items measure the ability to:
Inhibit	control impulses and stop certain behaviors at appropriate times
Shift	move from task to task and solve problems flexibly
Emotional Control	regulate emotional responses appropriately
Self-Monitor	recognize and monitor effect of own behavior on others
Initiate	initiate tasks and generate ideas
Working Memory	keep information being used in mind while completing a task
Plan/Organize	set goals and effectively plan and execute tasks necessary for attaining said goal
Task Monitor	check one's own work and assess personal performance
Organization of Materials	keep workspaces, living areas, and materials orderly

Roth RM, et al. Arch Clin Neuropsychol. 2013 Aug;28(5):425-34; https://www.additudemag.com/7-executive-function-deficits-linked-to-adhd/

Adults with ADHD Have Lower-Than-Expected Educational and Occupational Attainments





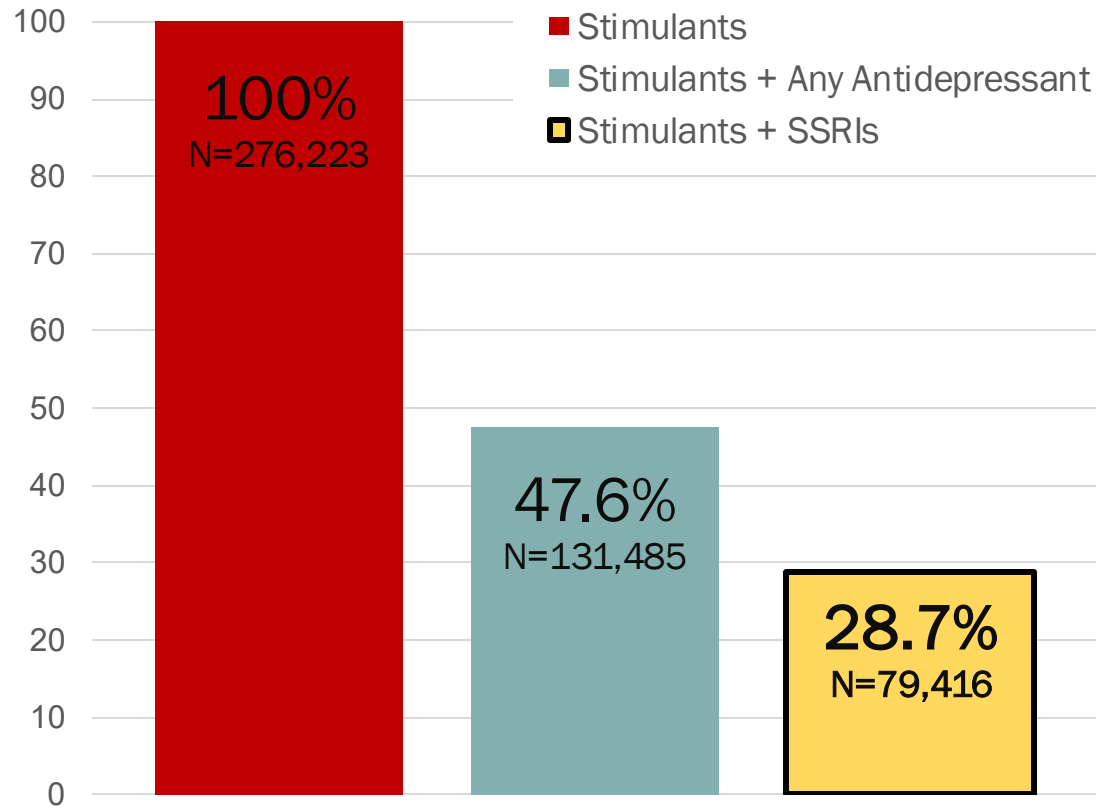
Although adults with ADHD had the intellectual potential for far higher educational attainment, **~50%** only completed college, and only **~20%** earned graduate degrees

Although 80–95% of adults with ADHD were expected to reach professional or managerial occupational levels,
only 58% achieved these roles

Biederman J, et al. *J Clin Psychiatry*. 2008;69(8):1217-1222.

High Stimulant and SSRI Co-Prescribing: Could Serotonin Be A Missing Piece in ADHD?

In an observational study of commercially insured U.S. adults prescribed Schedule II stimulants,
nearly 30% using stimulants also received SSRIs



High SSRI co-prescribing indicates compensation for symptoms **not fully addressed by stimulants**

Serotonergic pathways may indicate an important therapeutic target in ADHD, particularly for symptoms associated with **emotional dysregulation**

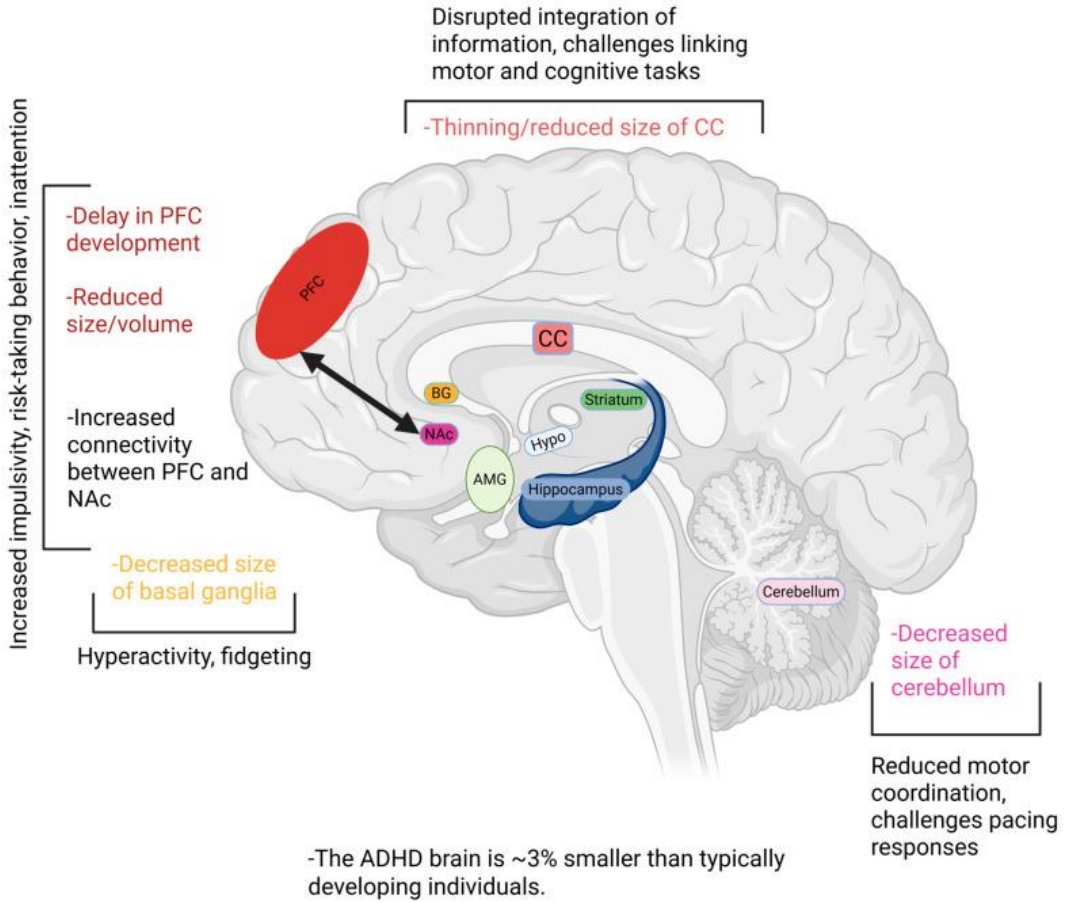
Moore TJ, et al. BMJ Open. 2023;13(4):e069668.

Neurobiological Systems Implicated in ADHD

Brain Regions Altered in ADHD

In ADHD, there are many ‘macro’ pathologies

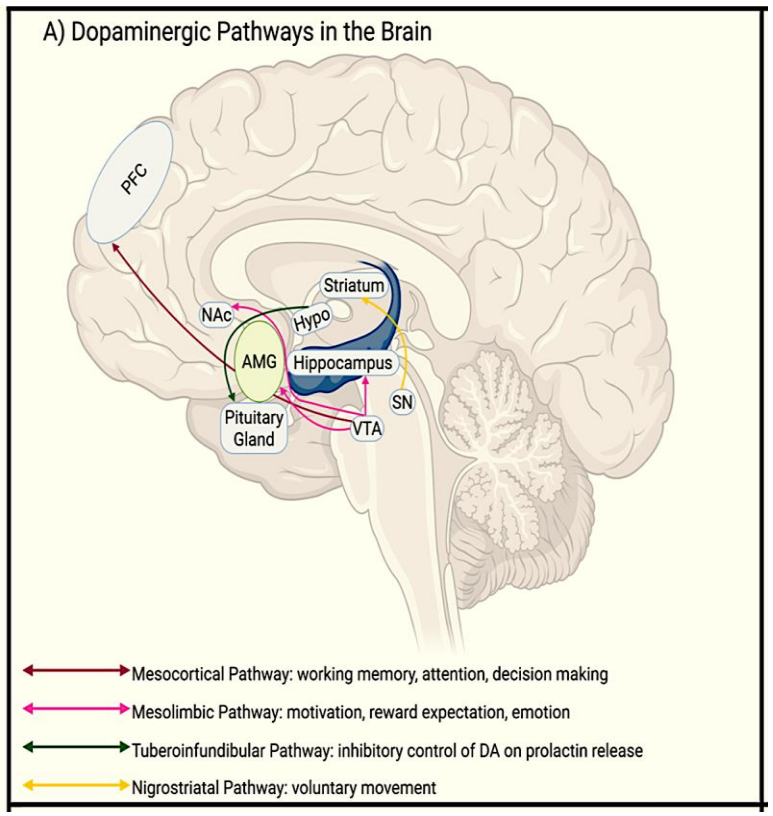
1. Brain size abnormalities
2. Brain connectivity abnormalities
3. These map onto the ‘classic’ symptoms of ADHD (inattention, hyperactivity, impulsivity)
4. Importantly, **they also map onto areas involved in emotional dysregulation and executive dysfunction in ADHD**

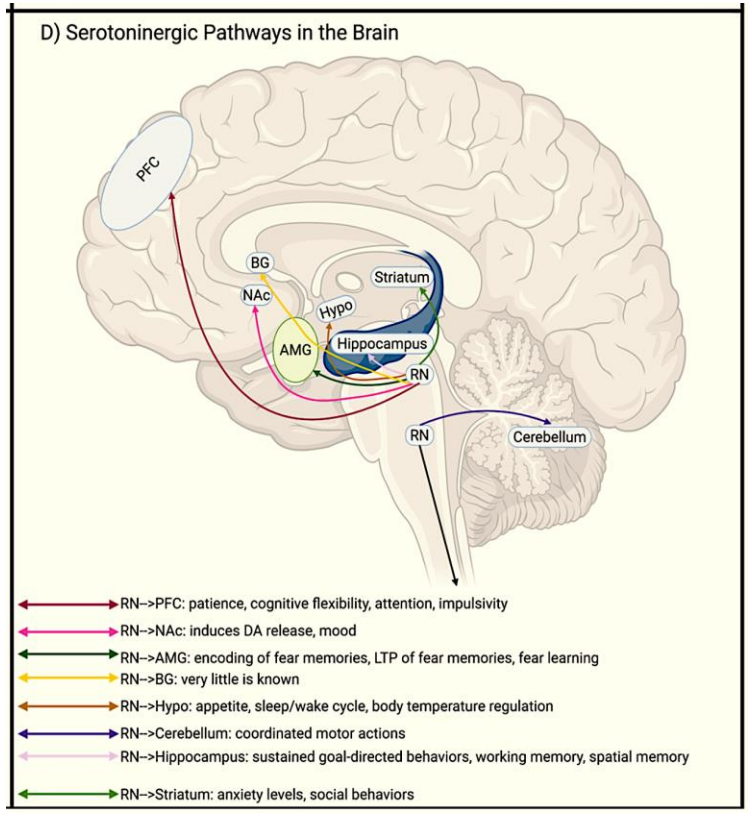


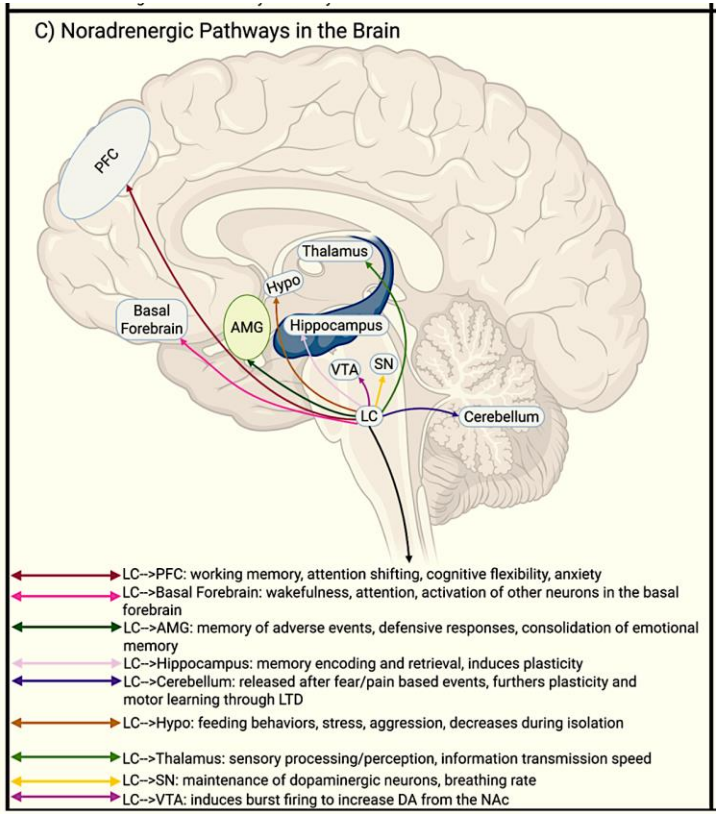
There is an overall decrease in total brain volume in ADHD: a loss of white matter volume (10.7%) and grey matter volume (3.9%), which is approximately **3% total decrease in brain volume.**

