Evaluation for and Treatment of Attention-Deficit/Hyperactivity Disorder in Adults

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Objectives

1) Identify diagnostic criteria, etiology, and neurobiology of Adult ADHD.
2) Describe a practical approach to diagnosing ADHD in adults.
3) Differentiate treatment options for ADHD in adults.
Attention Deficit/ Hyperactivity Disorder
Attention-Deficit/Hyperactivity Disorder

Edward Hallowell, MD
Psychiatrist and NY Times Best-Selling Author

"...the term 'attention deficit' is a misnomer. It is a matter of attention inconsistency. While it is true that the ADD mind wanders when not engaged, it is also the case that the ADD mind fastens on to its subject fiercely when it is engaged."

Edward Hallowell, MD
Psychiatrist and NY Times Best-Selling Author
1) Identify diagnostic criteria, etiology, and neurobiology of ADHD.
To Know ADHD in adults you have to know ADHD in kids

George Frederic Still (1868–1941) - “father of British paediatrics”

• 1902 – presented case series of 43 children with difficulties with sustained attention, but no intellectual disability.
• “there is a defect of moral consciousness which cannot be accounted for by any fault of the environment”
• noted potential heritability, as several children had parents with similar psychiatric concerns.

Charles Bradley, MD (1902–1979) - Medical director of Emma Pendleton Bradley Home

• 1937 – trialed Benzedrine (amphetamine) to reduce post-pneumoencephalography headaches
• 14/30 children with pre-existing behavioral problems showed “spectacular change in behavior . . . remarkably improved school performance” during 1 week of post-procedural treatment with Benzedrine.
• Children themselves noticed the improvement and called the medicine “arithmetic pills”.

9

10
ADHD Diagnostic Evolution

1952 - Minimal Brain Dysfunction
1968 - Hyperkinetic Reaction of Childhood
1980 - ADD with or without hyperactivity
1994 - ADHD: [subtypes]
2013 - ADHD: [presentations]

ICD10 lists “Hyperkinetic Disorder of Childhood” (a more stringent diagnosis with lower prevalence), which some have used to warrant concern that ADHD is over-diagnosed in US by DSM5 criteria.

ICD11 (2022) is removing “Hyperkinetic Disorder of Childhood” and replacing with almost verbatim DSM5 criteria – with even slightly more liberal age when sx start (“early to mid-childhood”).

DSM-5 criteria for ADHD

Inattention
(a) Lack of attention to details / careless mistakes
(b) Difficultly sustaining attention
(c) Does not seem to listen
(d) Does not follow through on instructions (easily side-tracked)
(e) Difficulty organising tasks and activities
(f) Avoids sustained mental effort
(g) Loses and misplaces objects
(h) Easily distracted
(i) Forgetful in daily activities

Hyperactivity / Impulsivity
(a) Fidgetiness (hand or feet) / squirms in seat
(b) Leaves seat frequently
(c) Running about / feeling restless
(d) Excessively loud or noisy
(e) Always “on the go”
(f) Talks excessively
(g) Blurts out answers
(h) Difficulty waiting his or her turn
(i) Tends to act without thinking

• >=6 for kids! in either
• 26 symptoms per category in adults, 26 months
• Age of onset ≤12 years
• Noticeable in ≥2 settings
• Impact on social, academic or occupational functioning; not better accounted for by another mental disorder

World Health Organization

11/4/2019
*During tasks requiring inhibition, individuals with ADHD, as compared to controls, several brain areas show decreased activation.

<table>
<thead>
<tr>
<th>Inhibition Tasks</th>
<th>Area/Variation</th>
<th>Resultant Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Inferior Prefrontal Cortex/Insula</td>
<td>Reduced Verbal Inhibition</td>
<td></td>
</tr>
<tr>
<td>Supplementary Motor Area</td>
<td>Reduced Motor Inhibition</td>
<td></td>
</tr>
<tr>
<td>Cognitive Anterior Cingulate Cortex</td>
<td>Reduced error detection</td>
<td></td>
</tr>
<tr>
<td>Left Caudate</td>
<td>Decreased goal evaluation and selection</td>
<td></td>
</tr>
<tr>
<td>Right mid-thalamus</td>
<td>Functional relay</td>
<td></td>
</tr>
</tbody>
</table>

*During tasks requiring attention, individuals with ADHD, as compared to controls, several brain areas show decreased activation. A few areas show increased activation.

