

ADHD QUIZ!!!!

The average genetic contribution to adhd is:

80%, 60%, 40%, or 20%

If your child is adhd, the probability you have it is:

70%, 50%, or 20%

The first accurate description of the adhd syndrome was in: 1798, 1842, 1913. 1974

In any given patient, all stimulants (dextroamphetamine or ritalin) are all about equally effective: true or false?

Who refills their adhd med prescriptions the least? Kids, adolescents, college kids, or elderly?

Psychostimulants help non-adhd individuals drive better? True or false?

It is proven that psychostimulants are effective boosters to antidepressants. True or false?

Fidgety Phil (Heinrich Hoffmann 1809–1894)



"Dr. Tuggle's Compound Syrup of Globe Flower"

COCA-COLA

SYRUP * AND * EXTRACT.

For Soda Water and other Carbonated Beverages.

This "INTELLECTUAL BEVERAGE" and TEMPERANCE DRINK contains the valuable TONIC and NERVE STIMULANT properties of the Coca plant and Cola (or Kola) nuts, and makes not only a delicious, exhilarating, refreshing and invigorating Beverage, (dispensed from the soda water fountain or in other carbonated beverages), but a valuable Brain Tonic, and a cure for all nervous affections — SICK HEAD-ACHE, NEURALGIA, HYSTERIA, MELANCHOLY, &c.

The peculiar flavor of COCA-COLA delights every palate; it is dispensed from the soda fountain in same manner as any of the fruit syrups.

J. S. Pemberton;

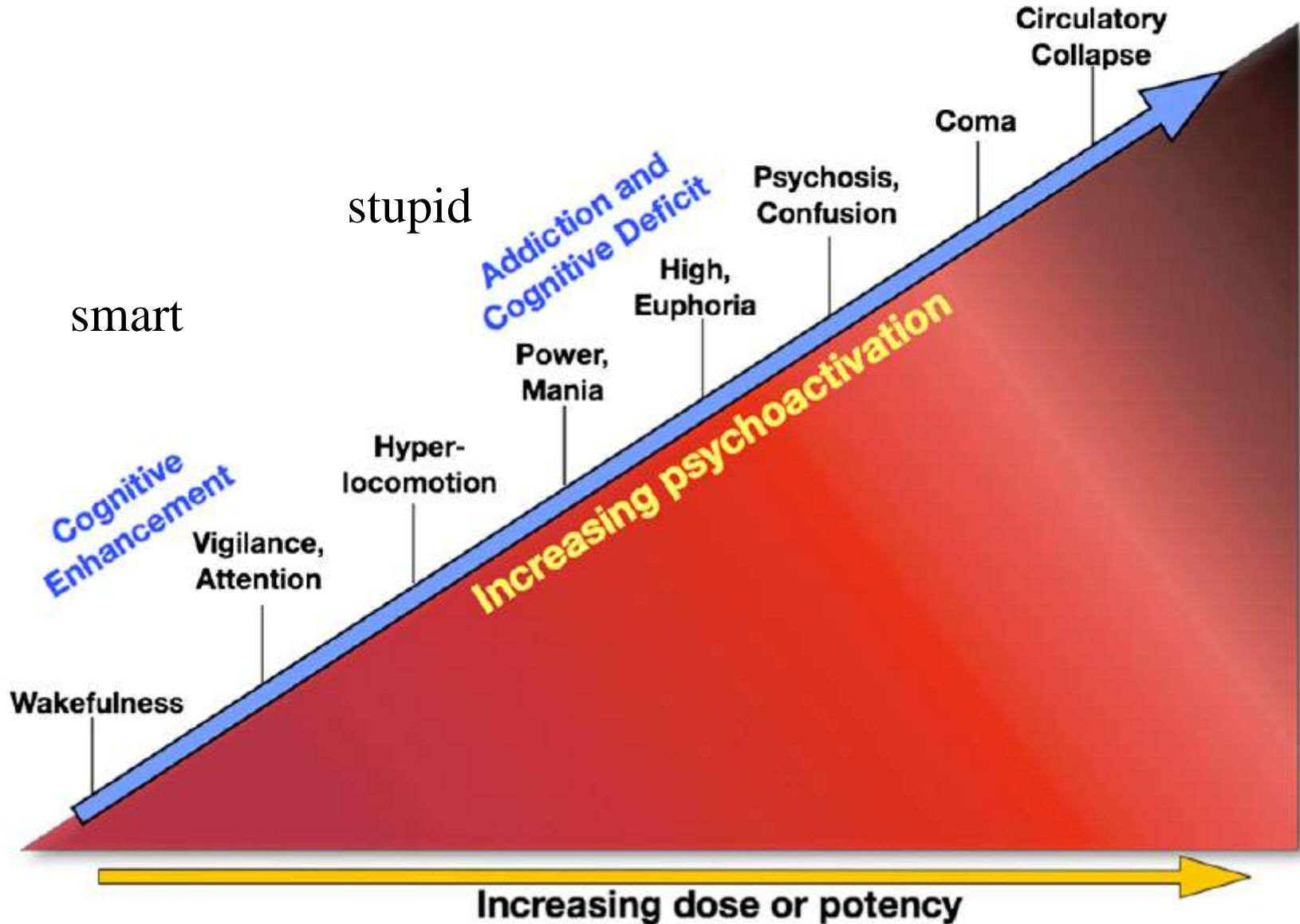
Chemist,

Sole Proprietor, Atlanta, Ga.

Your mission:

- **Early comprehensive screening**
- **You have the tools, don't neuropsych!**
- **Rule out BPD early on; depression, GAD, bipolarity as treatment unfolds**
- **Use rational pharmacotherapy, adjuvants should be rare**
- **Be ready to bounce between compounds based on side effects and response**
- **Learn to refer to key sites, texts, education**

Continuum of Psychostimulant Activation



Do Stimulants Really Make the “Normal” Brain Work Better?

It's easy to imagine the potential advantages if they do—better grades, greater productivity, more creativity

Repeated recent placebo controlled studies in students show students “feel” better in confronting difficult cognitive tasks, but show no difference in capacity or grades

While this may be a questionable benefit, it also advances the concept of doing “stupid things faster” rather than enhancing function

The questions clinicians want answered:

- How do I diagnose adult ADHD in the outpatient setting?
 - Highest specificity in particular
- How do I decide on which stimulant or non-stimulant to use and at what doses?
- How to deal with co-morbid substance use?
- How do I deal with the comorbidity as regards:
 - What do I treat first?
 - Contraindications to stimulant use?

DSM-5 Criteria for ADHD: Hyperactive/Impulsive Symptoms (6/9 age <17 years; 5/9 ≥17 years)



American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Arlington, VA: American Psychiatric Association; 2013.

1-DAY Health Care REGIONAL MEETINGS

DOMAINS OF EXECUTIVE FUNCTIONING

These clusters operate in an integrated way. ADHD patients tend to have impairments in at least some aspects of each cluster:

ACTIVATION

Organizing
Prioritizing
Initiating

FOCUS

Focus
Sustaining and changing tasks

ACTION

Monitoring self-control
Regulating action

EFFORT

Alertness
Sustaining effort and processing

MEMORY

Working memory
Information recall

EMOTION

Managing frustration
Controlling emotions

Adapted from: Brown, T. E. Yale University press health & wellness: Attention deficit disorder: The unfocused mind in children and adults. New Haven, CT, US: Yale University Press; 2005.

VIEWS

DSM-5 Criteria for ADHD: Inattentive Symptoms (6/9 age <17 years; 5/9 ≥17 years)



American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Arlington, VA: American Psychiatric Association; 2013.

1-DAY Health Care REGIONAL MEETINGS

ADHD: An Enormously Common and Impairing Disorder

Prevalence 18- to 44-year-olds: 4.4%

Percentage of adults with ADHD who received treatment within the previous 12 months: 11%

High degree of psychiatric comorbidities, eg, major depression, anxiety disorders, bipolar disorder, SUD, etc

Impairment in multiple domains (home, social, school, work)

Chronic course

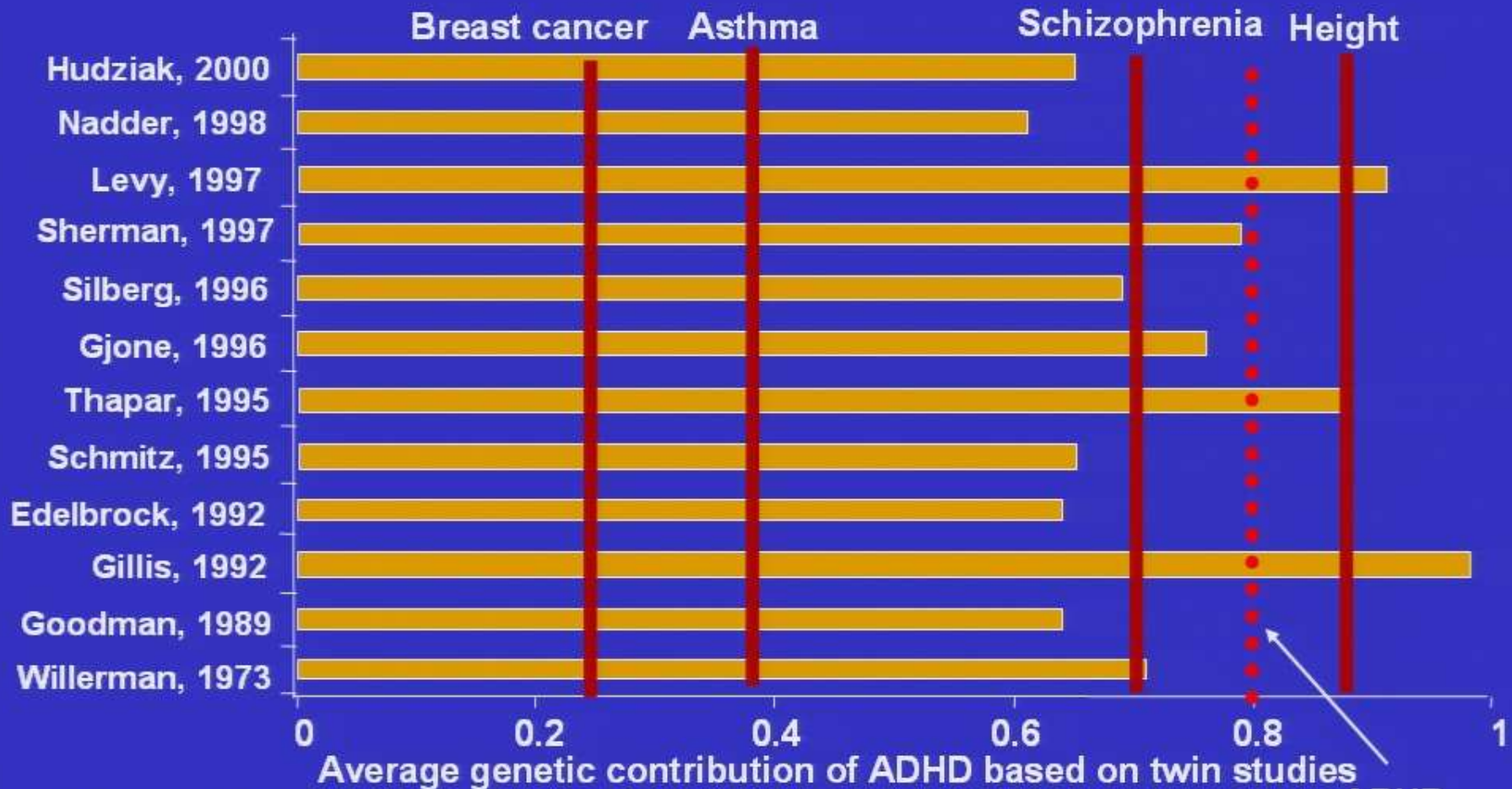
~75% persistence from childhood into adolescence

~50% persistence from childhood into adulthood

SUD = substance use disorder.

Froehlich TE, et al. *Arch Pediatr Adolesc Med.* 2007;161(9):857-864. Kessler RC, et al. *Am J Psychiatry.* 2006;163(4):716-723. Wilens TE, et al. *Postgrad Med.* 2010;122(5):97-109.

Twin Studies Show ADHD Is a Genetic Disorder



Faraone. *J Am Acad Child Adolesc Psychiatry*. 2000;39:1455-1457.

Hemminki. *Mutat Res*. 2001;25:11-21.