Yacoub, M.W.; et al. Cells 2025, 14, 1367

These Regions Are Innervated by Dopamine, Serotonin, and Norepinephrine





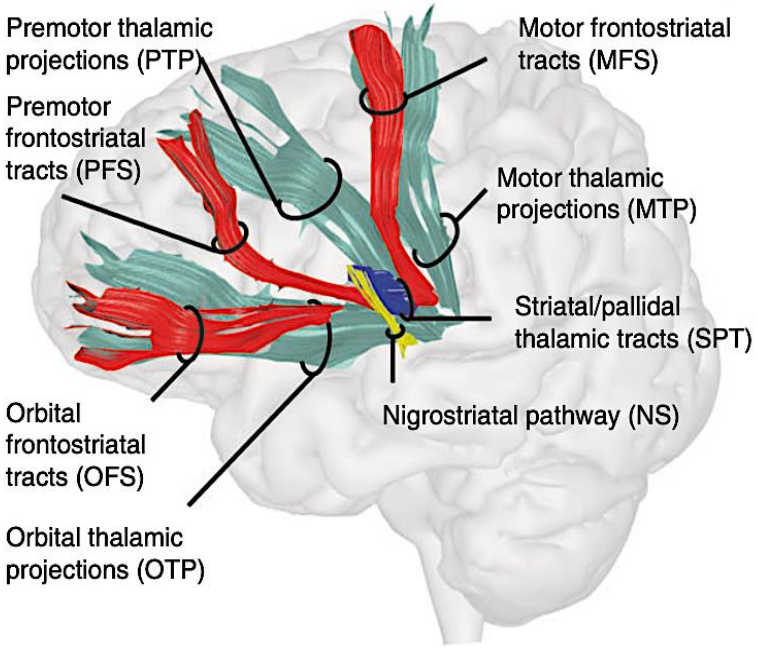


DA, 5-HT, and NE are the three neurotransmitters binding **attention**, **impulsivity**, and **emotional regulation** centers of the brain

Yacoub MW, et al. *Cells*. 2025;14(17):1367.

White Matter Alterations in ADHD

Frontostriatal and thalamic projections

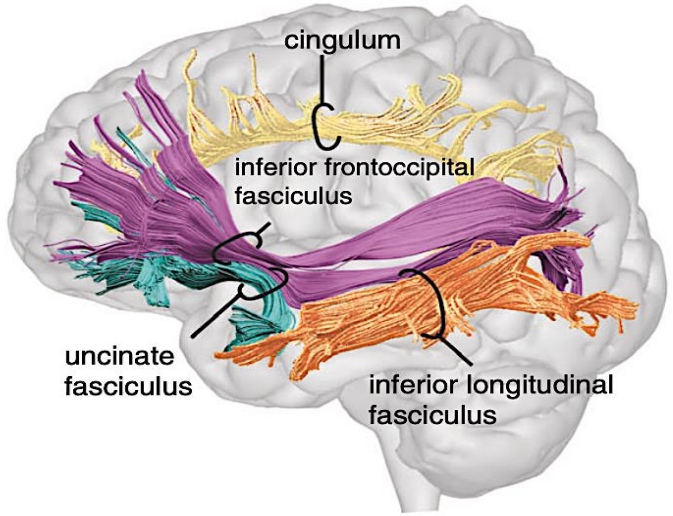


Associated impairment

FS pathways: inattention, impulsivity, executive dysfunction, poor schooling, ADHD symptom severity.

Thalamus and ATR: inattention, impulsivity, ADHD symptom severity.

Other association tracts



Associated impairment

CING: inattention, executive dysfunction, poor working memory, ADHD symptom severity and age-related remission of hyperactive-impulsive symptoms, emotional problems.

UNC: inattention, impulsivity, poor working memory and verbal intelligence, inattentive symptoms, emotional problems, and callous-unemotional behaviors.

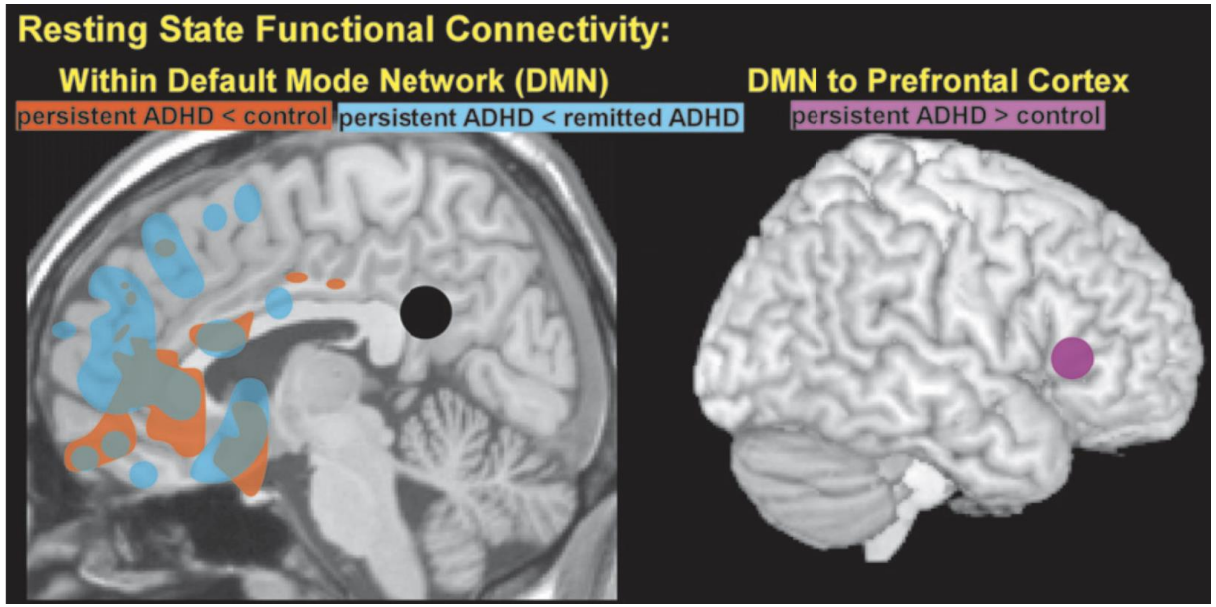
ILF: inattention and executive dysfunction, ADHD symptom severity, poor adaptive functioning, emotion dysregulation.

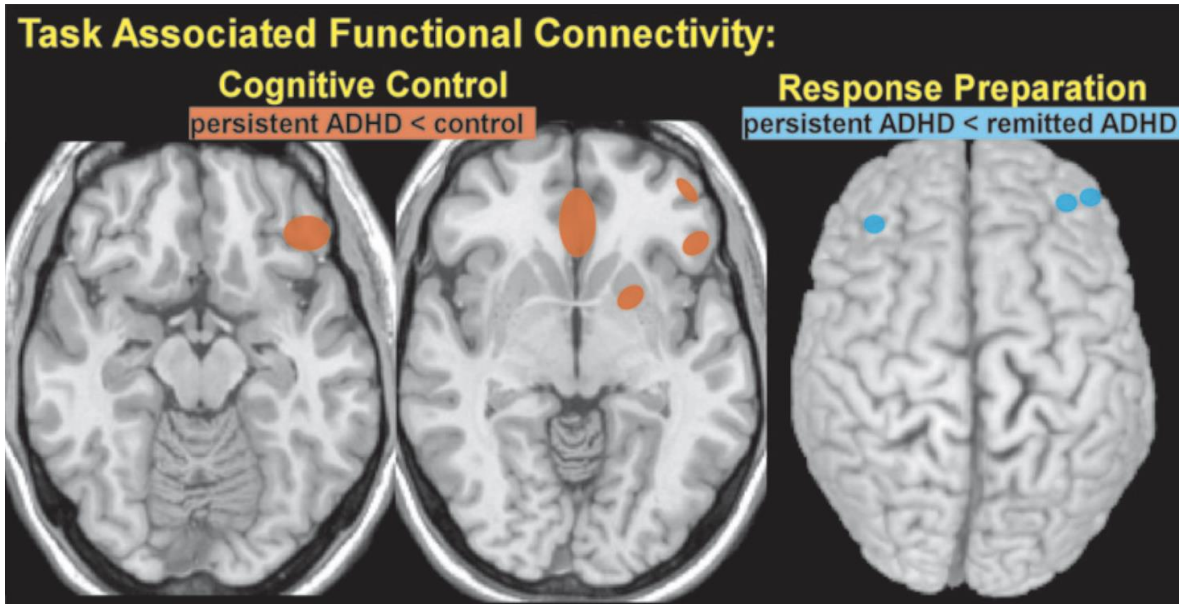
IFOF: inattention, ADHD symptom severity, poor adaptive functioning, emotion dysregulation, callous-unemotional behaviors.

Parlatini V et al. Molecular Psychiatry (2023) 28:4098–4123

Functional Differences in ADHD

DMN abnormalities are shared between ADHD and ‘classic’ mood disorders, such as MDD and BD, and are associated with **increased impulsivity, greater emotional dysregulation,** and **even suicidality.**



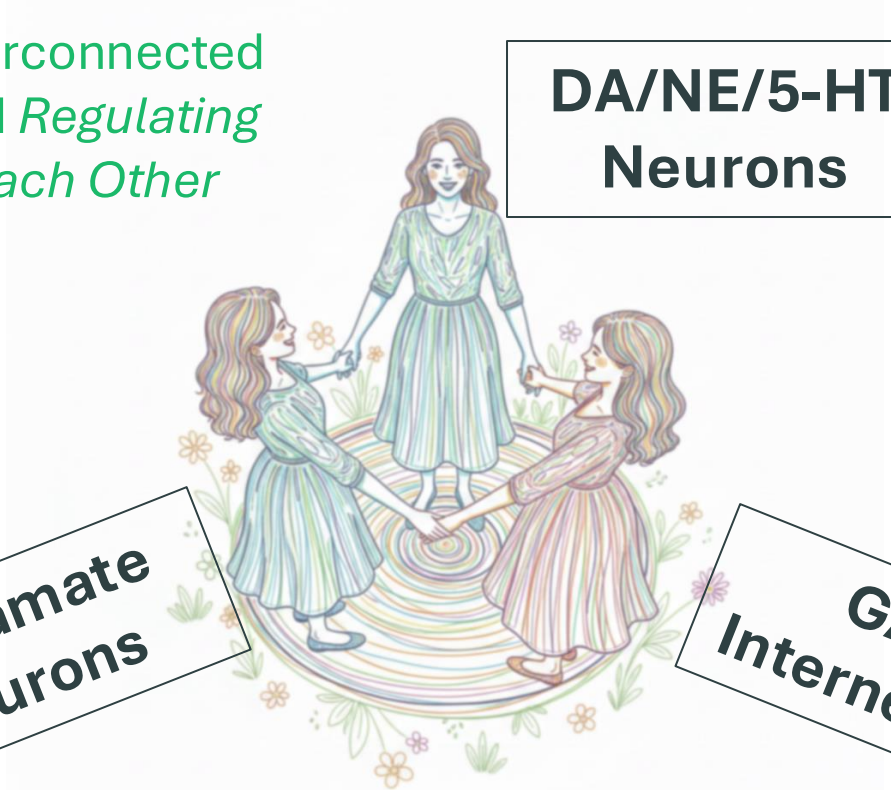


MDD = major depressive disorder; BD = bipolar disorder.

Jadidian A et al. J Neuropsychiatry Clin Neurosci 27:3, Summer 2015; We Y et al. J Psych Research 2024. Sept 177; 2111-218; Huang W-S, et al. J Clin Psychiatry 2025 Nov 19;87(1):25m15906

Neurons, Interneurons, Glutamate, GABA, and the ‘Classic Three’ (DA, NE, and 5-HT)

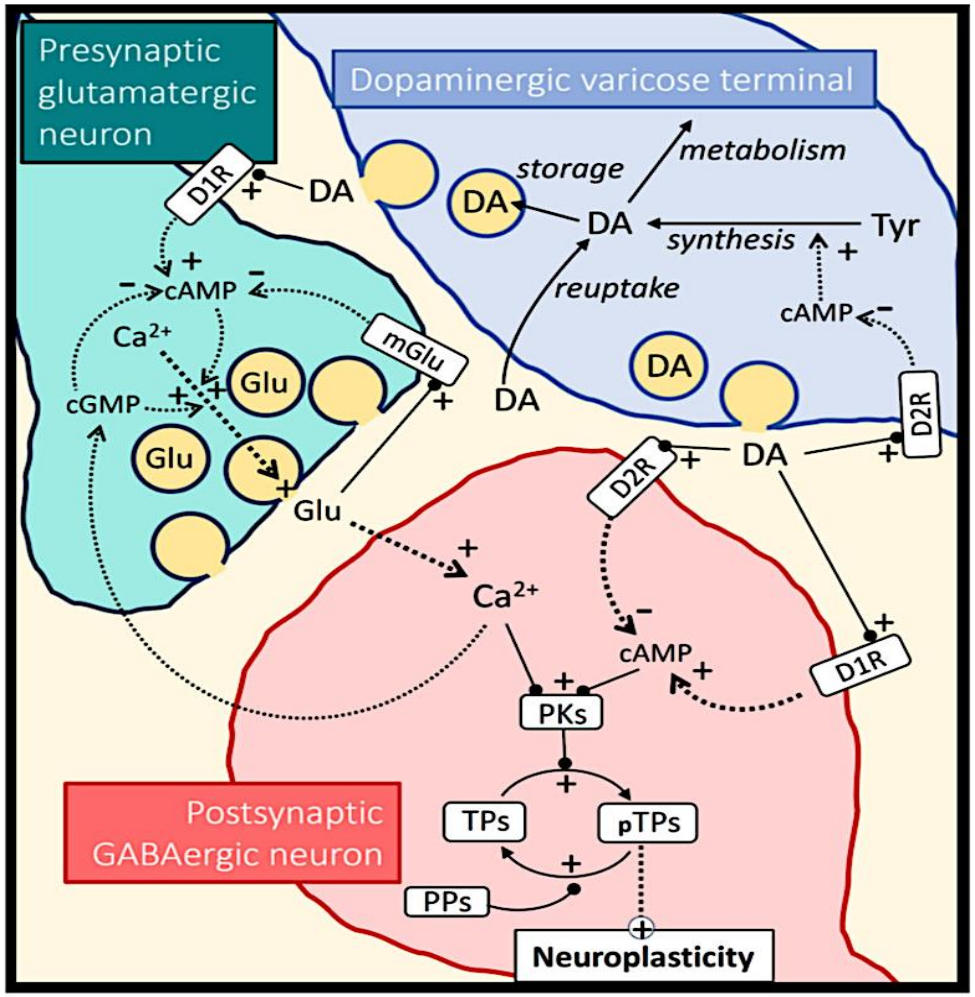
Interconnected and *Regulating Each Other*