<table>
<thead>
<tr>
<th>Attention Tasks</th>
<th>Area/Variation</th>
<th>Resultant Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Dorsolateral Prefrontal Cortex</td>
<td>Decreased executive function</td>
<td></td>
</tr>
<tr>
<td>Left Globus Pallidus</td>
<td>Decreased motor inhibition</td>
<td></td>
</tr>
<tr>
<td>Right Posterior Thalamus</td>
<td>Decreased proprioceptive relay</td>
<td></td>
</tr>
<tr>
<td>Right Inferior Parietal Lobe</td>
<td>Reduced integration of sensory info</td>
<td></td>
</tr>
<tr>
<td>Right Precuneus and Superior Temporal Lobe</td>
<td>Reduced attentional shifting</td>
<td></td>
</tr>
<tr>
<td>Left Cuneus</td>
<td>Higher visual attention</td>
<td></td>
</tr>
<tr>
<td>Right cerebellum</td>
<td>Higher compensatory activation</td>
<td></td>
</tr>
</tbody>
</table>
*There are differences in fMRI in Adults with ADHD vs Children with ADHD

- ADHD continues into adulthood for approximately 50% of those diagnosed in childhood.
- Prevalence of ADHD in adults is estimated at about 5%.

**Hot Topic**

**Is there a true adult-onset ADHD?**

**TABLE 2. Results of Stepped Procedure for Evaluating the Validity of Late-Onset ADHD Cases**

<table>
<thead>
<tr>
<th>Result</th>
<th>Adolescent-Onset</th>
<th>Adult-Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meets DSM-5 ADHD symptom criteria</td>
<td>96</td>
<td>47</td>
</tr>
<tr>
<td>Clinically significant impairment</td>
<td>32</td>
<td>40</td>
</tr>
<tr>
<td>Late-onset</td>
<td>21</td>
<td>40</td>
</tr>
<tr>
<td>Not due to substance abuse</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Not attributable to other mental disorder</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>Cross-situational symptoms</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Absence of subthreshold childhood symptoms</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>Childhood symptoms (less than three childhood symptoms of inattention and hyperactivity/impulsivity)</td>
<td>1.3</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Even in the patients identified with onset of ADHD sx during adult when no other confounders, there were previously-occurring conditions that may have influenced cognitive neurobiology.

- No fMRIs to confirm similar process to child-onset ADHD
Objective Milestone 1

- Identify diagnostic criteria, etiology, and neurobiology of Adult ADHD.
  - ADHD in adults almost assuredly started during childhood.
  - ~50% of children dx with ADHD retain the diagnosis into adulthood.
  - ADHD presentations (not “types”) can be:
    - Primarily inattentive
    - Primarily hyperactive/impulsive
    - Combined
  - Presentations can change over time
  - ADHD functional neurobiology is characterized by variance in function of multiple brain areas involved in “inhibition” and “attention” cognitive tasks.
    - Functional variance in some areas resolves by adulthood, but remains in others.

2) Describe a practical approach to diagnosing ADHD in adults.
Canadian ADHD Practice Guidelines
Fourth Edition

ADHD SUSPECTED

STEP 1 - INITIAL INFORMATION GATHERING

QUESTIONNAIRES FOR PATIENTS
- ASRS [Adult ADHD self-Report Scale]
  Consider also using a functional impairment scale (e.g.
  WFIRS-5) (Weiss Functional Impairment Rating Scale - Self)

QUESTIONNAIRES FOR SOMEONE
WHO KNOWS THE PATIENT WELL (e.g.
spouse, other)
- ASRS [Adult ADHD Self-Report]

QUESTIONNAIRES FOR SOMEONE WHO
KNOW THE PATIENT AS A CHILD (if possible)
- SNAP-IV

STEP 2 - MEDICAL REVIEW

EXCLUDE ANY MEDICAL CAUSES
THAT CAN MimIC OR AGGRAVATE
ADHD SIGNS OR SYMPTOMS

REVIEW NUTRITION AND LIFESTYLE HABITS:
Sleep, exercise, screen time, high-risk activities, substance use, sexual activity
(if applicable), accidents

EVALUATE POTENTIAL CONTRAINDICATIONS TO
ADHD MEDICATIONS

STEP 3 - ADHD SPECIFIC INTERVIEW

DISCUSS PATIENT’S STRENGTHS AND
OBSERVE PATIENT DURING INTERVIEW

REVIEW DEVELOPMENTAL HISTORY
AND OBTAIN COLLATERAL
INFORMATION FROM PARENTS/CLOSE
RELATIVES

REVIEW THE QUESTIONNAIRES
USED IN ASSESSMENT

CONSIDER CONTRIBUTIONS OF OTHER PSYCHIATRIC,
PSYCHOSOCIAL FACTORS OR LEARNING DISORDERS
TO THE PRESENTING SYMPTOMS
Consider specialist referral if necessary.

Canadian ADHD Practice Guidelines
Fourth Edition

SUSPECT

INFORMATION GATHERING

MEDICAL REVIEW
What could lead a physician to suspect ADHD?

