Assessment of ADHD in Adults

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Overview

- DSM-5 TR Diagnostic Criteria
- The importance of a thorough ADHD assessment
- The importance of accurate ADHD diagnosis
- Components of a good ADHD evaluation
- Factors complicating diagnosis

DSM-5 TR Diagnostic Criteria (APA, 2022)

A. persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development, as characterized by (1) and/or (2):

1. **Inattention:** Six (or more) symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities.
2. **Hyperactivity and impulsivity:** Six (or more) symptoms have persisted for at least 6 months to a degree that is inconsistent with developmental level and that negatively impacts directly on social and academic/occupational activities.

Note: The symptoms are not solely a manifestation of oppositional behavior, defiance, hostility, or a failure to understand tasks or instructions. For older adolescents and adults (age 17 and older), at least five symptoms are required.

DSM-5 TR Diagnostic Criteria (APA, 2022)

B. Several inattentive or hyperactive-impulsive symptoms were present prior to age 12 years.

C. Several inattentive or hyperactive-impulsive symptoms are present in two or more settings (e.g., at home, school, or work; with friends or relatives; in other activities).

D. There is clear evidence that the symptoms interfere with, or reduce the quality of, social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of schizophrenia or another psychotic disorder and are not better explained by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder, substance intoxication or withdrawal).

DSM-5 TR Diagnostic Criteria (APA, 2022)

Specify whether:

(F90.2) Combined presentation: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.

(F90.0) Predominantly inattentive presentation: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.

(F90.1) Predominantly hyperactive/impulsive presentation: If Criterion A2 (hyperactivity-impulsivity) is met and Criterion A1 (inattention) is not met for the past 6 months.

Importance of Psychological Assessment

- Many mental health and developmental disorders can look like ADHD
  - Depression (lack of motivation, anhedonia)
  - Anxiety (problems focusing, restlessness)
  - Borderline Personality Disorder (impulsivity)
  - Specific Learning Disorders
  - Insomnia
  - Intellectual Developmental Disorder
  - Early symptoms of Schizophrenia
- Many people commonly experiencing symptoms of ADHD, just not at an impairing level
  - Spectrum of impairment
  - Social media

Importance of Psychological Assessment

- Diversion of stimulant medications, especially among young adults on college campuses (Faraone et al., 2022)
- Risks associated with stimulant medications
  - Exacerbation of anxiety, depression, mood, or psychosis symptoms (Keith et al., 2022)
  - Abuse potential (Shellenberg et al., 2020)
- Uncovering comorbid disorders that will inform treatment approach

Importance of Accurate Diagnosis

- Educational Outcomes
  - Lower grades and achievement
- Occupational/Economic Functioning
  - Job loss/lower career aspirations/financially dependent on parents
- Mental Health
- Physical Health
  - Approximately 10-year lower life expectancy
- Substance Use
- Antisocial Behavior
- Driving
  - More car accidents/license suspensions

Cherkasova et al., 2022

Components of an ADHD Evaluation

- Clinical Interview
  - Thorough review of mental health symptoms
  - Review of current stressors
  - Information regarding childhood
  - Medical, academic, employment history
  - Trauma history
  - Family history of mental health issues

Component of an ADHD Evaluation

- Self-report and observer (if possible) ratings of ADHD symptoms both as a child (if possible) and as an adult
- Establish impairment relative to the average person
- Obtain corroboration of symptoms and impairment (interviews, academic records, performance improvement plans)
- Rule out other mental health disorders that may be causing symptoms
  - Assessment of anxiety, depression, and other relevant issues
- Rule out developmental intellectual disorder and specific learning disorders as cause of inattention symptoms

Barkley & Newcorn, 2009

Factors Complicating Accurate Diagnosis

- Severe anxiety and/or depression
- Active PTSD symptoms
- Regular marijuana/substance use
- Poor sleep

Treatment of these issues prior to psychological assessment of ADHD can provide additional information to inform diagnosis



Attention Deficit Hyperactivity Disorders

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ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) TREATMENT