DA/NE/5-HT Neurons

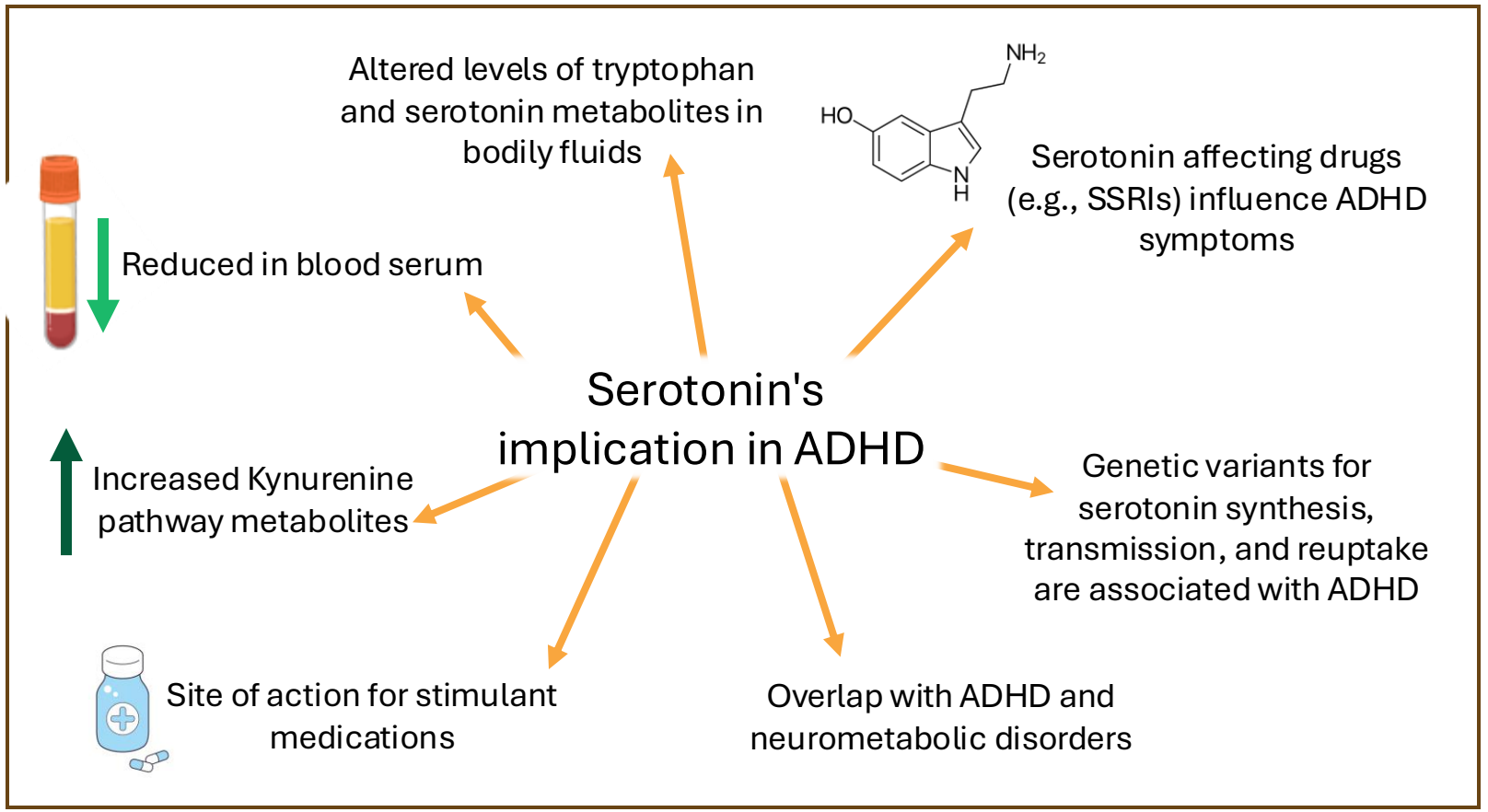
Glutamate Neurons

GABA Interneurons



Campusano JM et al. Front. Psychiatry 15:1492126

Evidence for Serotonin Dysfunction in ADHD Is Rapidly Gathering Steam

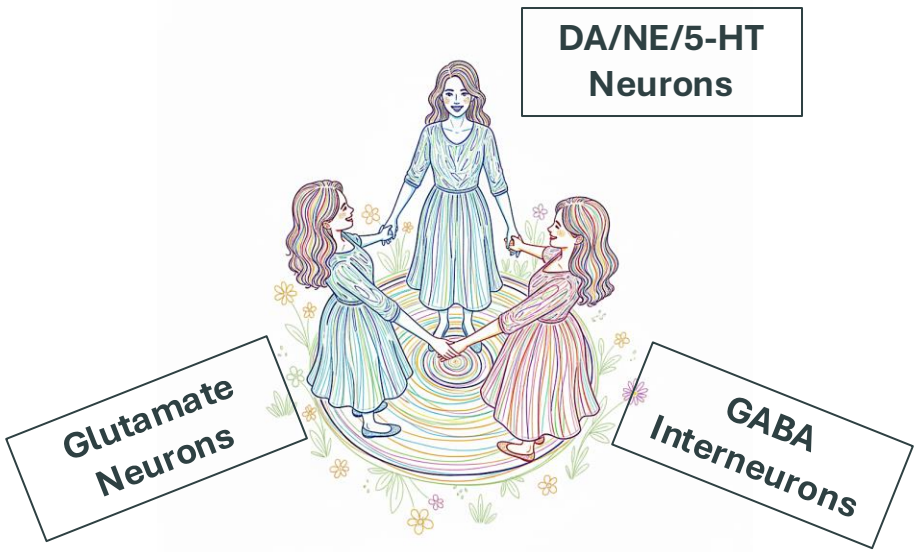


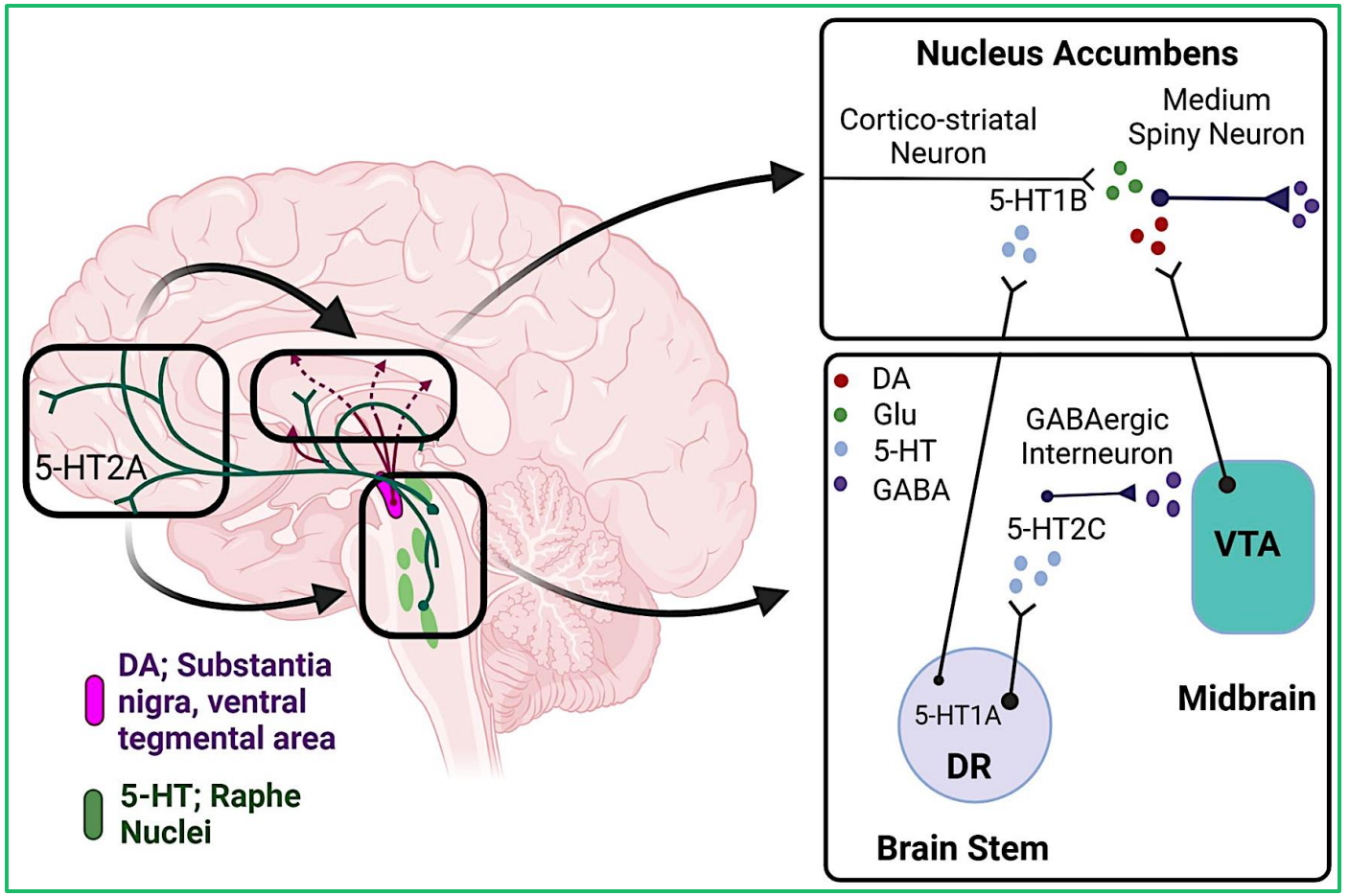
The role of serotonin in the following is well established:

- Major depression
- Impulsivity
- Emotional dysregulation
- Sleep

Jackson et al. Journal of Neurodevelopmental Disorders (2025) 17:2.

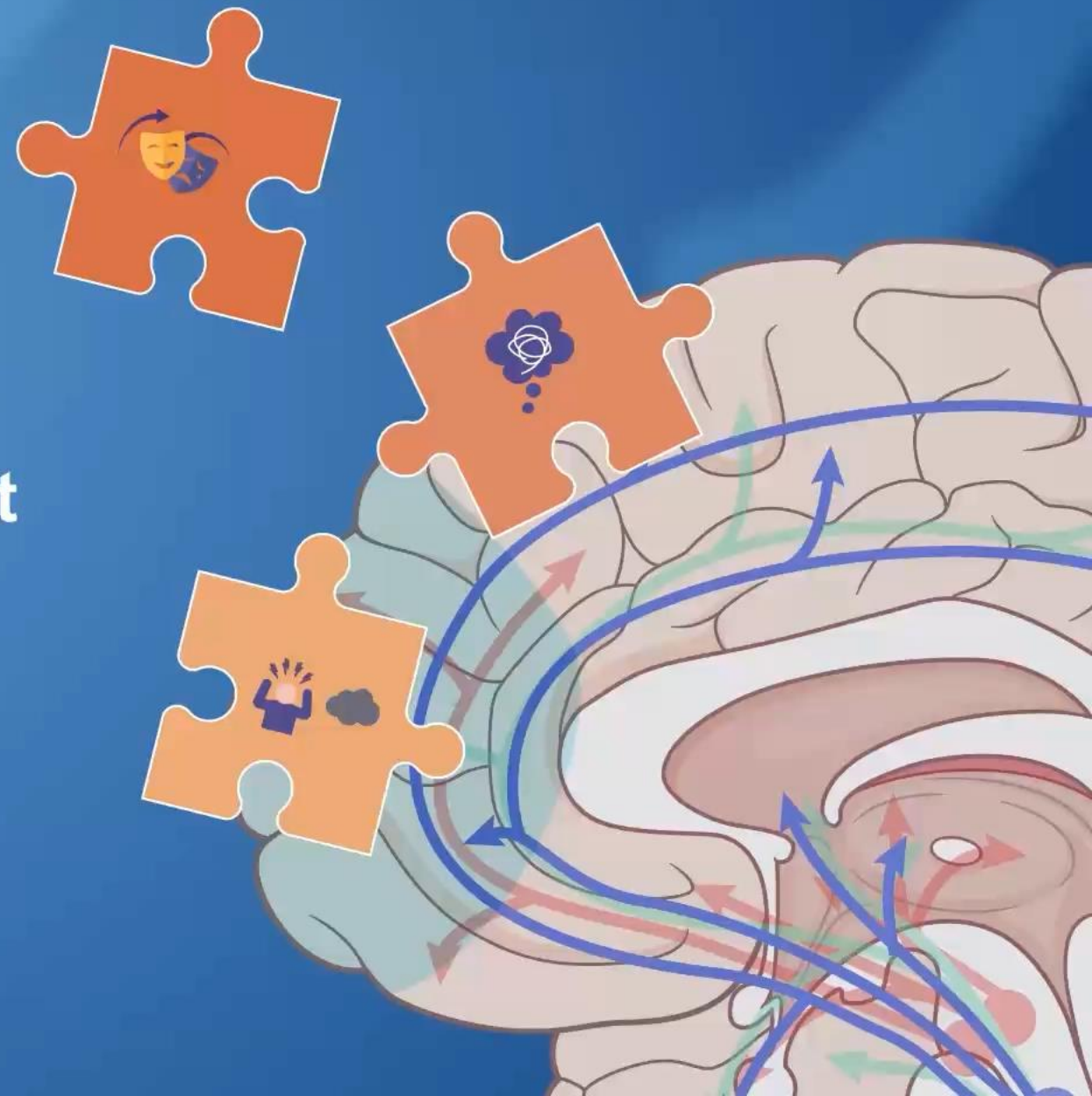
ADHD Is a Story of Autoreceptors, Heteroreceptors, And Interactions of Multiple Neurotransmitters





Solomon M, et al. Clinical Drug Investigation (2025) 45:701–742.