**Societal Expectations**
- Increase

**Dangerous Temptations**
- Increase

Among those with ADHD, which risk factors were additionally associated with Conviction and Incarceration?
- Male status (HR 2.7 [C] and 3.9 [I])
- Substance use disorder (HR 2.9 [C] and 3.2 [I])
- Oppositional defiant disorder (HR 2.7 [C] and 3.9 [I])
- Low family socioeconomic status (HR 1.4 [C] and 1.5 [I])
- Parental incarceration (HR 1.4-1.7 [C] and 1.6-1.7 [I])
- Parental Separation/Divorce (HR 1.4 [C] and 1.4 [I])

**TABLE 2: Prevalence of Outcomes Among Participants With and Without Attention-Deficit/Hyperactivity Disorder (ADHD)**

<table>
<thead>
<tr>
<th></th>
<th>ADHD (n = 4,231)</th>
<th>Controls (n = 19,995)</th>
<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convictions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No with a conviction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2 Convictions</td>
<td>1,355</td>
<td>2.0</td>
<td>15.6</td>
<td>.868</td>
</tr>
<tr>
<td>Percentage with ≥2</td>
<td>868</td>
<td>20.5</td>
<td>6.7</td>
<td>.799</td>
</tr>
<tr>
<td>convictions among</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>convicted</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penal code</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual offenses</td>
<td>109</td>
<td>2.6</td>
<td>95</td>
<td>.3</td>
</tr>
<tr>
<td>Violence</td>
<td>531</td>
<td>12.6</td>
<td>629</td>
<td>2.2</td>
</tr>
<tr>
<td>Murder</td>
<td>&lt;5 &lt;0.0</td>
<td>&lt;5 &lt;0.0</td>
<td>1.3</td>
<td>.179</td>
</tr>
<tr>
<td>Property offenses</td>
<td>896</td>
<td>21.2</td>
<td>1,391</td>
<td>.7</td>
</tr>
<tr>
<td>Traffic code</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Driving under the</td>
<td>229</td>
<td>5.4</td>
<td>474</td>
<td>2.4</td>
</tr>
<tr>
<td>influence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special law</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td>405</td>
<td>11.7</td>
<td>761</td>
<td>3.9</td>
</tr>
<tr>
<td>Weapon</td>
<td>270</td>
<td>6.4</td>
<td>284</td>
<td>1.5</td>
</tr>
<tr>
<td>Tax laws</td>
<td>25</td>
<td>0.6</td>
<td>37</td>
<td>0.2</td>
</tr>
<tr>
<td>Incarcerations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No with an</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>incarceration</td>
<td>786</td>
<td>18.6</td>
<td>1,329</td>
<td>6.8</td>
</tr>
<tr>
<td>≥2 Incarcerations</td>
<td>435</td>
<td>10.3</td>
<td>515</td>
<td>2.6</td>
</tr>
<tr>
<td>Percentage with ≥2</td>
<td>553</td>
<td>11.7</td>
<td>388</td>
<td>3.4</td>
</tr>
<tr>
<td>among incarcerated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Red flags to evaluate for ADHD in adults

- Organizational skill problems (time management difficulties, missed appointments, frequent late and unfinished projects).
- Erratic work/academic performance.
- Anger control problems.
- Family/marital problems.
- Difficulty in maintaining organized household routines, sleeping patterns and other self-regulating activities.
- Difficulty managing finances.
- Addictions such as substance use, compulsive shopping, sexual addiction, overeating, compulsive exercise, video gaming or gambling.
- Frequent accidents either through recklessness or inattention.
- Problems with driving (speeding tickets, serious accidents, license revoked).
- Having a direct relative who has ADHD.
- Having to reduce their course load, or having difficulty completing assignments in school.
- Low self-esteem or chronic under-achievement.
What could lead a physician to suspect ADHD?

<table>
<thead>
<tr>
<th>Diagnosed as Children</th>
<th>Diagnosed as Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M&gt;F</strong></td>
<td><strong>M=F</strong></td>
</tr>
<tr>
<td>Higher frequency of hyperactive sx</td>
<td>Inattention sx most common reason for presentation</td>
</tr>
<tr>
<td>Less likely to have developed behavioral self-management strategies prior to dx</td>
<td>More likely to have developed behavioral self-management strategies prior to dx</td>
</tr>
<tr>
<td>May experience most sx at school</td>
<td>May experience most sx at home</td>
</tr>
<tr>
<td>Parents/Teachers are more often driving force for eval and reporters of treatment response.</td>
<td>Patient is more often driving force for eval and main reporter of treatment response.</td>
</tr>
</tbody>
</table>

Current Symptom/Function

Because accurate recollection of childhood symptoms and developmental history is difficult to obtain in adults, it is suggested to obtain, when possible, the point of view of a parent or a close family member who knows the individual’s early history.