- ADHD is a neurodevelopmental disorder with onset before age 12
- ADHD symptoms cause impairment in all spheres of functioning
- The estimated prevalence of Adult ADHD in the United States is around 6%, with a male to female ratio of only 1.6:1
- Effective treatment is possible, and it leads to significant improvement in the quality of life

TREATMENT GOALS

- IMPROVED FOCUS
- IMPROVED ABILITY TO INITATE TASKS
- IMPROVED ABILITY TO SUSTAIN MENTAL EFFORT AND COMPLETE TASKS
- DECREASED DISTRACTIBILITY
- DECREASED FORGETFULNESS
- IMPROVED IMPULSE CONTROL

TREATMENT GOALS, continued

- As core symptoms improve, patients experience an improved ability to complete tasks and regulate their emotions and behaviors
- Consistent improvement in everyday functioning leads to improved self –esteem and self-confidence, less performance anxiety and improved overall life experiences and quality of life

PHARMACOLOGICAL TREATMENT HISTORY

- Certain natural substances have been known to improve cognitive and physical performance since ancient times
- Ephedrine is a plant-derived substance first used in China more than 5,000 years ago for its stimulant properties
- Ephedrine and related chemicals have sympathomimetic properties
- They act similarly to the endogenous agonists of the sympathetic nervous system called catecholamines (epinephrine or adrenaline, norepinephrine or noradrenaline, and dopamine)

PHARMACOLOGICAL TREATMENT HISTORY, continued

- Due to the scarcity of the naturally derived ephedrine, chemists sought ways to synthesize it
- In 1885 the Japanese chemist Nagai Nagayoshi isolated ephedrine from Ephedra vulgaris and later synthesized it
- In 1887, in Germany, the Romanian chemist Lazar Edeleanu produced amphetamine entirely synthetically from phenyl-2-propranone
- In 1893 Nagayoshi synthesized methamphetamine from ephedrine

PHARMACOLOGICAL TREATMENT HISTORY, continued

- In 1927 the American chemist Gordon Alles (1901 – 1963) independently resynthesized amphetamine and described its sympathomimetic properties
- The American pharmaceutical company Smith, Kline & French (SKF) bought the patent
- The company started marketing amphetamine as a nonaddicting substitute for ephedrine in several products such as Benzedrine pills and inhalers, Dexedrine pills and Dexamyl tablets

PHARMACOLOGICAL TREATMENT HISTORY, continued

- Benzedrine sulfate started being used worldwide to treat a wide variety of medical conditions
- In 1937, Dr. Charles Bradley M.D. (1902 – 1979), an American psychiatrist, treated headaches in hospitalized children with Benzedrine and noticed significant improvement in the children's attention, concentration and academic performance
- Most of the research and development of ADHD medications since has been based in his findings

PHARMACOLOGICAL TREATMENT

- The first line of treatment for ADHD are drugs with sympathomimetic properties called stimulants
- Their effectiveness in reducing the core symptoms of ADHD (distractibility, impulsivity, hyperactivity) has been demonstrated by numerous studies over the past few decades
- Stimulants actively increase the metabolic activity and the levels of norepinephrine and dopamine in areas of the brain important for executive function

STIMULANTS

There are two groups of stimulants

methylphenidate based

amphetamine based

- Both groups inhibit the norepinephrine and dopamine re-uptake, with subtle differences in the balance of dopamine and norepinephrine

STIMULANTS, continued

- Stimulants can be immediate - release (short - acting) and extended - release (long - acting) products
- The extended - release products vary by the active-drug delivery system they employ
- Most products are administered orally as tablets, caplets, capsules, spansules, sprinkles, liquids
- Two products are administered transdermally, as patches

STIMULANT SIDE EFFECTS

- Common side effects include appetite suppression, insomnia, gastrointestinal upset, headaches
- Some patients may experience new onset of tics or worsening of pre-existent tics
- Some patients may experience a stimulant rebound effect - a return in symptoms, sometimes with heightened intensity, once the medication wears off