Balancing Monoamines for the Complexities of ADHD Treatment



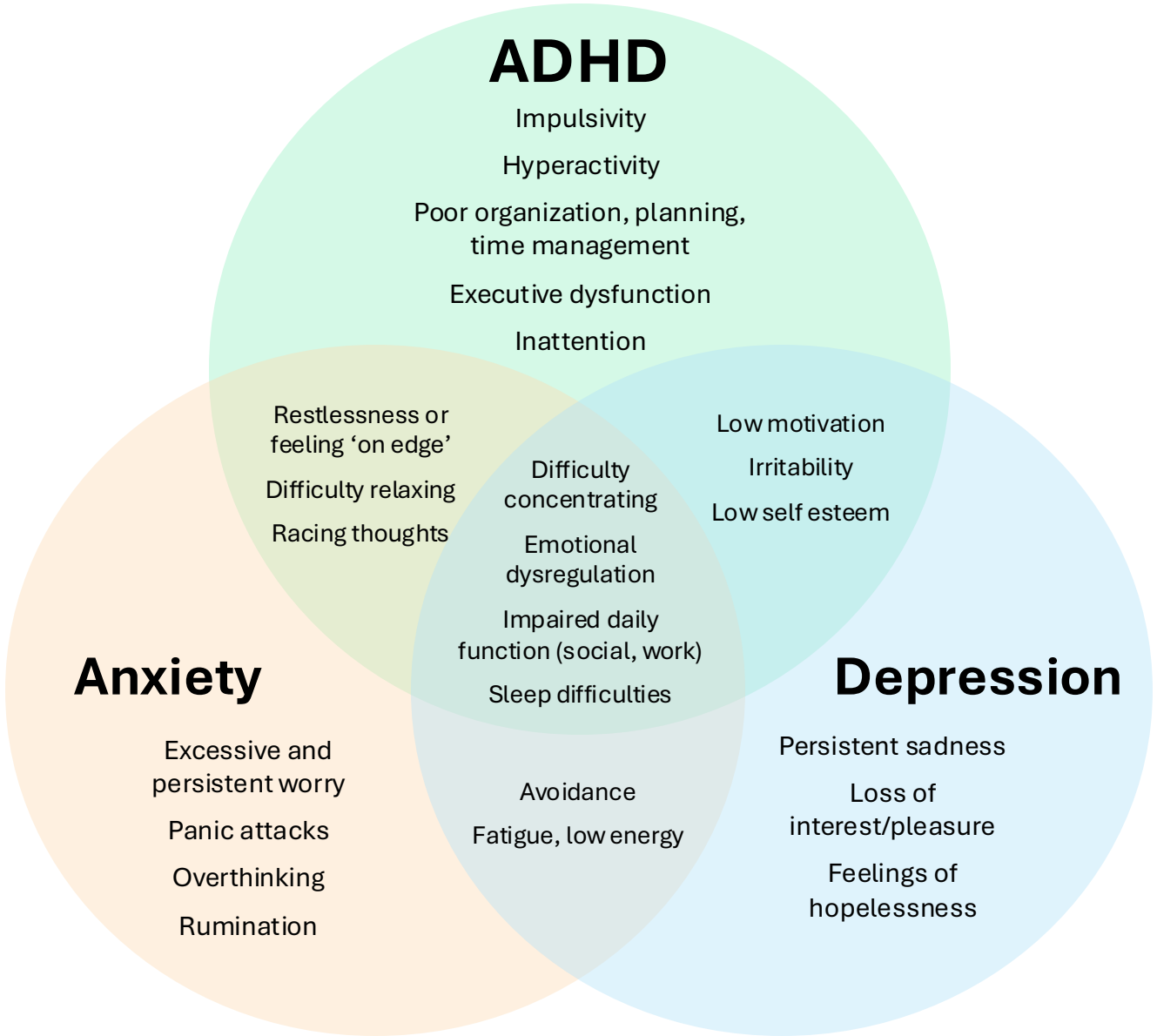
Creative services provided by infograph-ed™ your data, visualized

Key Learning Points

- ADHD is characterized by more than just inattention and hyperactivity; it may include executive dysfunction, emotional dysregulation, relationship strain, and functional impairment
- The serotonergic system may represent an important, yet neglected therapeutic target in ADHD, particularly for symptoms of emotional dysregulation
- Neurobiology reveals structural and functional abnormalities in the brain that tie the ‘classic’ symptoms of ADHD to emotional dysregulation and executive dysfunction
  - At the receptor level, DA, NE, and 5-HT, along with glutamate and GABA (and their auto- and hetero-receptors) are implicated in ADHD and emotional and executive function dysregulation

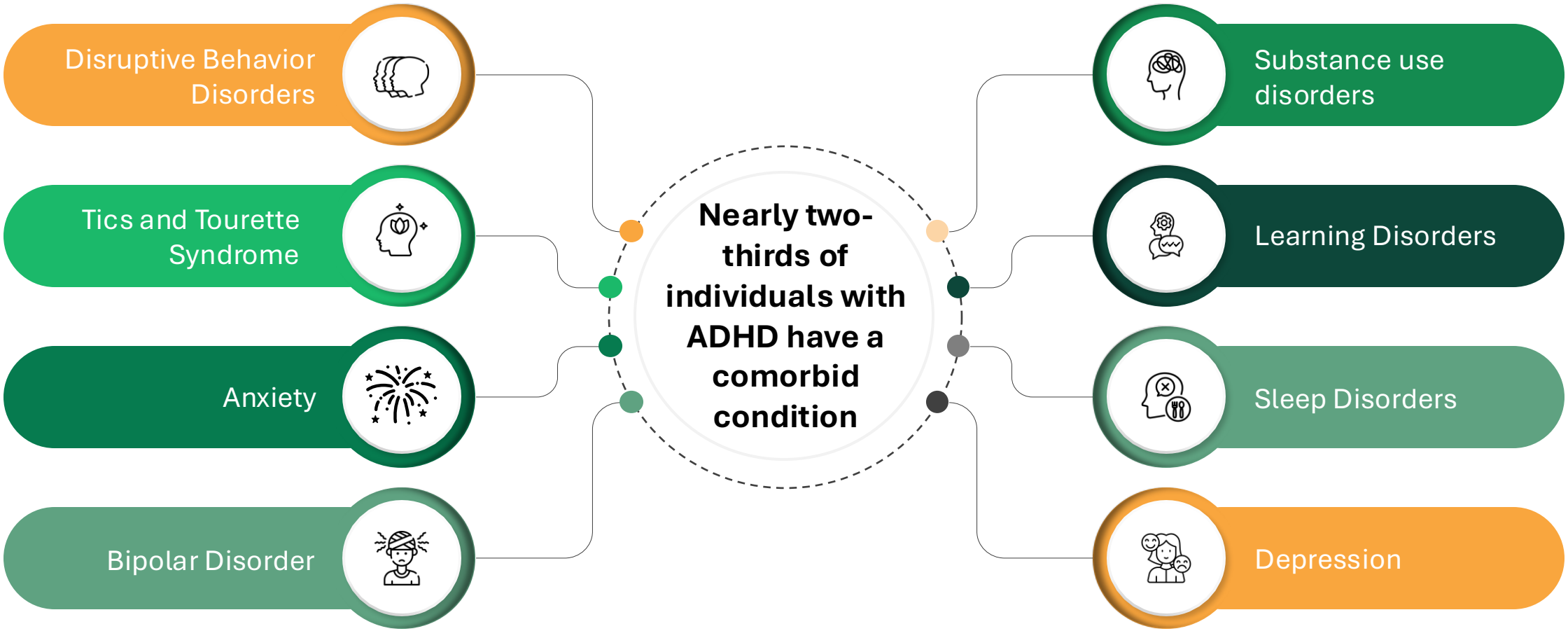
Comprehensive Recognition and Assessment of ADHD

Differentiating ADHD from Depression and Anxiety



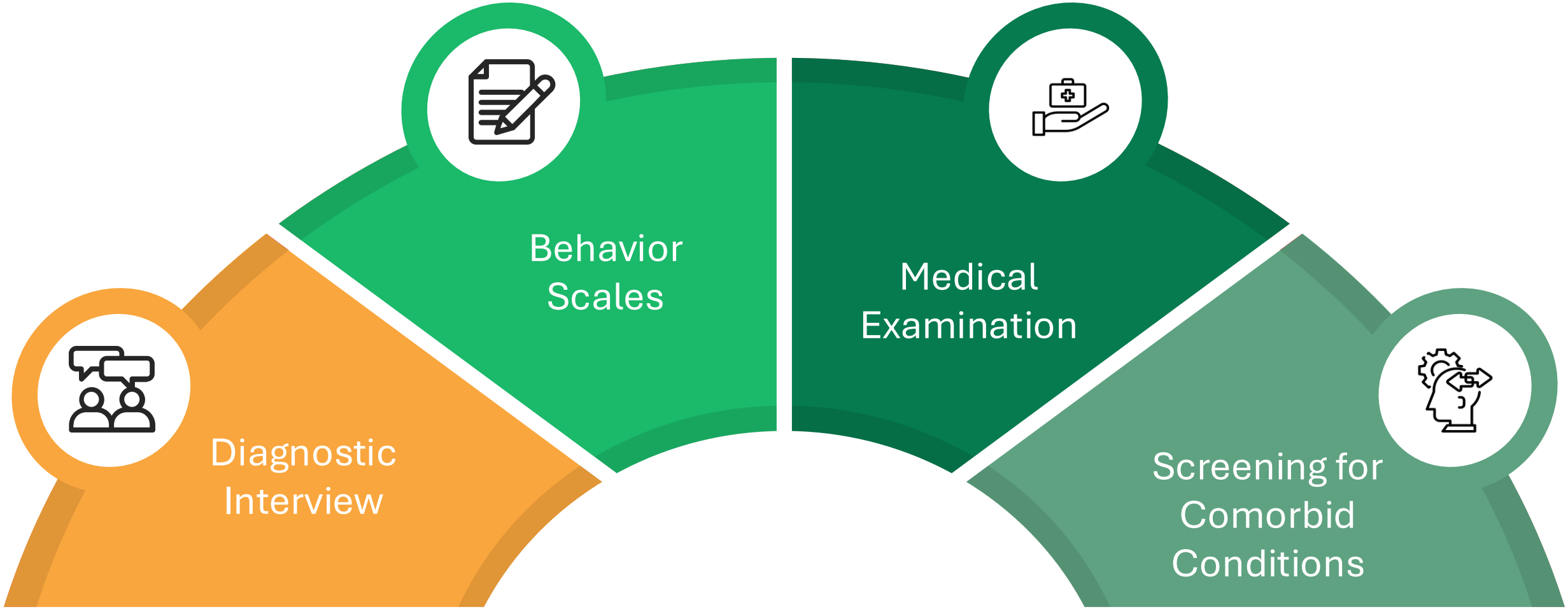
Fu X et al. *Front Psychiatry*. 2025;16:1597559; Becker SP, et al. *J Clin Child Adolesc Psychol*. 2015;44(6):1015-1029.

ADHD Rarely Occurs Alone



Pliszka SR. Comorbid psychiatric disorders in children with ADHD. In: Barkley RA, ed. *Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment*. 4th ed. New York, NY: Guilford Press; 2015:140-168

ADHD Assessment



Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). *Diagnosis of ADHD in Adults*. CHADD website. Accessed May 2026. https://chadd.org/for-adults/diagnosis-of-adhd-in-adults/

Assessing Emotional Dysregulation and Executive Dysfunction

Thinking of Reba and Sara:

- **What contextual factors should we consider?**
- **What questions should we ask?**
- **What is your differential diagnosis?**

Screening Tools

BDEFS Short Form

- 20 item assessment tool
- Score ranges from 20-80, with higher scores = greater deficits
- Evaluates areas of:
  - Time management
  - Self-restraint
  - Organization and problem solving
  - Self-motivation
  - Self-regulation of emotion

ASRS v1.1

- One the most widely used ADHD screeners
- Brief, validated, easy to use
- Indirectly screens for executive dysfunction and emotional dysregulation

BDEFS = Barkley Deficits in in Executive Functioning Scale. ASRS= Adult ADHD Self-Report Scale.

Kamradt JM, Nikolas MA, Burns GL, et al. Validation of the Barkley Deficits in Executive Functioning Scale (BDEFS) in a large multisite college sample. *Assessment*. 2021;28(3):964-976. doi:10.1177/1073191119869823. Kessler RC, Adler L, Ames M, et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol Med*. 2005;35(2):245-256. .

Key Learning Points

- ADHD frequently overlaps with depressive and anxiety disorders, and emotional dysregulation or executive dysfunction may overshadow classic attentional symptoms
- Comprehensive ADHD assessment should include developmental history, functional impairment, contextual factors, comorbidities, and collateral information, not just symptom checklists alone

Evaluation of Current and Emerging Pharmacotherapies to Address Unmet Needs

Strengths and Limitations of Conventional Stimulant Pharmacotherapies

Some Strengths of Conventional Stimulants	Some Limitations of Conventional Stimulants
High efficacy in reducing core ADHD symptoms in children and adults (70-80% response rates)	Common adverse effects: appetite suppression, insomnia, irritability, headache, anxiety, dizziness, nausea
Rapid onset of action with noticeable improvement within hours to days	Growth concerns in youth due to appetite/weight suppression
Strong evidence base with decades of clinical research and guideline support	Increased cardiovascular risk; increased heart rate and blood pressure; requires monitoring
Multiple formulations (IR, ER, prodrug) allow individualized treatment; long-acting options improve adherence and convenience	Risk of misuse/diversion, especially in adolescents and adults
Improves academic, occupational, executive, and social functioning	Schedule II classification creates prescribing and refill restrictions; potential shortages
Well-established dosing/titration strategies familiar to clinicians	May cause or worsen sleep disturbances, aggression, irritability, hostility, anxiety, mood swings

Kolar D, et al. *Neuropsychiatr Dis Treat*. 2008;4(2):389-403; Wolraich ML, et al. *Pediatrics*. 2019;144(4):e20192528.