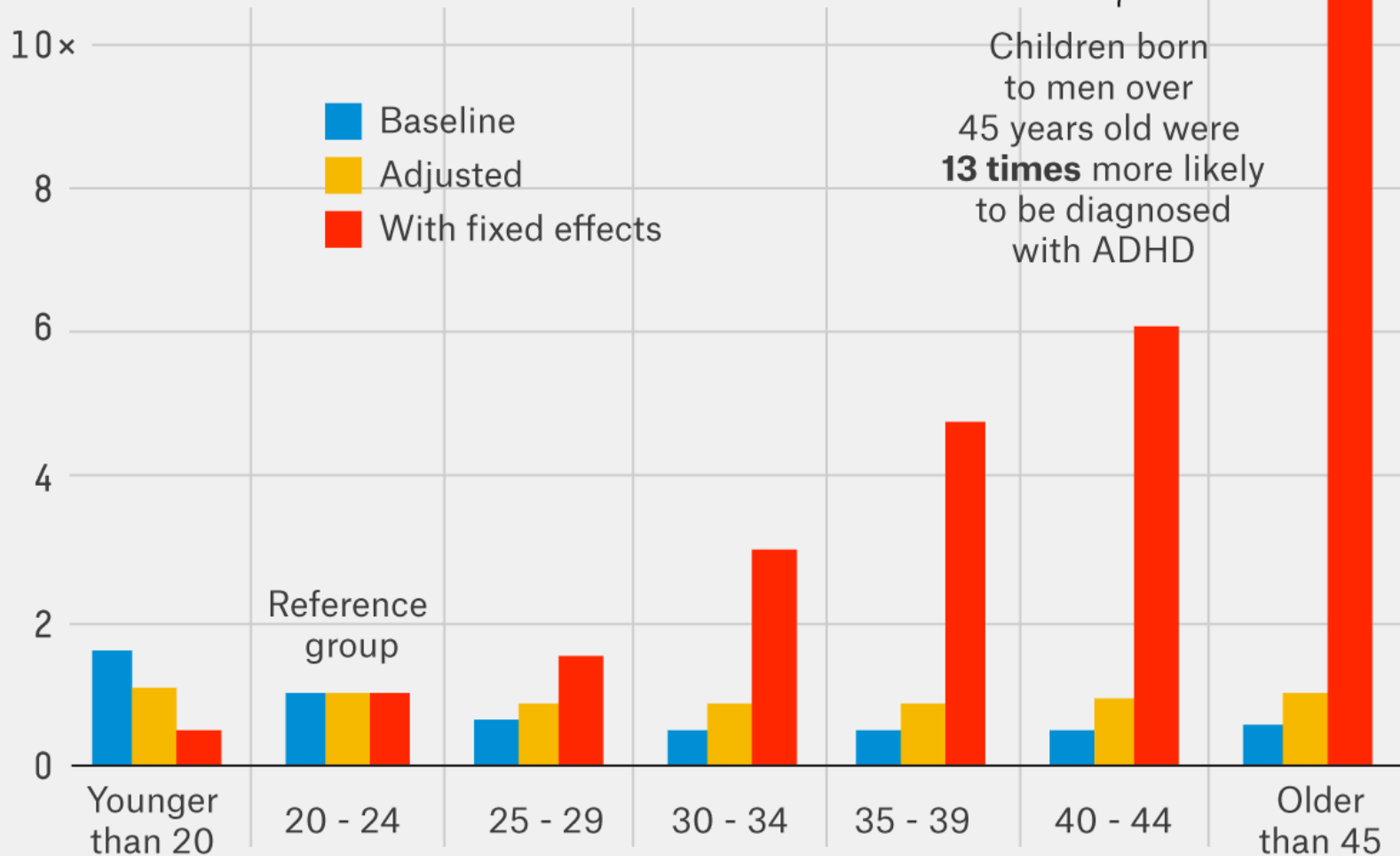
Palmer. *Eur Resp J*. 2001;17:696-702.

Issue of heritability vital in interview:

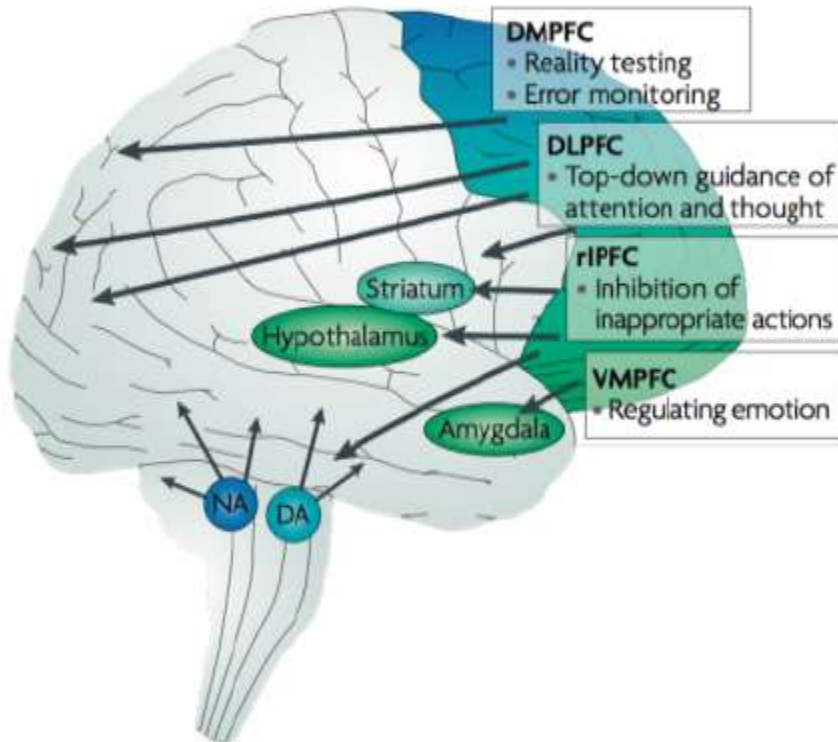
- If you are ADHD, each of your parents has a 30% odds of having suffering from it
- If your child is ADHD, you have a 50% probability of having silently suffered from it

Likelihood of Child's ADHD Diagnosis

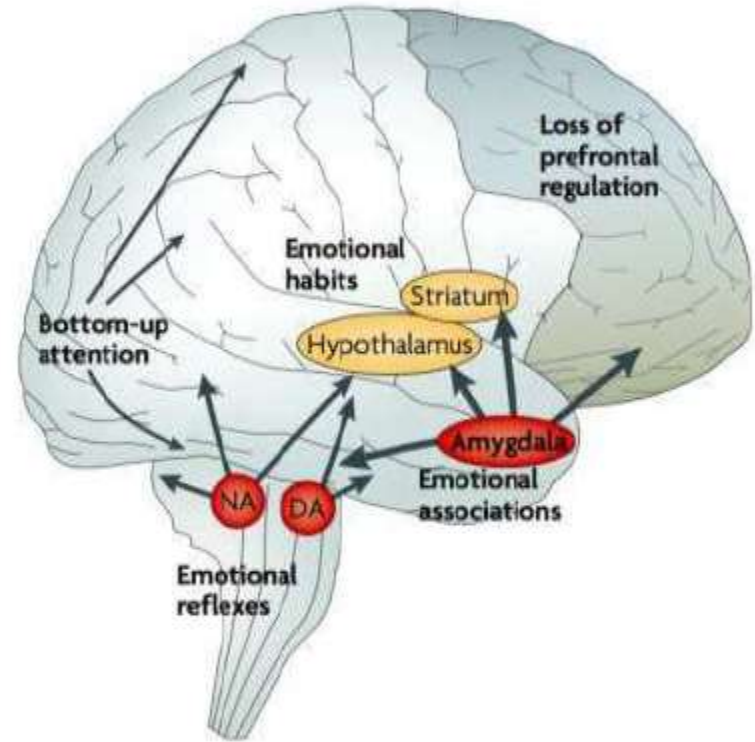
By paternal age group, based on longitudinal study of Swedish men



Examining the Cognitive and Emotional Dysregulation Pathways in Adults with ADHD (Stressed vs Non-Stressed Situations)



Prefrontal Regulation during Alert, Non-Stress Conditions



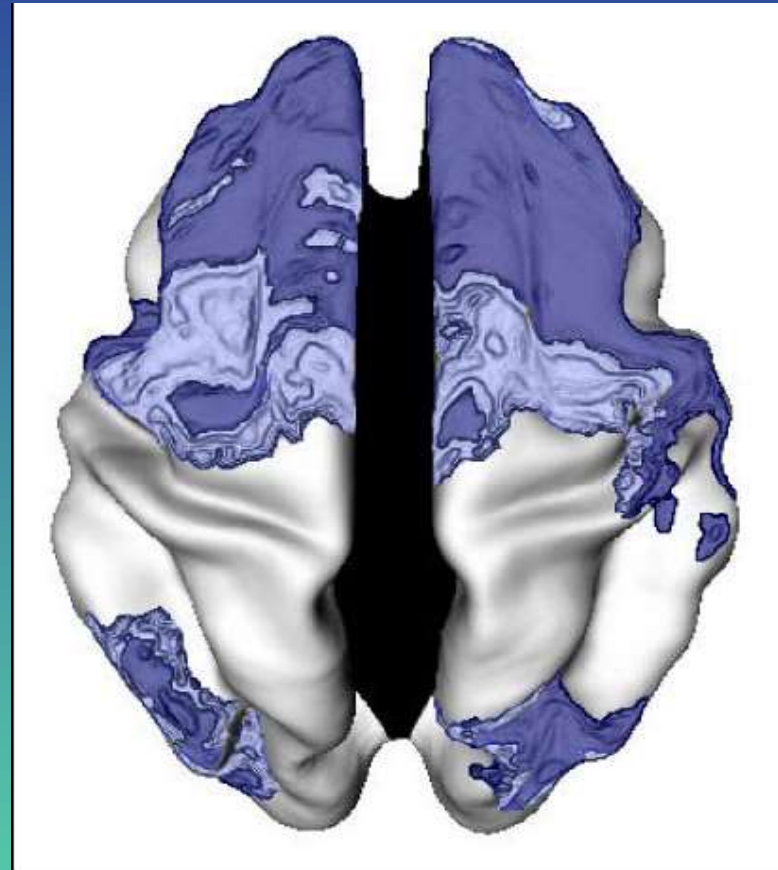
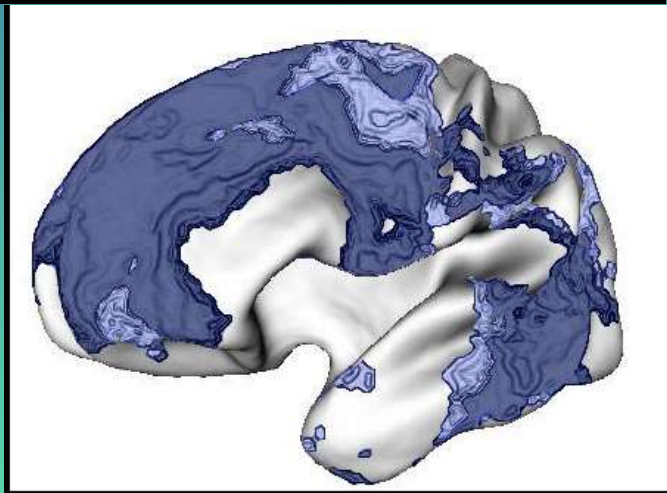
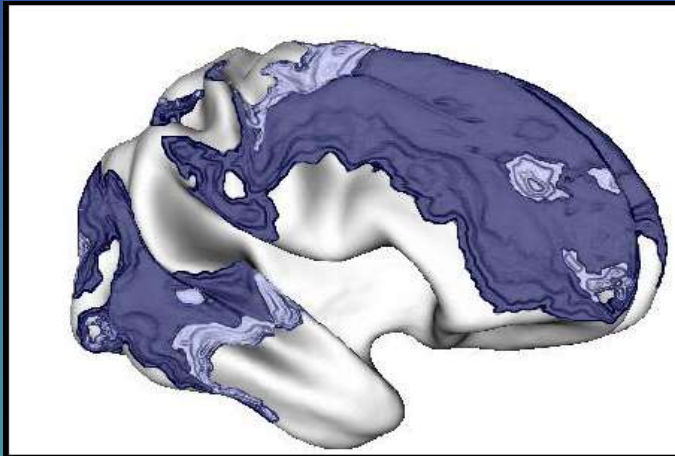
Amygdala Control during Stress Conditions

DMPFC = dorsal medial prefrontal cortex; DLPFC = dorsal lateral prefrontal cortex; rIFFC = rostral lateral prefrontal cortex; VMPFC = ventral medial prefrontal cortex; NA = noradrenaline; DA = dopamine.

Arnsten AF. *Nat Rev Neurosci.* 2009;10(6):410-422.

Delayed brain growth in ADHD (3 yrs.)

From Shaw, P. et al. (2007). ADHD is characterized by a delay in cortical maturation. *Proceedings of the National Academy of Sciences*, 104, 19649-19654.



Greater than 2 years' delay
0 to 2 years delay

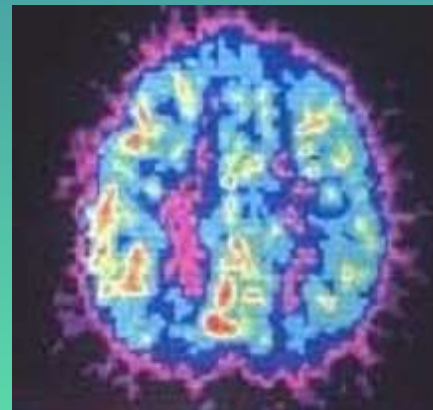
Ns: ADHD=223; Controls = 223

Cerebral Glucose Metabolism in Adults with Hyperactivity of Childhood Onset

- Global and regional glucose metabolism by PET scan reduced in adults who have been hyperactive since childhood
- Largest reductions in:
 - Premotor cortex
 - Superior prefrontal cortex