STIMULANT SIDE EFFECTS

- Stimulants may cause psychosis and may worsen symptoms in patients with depression, anxiety, bipolar disorder and pre-existing psychotic disorders
- Combining stimulants and MAOI's can cause dangerously high blood pressure and even death. Patients must be off MAOI's for at least 14 days before starting a stimulant

There is clinical evidence that stimulants may lower the convulsive threshold and increase the risk for seizures in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures

STIMULANT SIDE EFFECTS

- Stimulants may increase blood pressure and must be used cautiously in patients with a history of hypertension or other heart problems
- When treating adult ADHD, it is important to start with a comprehensive medical work-up to screen for hypertension and other cardiac risk factors
- In 2006 an FDA panel recommended that the potential cardiovascular risks of stimulant medications be included in a black box warning on the medications

STIMULANT SIDE EFFECTS

- Stimulants may increase or decrease the activity of certain cytochrome P450 enzymes and can interfere with the metabolism of a variety of medications such as coumarin anticoagulants, certain anticonvulsants, phenylbutazone, and tricyclic drugs (imipramine, clomipramine, desipramine)
- Alcohol may increase the blood levels of stimulants and increase the risk for side effects

STIMULANTS AND PREGNANCY

There are no adequate studies in humans

- Potential benefits may warrant the use of stimulants in pregnant women when benefits significantly outweigh potential risks
- Premature delivery and low birth weight infants have been reported
- Stimulants are excreted in breast milk
  Breastfed infants should be monitored for adverse reactions, such as agitation, insomnia, anorexia, and reduced weight gain

STIMULANTS AND PREGNANCY

- Long term neurodevelopmental effects on infants from CNS stimulant exposure have not been studied
- Some authorities advise against maternal use during pregnancy and breastfeeding for safety reasons

- There is a US pregnancy registry that monitors pregnancy outcomes in women exposed to psychostimulants during pregnancy
- Healthcare providers are encouraged to register patients with the National Pregnancy Registry for Psychostimulants at 1-866-961-2388

STIMULANTS AND ADDICTION

Stimulants are addictive drugs

The Drug Enforcement Agency (DEA) categorizes stimulants as Schedule II non-narcotic drugs (substances or chemicals with a high potential for abuse, with use potentially leading to severe psychological or physical dependence)

Stimulants come with a warning regarding their addictive potential

METHYLPHENIDATE BASED PRODUCTS

- Ritalin (approved December 1955) - methylphenidate hydrochloride, tablets
- Methylin (approved May 2000) – methylphenidate hydrochloride, tablets
- Concerta (approved August 2000) – methylphenidate hydrochloride, extended-release tablets
- Metadate CD (approved April 2001) – methylphenidate extended release, capsules
- Ritalin LA (approved June 2002) - methylphenidate extended release, capsules

METHYLPHENIDATE BASED PRODUCTS, continued

- Methylin (approved December 2002) - methylphenidate hydrochloride, tablets
- Daytrana (approved 2006) – methylphenidate, patch
- Quillivant XR (approved September 2012) – methylphenidate hydrochloride, powder for oral suspension, extended release
- Methylin ER (FDA approved in 2012) methylphenidate, controlled release tablets
- Methylin chewable tablets (FDA approved in 2015) – methylphenidate, tablets, chewable

METHYLPHENIDATE BASED PRODUCTS, continued

- Aptensio XR (approved April 2015) – methylphenidate hydrochloride, extended release, capsules
- Quillichew ER (approved December 2015) - methylphenidate hydrochloride, extended release, chewable tablets
- Cotempla XR-ODT (approved June 2017) – methylphenidate, extended release, disintegrating tablets
- Relexxii (approved July 2017) - methylphenidate hydrochloride, extended release, tablets
- Jornay PM (approved August 2018) - methylphenidate hydrochloride, extended release, capsules

METHYLPHENIDATE BASED PRODUCTS, continued

- Adhansia XR (approved February 2019) - methylphenidate hydrochloride, extended release, capsules