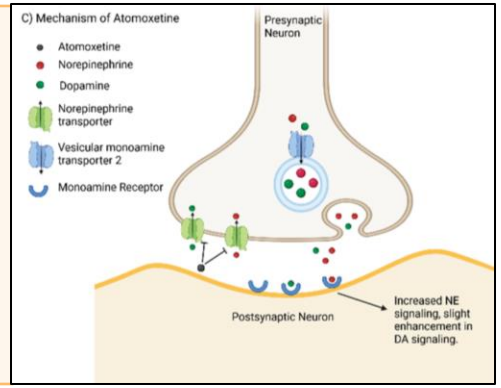
Current Availability of Nonstimulant ADHD Medications

- Nonstimulants
  - Not FDA Approved
    - **Historical**: TCAs, modafinil/armodafinil, bupropion
    - **In development**: centanafadine, solriamfetol
  - FDA Approved
    - Atomoxetine
    - Alpha 2 agonists (clonidine XR and guanfacine XR)
    - Viloxazine ER

MOA: norepinephrine reuptake inhibitor (NRI)

Showed significant improvement in ADHD symptoms in 4 studies in children/adolescents and 2 studies in adults

- Studies have also shown efficacy for: Function (WIFRS), Quality of Life (CHQ, AAQoL), Executive function (BRIEF), Oppositionality (CPRS), Emotional lability (WRAADDS), Anxiety (PARS, LSAS), but NOT for depression

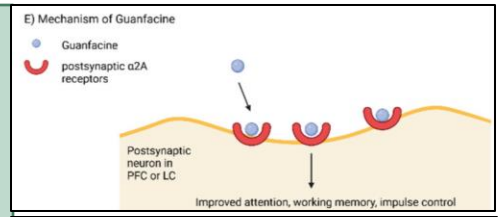


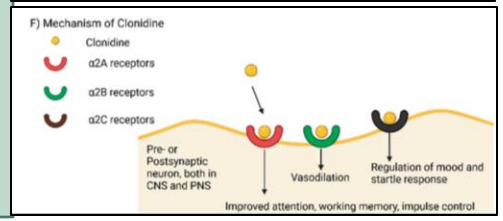
MOA: agonism of noradrenergic alpha 2A (presynaptic) and 2C (postsynaptic) receptors

Both approved (XR only) as monotherapy or adjunct to stimulants, but only for ages 6-17. Both also used for ODD and emotional dysregulation.

Clonidine XR is now available as tablet (BID) or liquid (QHS)

Guanfacine XR "selective" for alpha 2A?

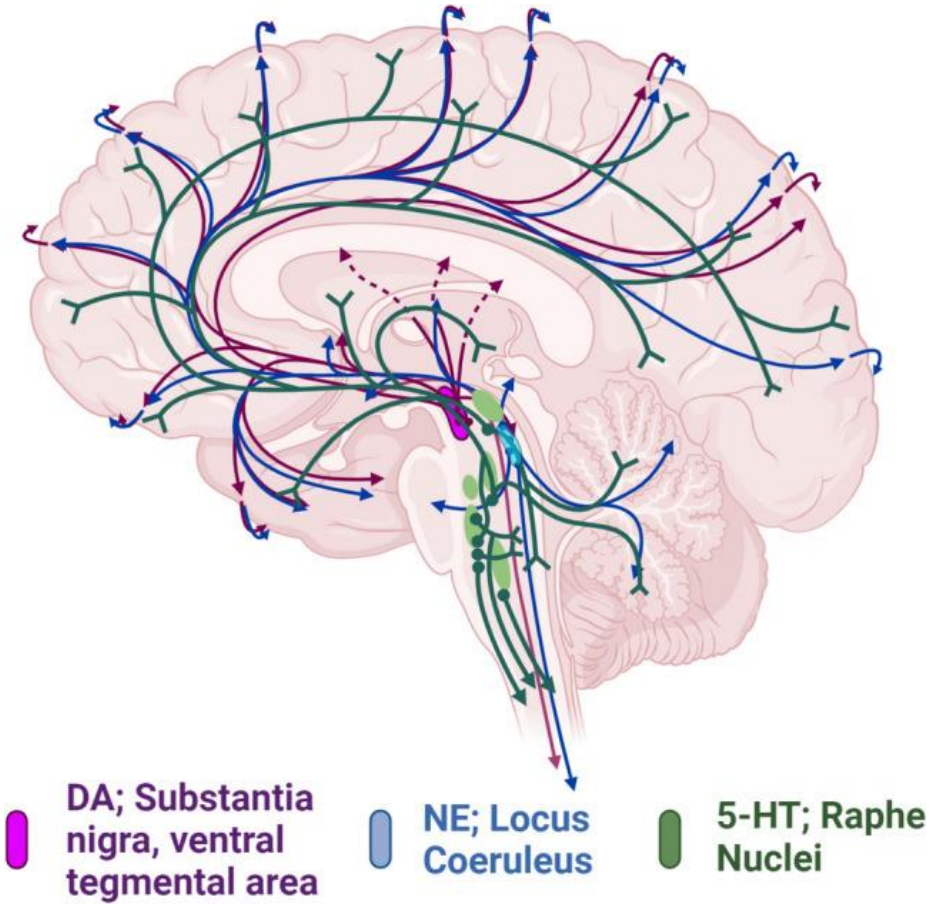




AAQoL=Adult ADHD QoL Measure; BRIEF=Behavior Rating Inventory of Executive Function; CHQ=Children's Health Questionnaire; CPRS=Conners Parent Rating Scale; LSAS=Liebowitz Social Anxiety Scale; MOA=Mechanism of action; PARS=Pediatric Anxiety Rating Scale; WIFRS=Weiss; WRAADDS=Wender-Reimherr Adult Attention Deficit Disorder Scale

Childress AC. Therapeutics and Clinical Risk Management 2016:12 27–39. Schwartz S and Correll C. J Am Acad Child Adolesc Psychiatry. 2014 Feb;53(2):174-87.Bellato A, et al. J Am Acad Child Adolesc Psychiatry 2025;64(3):346-361. Sallee FR. Postgrad Med. 2010 Sep;122(5):78-87. Ming X, et al. Adolesc Health Med Ther. 2011 Sep 30;2:105–112. Yacoub MW, et al. Cells. 2025;14(17):1367

...But What About Serotonin?



Serotonin signaling is closely tied to dopamine and norepinephrine

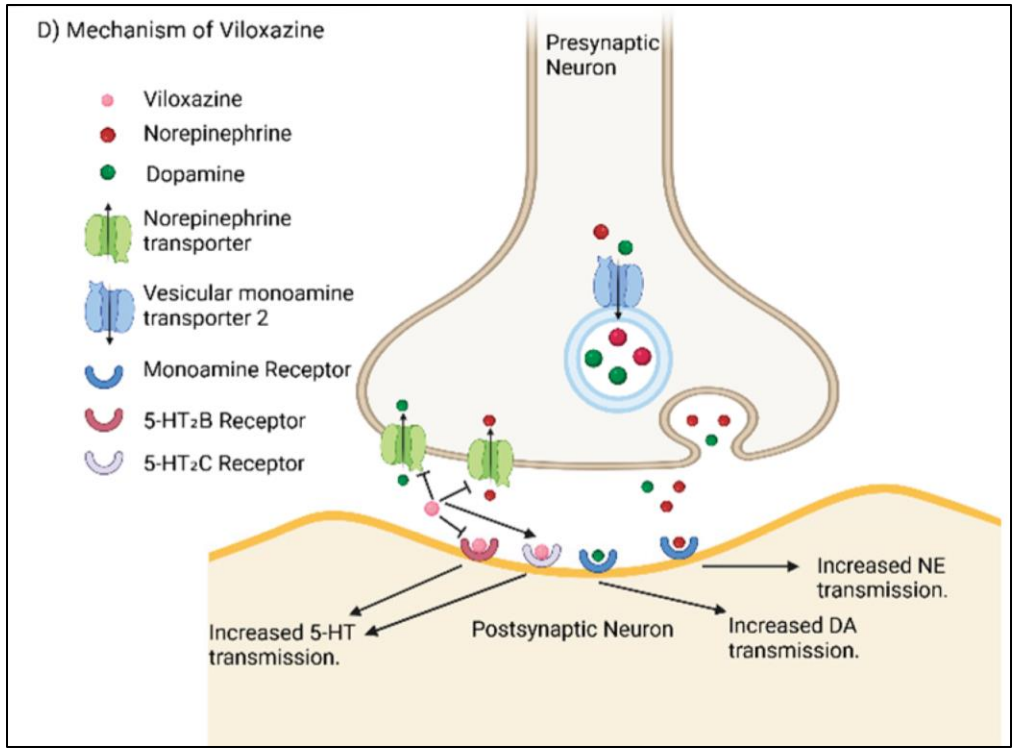
How can we target this system pharmacologically?

Solomon MB, et al. Clin Drug Investig. 2025;45(10):701-742.

Viloxazine ER

Viloxazine ER

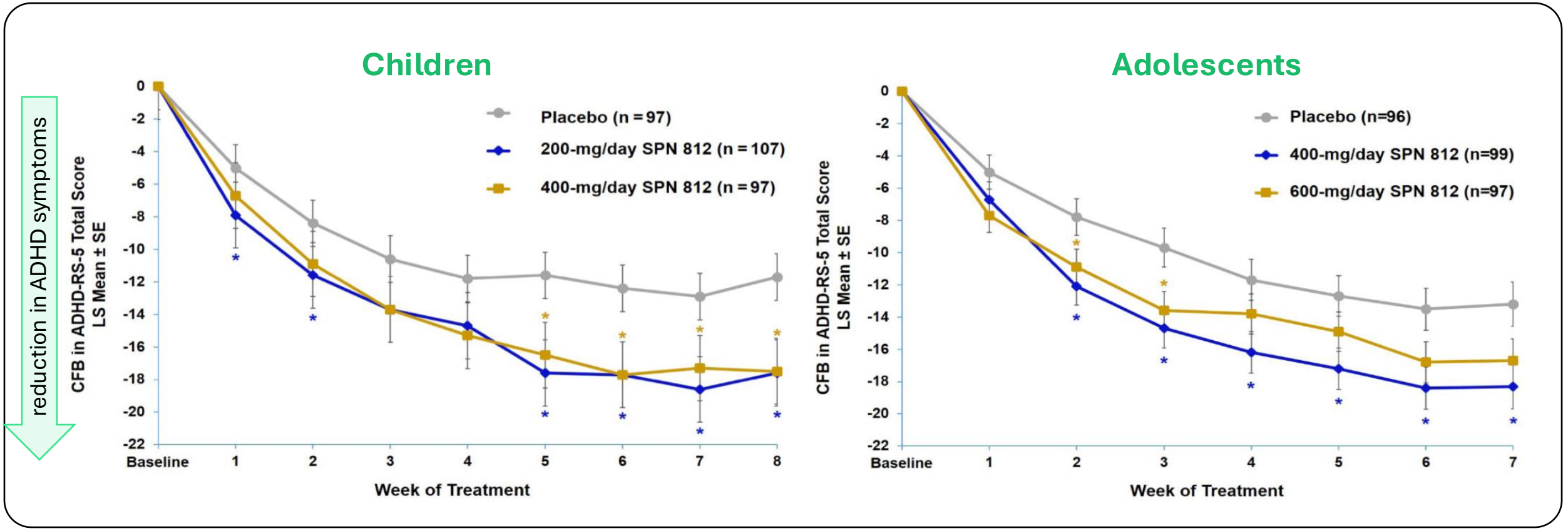
- **MOA**: NRI and 5HT2C partial agonist, 5HT2B & 5HT7 antagonist
  - IR formulation approved for MDD in the EU, but never in the US
- FDA approved for children, adolescents, and adults



MOA=mechanism of action.