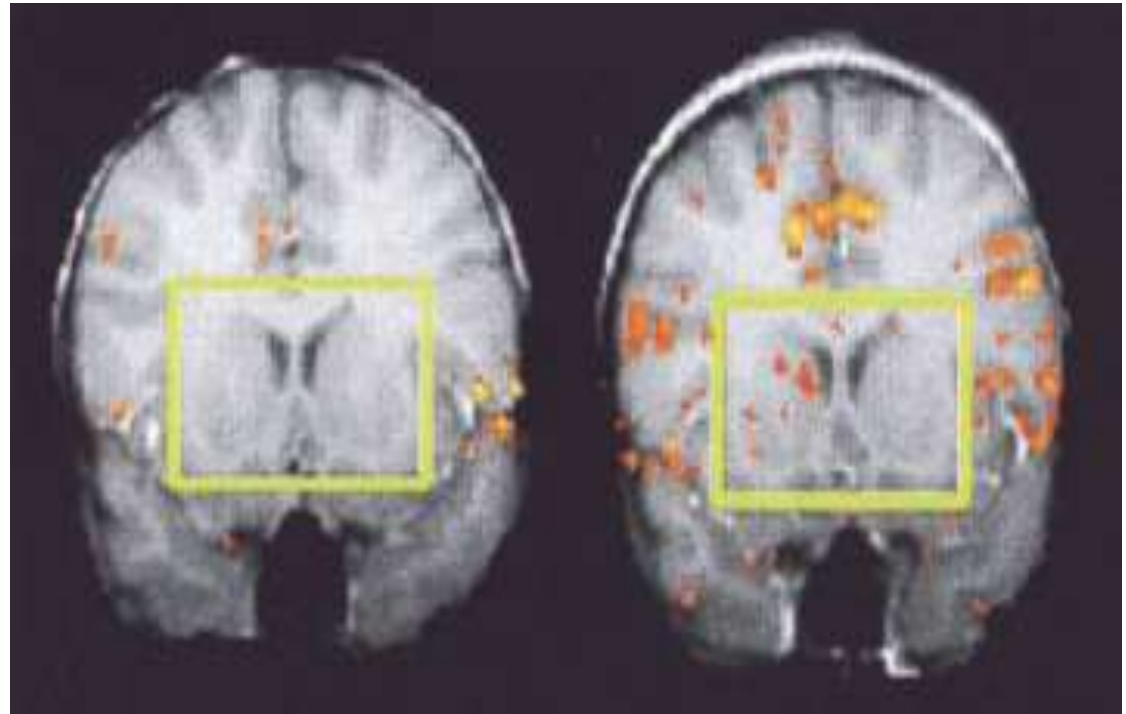


Normal



With ADHD

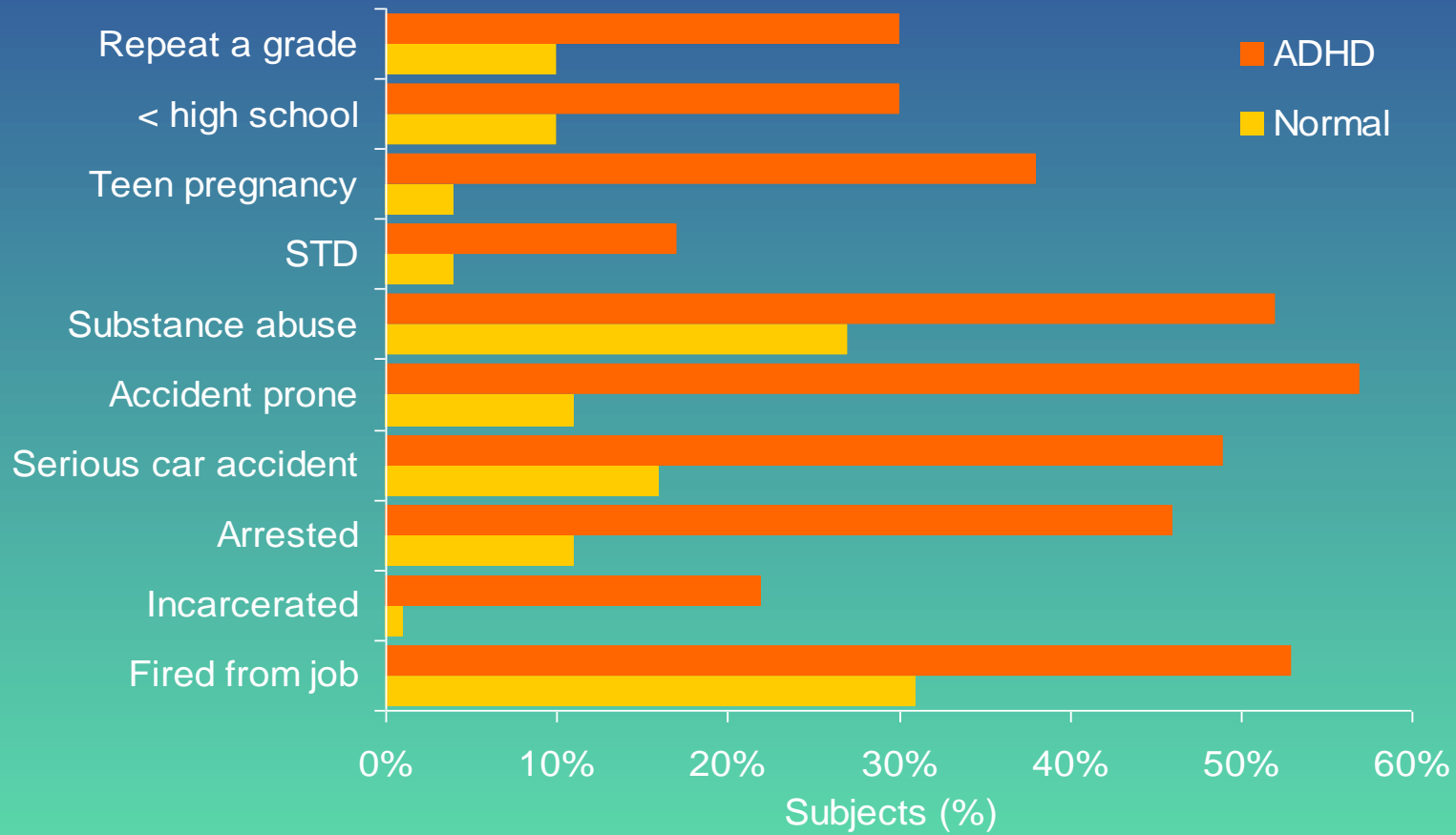
STIMULANTS
AFFECT
UNDERACTIVE
AREAS



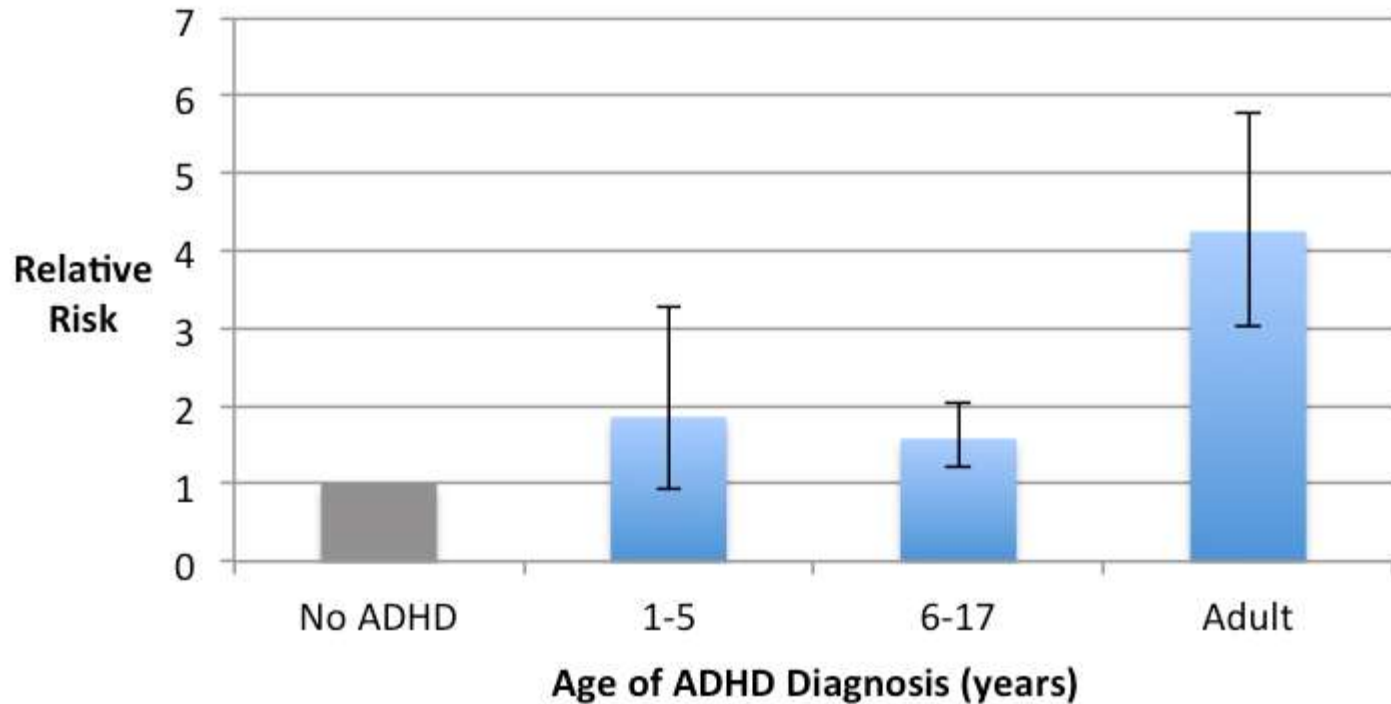
Setting us straight

- **ADHD is a developmental neurobehavioral disorder with biopsychosocial risk factors**
 - **Maternal-fetal variables such as smoking, alcoholism, obstetrical complications, low birth weight**
 - **Psychological variables such as abuse, deprivation, co-morbid mental health disorders**
 - **Genetic loci: dopamine receptor polymorphisms, dopamine reuptake protein**
 - **Strong neuroimaging correlates to all the above**

Functional Impairment in Patients with ADHD Compared to Those Without



Relative Risk of Death over Follow-up by Age of ADHD Dx



The increased risk of death for persons diagnosed with ADHD averaged 70% for death by natural causes and 140% for death by unnatural causes of death (mostly accidents)

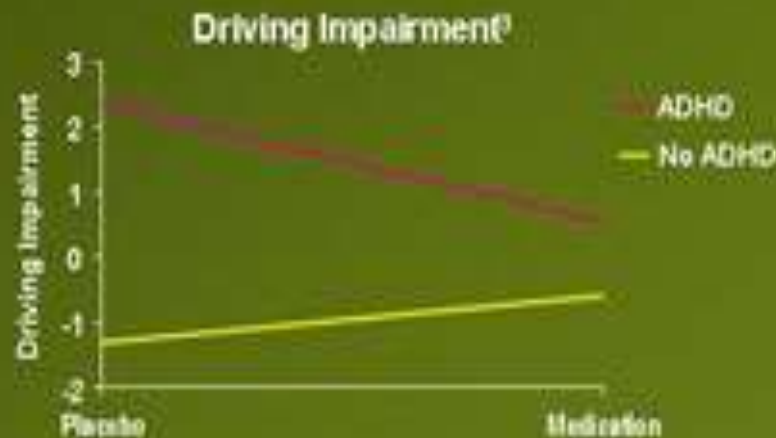
SLIDE 4

Common Comorbid Psychiatric Disturbances in Adolescents with ADHD¹²⁻¹⁷

<u>Comorbidity</u>	<u>Prevalence Among Adolescents with ADHD</u>	<u>Prevalence in General Adolescent Population</u>
Academic impairment	20–60%	5–15%
Major depressive disorder	9–32% (average 25%)	3–5%
Anxiety disorders	10–40% (average 25%)	3–10%
Conduct disorder	20–56%	Unknown
Oppositional defiant disorder	20–67% (average 35%)	2–16% (average 7–8%)
Bipolar disorder	~6–10%	3–4%

ADHD=attention-deficit/hyperactivity disorder.

Example: ADHD and Driving



1. Fried R et al. *J Clin Psychiatry*. 2006;67:567-574. 2. Barkley RA et al. *J Int Neuropsychol Soc*. 2002;8:655-672. 3. Cox DJ et al. *J Nerv Ment Dis*. 2000;188:230-234.

JAMA Psychiatry | [Original Investigation](#)

Association Between Medication Use for Attention-Deficit/ Hyperactivity Disorder and Risk of Motor Vehicle Crashes

Zheng Chang, PhD, MSc; Patrick D. Quinn, PhD; Kwan Hur, PhD; Robert D. Gibbons, PhD; Arvid Sjolander, PhD;
Henrik Larsson, PhD; Brian M. D'Onofrio, PhD

CONCLUSIONS AND RELEVANCE Among patients with ADHD, rates of MVCs were lower during periods when they received ADHD medication. Considering the high prevalence of ADHD and its association with MVCs, these findings warrant attention to this prevalent and preventable cause of mortality and morbidity.

Adult ADHD and Car Accidents: What is Known about the Disorder's Impact, and Its Treatment's Impact on Outcomes

OBJECTIVES To estimate the association between ADHD and the risk of serious transport accidents and to explore the extent to which ADHD medication influences this risk among patients with ADHD.

DESIGN, SETTING, AND PARTICIPANTS In total, 17 408 patients with a diagnosis of ADHD were observed from January 1, 2006, through December 31, 2009, for serious transport accidents documented in Swedish national registers. The association between ADHD and accidents was estimated with Cox proportional hazards regression. To study the effect of ADHD medication,

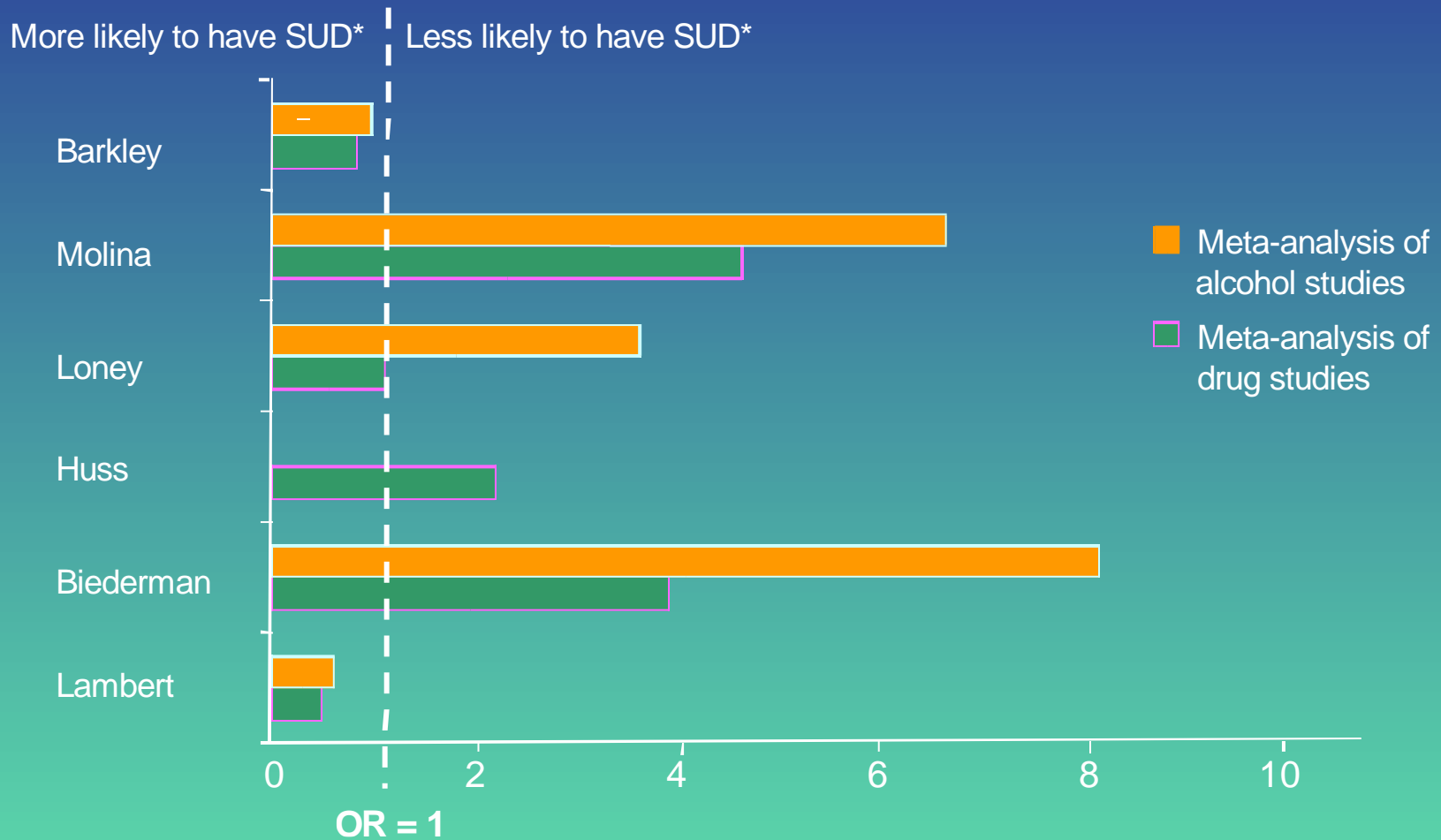
Relevant Points

- Males with ADHD had a 1.47 hazard ratio of serious car accidents
- Females had a hazard ratio of 1.45 of serious car accidents
- In males, taking medications for ADHD lead to a 58% risk reduction (in females it was statistically insignificant)

attributable fractions suggested that 47% to 49% of the accidents in male patients with ADHD could have been avoided if they had been receiving treatment during the entire follow-up.