A complete review would explore:
- Perinatal history
- Developmental milestones.
- Childhood medical/psychiatric/trauma history
- Social Hx re: learning, socialization and independent functioning.
- Symptoms of ADHD prior to the age of 12.
Assessment of Current Symptom/Function

Assessment Symptom/Function at age <12

SNAP-IV 26-Item Teacher and Parent Rating Scale
James M. Swanson, Ph.D., University of California, Irvine, CA 92715

Patient/Client Name:
Date of birth:
Grade:
Type of class:
Class size:
Completed by:
Date:
Physician Name:

For each item, check the column which best describes this child/adolescent:

<table>
<thead>
<tr>
<th>Item</th>
<th>Not at all</th>
<th>Just a little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Often fails to give close attention to details or makes careless mistakes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Medical Rule-Outs:
1. Sensory Deficits
2. Learning Disabilities
3. Seizures & other Neurologic Disorders
4. Sleep/Wake Disorders
5. Thyroid Dysfunction
6. Hypoglycemia
7. Anemia
8. Medications
   • Meds → Cognitive slowing
   • Meds → Agitation/Anxiety
9. Other Psychiatric Disorders

Lifestyle Habit Review:
1. Nutrition
2. Sleep
3. Exercise
4. Screen Time
5. High-Risk pursuits
6. Substance Use
7. Sexual Activity
8. Accidents

Contraindications to medications used to treat ADHD:
Generally (review HOPE for treatment in ADHD):
• Heart/Vascular
• Ophthalmologic
• Psychiatric
• Endocrine

See Next Slide for details
## MEDICAL REVIEW

### Cardiac Risks of ADHD Medications

In young and middle aged adults, when pre-existing cardiac status accounted for, psychostimulants and atomoxetine did NOT increase risk of MI, sudden cardiac death or stroke.

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<table>
<thead>
<tr>
<th>Medication Type</th>
<th>Contraindications</th>
<th>Precautions</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychostimulants</strong></td>
<td>Heart/Vascular • Symptomatic Cardiac Dz • Mod-&gt;Sev hypertension • Advanced Arteriosclerosis Ophthalmologic • Narrow Angle glaucoma Endocrine • Untreated hyperthyroidism • Pheochromocytoma Psychiatric • Tx with MAOI in last 14 days • Hx of Mania or Psychosis</td>
<td>Heart/Vascular • Non-symptomatic cardiac dz • Peripheral vasculopathy Psychiatric • Tic Disorders • Hx of substance use disorder • Anxiety Other • Pregnancy/Lactation • Renal impairment • Epilepsy</td>
<td>Vitals • Ht/wt, growth retardation, appetite probs • BP/HR increases, new peripheral vasculopathy Psychiatric • New psychiatric sx, incl irritability, aggression • New suicidal thoughts • New substance use • New sleep problems Other • Priapism</td>
</tr>
<tr>
<td><strong>Atomoxetine</strong></td>
<td>*all bold above</td>
<td>*all bold above • Asthma • Poor CYP2D6 metabolizers</td>
<td>*all bold above</td>
</tr>
<tr>
<td><strong>Alpha-2 Agonists</strong></td>
<td>• Inability for patient to adhere to regular daily dosing (d/t rebound hypertension)</td>
<td>• Hepatic impairment • Renal impairment</td>
<td>• BP/HR decreases during use • BP/HR increases upon withdrawal • QTc interval (monitor if other conditions/meds at risk of prolonging) • Somnolence and sedation</td>
</tr>
</tbody>
</table>
Cardiac Risks of ADHD Medications

A Randomized, Placebo-Controlled Trial of OROS Methylphenidate in Adults with Attention-Deficit/Hyperactivity Disorder
J. Biederman, Eric Mick, Craig Surman, Robert Doyle, Paul Hammerness, Theresa Harpold, Stephanie Durkel, Meghan Dougherty, Megan Alward, and Thomas Spencer

Increase:
- SBP/DBP
- HR

Did not affect:
- PR interval
- QRS interval
- QTC interval

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**Cardiac Risks of ADHD Medications**

**FDA Drug Safety Communication: Safety Review Update of Medications used to treat Attention-Deficit/Hyperactivity Disorder (ADHD) in adults**

**[12-12-2011] last update**

“FDA recommendations for the use of medications to treat ADHD have not changed. Healthcare professionals should continue to take special note that:

- Stimulant products and atomoxetine should generally not be used in patients with serious heart problems, or for whom an increase in blood pressure or heart rate would be problematic.
- Patients treated with ADHD medications should be periodically monitored for changes in heart rate or blood pressure.

Patients should continue to use their medicine for the treatment of ADHD as prescribed by their healthcare professional.”


**Hot Topic**

What if there are multiple psychiatric conditions?