Edinoff AM, et al. Front Psychiatry. 2021 Dec 17;12:789982. Nasser A, et al. CNS Drugs. 2022 Jul;36(8):897-915. Childress AC, et al. J Child Adolesc Psychopharmacol. 2025 Apr;35(3):155-166. Yacoub MW, et al. Cells. 2025;14(17):1367

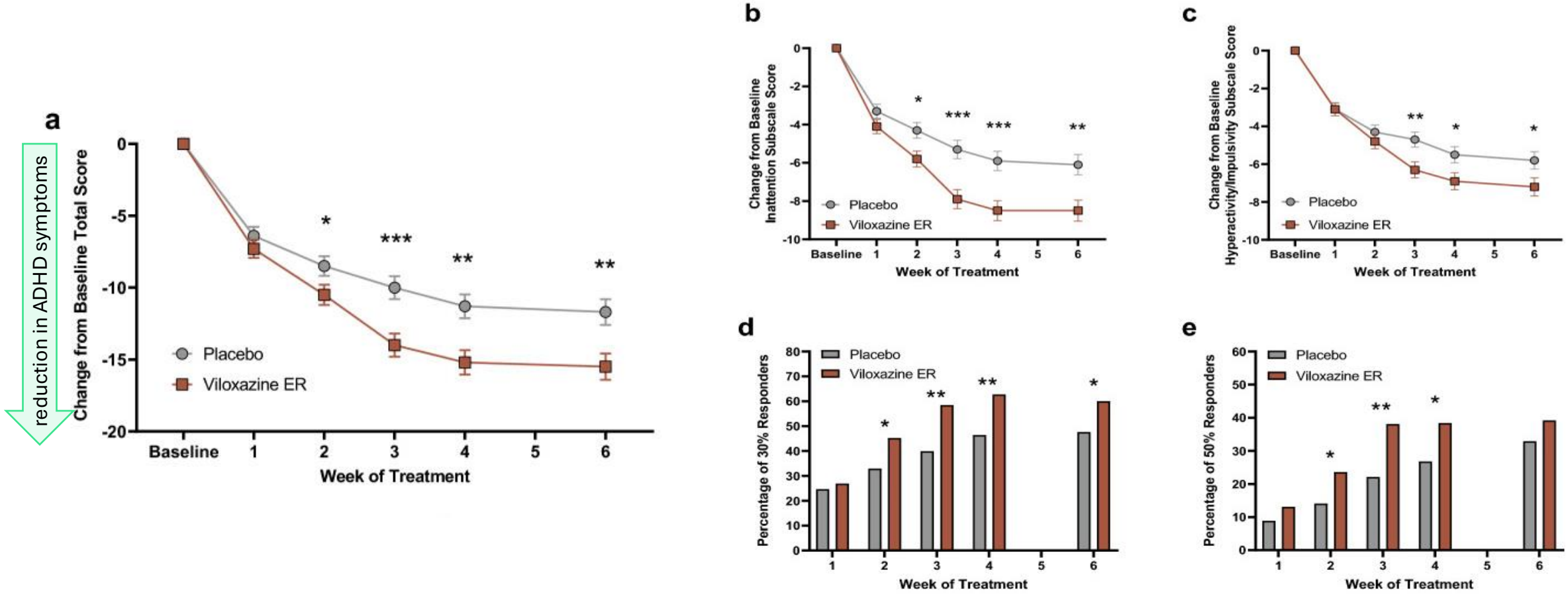
Viloxazine ER Efficacy: Children & Adolescents



Across pediatric and adolescent trials, viloxazine ER (SPN-812) demonstrated significant and sustained reductions in ADHD symptoms over 6–8 weeks compared to placebo.

Nasser A, et al. Clin Ther. 2021;43(4):684-700; Nasser A, et al. Psychopharmacol Bull. 2021;51(2):43-64. Nasser et al. The Efficacy and Safety of SPN-812 (Viloxazine Extended-Release) for the Treatment of ADHD in Children and Adolescents. NEI Virtual Meeting 2021

Viloxazine ER for Adult ADHD



In an adult trial, **viloxazine ER significantly reduced overall ADHD symptoms**, including inattention and hyperactivity/impulsivity, over 6 weeks of treatment compared to placebo.

Nasser A, et al. CNS Drugs. 2022 Jul 27;36(8):897–915.

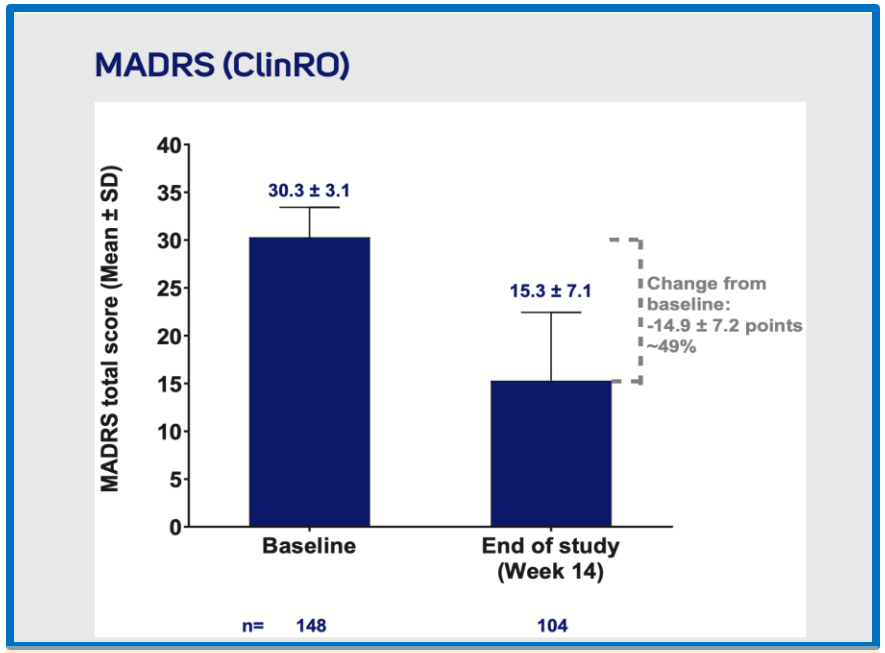
Viloxazine ER for Adults with ADHD and Comorbid Mood and Anxiety Symptoms

All clinician and patient reported outcomes were significant and showed > 50% improvement

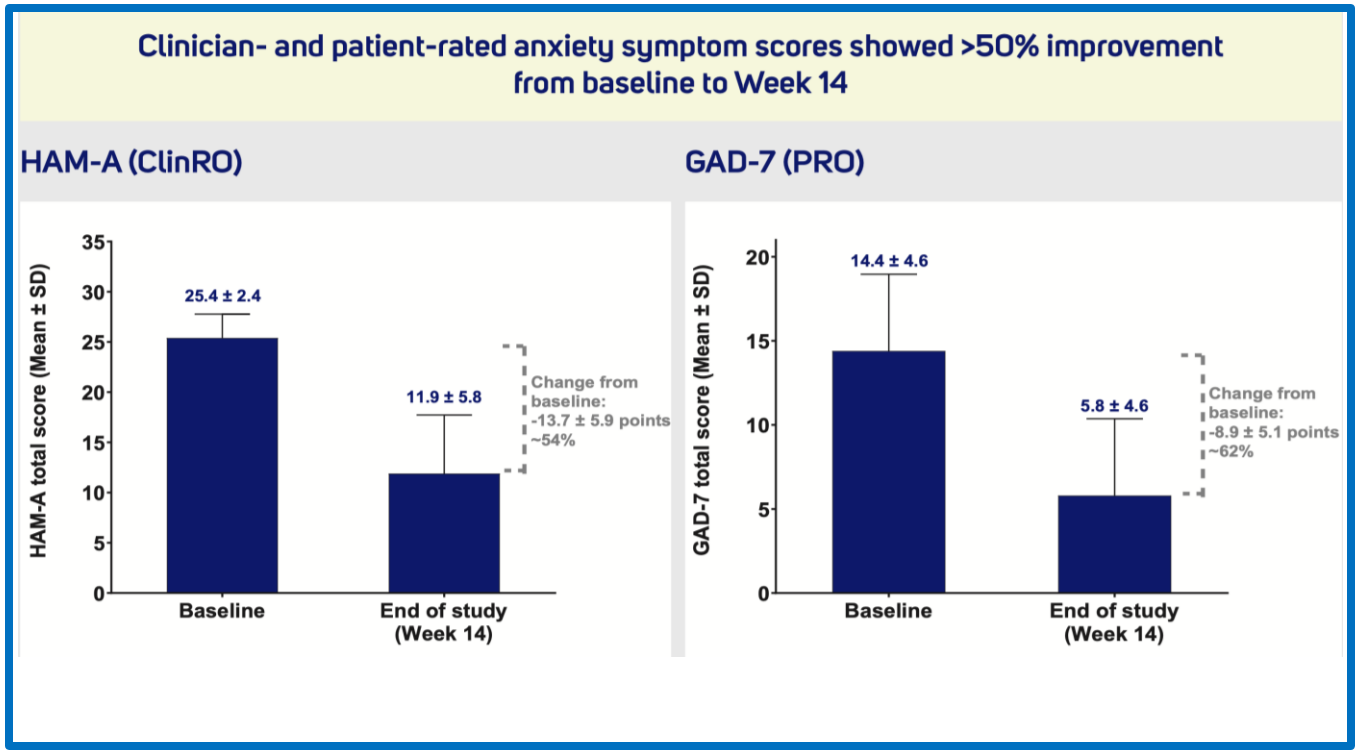
Safety population, N=161	
Age (years), mean ± SD	39.5 ± 10.6
Sex, female	75.2%
Race, white	79.5%
BMI (kg/m^2), mean ± SD	31.7 ± 9.0
College degree (2 or 4 year)	36.0%
Currently employed	72.1%
Married	37.9%
Total AISRS, mean ± SD	37.4 ± 6.5
Total MADRS, mean ± SD	30.3 ± 3.1
Total HAM-A, mean ± SD	25.4 ± 2.3
Total MADRS >22	100%
Total HAM-A >22	99.4%
Total MADRS >22 and HAM-A >22	99.4%

Adler L, Mattingly GW et al. Nevada Psychiatric Association Meeting, Las Vegas, NV, Feb 2025 (Poster)

Viloxazine ER for Depression and Anxiety in ADHD



Clinician-rated depressive symptom scores showed
~49% improvement from baseline to Week 14

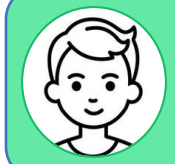


Adler L, Mattingly GW et al. Nevada Psychiatric Association Meeting, Las Vegas, NV, Feb 2025 (Poster)

Viloxazine ER Safety and Tolerability

Across age groups, viloxazine ER was **generally safe** and **well-tolerated**

In children (6-11yo), **55.1%** of participants treated with SPN-812 experienced an AE
- Most common: somnolence, decreased appetite, fatigue, headache, and upper abdominal pain



In adolescents (12-17yo), **56.8%** of participants treated with SPN-812 experience an AE
- Most common: somnolence, fatigue, headache, nausea, and decreased appetite

In adults (18-65yo), **60.3%** of participants randomized to viloxazine ER experienced a TEAE
- Most common: insomnia, fatigue, nausea, decreased appetite, dry mouth, and headache

AE=adverse event; TEAE=treatment-emergent adverse event

Nasser A, et al. Clin Ther. 2021;43(4):684-700; Nasser A, et al. Psychopharmacol Bull. 2021;51(2):43-64; Nasser A, et al. CNS Drugs. 2022 Jul 27;36(8):897–915.