CONCLUSIONS AND RELEVANCE Attention-deficit/hyperactivity disorder is associated with an increased risk of serious transport accidents, and this risk seems to be possibly reduced by ADHD medication, at least among male patients. This should lead to increased awareness among clinicians and patients of the association between serious transport accidents and ADHD medication.

Impact of ADHD Pharmacotherapy on Later Substance Use Disorders



SUD = substance use disorder
*Compared to unmedicated youth with ADHD

A systematic review and analysis of long-term outcomes in attention deficit hyperactivity disorder: effects of treatment and non-treatment

Monica Shaw^{1†}, Paul Hodgkins^{2*†}, Hervé Caci³, Susan Young⁴, Jennifer Kahle⁵, Alisa G Woods⁶ and L Eugene Arnold⁷

Treatment Benefit by Outcome Group compared with untreated ADHD

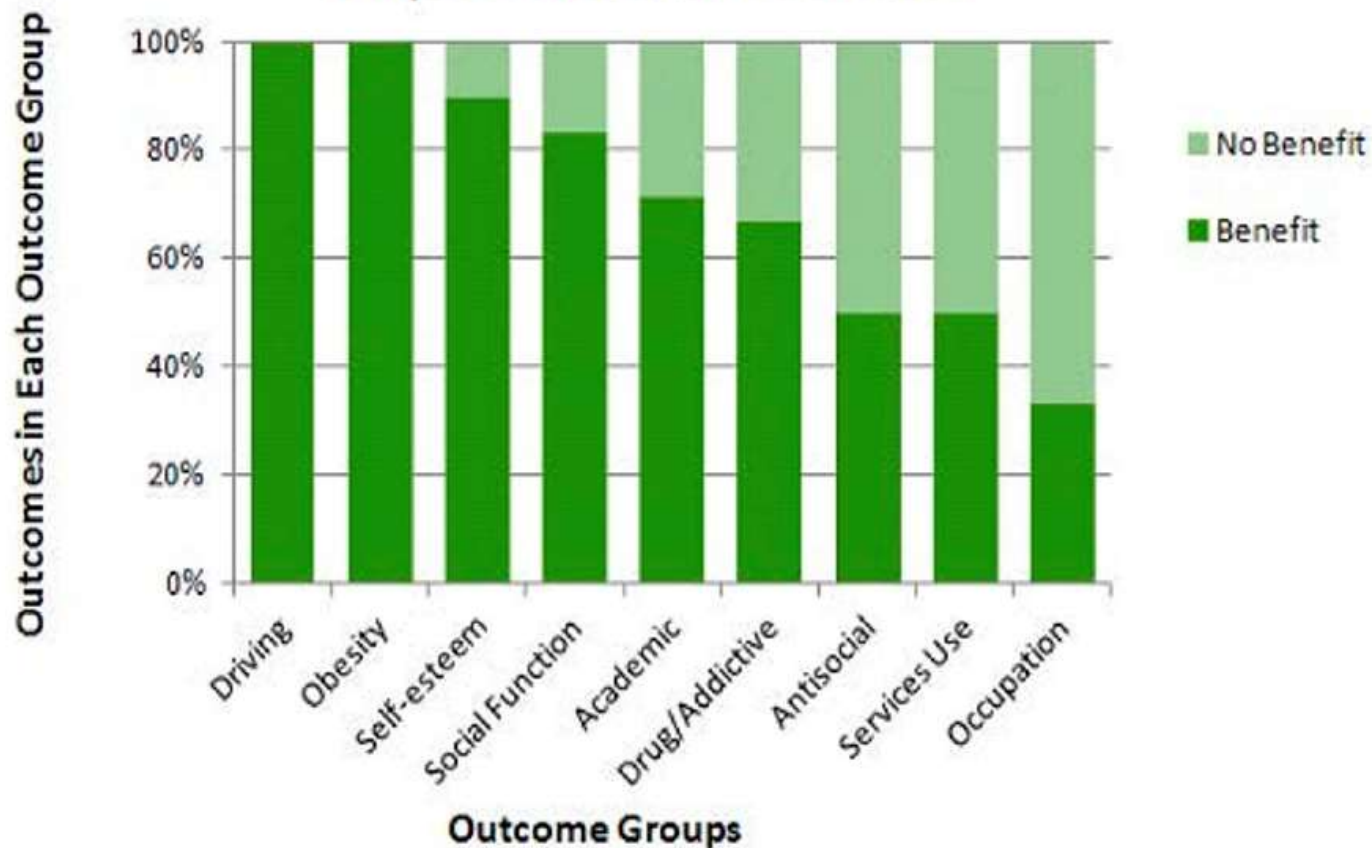


Figure 6 Benefit and no benefit with treatment by outcome group. This graph shows benefit (dark green bars) or no benefit (light green bars) by outcome group in treated participants with attention deficit hyperactivity disorder (ADHD) versus untreated ADHD. Improvement was reported most often in studies of driving and obesity outcomes (left side), with a greater proportion of outcomes reported to exhibit no benefit following treatment compared with no treatment in studies of occupation (right side). An intermediate proportion of studies of self-esteem, social function, academic, drug use/addictive behavior, antisocial behavior, and services use outcomes reported benefit with treatment.

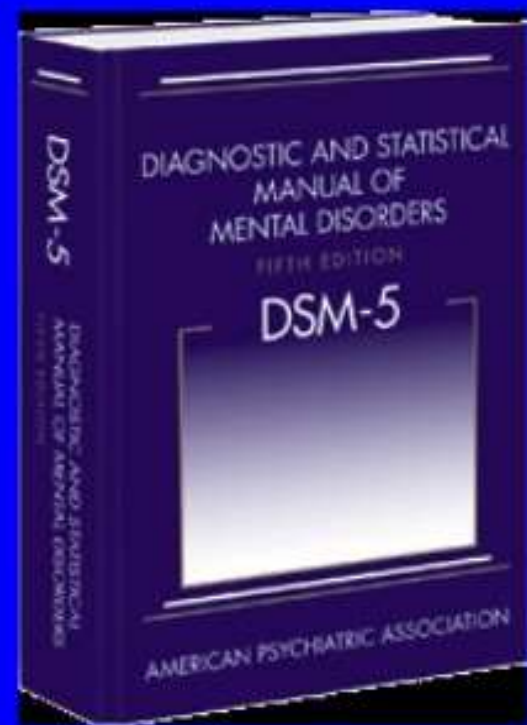
Childhood Attention-Deficit/Hyperactivity Disorder and the Emergence of Personality Disorders in Adolescence: A Prospective Follow-Up Study

- **Individuals diagnosed with childhood ADHD are at increased risk for personality disorders in late adolescence, specifically borderline (OR = 13.16), antisocial (OR = 3.03), avoidant (OR = 9.77), and narcissistic (OR = 8.69) personality disorders.**
- **Those with persistent ADHD were at higher risk for antisocial (OR = 5.26) and paranoid (OR = 8.47) personality disorders but not the other personality disorders when compared to those in whom ADHD remitted.**

Adult Adhd: presentation, diagnosis, differential

DSM-V Revisions to ADHD

- Same criteria as DSM-IV
- Onset before age 12 (age 7 in DSM-IV)
- 5 symptom criteria in adults (6 in DSM-IV)
- Removed autism-spectrum d/o from excluders
- Elaborated ADHD criteria descriptions (more examples for adults)



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Am J Psychiatry. 2015 October 1; 172(10): 967–977. doi:10.1176/appi.ajp.2015.14101266.

Is adult ADHD a childhood-onset neurodevelopmental disorder? Evidence from a 4-decade longitudinal cohort study

**Terrie E. Moffitt, PhD^{1,2,3,4}, Renate Houts, PhD¹, Philip Asherson, MD⁴, Daniel W Belsky^{1,9},
David L Corcoran³, Maggie Hammerle¹, Honalee Harrington, BA¹, Sean Hogan, MSW⁵,
Madeline Meier, PhD⁶, Guilherme V. Polanczyk, MD⁷, Richie Poulton, PhD⁵, Sandhya**

and treatment contact. Unexpectedly, the childhood-ADHD and adult-ADHD groups comprised virtually non-overlapping sets; 90% of adult-ADHD cases lacked a history of childhood ADHD. Also unexpectedly, the adult-ADHD group did not show tested neuropsychological deficits in childhood or adulthood, nor did they show polygenic risk for childhood ADHD.

Conclusion—Findings raise the possibility that adults presenting with the ADHD symptom picture may not have a childhood-onset neurodevelopmental disorder. If this finding is replicated, then the disorder's place in the classification system must be reconsidered, and research must investigate the etiology of adult ADHD.

Original Investigation

Attention-Deficit/Hyperactivity Disorder Trajectories From Childhood to Young Adulthood

Evidence From a Birth Cohort Supporting a Late-onset Syndrome

CONCLUSIONS AND RELEVANCE The findings of this study do not support the assumption that adulthood ADHD is necessarily a continuation of childhood ADHD. Rather, they suggest the existence of 2 syndromes that have distinct developmental trajectories.

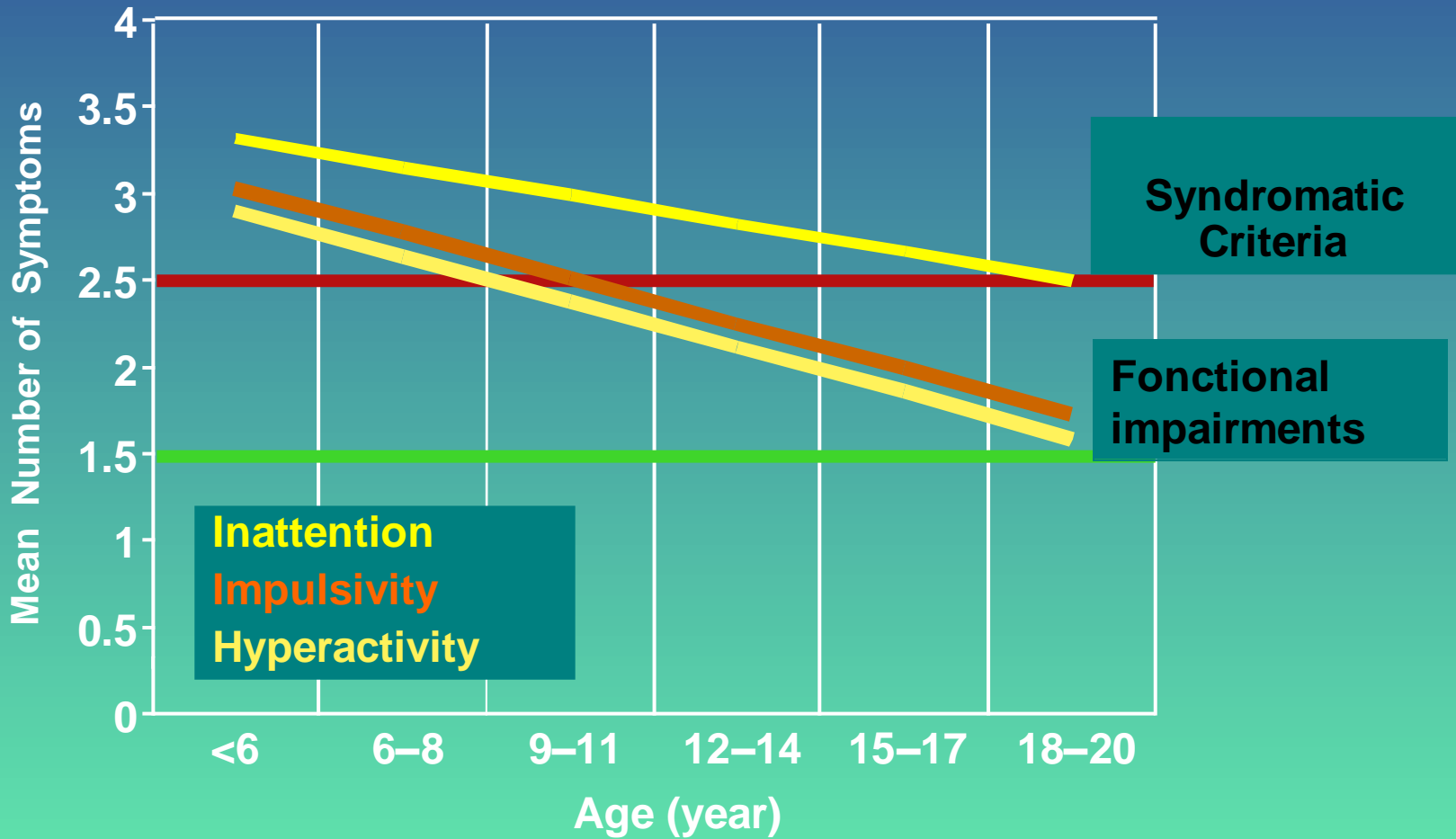
Original Investigation

Evaluation of the Persistence, Remission, and Emergence of Attention-Deficit/Hyperactivity Disorder in Young Adulthood

Jessica C. Agnew-Blais, ScD; Guilherme V. Polanczyk, MD, PhD; Andrea Danese, MD, PhD;
Jasmin Wertz, MSc; Terrie E. Moffitt, PhD; Louise Arseneault, PhD

CONCLUSIONS AND RELEVANCE We identified heterogeneity in the *DSM-5* young adult ADHD population such that this group consisted of a large, late-onset ADHD group with no childhood diagnosis, and a smaller group with persistent ADHD. The extent to which childhood-onset and late-onset adult ADHD may reflect different causes has implications for genetic studies and treatment of ADHD.