<table>
<thead>
<tr>
<th>Comorbid Psych Diagnosis/Sx</th>
<th>Treat comorbid dx/sx first</th>
<th>Treat ADHD First</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI/HI</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Substance Use Disorder</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Psychosis</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Severe Major Depressive Disorder</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Moderate Major Depressive Disorder</td>
<td>* if ADHD sx more severe + high likelihood that ADHD sx significantly contribute to factors leading to onset of mood sx</td>
<td></td>
</tr>
<tr>
<td>Mild Major Depressive Disorder</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>OCD</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>PTSD</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Severe Anxiety Disorder</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Moderate Anxiety Disorder</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Mild Anxiety Disorder</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Borderline Personality Disorder</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

**ODDS OF HAVING COMORBID DISORDERS AMONG PERSONS WITH ADHD**

**Hot Topic**

**ADHD or Bipolar Disorder?**

ADHD more likely:

- Chronic inattention or hyperactivity (BPAD=only episodic)
- Normal number of thoughts, just unfiltered expression (BPAD=increased number of thoughts, “flight of ideas”, “crowded thoughts”)
- Bedtime resistance, delayed sleep onset, normal sleep duration (BPAD= decreased need for sleep)
- Mood contingent upon frustration with cognitive load. (BPAD=+euphoria, sometimes delusionally grandiose, very frequent mood changes, not contingent upon cognitive load)


**TABLE. Clinical presentation of ADHD, BD and BPD**

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>ADHD</th>
<th>BD mania</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inattention</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Does not complete tasks</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>All day, worse when prolonged attention or on-task behavior is expected</td>
<td>Fluctuation in activity levels day/night</td>
</tr>
<tr>
<td>Racing/crowded thoughts</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Pressured speech</td>
<td>Can be redirected and focused</td>
<td>Difficult to stop and focus</td>
</tr>
<tr>
<td>Impairability</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Decreased need for sleep</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sleep difficulties</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Early insomnia</td>
<td>No</td>
<td>Difficulty getting to sleep, awareness in the night</td>
</tr>
<tr>
<td>Disruptive sleep/wake patterns</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Euphoria/hallucination</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Irritability</td>
<td>Not frequent, other symptoms by enactment of achieved</td>
<td>Very frequent, especially on morning arousal</td>
</tr>
<tr>
<td>Mood swings</td>
<td>Not frequent, usually related to demands of learning</td>
<td>Very frequent rapid mood shifts</td>
</tr>
<tr>
<td>Self-esteem</td>
<td>Usually worsens over time</td>
<td>Generally inflated</td>
</tr>
<tr>
<td>Psychotic symptoms</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hypersexuality</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Verbal aggressiveness</td>
<td>Due to frustration</td>
<td>Deliberate</td>
</tr>
<tr>
<td>Physical aggressiveness</td>
<td>Rare</td>
<td>Deliberate</td>
</tr>
<tr>
<td>Destruction of property</td>
<td>Due to irritation</td>
<td>Deliberate</td>
</tr>
<tr>
<td>Suicidal ideation/attempts</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

(ADHD: attention deficit/hyperactivity disorder; BD: bipolar disorder; BPD: borderline personality disorder)

**Hot Topic**

**Cannabis Use and ADHD**

The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research, National Academies of Sciences, Engineering, Medicine, Jan 2017

- Moderate evidence that cannabis use is associated with increased risk of learning, memory, attention in acute use
- Limited evidence that cannabis use increases risk of substance use disorder for alcohol, tobacco, and other substances.
Hot Topic
Cannabis Use and ADHD

ORIGINAL ARTICLE
Deficits in striatal dopamine release in cannabis dependence
E van de Giessen1,3,4, JJ Weinstein1,2,3, CM Cassidy1,2, M Haney1,2, Z Dong1,2, R Ghazzouli1,2, N Ojel1,2, LS Kogele1,5, X Xu1,2, NP Vadhan1,3, ND Volkow1, M Sifftstein1,2 and A Al-Dargham1

Most drug of abuse lead to a general blunting of dopamine release in the chronic phase of dependence, which contributes to poor outcome. To test whether cannabis dependence is associated with a similar dopaminergic deficit, we examined striatal and extrastriatal dopamine release in severely cannabis-dependent participants (CD), free of any comorbid conditions, including nicotine use. Eleven CD and 12 healthy controls (HC) completed two positron emission tomography scans with [11C]DOPAC, before and after oral administration of d-amphetamine. CD stayed inpatient for 5-7 days prior to the scans to standardize abstinence. Magnetic resonance spectroscopy (MRS) measures of glutamate in the striatum and hippocampus were obtained in the same subjects. Percent change in [11C]DOPAC binding potential (ΔBPND) was compared between groups and correlations with MRS glutamate, subclinical psychopathological and neurocognitive parameters were examined. CD had significantly lower ΔBPND in the striatum (P = 0.003), effect size (ES) = 1.68, including the associative nuclei (P = 0.001, ES = 1.74), ventromedial striatum (P = 0.003, ES = 1.41) and the pallidus (P = 0.012, ES = 3.16). Lower dopamine release in the associative striatum correlated with inattention and negative symptoms in CD, and with poorer working memory and probabilistic category learning performance in both CD and HC. No relationships to MRS glutamate and amphetamine-induced subclinical positive symptoms were detected. In conclusion, this study provides evidence that severe cannabis dependence—without the confounds of any comorbidity—associates with a deficit in striatal dopamine release. This deficit extends to extrastriatal areas and predicts subclinical psychopathology.