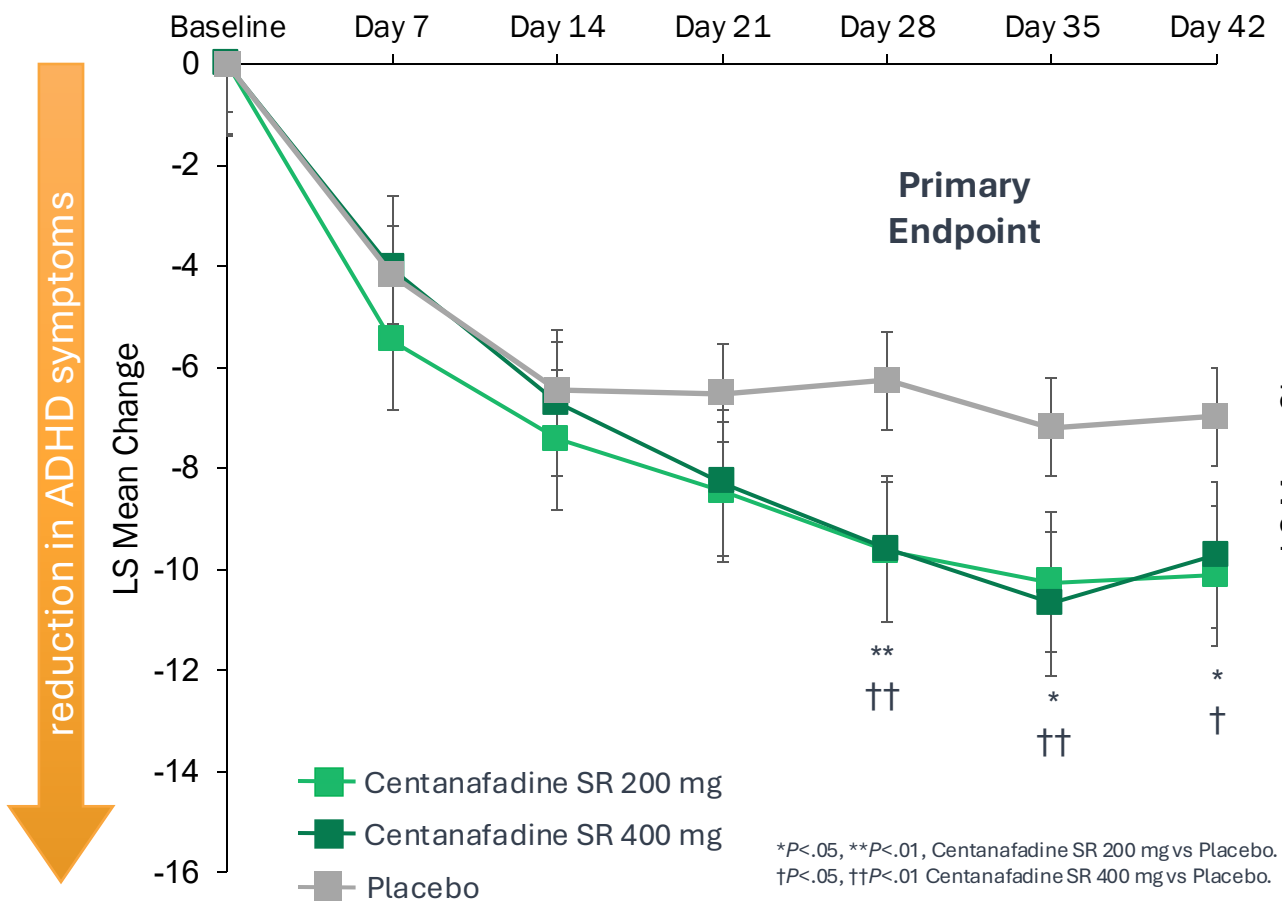
Centanafadine


Emotional dysregulation
Executive dysfunction
Anxiety and depression

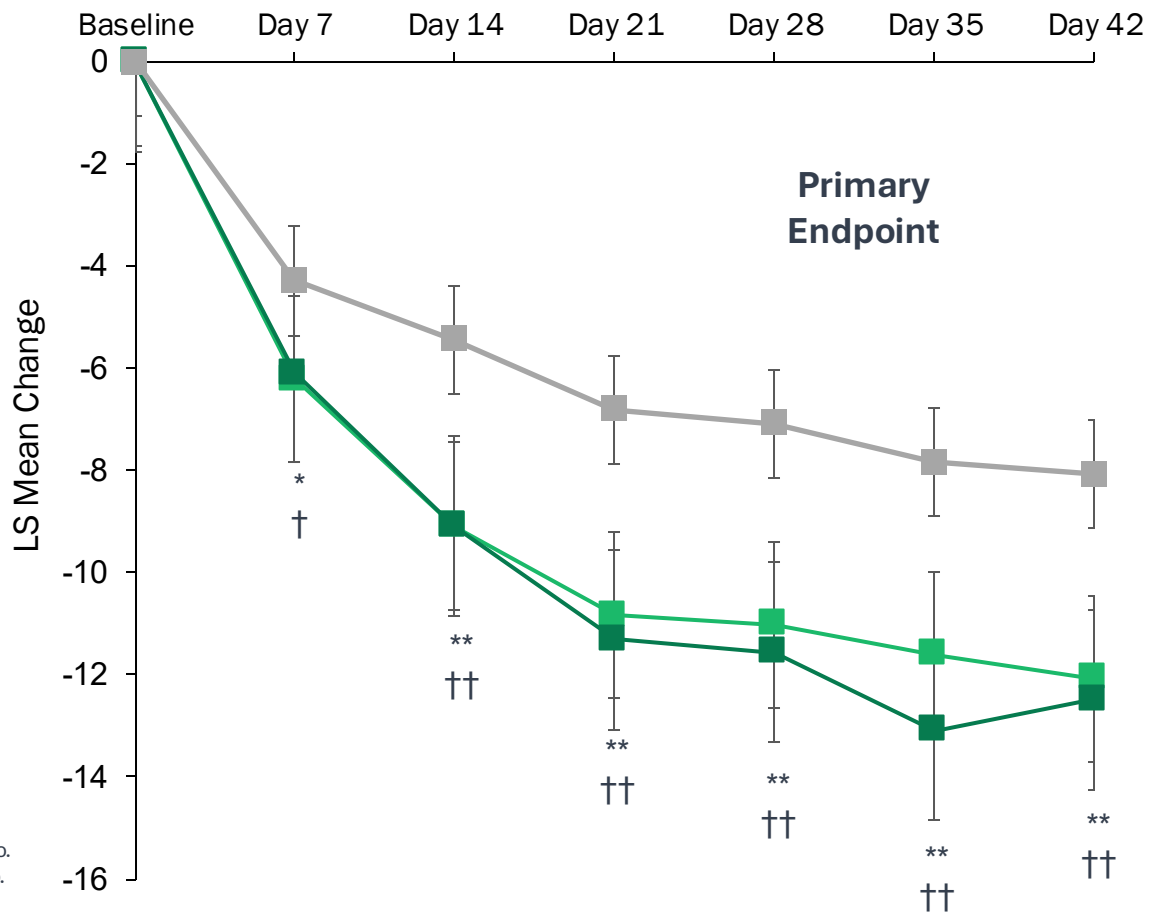
Serotonin

Centanafadine SR (200 and 400mg) Improved ADHD Symptoms in Adults

Study 1



Study 2

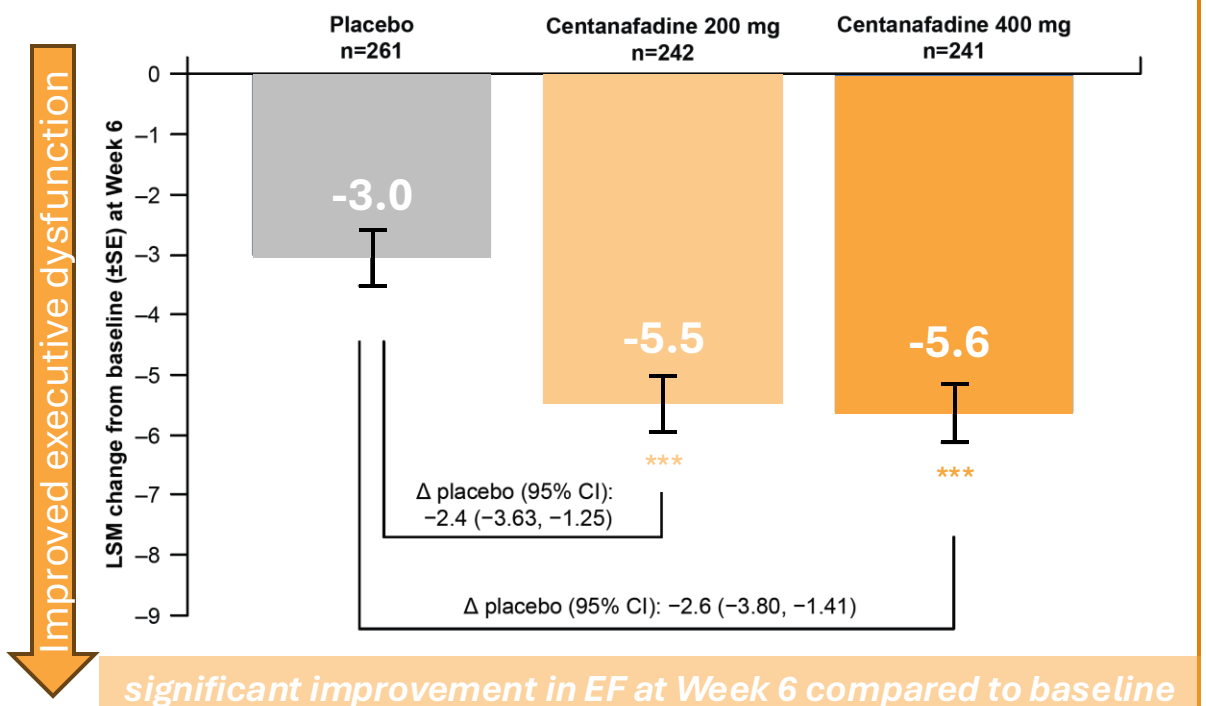


AISRS=ADHD Investigator Symptom Rating Scale; LS=least squares; MMRM=Mixed Models for Repeated Measures; SR=sustained release.
Adler LA, et al. J Clin Psychopharmacol. 2022 Sep-Oct;42(5):429-439.

Post-Hoc Analysis: Centanafadine Improved Executive Dysfunction and Emotional Dysregulation in Adults

Executive Function

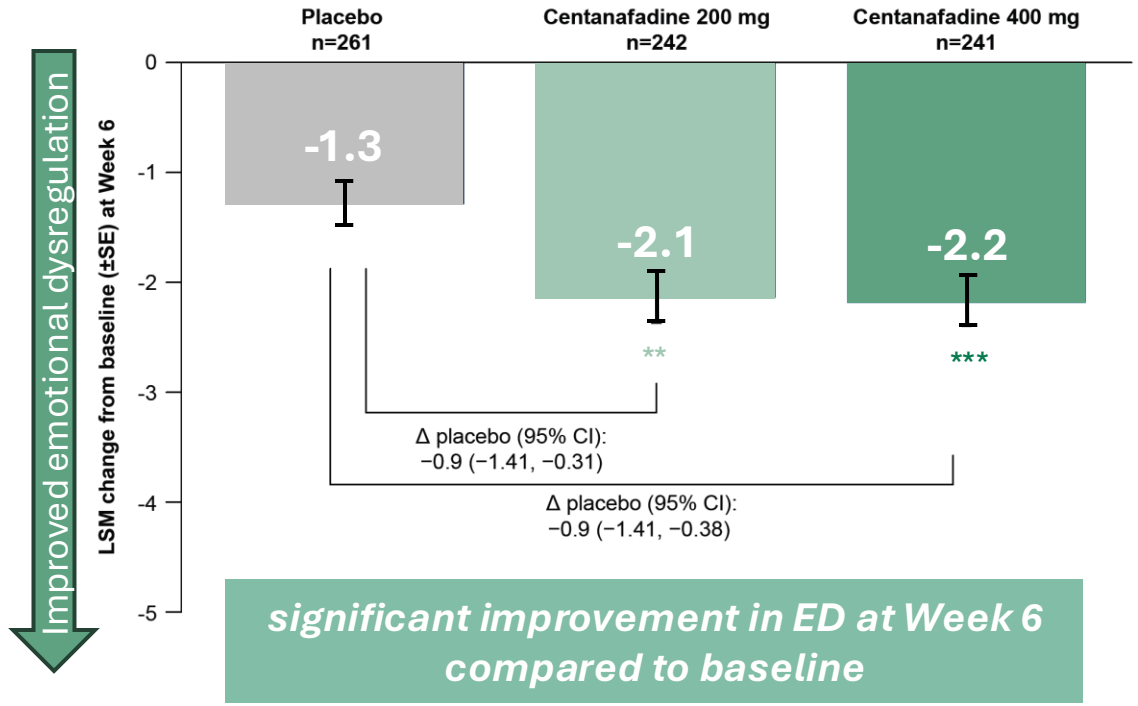
Measured with ASRS Expanded Version Executive Function (EF) subscale



significant improvement in EF at Week 6 compared to baseline

Emotional Dysregulation

Measured with ASRS Expanded Version Emotional Dyscontrol (ED) subscale



significant improvement in ED at Week 6 compared to baseline

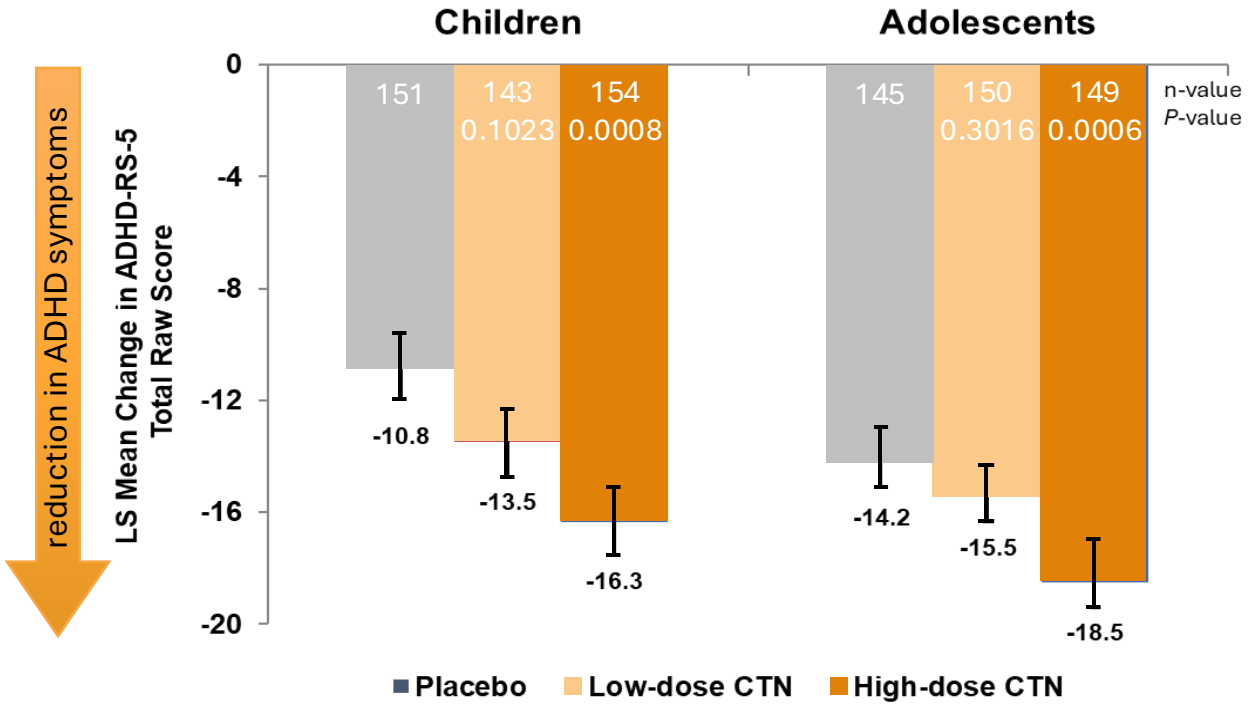
** *P*<0.01, ***P*<0.001 versus placebo. ASRS =adult ADHD Self-Report Scale; CI = confidence interval; LSM = least squares mean; SE = standard error.

Newcorn JH, et al. Poster #1: Emotional dysregulation symptom outcomes in adults with ADHD treated with centanafadine: a pooled post hoc analysis of two phase 3 trials; Poster #2: Executive function symptom outcomes in adults with ADHD treated with centanafadine: a pooled post hoc analysis of two phase 3 trials. Posters presented at: American Society of Clinical Psychopharmacology (ASCP) Annual Meeting; May 26-29, 2026; Miami, FL.