Age-dependent decline of ADHD Symptoms



■ Characteristics of Patients in Whom ADHD Should Be Suspected

- Life-long history of impairment, i.e., symptoms persist although they may change over time
- Have chaotic life-styles and are highly disorganized
- Have a family member with ADHD
- Have a comorbid psychiatric disorder such as a mood disorder that has not responded well to treatment
- Rely on substances such as alcohol, illicit drugs, or caffeine to function



Anyone with behavioral or emotional presentations

TABLE 3.

Differential Diagnosis of Attention-Deficit/ Hyperactivity Disorder

Psychiatric Disorders

Oppositional defiant disorder
Disruptive mood dysregulation disorder
Intermittent explosive disorder
Bipolar disorder
Autism spectrum disorder

Anxiety disorders

Intellectual developmental disorder

Substance use disorders

Personality disorders

Psychosocial Conditions

Abuse and/or neglect
Poor nutrition
Neighborhood violence
Chaotic family situation
Being bullied

Medical Disorders

Medication-induced symptoms
(eg, asthma medications)
Sensory impairments (poor eyesight or
hearing)
Seizure disorder
Thyroid abnormality
Heavy metal poisoning
Head trauma

Apnea or other sleep disorders

ASRS Screener v1.1

1. Inattention	Never	Rarely	Sometimes	Often	Very Often
How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?	0	1	2*	3*	4*
How often do you have difficulty getting things in order when you have to do a task that requires organization?	0	1	2*	3*	4*
When you have a task that requires a lot of thought, how often do you avoid or delay getting started?	0	1	2	3*	4*
How often do you have problems remembering appointments or obligations?	0	1	2*	3*	4*
1. Hyperactivity/Impulsivity					
How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?	0	1	2	3*	4*
How often do you feel overly active and compelled to do things, like you were driven by a motor?	0	1	2	3*	4*

Significant items in Red (*p=0.5); Likely to have ADHD with ≥ 4 significant items

Adult ASRS Screener and Question list

- Standardized and useful screening, diagnostic, and follow up tool
 - Use all the questions on the ASRS list, not just screener in interview
- Threshold for Likely to Have ADHD: ≥ 4 significant items on screener
- Screener Sensitivity = 68.7%
- Screener Specificity = 99.5%
- Positive predictive value (PPV) using 3% estimate of prevalence = 80%
- More follow up done on positive screener questions, higher the PPV
- Total ASRS designed and useful to track treatment response

Is he DISTRACTED? Considerations when diagnosing ADHD in an adult

Richard C. Christensen, MD, MA

Adult attention-deficit/hyperactivity disorder (ADHD) can be challenging to assess accurately. Adult ADHD differs significantly from childhood ADHD, in that hyperactivity often is absent or greatly diminished, comorbid disorders (depression or substance use) are common, and previously compensated attention deficits in school can manifest in the patient's personal and professional life.¹

The mnemonic **DISTRACTED** can help when recalling key components in assessing adult ADHD.² Because ADHD is a developmental disorder—there are signs of onset in childhood—it is important to maintain a longitudinal view when asking about patterns of behavior or thinking.

Distractibility. Is there a pattern of getting “off track” in conversations or in school or work situations because of straying thoughts or daydreams? Is there a tendency to over-respond to extraneous stimuli (eg, cell phones, computers, television) that impedes the patient's ability to converse, receive information, or follow directions?

Impulsivity. Does the patient have a history of saying things “off the cuff,” interrupting others, or “walking on” someone else's words in a conversation? Is impulsivity evident in the person's substance use or spending patterns?

School history. This domain is important in diagnosing ADHD in adults because there needs to be evidence that the disorder was present from an early age. How did the patient perform in school (ie, grades, organization, completion of homework as-

signments)? Was there a behavioral pattern that reflected hyperactivity (could not stay seated) or emotional dysregulation (frequent outbursts)?

Task completion. Does the patient have trouble finishing assignments at work, staying focused on a project that is considered boring, or completing a home project (eg, fixing a leaky faucet) in a timely fashion?

Rating scales. Rating scales should be used to help support the diagnosis, based on the patient's history and life story. There are >12 scales that can be utilized in a clinical setting³; the ADHD/Hyperactivity Disorder Self-Report Scale is a brief and easy measure of core ADHD symptoms.

Accidents. Adults with ADHD often are accident-prone because of inattention, hyperactivity, or impulsivity. Does the patient have a history of unintentionally hurting himself because he “wasn't paying attention” (falls, burns), or was too impatient (traffic accidents or citations)?

Commitments. Does the patient fail to fulfill verbal obligations (by arriving late, forgetting to run errands)? Has this difficulty to commit created problems in relationships over time?

Time management. How difficult is it for the patient to stay organized while balancing work expectations, social obligations, and family needs? Is there a pattern of chaotic scheduling with regard to meals, work, or sleeping?

Employment. Has the patient changed jobs because the work becomes “too boring” or “uninteresting”? Is there a pattern of being terminated because of poor work quality based on time management or job performance?

Decisions. Adults with ADHD often make hasty, ill-informed choices or procrastinate so that they do not have to make a decision. Does the patient’s decision-making reveal a pattern of being too distracted to hear the information needed, or too impatient to consider all the details?

Remember: No single component of this mnemonic alone suffices to make a diagnosis of adult ADHD. However, these considerations will help clarify what lies behind your **DISTRACTED** patient’s search for self-understanding and appropriate medical care.

References

1. Barkley RA, Brown TE. Unrecognized attention-deficit/hyperactivity disorder in adults presenting with other psychiatric disorders. *CNS Spectr.* 2008;13(11):977-984.
2. Barkley R. *Taking charge of adult ADHD.* New York, NY: Guilford Press; 2010.
3. Attwell C. ADHD, rating scales, and your practice today. *The Carlat Psychiatry Report.* 2012;10(12):1,3,5-8.

JAMA Psychiatry | [Original Investigation](#)

The World Health Organization Adult Attention-Deficit/ Hyperactivity Disorder Self-Report Screening Scale for *DSM-5*

Berk Ustun, MS; Lenard A. Adler, MD; Cynthia Rudin, PhD; Stephen V. Faraone, PhD; Thomas J. Spencer, MD;
Patricia Berglund, MBA; Michael J. Gruber, MS; Ronald C. Kessler, PhD

Table 1. Questions in the Optimal RiskSLIM *DSM-5* ASRS Screening Scale^a

1. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly? (*DSM-5 A1c*)
2. How often do you leave your seat in meetings or other situations in which you are expected to remain seated? (*DSM-5 A2b*)
3. How often do you have difficulty unwinding and relaxing when you have time to yourself? (*DSM-5 A2d*)
4. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to before they can finish them themselves? (*DSM-5 A2g*)
5. How often do you put things off until the last minute? (*Non-DSM*)
6. How often do you depend on others to keep your life in order and attend to details? (*Non-DSM*)

Abbreviations: ADHD, attention-deficit/hyperactivity; ASRS, Adult ADHD Clinical Diagnostic Scale; RiskSLIM, Risk-Calibrated Supersparse Linear Integer Model.

^a Response categories are never, rarely, sometimes, often, and very often. The never response option is scored 0 for all questions; the highest scores are 5 for questions 1 and 2, 4 for question 5, 3 for question 6, and 2 for question 4, resulting in a scale with scores in the range 0 of 24.

McLean Screening Instrument for Borderline Personality Disorder

1. Have any of your closest relationships been troubled by a lot of arguments or repeated breakups? **1 = yes 0 = no**
2. Have you deliberately hurt yourself physically (e.g., punched yourself, cut yourself, burned yourself)? How about made a suicide attempt? **1 = yes 0 = no**
3. Have you had at least two other problems with impulsivity (e.g., eating binges and spending sprees, drinking too much and verbal outbursts)? **1 = yes 0 = no**
4. Have you been extremely moody? **1 = yes 0 = no**
5. Have you felt very angry a lot of the time? How about often acted in an angry or sarcastic manner? **1 = yes 0 = no**
6. Have you often been distrustful of other people? **1 = yes 0 = no**
7. Have you frequently felt unreal or as if things around you were unreal? **1 = yes 0 = no**
8. Have you chronically felt empty? **1 = yes 0 = no**
9. Have you often felt that you had no idea of who you are or that you have no identity? **1 = yes 0 = no**
10. Have you made desperate efforts to avoid feeling abandoned or being abandoned (e.g., repeatedly called someone to reassure yourself that he or she still cared, begged them not to leave you, clung to them physically)? **1 = yes 0 = no**

Moreover, ADHD and BPD frequently co-occur, with rates of BPD among adults with ADHD ranging from 19% to 37% (e.g., Miller et al.). Finally, there is evidence to suggest that childhood ADHD may be a risk factor

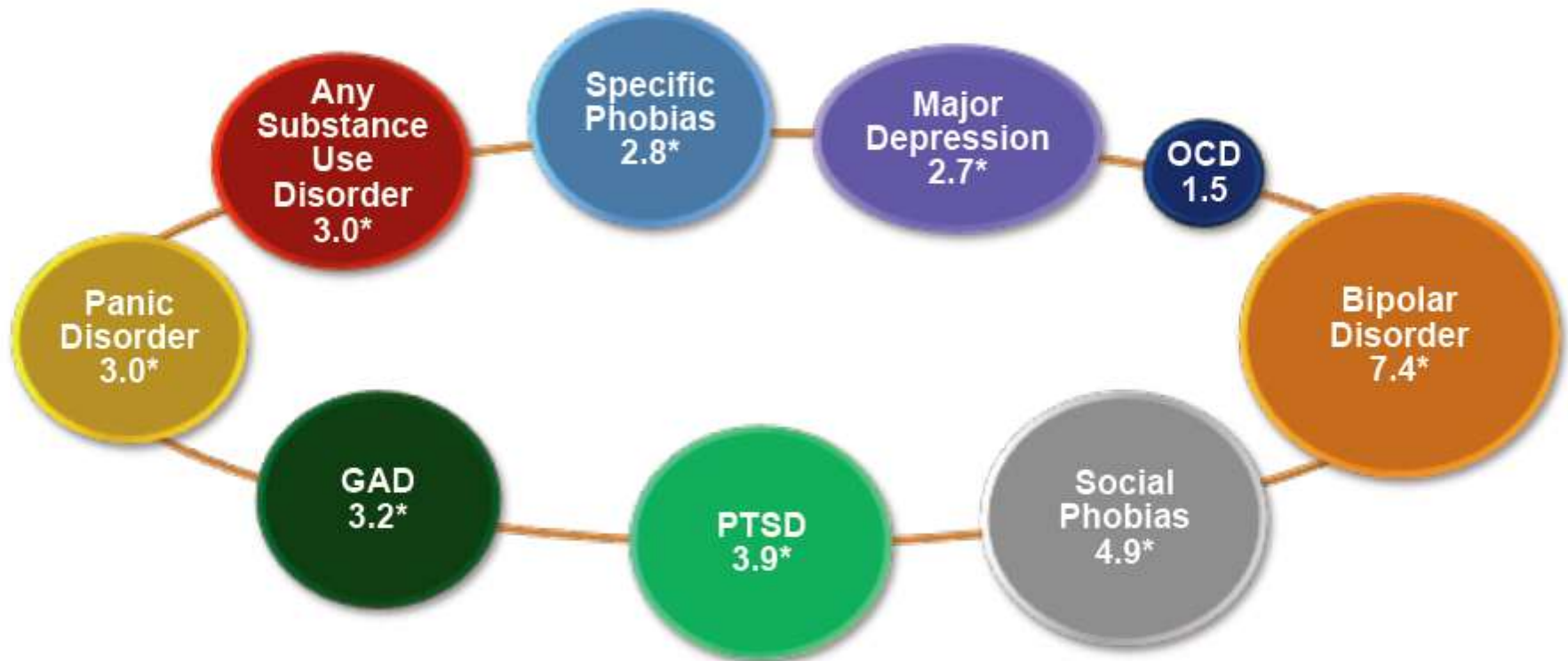
Neuropsychological testing

- **Not to be routinely done**
- **Possible indications:**
 - To rule out school or workplace difficulties that appear unrelated to attentional deficits: learning disabilities, IQ issues
 - Question of organic or congenital brain lesions or neurological trauma donating to disability
 - To rule out psychiatric diagnoses that imitate or are comorbid to the cardinal ADHD symptoms but are difficult to identify
 - Lack of treatment response
 - Malingering or factitious disorders suspected

Diagnostic considerations: Summary

- While the ASRS cannot replace the diagnostic interview, it should be given to all higher risk clients outlined and used to follow treatment results
- The ASRS results should form a basis for further questioning, using the positive test items as a base (DISTRACTED)
- Corroboration by previous scholastic history, marks, childhood, and everyday behaviors by relatives/parents/spouse very helpful
- Comorbidity is the rule rather than the exception and mood/anxiety disorders common

Adult ADHD Link of the NCS-R: Psychiatric Comorbidities



Odds Ratio (95% CI). * $P < .05$.

GAD = generalized anxiety disorder; NCS-R = National Comorbidity Survey Replication; OCD = obsessive-compulsive disorder; PTSD = posttraumatic stress disorder.