Molecular Psychiatry (2017) 22, 68–75; doi:10.1038/mp.2016.21; published online 22 March 2016

Hot Topic
Is there a place for Neuropsychological testing in adults?

Can be helpful when...
1) Sx could be something related to else:
   • Suspicion of low cognitive ability
   • Suspicion of other learning/sensory deficit
   • Need to differentiate between coexisting psychiatric disorders (patient where empirical treatment trial carries significant risks).
   • If needed to increase validity of diagnostic impressions (patient with inability to provide age<12 contact or potential malingering).

2) You need more information:
   • You want to provide better detail on cognitive strengths and weaknesses to make recommendations for interventions or educational planning.
Objective Milestone 2

Describe a practical approach to diagnosing ADHD in adults.

- Suspect ADHD
- Gather Information on sx and function currently and prior to age 12.
  - Current: Get ASRS and lifestyle review from patient
  - At age<12: Get SNAP IV and childhood history from parent/early childhood parental figure
- Medical Review
  - Alternative causes
    - Medical conditions (sleep, endocrine, anemia, metabolic disorders)
    - Psychiatric conditions (psychosis, mood, anxiety, substance use disorders)
    - Sensory/Learning conditions
    - Medications (cognitive impairers and agitators)
  - Lifestyle contributors
  - Contradictions to ADHD treatments
    - HOPE

3) Differentiate treatment options for ADHD in adults.
Educatn patient and families on ADHD

<table>
<thead>
<tr>
<th>Core Goal of Education</th>
<th>Specifics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instill Hope</td>
<td>Patients feel and do better after treatment</td>
</tr>
<tr>
<td>Empathize</td>
<td>Express understanding of challenges and frustrations</td>
</tr>
</tbody>
</table>
| Explain               | - core symptoms  
|                       | - common associated mood/sleep changes  
|                       | - treatment rationale |
| Be Sensitive          | Listen to how cultural, ethnic, gender issues may shape beliefs re: ADHD and tx |
| Encourage             | Identify Strengths, encourage families to nurture talents |
| Balanced Lifestyle    | Emphasize benefit of:  
|                       | - regular exercise  
|                       | - sleep hygiene  
|                       | - nutrition  
|                       | - relaxation |
| Give Resources        | Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD)  
|                       | Canadian ADHD Resource Alliance (CADDRA)  
|                       | Centre for ADHD Awareness Canada (CADDAC)  
|                       | ADDitude Magazine/Website  
|                       | Books: Hallowell's Driven to Distraction |
Treatment of ADHD in Adults

**NON-PHARMACOLOGICAL STRATEGIES**

- Structure
- Set attainable goals
- Prioritize
- Visual Reminders
- Timers
- White noise
- Plan frequent breaks during long tasks

**PHARMACOLOGICAL STRATEGIES**

- Workplace Accommodations
- Regular Meetings with manager
- Short Term Goals
- Time Management Strategies
- Declutter
- Organizational Apps
- Executive Function Coaching

* + Cognitive-Behavioral Therapy
  - CBT+meds>meds alone
  - Mindfulness Training


Amphetamines increase synaptic release of:
- Dopamine
- Norepinephrine
- Serotonin

● DOP/NE/SER Dump into synapse

Lisdexamfetamine dimesylate

Methylphenidate reduces re-uptake of:
- Dopamine
- Norepinephrine

? Increases release of Dop/NE

= Rapid/Potent DOP/NE Backup in synapse
### Treatment of ADHD in Adults

#### PHARMACOLOGICAL STRATEGIES

**NON-STIMULANTS**

- **atomoxetine**
- **bupropion**
- **modafinil**
- **guanfacine**
- **clonidine**

Reduces re-uptake of NE = Potent NE Backup in synapse

Reduces re-uptake of Dop>NE = SLOW Dop>NE Backup in synapse

Mechanism not completely known – some effect on Dop re-uptake, some Dop/NE agonism, glut/Gaba effects