Centanafadine XR in Children and Adolescents

Children: mean change from baseline in ADHD-RS-5 at Week 6 was −16.3 for high-dose CTN versus −10.8 for placebo (*P=0.0008*), with benefit seen as early as Week 1 (*P=0.0009*)

Adolescents: mean change from baseline in ADHD-RS-5 at Week 6 was −18.5 for high-dose CTN versus −14.2 for placebo (*P=0.0006*), with benefit seen as early as Week 1 (*P=0.001*)



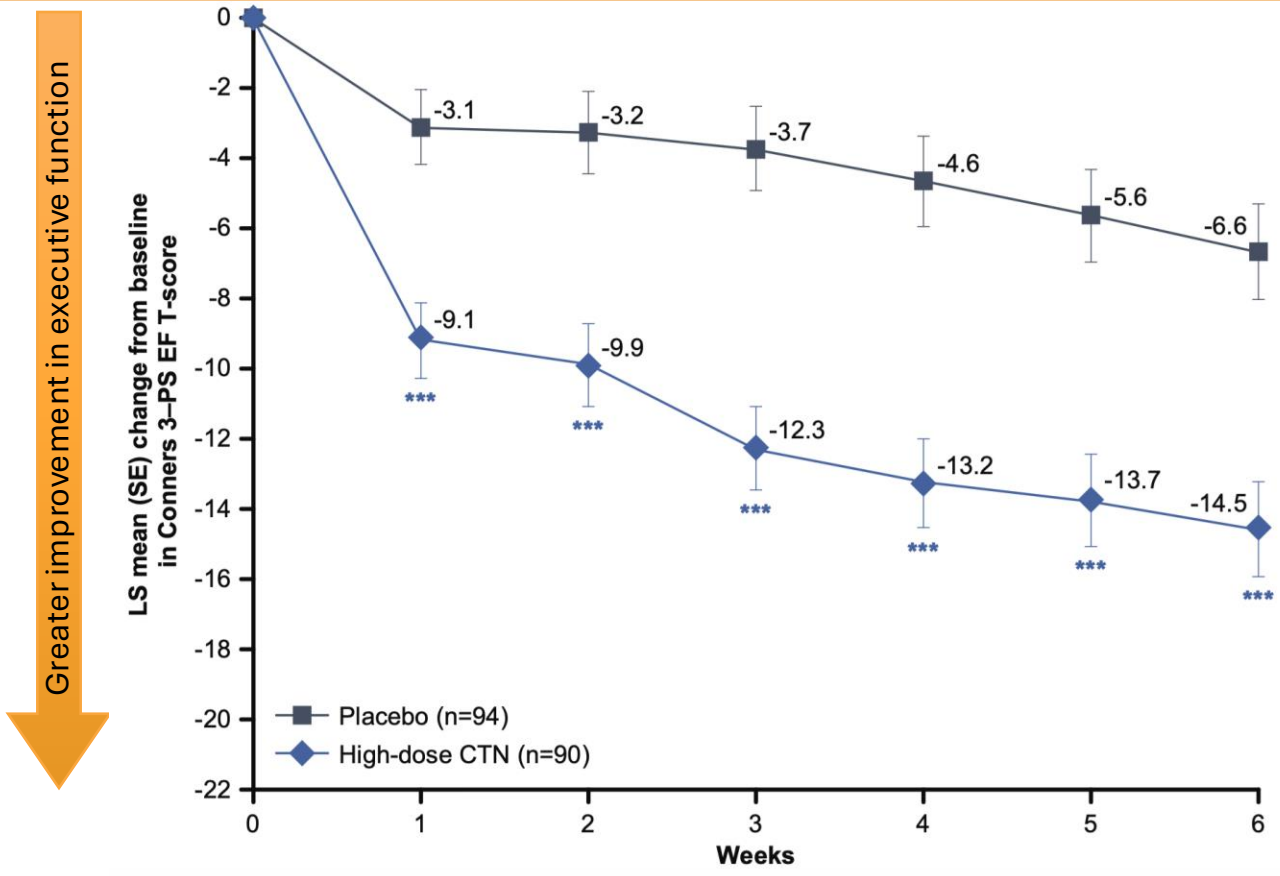
Children (weight-based dosing)
Low Dose: 41.1mg, 82.2 mg,123.3mg, 164.4mg
High Dose: 82.2mg, 164.4mg, 246.6mg, 328.8mg

Adolescents
Low Dose: 164.4mg
High Dose: 328.8mg

Ward et al., Efficacy and Safety of Once-Daily Extended Release Centanafadine for the Treatment of Attention-Deficit/Hyperactivity Disorder in Pediatric Patients. Poster presented at the NEI Congress 2024; November 7-10, 2024 (Colorado Springs, CO)

High-Dose Centanafadine Improved Executive Function in Children and Adolescents with High Baseline Emotional Dysregulation

A post-hoc analysis of data pooled from two phase 3 clinical trials in children (6-12yo) and adolescents (13-17yo) with **ADHD** and **high baseline emotional dysregulation**†



For participants with high baseline emotional dysregulation†:

High-dose CTN produced significantly **greater improvements in parent-rated executive function** compared with placebo at all time points over 6 weeks

† High baseline emotional dysregulation was defined by a baseline Conners 3–PS Defiance/Aggression content scale T-score of ≥70.
***P<0.001

CTN = centanafadine; Conners 3-PS = Conners 3rd Edition-Parent Short; EF = Executive Function.

Ward CL, et al. Efficacy of centanafadine in children and adolescents with ADHD and high baseline emotional dysregulation: post hoc analysis of two phase 3 trials. Poster presented at: American Professional Society of ADHD and Related Disorders (APSARD) Annual Meeting; January 15–18, 2026; San Diego, CA.

Centanafadine Safety and Tolerability

Across age groups, safety and tolerability were **generally favorable**

In children (6-12yo), ~**37%** of participants treated with centanafadine experienced an AE
- Most common: decreased appetite, rash, and vomiting

In adolescents (13-17yo), **~41%** of participants treated with centanafadine experienced an AE
- Most common: decreased appetite, nausea, headache, and rash

In adults (18-55yo), **41.1%** of participants receiving centanafadine experience a TEAE
- Most common: gastrointestinal disorders (diarrhea), dry mouth, nausea, decreased appetite, headache, and insomnia

AE=adverse event; TEAE=treatment-emergent adverse event.

Ward CL, et al. Pediatr Open Sci. 2025;1(3):1-11; Ward CL, et al. J Am Acad Child Adolesc Psychiatry. Published online July 4, 2025; Adler LA, et al. J Clin Psychopharmacol. 2022 Sep-Oct;42(5):429-439.

Optimal Selection and Initiation of Non-Stimulant Pharmacotherapies

Thinking of Reba and Sara:

- **What are the primary symptom targets for Reba and Sara?**
- **Would a non-stimulant medication be a better fit than a conventional stimulant?**
- **If so, which one?**

Key Learning Points

- Conventional stimulant pharmacotherapies remain highly effective for ADHD but may be limited by tolerability concerns, misuse/diversion risk, sleep and appetite effects, or co-occurring psychiatric conditions.
- Non-stimulant pharmacotherapies—including bupropion, atomoxetine, alpha-2 agonists, viloxazine ER, and emerging agents such as centanafadine ER—offer distinct mechanisms of action and may address emotional dysregulation, executive dysfunction, anxiety, and depressive symptoms alongside core ADHD symptoms.
- Optimal selection and initiation of non-stimulant treatments require individualized assessment of symptom profile, comorbidities, functional impairment, prior treatment response, safety considerations, and patient/family preferences.

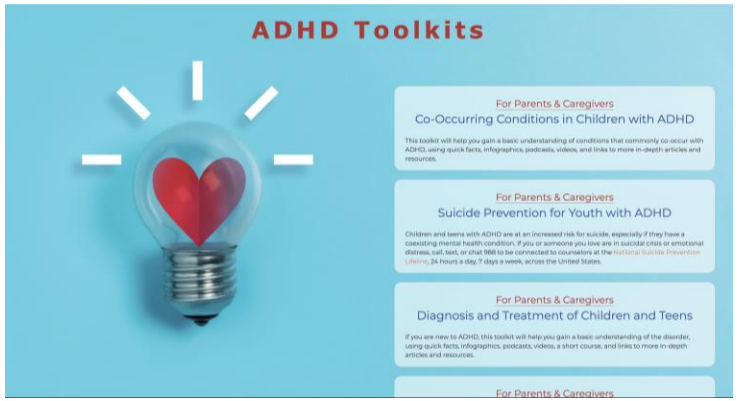
Faculty Panel Discussion: Practical Strategies to Improve Recognition and Treatment of ADHD

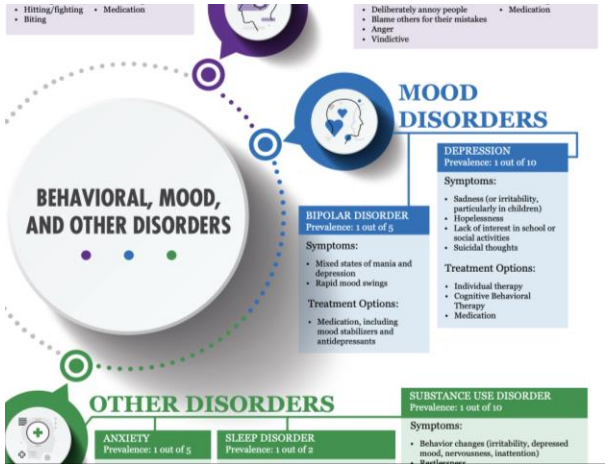
Recognition of Emotional Dysregulation and Executive Dysfunction

Collaboration with Patients and Family Members/Care Partners in Treatment Planning

Developmental and Cultural Contexts

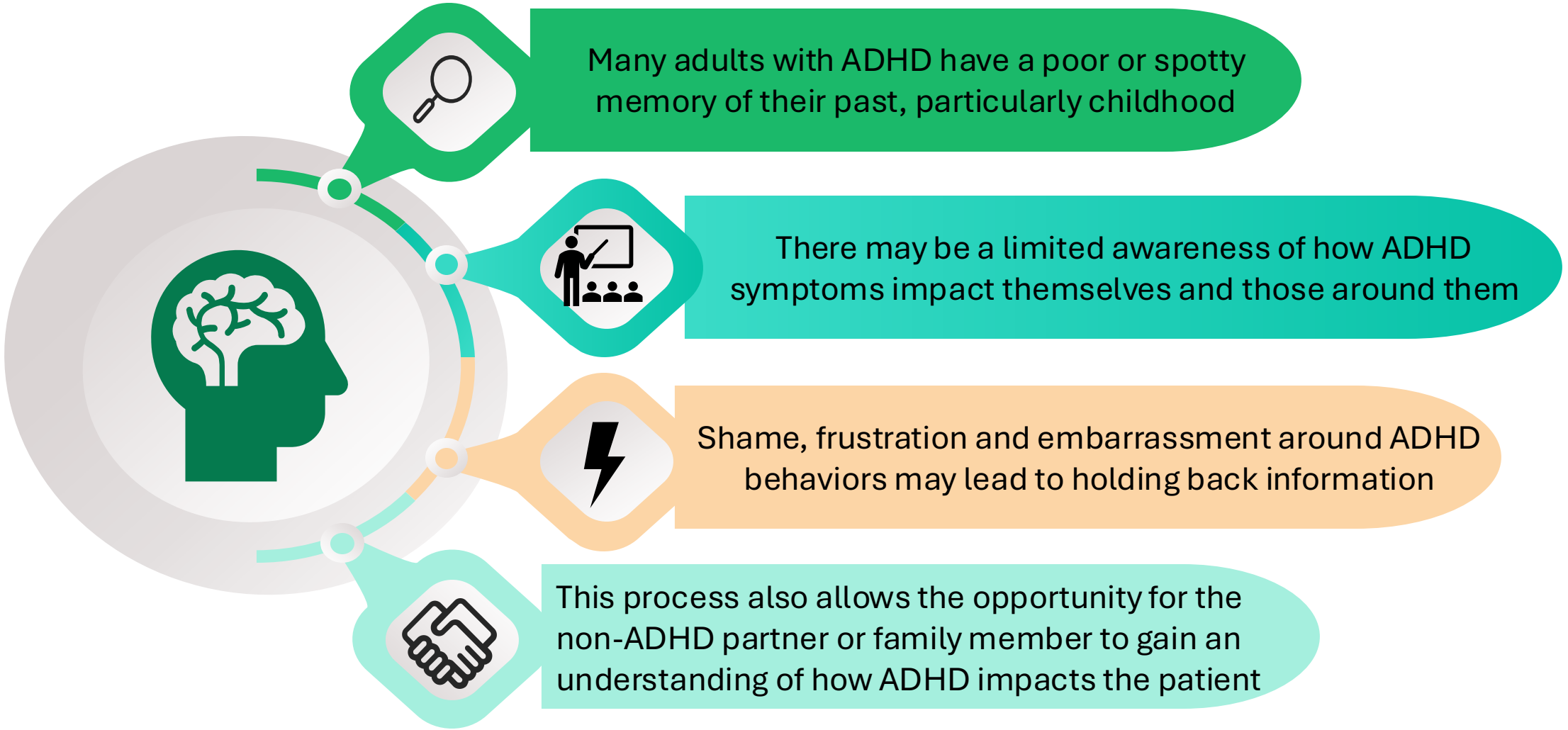
Tools for Recognition of Emotional Dysregulation and Executive Dysfunction





Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). *CHADD*. Accessed May 2026. https://chadd.org/

Collaboration in Diagnosis/Treatment Planning



CHADD. *Diagnosis of ADHD in Adults*. Accessed May 19, 2026. CHADD ADHD Diagnosis Resource. Wolraich, M. & DuPaul, G. (2010). *ADHD diagnosis and management: A practical guide for the clinic and the classroom*. Baltimore, MD: Brooks Publishing.

Cultural Considerations in ADHD Diagnosis and Treatment

ADHD affects children and adults of all ethnicities

- 12% of African American children have been diagnosed with ADHD
- 10% of Latino/Hispanic Children have been diagnosed with ADHD
- 1 in 10 military service members are diagnosed with ADHD.

Cultural beliefs may influence how ADHD sx are perceived and reported

- Expressions of hyperactivity, impulsivity, emotional regulation may vary depending on culture and environment .
- Stigma, language barriers, and health literacy may delay diagnosis and treatment

Shared decision making and culturally responsible communication improves outcomes

- Collateral information from caregivers and patients should be interpreted with cultural humility and awareness of implicit bias
- Cultural norms for academic/work performance, emotional expression, and behaviors should be considered during assessment

Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). *Diversity, Equity, Inclusion, and Belonging*. CHADD website. Accessed May 19, 2026. CHADD Diversity Page

Key Learning Points

- ADHD frequently overlaps with depressive and anxiety disorders, and emotional dysregulation or executive dysfunction may overshadow classic attentional symptoms
- Comprehensive ADHD assessment should include developmental history, functional impairment, contextual factors, comorbidities, and collateral information—not symptom checklists alone.
- Emotional dysregulation and executive dysfunction are highly impairing features of ADHD that significantly affect academic, interpersonal, occupational, and quality-of-life outcomes