Kessler RC, et al. *Am J Psychiatry*. 2006;163(4):716-723.

National Comorbidity Survey Replication: Mood Disorders in Adult ADHD

N=3199

**Adult
ADHD**

**Major
Depression
18.6%**

**Bipolar
Disorder
19.4%**

**Dysthymia
12.8%**

**Any Mood
Disorder
38.3%**

ADHD and SUD: Increased Risks across the Board

Population-based sample of Swedish adult twins (N = 18,167)

Associations of ADHD Symptoms with SUD (Adjusted for Sex, Age, and Education and Controlled for the Random Effect of Twins) Compared with Controls/Twins with No ADHD Symptoms

Substance Abuse	All Twins, n (%)	ADHD OR
Alcohol		
Alcohol abuse	543 / 17,940 (3.06)	1.88
Alcohol dependence	1878 / 17,784 (10.56)	2.58
Drugs		
Stimulants	107 / 17,940 (0.59)	1.88
Opioids	107 / 17,940 (0.59)	1.88
Cannabis	107 / 17,940 (0.59)	1.88
Illicit drugs	107 / 17,940 (0.59)	1.88
Poly-substance use including alcohol	1704 / 18,027 (9.42)	2.78
Nicotine (smoke and/or "snus")		
Regular nicotine use	3115 / 18,167 (17.15)	1.33

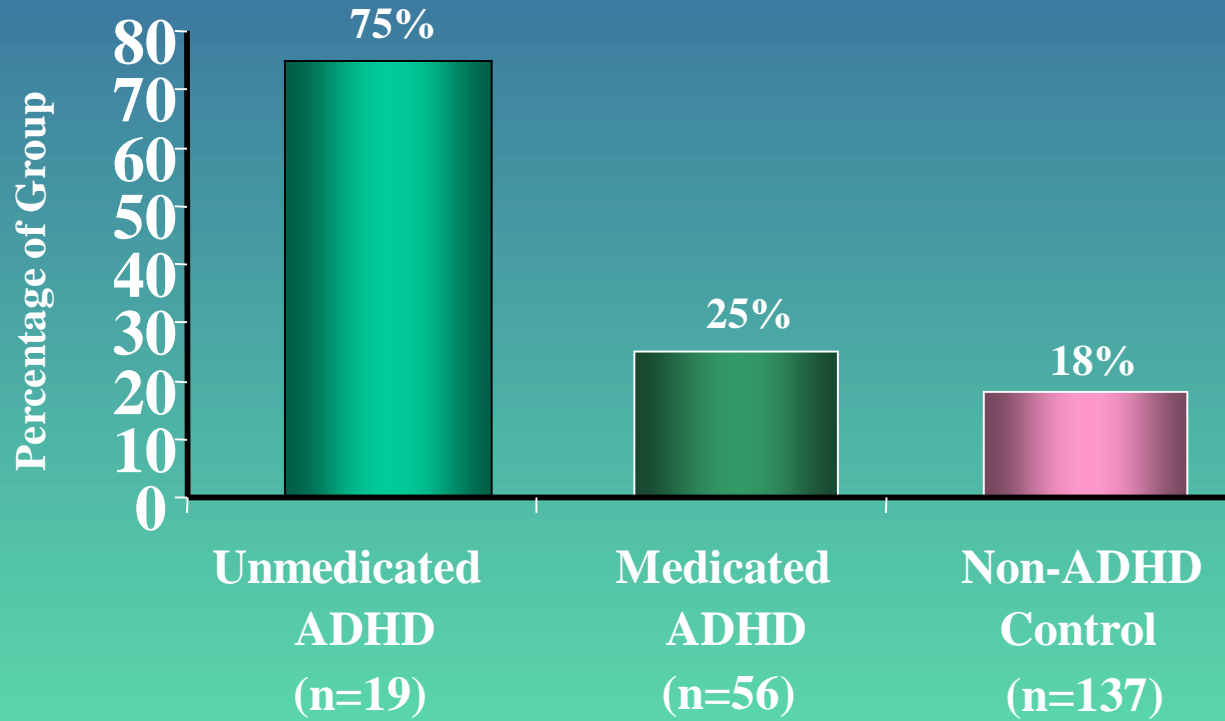
ADHD Sxs and subtypes are associated with increased risks for all SUD outcomes; no difference between ADHD subtypes, no substance preference, and no sex differences for the comorbidity

$P \leq .001$. Calculated from multilevel logistic regression adjusted for sex, age, and education and controlled for the random effect of twins.

Capusan AJ, et al. *J Atten Disord*. 2016;[Epub ahead of print].

Prevalence of SUD: Prospective 4-Year Follow-up Study

Overall Rate of Substance Use Disorder



$P < .001$ across groups.

Biederman J, et al. *Pediatrics*. 1999;104:e20.

ADHD Medication and Substance-Related Problems

American Journal of Psychiatry, Volume 174, Issue 9, [September 01, 2017](#), pp. 877-885

- *In the largest study to examine whether ADHD medications are associated with differences in risk for substance-related problems, researchers identified 3 million individuals aged 13 years or older who received either an ADHD diagnosis or treatment for ADHD*
- *Models showed that use of ADHD medication was associated with 35% lower odds of concurrent substance-related events among men and 31% lower odds among women.*

Dealing with comorbidity in treatment

SUD:

determine pattern and severity and potential risk of med interactions or medication diversion

Detox-rehab needed to clear sud-related symptoms

When some results achieved, use either atomoxetine or long acting stimulants, depending on relapse risk.

Mood disorders:

Treat the primary affective state with antidepressants or mood stabilizers;

If the core inattentive symptoms persist, add on extended release stimulants or atomoxetine;

Odds of manic switch appear rare with mood stabilizers in place

ADHD and Bipolarity: Controversial

Potentially huge rates of ADHD comorbidity have been found in children with Manic-Depressive disorder, but this is hotly disputed, and is an issue in adults as well

22% of ADHD adults appear to suffer from bipolarity,
men=women

Treat the bipolarity first with mood stabilizers, consider all treatment options thereafter if ADHD symptoms remain and are disabling; little evidence that one treatment creates more switches into mania than any other if already stabilized.

Distinguishing the symptoms of mania from ADHD is a concern, features that help include:

- Discrete but prolonged dysphoric or euphoric episodes

- Psychotic symptoms such as delusions

- Decreased need for sleep

- Grandiosity, hypersexuality, bizarreness

- ADHD has significant and chronic attention deficits

Case Presentation: Diagnostic Prioritization for Pharmacotherapy

Borderline Personality
Alcohol and substance abuse

Mood disorders

Bipolar and MDD

Anxiety disorders

Obsessive-compulsive disorder,
generalized anxiety disorder, panic

ADHD



Order of Treatment

Order of treatment also considers the severity of the concurrent disorders.

Goodman D. Treatment and assessment of ADHD in adults. In: Biederman J, ed. *ADHD Across the Life Span: From Research to Clinical Practice - An Evidence Based Understanding*. Hasbrouck

ADHD: Options

Pharmacologic Treatment

Stimulants

Methylphenidate
Dexedrine
Amphetamine (compounds)



FDA Approved
(all in Peds, some in
Adults)

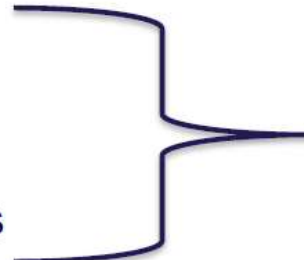
Atomoxetine



FDA Approved

Alpha-agonists

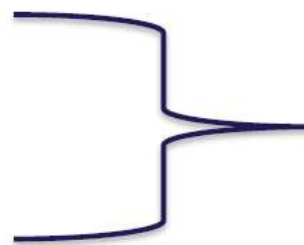
Guanfacine XR
Clonidine XR
Guan XR / Clon XR + Stimulants



FDA Approved
(Peds only)

Antidepressants

Bupropion
Tricyclics
Modafinil
Combinations



Not FDA Approved

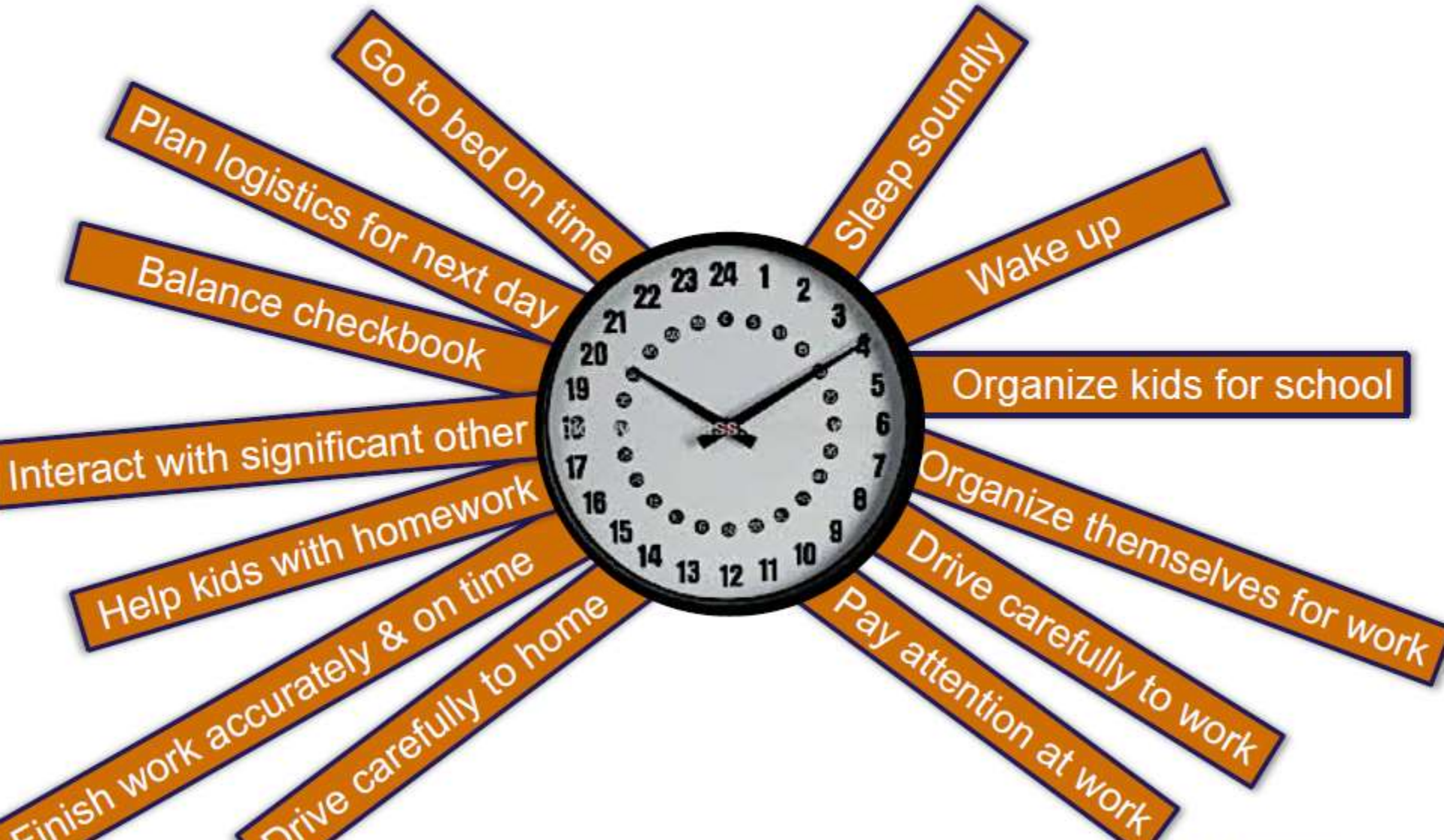
J Consult Clin Psychol. 2017 May 15

Meta-Analysis of Cognitive-Behavioral Treatments for Adult ADHD.

Knouse LE, Teller J, Brooks MA

Effect sizes were heterogeneous for most outcome measures. **Studies with active control groups showed smaller effect sizes.** Neither participant medication status nor treatment format moderated pre-to-post treatment effects, and longer treatments were not associated with better outcomes.