α₂a receptor agonist = DECREASE sympathetic tone

α₂a receptor agonist = DECREASE sympathetic tone

*may also impact functional connections in prefrontal cortex

*FDA Approved for tx of ADHD

### Treatment of ADHD in Adults

#### PHARMACOLOGICAL STRATEGIES

<table>
<thead>
<tr>
<th>Receptor</th>
<th>d(l)-amphetamine*</th>
<th>d(l)-methylphenidate*</th>
<th>Atomoxetine*</th>
<th>bupropion</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAT antag</td>
<td>-</td>
<td>121 nm</td>
<td>1451 nm</td>
<td>526 nm</td>
</tr>
<tr>
<td>NET antag</td>
<td>-</td>
<td>788 nm</td>
<td>5 nm</td>
<td>(poss metabolites)</td>
</tr>
<tr>
<td>SERT antag</td>
<td>-</td>
<td>&gt;10000 nm</td>
<td>77 nm</td>
<td>-</td>
</tr>
<tr>
<td>TAAR1 ag</td>
<td>-&gt;dop/ne release</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Time to peak (single dose)</td>
<td>2h</td>
<td>4.7h (SR)</td>
<td>1-2 h</td>
<td>3h (SR)</td>
</tr>
<tr>
<td>T ½</td>
<td>3.5h</td>
<td>5h</td>
<td>21 h</td>
<td></td>
</tr>
<tr>
<td>CYP Metabolism</td>
<td>2D6</td>
<td>none</td>
<td>2D6</td>
<td>2B6</td>
</tr>
</tbody>
</table>

Notes: d-enantiomer more potent effect than l-enantiomer

*FDA Approved for tx of ADHD
Treatment of ADHD in Adults

PHARMACOLOGICAL STRATEGIES


Clinician Reported ADHD Sx Improvement


Meta-analyses strongly favor psychostimulant treatment over placebo for symptoms improvement in ADHD.

53

54
Meta-analysis even favors bupropion over placebo for improvement in ADHD sx, although not as robustly as psychostimulants.


Risk of dependence and physical/social harm from psychostimulants must be factored into treatment decisions.

<table>
<thead>
<tr>
<th>Age Category</th>
<th>% of pop with Rx stimulant use disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall 12+</td>
<td>0.2%</td>
</tr>
<tr>
<td>12-17</td>
<td>0.2%</td>
</tr>
<tr>
<td>18-25</td>
<td>0.5%</td>
</tr>
<tr>
<td>26+</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

Comparison of ADHD treatment options.
Treatment of ADHD in Adults

- Risk of misuse/use disorder of amphetamine > risk of methylphenidate
- Few countries allow treatment of ADHD with amphetamine containing medications, some only lisdexamfetamine
- Even fewer allow with IR preps


Extended Release formulations lead to fewer ER visits.
**Treatment of ADHD in Adults**

**ADHD Treatment Decision Tree**

**Decision points:**
- Is treatment of comorbid condition a priority?
- Are there contraindications to/preference against psychostimulants? (if so, go to 2 below)

**Basic approach:**
1. Start stimulant trial fist
   - If higher risk of diversion/misuse, start with XR forms
   - **Methylphenidate preferred**
     - Usually start IR 5mg qam/qpnoon
     - Increase by 10mg total dose, every 5-7 days to max tolerable dose, max dose **60mg**.
     - Convert total dose to XR form
   - If Methylphenidate ineffective at max dose, start **mixed amphetamine salts**
     - Usually start IR 5mg qam/qpnoon
     - Increase by 10mg total dose, every 5-7 days to max tolerable dose, max dose **40mg**.
     - Convert total dose to XR form
2. If methylphenidate and mixed amphetamine salts helpful, but intolerable side effects, trial **atomoxetine**.
3. If methylphenidate and mixed amphetamine salts make worse, consider **guanfacine or clonidine**.

---

**Adverse effect and response level**

Low dose PRN IR for necessary activity in am or evening if using XR primarily.
## Treatment of ADHD in Adults

<table>
<thead>
<tr>
<th>Medication</th>
<th>Prep</th>
<th>Cost/30d (Good Rx 10/2019)</th>
<th>Insurance Tier</th>
</tr>
</thead>
<tbody>
<tr>
<td>D(I)-amphetamine</td>
<td>Mixed amphetamine salts IR</td>
<td>$28-39</td>
<td>Select</td>
</tr>
<tr>
<td>methylphenidate</td>
<td>IR</td>
<td>$25-41</td>
<td>Select</td>
</tr>
<tr>
<td>atomoxetine</td>
<td>Strattera</td>
<td>$65-120</td>
<td>Select (QL)</td>
</tr>
<tr>
<td>bupropion</td>
<td>Wellbutrin XL</td>
<td>$18-50</td>
<td>Select (QL)</td>
</tr>
<tr>
<td>Guanfacine</td>
<td>Intuniv (ER)</td>
<td>$18-84</td>
<td>Select (QL)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Kapvay (ER)</td>
<td>$73-100</td>
<td>Select (QL)</td>
</tr>
</tbody>
</table>

Insurance coverage and cost can be barriers to safer treatments.

---

### Medication Availability

- **Methylphenidate (Ritalin, etc)**: X (1st line) X (2nd line) *long acting only* X (1st line) X (2nd line) *long acting only* X (1st line) X (2nd line) *long acting only, and only if started during childhood*

- **Amphetamine Mixed salts (Adderall, etc)**: X (1st line) X (2nd line) *if can't tolerate long action of lisdex* X (1st line) X (2nd line) *only if started during childhood*

- **Dexamfetamine (Dexedrine)**: X (1st line) X (2nd line) *long acting only* X (1st line) X (2nd line) *long acting only*

- **Lisdexamfetamine (Vyvanse)**: X (1st line) X (2nd line) X (1st line) X (2nd line) *only if started during childhood*

- **Atomoxetine (Strattera)**: X (1st line) X (2nd line) X (1st line) X (2nd line) X (1st line) X (2nd line) X (1st line) X (2nd line)

- **Guanfacine ER (Intuniv)**: X (1st line) X (2nd line) X (1st line) X (2nd line)

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### References

Differentiate treatment options for ADHD in adults.

- Psychoeducation and community resources provide solid ground for initiating treatment.
- Non-pharmacological interventions:
  - can be helpful at reducing impact of sx, reducing stress, depression, anxiety related to ADHD.
  - may not be as practical, as adult environments (work, adult relationships) may be harder to manipulate from clinic.
- Pharmacological Interventions:
  - Are more effective than non-pharm interventions at decreasing core ADHD sx
  - Amphetamine and Methylphenidate have greatest effectiveness, but have higher risk of misuse and use disorder (AMP>MPH).
  - Young adults most likely to misuse prescription stimulants.
  - Adult work schedules/home demands may benefit from mixed dosing of XR and IR preps.
“Dear Ricky,

I’m writing to you from more than 50 years in the future. You’re a lot older now, and while you’ve lived a happy and healthy life with no regrets, I have some advice for you. You know how you love to play outdoors and explore the world around you? Never stop doing that. Always seek adventure. Learn to swim, find your own way home, and climb trees with Lindy, Vanessa and your friends. The spirit of adventure will keep you curious, open your mind to great opportunities, and steer you on a lifelong quest to prove that impossible is just a word. You will have many wonderful adventures in your life with the most incredible people - I won’t give away exactly what they are, as I don’t want to spoil the fun.

On the topic of imagination, never stop dreaming and creating. Children are too often told that they cannot do this, and they shouldn’t do that - ignore them. Don’t ever let anyone prevent you from going after your dreams. Balloons, trains, planes and spaceships - whatever comes into your imagination, continue to dream big.

Your imagination is one of your greatest gifts - this will become more and more apparent when you enter secondary school. You will face many challenges, and often feel like you don’t fit in and that you can’t always keep up. Don’t let this hold you back. Use your imagination to find inventive ways around it. Your ability to think differently will become one of your biggest advantages in life - taking you places where most straight-A students will never go.

Challenges will be a constant in your life. You will make a lot of mistakes and fail time and time again. But don’t let this discourage you. Failure teaches us life’s greatest lessons, and often shows us a better way of doing things. Don’t let failure get you down. Everyone fails. Your biggest heroes - including Douglas Bader, Ernest Shackleton and Scott of the Antarctic (did you know you’re related?) - have all failed at some point, but look what they achieved in the end.

And when you do make mistakes, know that your parents will always be there for you. While you may get in trouble at times, they always have your best interest at heart and love you unconditionally. You will understand this better when you become a father yourself. Be nice to your family and listen to your mum and dad - they will guide you through life and be there for you at every turn. Remember to treat others as you would want to be treated.

Above all, always remember to have fun. As you grow older you will realize just how important it is to do what you love and love what you do. Don’t waste your time doing things that don’t excite you. Find your passions and go out there and grab at them with both hands. Life is for living and try to enjoy every day.

Good luck
Richard”

Edward Hallowell, MD
Psychiatrist and NY Times Best-Selling Author

“THE SEVEN HABITS OF HIGHLY EFFECTIVE ADD ADULTS
1. Do what you’re good at. Don’t spend too much time trying to get good at what you’re bad at. (You did enough of that in school.)
2. Delegate what you’re bad at to others, as often as possible.
3. Connect your energy to a creative outlet.
4. Get well enough organized to achieve your goals. The key here is “well enough.” That doesn’t mean you have to be very well organized at all—just well enough organized to achieve your goals.
5. Ask for and heed advice from people you trust—and ignore, as best you can, the dream-breakers and finger-waggers.
6. Make sure you keep up regular contact with a few close friends.
7. Go with your positive side. Even though you have a negative side, make decisions and run your life with your positive side.”
Evaluation for and Treatment of Attention-Deficit/Hyperactivity Disorder in Adults

Michael Sean Stanley, MD
Assistant Professor
Oregon Health & Science University
Department of Psychiatry