The 24-Hour Day of a Typical Adult and Why the Adult with ADHD Needs Longer than 8- to 12-Hour Coverage of Symptoms / Day



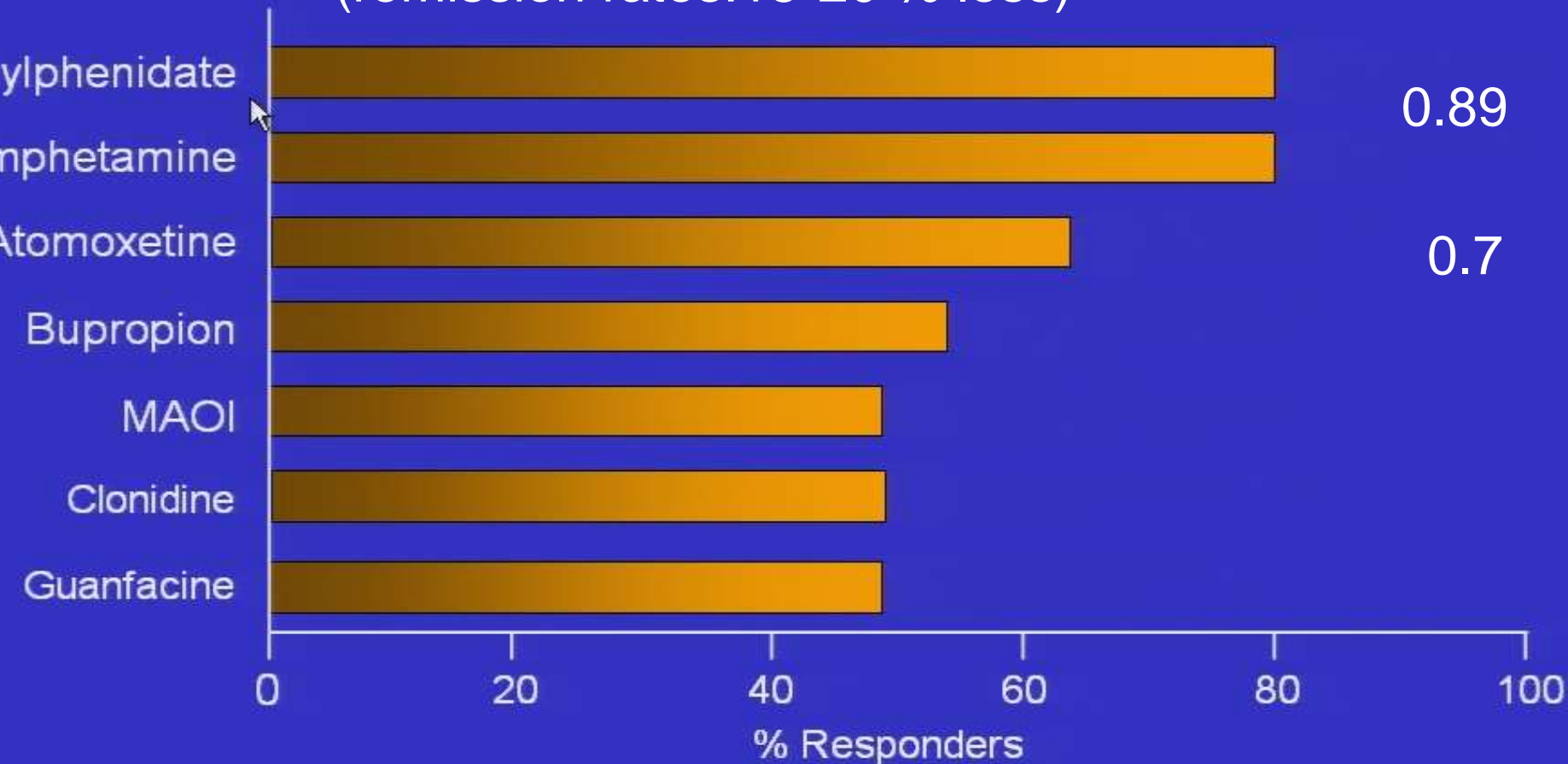
Important practical issues in pharmacotherapy:

- Stimulant therapy is the backbone of short and long term improvement in all facets of the disorder and social development
- Compliance can be terrible given the forgetfulness and disorganization (I.e BID, TID dosings)
- Meds act quickly and effect fades quickly once blood levels drop: over minutes!
- This lack of 12-18 hour medication coverage has daily functional consequences
- There can be a huge difference in perceived and measured side effects and effectiveness with different formulations, even of the same molecule.
- Tendency for abuse, tolerability, and medication interactions varies significantly with longer vs. shorter acting formulations
- Non stimulants take weeks, not days to work

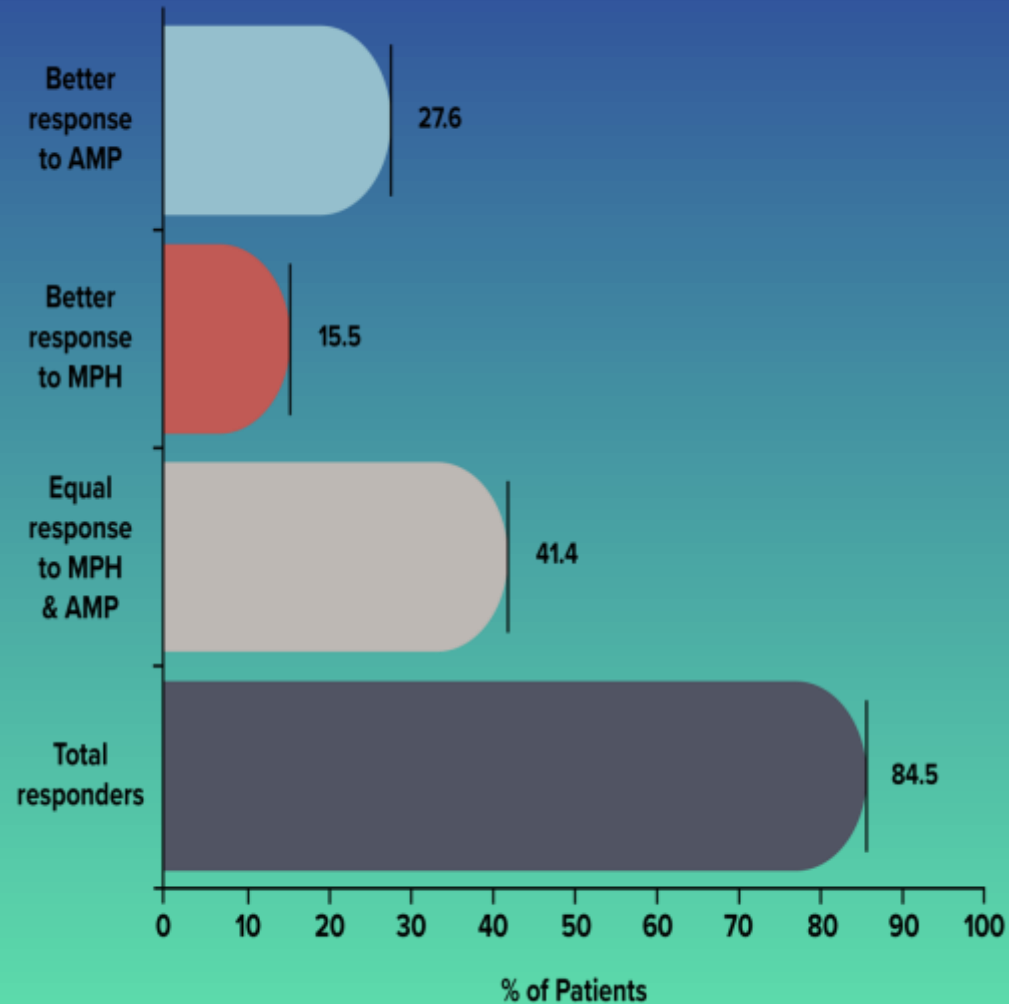
ADHD Pharmacotherapy – Responsiveness

(remission rates: 15-20 % less)









Effect size:



AMP VS MPH: RESPONDERS



CADDRA Guide to ADHD Pharmacological Treatments in Quebec - 2017

Medications available and illustrations	Characteristics	Duration of action ¹	Starting dose ²	Dose titration as per product monograph	Dose titration as per CADDRA www.caddra.ca	RAMQ-coverage (code)
AMPHETAMINE-BASED PSYCHOSTIMULANTS						
Dexedrine® tablets 5 mg Dexedrine® spansules 10, 15 mg 	Pill can be crushed ³ Spansule (not crushable)	~ 4 h ~ 6 - 8 h	Tablets = 2.5 to 5 mg BID Spansules = 10 mg q.d. a.m.	↑ 2.5 - 5 mg at weekly intervals; Max. dose/day: (q.d. or b.i.d.) All ages = 40 mg	↑ 2.5 - 5 mg/day at weekly intervals Max. dose/day: (q.d. or b.i.d.) Children and Adolescents = 20 - 30 mg Adults = 50 mg	Covered Covered
Adderall XR® Capsules 5, 10, 15, 20, 25, 30 mg 	Sprinkable Granules	~ 12 h	5 - 10 mg q.d. a.m.	↑ 5 - 10 mg at weekly intervals Max. dose/day: Children = 30 mg Adolescents and Adults = 20 - 30 mg	Children: ↑ 5 mg at weekly intervals Max. dose/day = 30 mg Adolescents and Adults: ↑ 5 mg at weekly intervals max. dose/day = 50 mg	Médicament d'exception program Child-Adolescent: (SNI03) Adult (SNI32)
Vyvanse® Capsules 10, 20, 30, 40, 50, 60 mg 	Capsule content can be diluted in water, orange juice and yogurt	~ 13 - 14 h	20 - 30 mg q.d. a.m.	↑ by clinical discretion at weekly intervals Max. dose/day: All ages = 60 mg	↑ 10 mg at weekly intervals Max. dose/day: Children = 60mg Adolescents and Adults = 70 mg	Médicament d'exception program Child-Adolescent: (SNI03) Adult (SNI32)
METHYLPHENIDATE-BASED PSYCHOSTIMULANTS						
Methylphenidate short acting, tablets 5 mg (generic) 10, 20 mg (Ritalin®) 	Pill can be crushed ³	~ 3 - 4 h	5 mg b.i.d. to t.i.d. Adult = consider q.i.d.	↑ 5 - 10 mg at weekly intervals Max. dose/day: All ages = 60 mg	↑ 5 mg at weekly intervals Max. dose/day: Children and Adolescents = 60 mg Adults = 100 mg	Covered
Biphentin® Capsules 10, 15, 20, 30, 40, 50, 60, 80 mg 	Sprinkable Granules	~ 10 - 12 h	10 - 20 mg q.d. a.m.	↑ 10 mg at weekly intervals Max. dose/day: Children and Adolescents = 60 mg Adults = 80 mg	↑ 5 - 10 mg at weekly intervals Max. dose/day: Children = 60 mg Adolescents and Adults = 80 mg	Médicament d'exception program Child-Adolescent: (SNI03) Adult (SNI32)
Concerta® Extended Release Tabs 18, 27, 36, 54 mg 	Pill needs to be swallowed whole to keep delivery mechanism intact	~ 12 h	18 mg q.d. a.m.	↑ 18 mg at weekly intervals Max. dose/day: Children = 54 mg Adolescents = 54 mg / Adults = 72 mg	↑ 9 - 18 mg at weekly intervals Max. dose/day: Children = 72 mg Adolescents = 90 mg / Adults = 108 mg	Médicament d'exception program Child-Adolescent: (SNI03) Adult (SNI32)
NON PSYCHOSTIMULANT - SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR						
Strattera® (Atomoxetine) Capsules 10, 18, 25, 40, 60, 80, 100 mg 	Capsule needs to be swallowed whole to reduce GI side effects	Up to 24 h	Children and Adolescents: 0.5 mg/kg/day Adults = 40 mg q.d. for 7-14 days	Maintain dose for a minimum of 7 - 14 days before adjusting: Children = 0.8 then 1.2 mg/kg/day 70 kg or Adults = 60 then 80 mg/day Max. dose/day : 1.4 mg/kg/day or 100 mg	Maintain dose for a minimum of 7 - 14 days before adjusting: Children = 0.8 then 1.2 mg/kg/day 70 kg or Adults = 60 then 80 mg/day Max. dose/day: 1.4 mg/kg/day or 100 mg	Médicament d'exception program Child-Adolescent Patient d'exception program Adult
NON PSYCHOSTIMULANT - SELECTIVE ALPHA-2A ADRENERGIC RECEPTOR AGONIST						
Intuniv XR® (Guanfacine XR) Extended release tabs 1, 2, 3, 4 mg 	Pills need to be swallowed whole to keep delivery mechanism intact	Up to 24 h	1 mg q.d. (morning or evening)	Maintain dose for a minimum of 7 days before adjusting by no more than 1 mg increment weekly Max. dose/day: Monotherapy: 6-12 years: 4 mg 13-17 years: 7 mg As adjunctive therapy to psychostimulants 6-17 years: 4 mg	Maintain dose for a minimum of 7 days before adjusting by no more than 1 mg increment weekly Max. dose/day: Monotherapy: 6-12 years: 4 mg 13-17 years: 7 mg As adjunctive therapy to psychostimulants 6-17 years: 4 mg	Médicament d'exception program Child-Adolescent Patient d'exception program Adult

Note: Illustrations do not reflect real size of pills/capsules. For specific details on how to start, adjust and switch ADHD medications, clinicians are invited to refer to the Canadian ADHD Practice Guidelines (www.caddra.ca)

¹ Pharmacokinetics and pharmacodynamic response vary from individual to individual. The clinician must use clinical judgment as to the duration of efficacy and not solely rely on reported values for PK and duration of effect



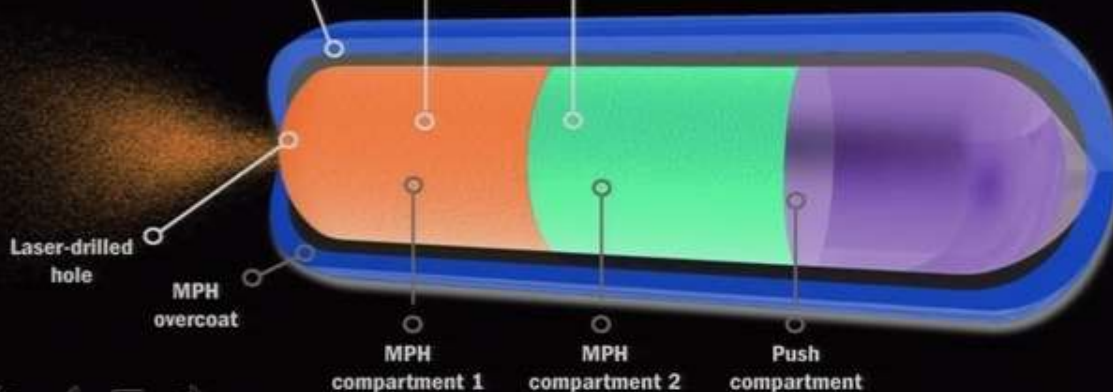
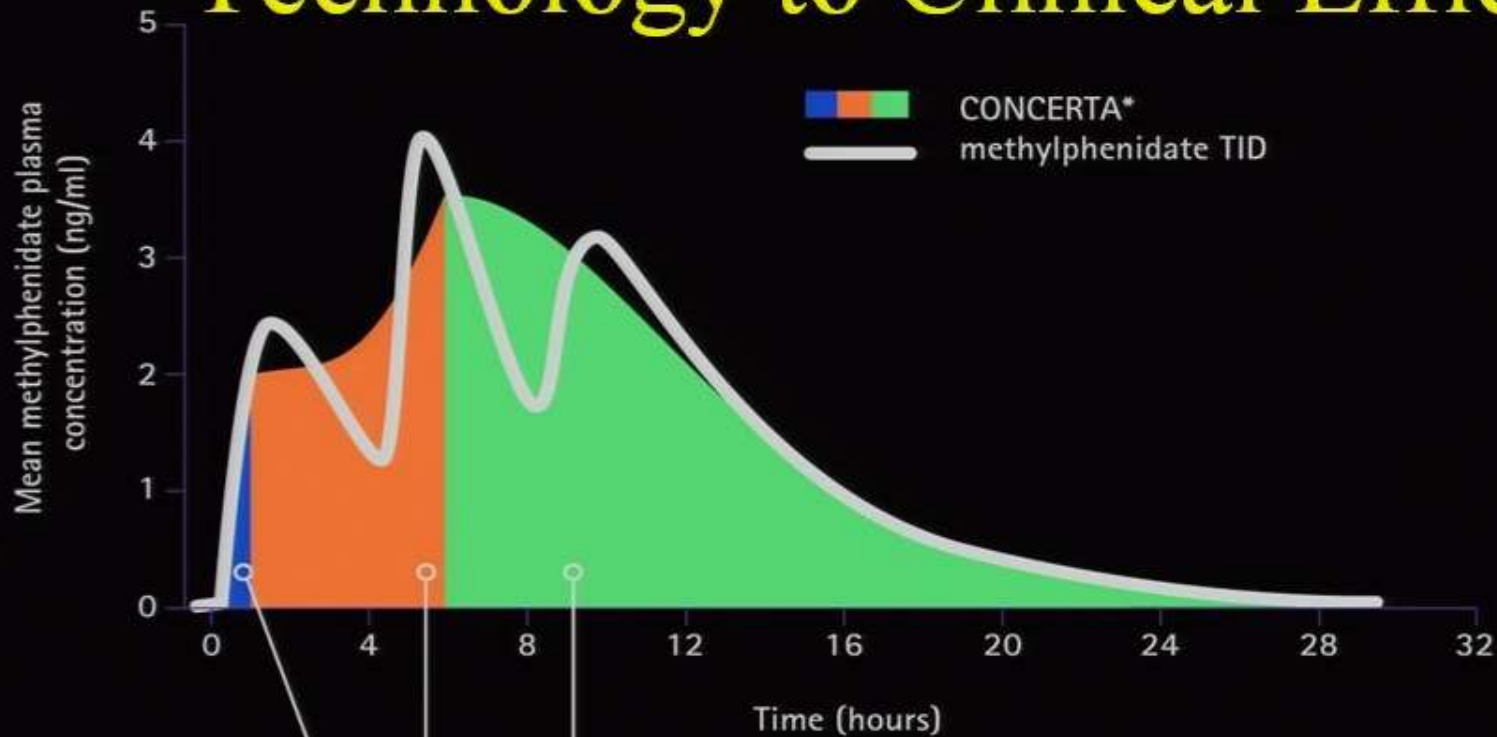
ADULT (18+) 1st LINE AGENTS

CADDRA First Line Treatment for ADHD - Adult (18+ Years)

Agent	Dosage Form (mg)	Starting Dose	Titration Schedule every 7 days	Max dose/day by PM	Max dose/day CADDRA
Adderall XR® (amphetamine mixed salts)	5, 10, 15, 20, 25, 30, mg cap	10 mg q.d. a.m.	↑ 10 mg	20-30 mg	50 mg
Biphentin® (methylphenidate)	10, 15, 20, 30, 40, 50, 60, 80 mg cap	10-20 mg q.d. a.m.	↑ 10 mg	80 mg	80 mg
Concerta® (methylphenidate)	18, 27, 36, 54 mg tab	18 mg q.d. a.m.	↑ 18 mg	72 mg	108 mg
Vyvanse® (lisdexamfetamine)	10, 20, 30, 40, 50, 60, 70 mg cap	20-30 mg q.d. a.m.	By clinical discretion	60 mg	70 mg
Foquest® (methylphenidate)	25, 35, 45, 55, 70, 85, 100 mg cap	25 mg q.d. a.m.	Increase 10 - 15 mg	100 mg	100 mg

CONCERTA*: OROS

Technology to Clinical Efficacy

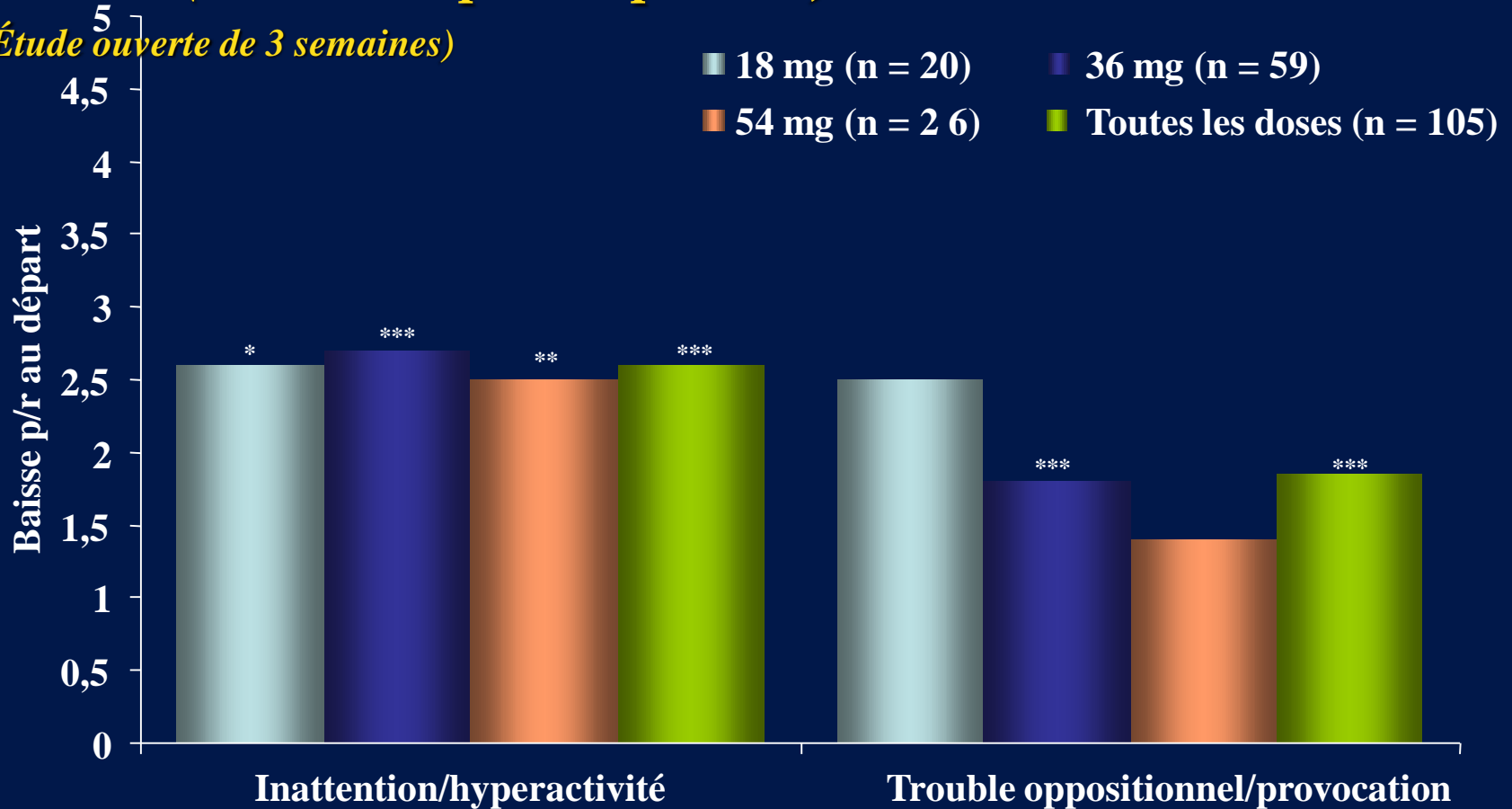


- 1 An initial dose dissolves within an hour
- 2 Specially engineered capsule releases a steadily rising concentration of methylphenidate
- 3 Design ensures that physiological activity lasts no longer than that seen with an immediate-release TID methylphenidate preparation

Remschmidt : passage de IR MPH à Concerta® Meilleure maîtrise des symptômes

Changement moyen des symptômes d'après l'échelle IOWA Conners (évaluation par les parents)

(Étude ouverte de 3 semaines)



*p < 0,05, **p < 0,01, ***p < 0,001 au jour 21 p/r au départ

Indications for Atomoxetine[®]

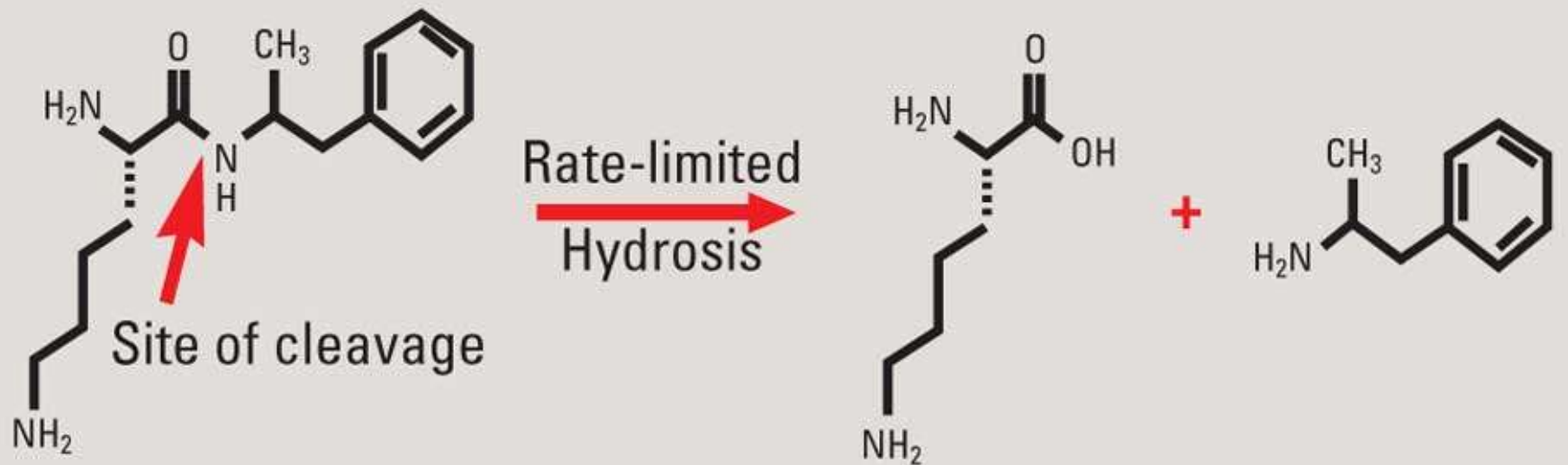
Substance abusers: active or with high relapse risk

- Patients not responsive to stimulants
- Patients with significant side effects to stimulants (e.g., rebound, tics)
- Patients with Tourette's Syndrome or chronic motor tic disorders
- Epilepsy
- Comorbid Anxiety
- Abuse or diversion is a concern

Bipolar disorder? Unstudied

SLIDE 4

Lisdexamfetamine – a prodrug that is therapeutically inactive until it is converted to active dextroamphetamine in the body

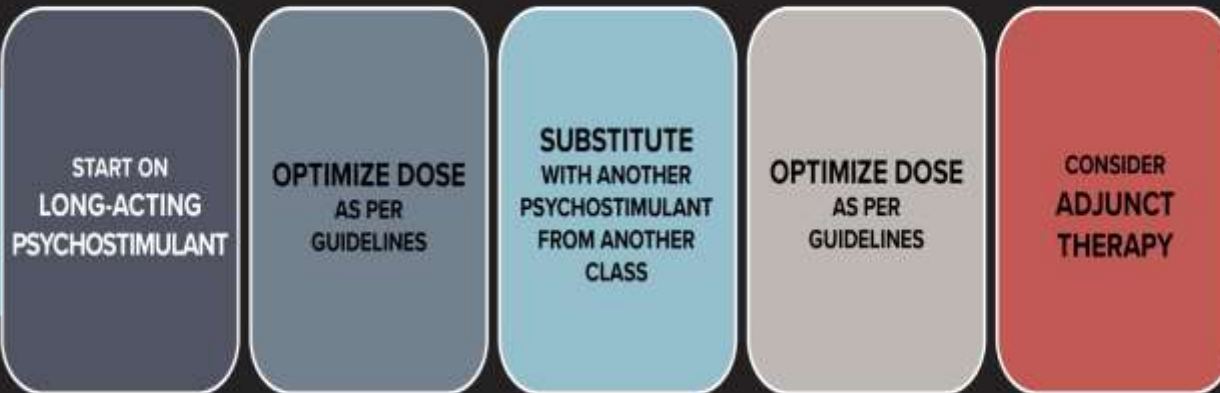


Lisdexamfetamine (prodrug)

L-lysine

**d-amphetamine
(active)**

ADHD MANAGEMENT



If the patient experiences substantial adverse effects, consider another ADHD agent

ACTION OF NEUROTRANSMITTERS

STIMULANTS

NON-STIMULANTS

DA = Dopamine
NE = Norepinephrine

ADDERALL® XR AMPHETAMINE		VYVANSE® AMPHETAMINE	
DA	NE	DA	NE
Strong	Strong	Strong	Strong

INTUNIV XR® GUANFACINE XR	
DA	NE
NOT KNOWN	

BIPHENTIN® METHYLPHENIDATE		CONCERTA® METHYLPHENIDATE		FOQUEST® METHYLPHENIDATE	
DA	NE	DA	NE	DA	NE
Strong	Weak	Strong	Weak	Strong	Weak

STRATTERA™ ATOMOXETINE	
DA	NE
Weak	Strong

Strong = Acts directly at synapse
Weak = Less effect or acts indirectly/remotely from its primary site of action

Treatment (continued)

Canadian Resources

- CADDRA (www.caddra.ca)
- CADDAC (www.caddac.ca)
- Teach ADHD (www.teachadhd.ca)
- Learning Disabilities Assn of Canada (www.ldac-taac.ca)
- Learning Disabilities Assn of Ontario (www.ldao.ca)
- Association Québécoise des troubles d'apprentissage (www.aqeta.qc.ca)
- CH.A.D.D. Canada (www.chaddcanada.org)
- PANDA (www.associationpanda.qc.ca)
- The AD/HD Foundation (www.adhdfoundation.ca)