Dexmethylphenidate products:

- Focalin (FDA approved in 2001) – dexmethylphenidate hydrochloride, tablets
- Focalin XR (FDA approved in 2005) – dexmethylphenidate, extended release, capsules
- Azstarys (approved March 2021) - once-daily capsule - combines the dexmethylphenidate prodrug serdexmethylphenidate (SDX) and immediate-release dexmethylphenidate

AMPHETAMINE BASED PRODUCTS, continued

Amphetamine

- Adzenys ER - Adzenys ER (FDA approved in 2007) – amphetamine, extended-release, liquid suspension
- Dyanavel XR – (FDA approved in 2015) – amphetamine, extended release, oral suspension
- Adzenys XR – ODT (FDA approved in 2016) - amphetamine, extended-release, disintegrating tablet

AMPHETAMINE BASED PRODUCTS, continued

Amphetamine – Dextroamphetamine

- Adderall (first approved for ADHD in 1996) - 75 percent dextroamphetamine and 25 percent levoamphetamine, tablet
- Adderall XR (first approved for ADHD in 2001) - 75 percent dextroamphetamine and 25 percent levoamphetamine, extended release, capsule
- Evekeo (FDA approved September 2014) – amphetamine sulfate, tablet
- Mydayis (approved in June 2017) – amphetamine and dextroamphetamine mixed salts, extended release, capsule
- Evekeo ODT (FDA approved April 2021) - 50% dextroamphetamine sulfate / 50 % levoamphetamine sulfate, oral disintegrating tablet

AMPHETAMINE BASED PRODUCTS, continued

Dextroamphetamine

- Dexedrine (FDA approved in 1976) – dextroamphetamine sulfate, tablets
- Dexedrine spansules - dextroamphetamine sulfate, spansules
- ProCentra (FDA approved 2013) - Dextroamphetamine Sulfate, oral Solution
- Zenzedi (FDA approved 2013) - Dextroamphetamine sulfate, tablets
- Xelstrym Transdermal System (FDA approved 2022) – dextroamphetamine, transdermal patch

AMPHETAMINE BASED PRODUCTS, continued

Lisdexamfetamine

- Vyvanse (lisdexamfetamine dimesylate) (FDA approved in) 2007 - amphetamine prodrug, capsules

Methamphetamine

Desoxyn (FDA approved in 2010) - methamphetamine hydrochloride, tablets

NON-STIMULANT MEDICATIONS

- Medications that are not stimulants can improve ADHD symptoms by also increasing dopamine and noradrenergic neurotransmission in brain regions involved in sustaining attention and regulating motor activity and emotion
- Most of the non-stimulant medications used off label to treat ADHD are antidepressants
- Some of the antidepressants have a boxed warning regarding the risk of suicide in patients younger than 24 years of age

NON-STIMULANT MEDICATIONS

- They are recommended for patients with conditions that preclude the use of stimulants, such as:
  - poor response to stimulants
  - significant side effects to stimulants
  - medical risk factors such as hypertension or cardiac disease
  - substance disorders and high risk for abuse
  - significant insomnia

NON-STIMULANT MEDICATIONS, continued

<u>Guanfacine</u>

- Guanfacine extended release (Intuniv) was FDA approved in September 2009
- Guanfacine hydrochloride (brand name Tenex) – off label use, tablets
- Guanfacine selectively stimulates the adrenergic α2A receptors subtype and appears to be more potent at postsynaptic receptors

NON-STIMULANT MEDICATIONS, continued

Clonidine

- Clonidine hydrochloride immediate release
- Clonidine hydrochloride extended release (Kapvay, Onyda XR) – FDA approved in 2010
- Clonidine stimulates all 3 subtypes of adrenergic α_2 receptors and tends to be more potent at the presynaptic receptors

NON-STIMULANT MEDICATIONS, continued

- Selective Norepinephrine reuptake inhibitors
- Strattera (FDA approved in 2002) – atomoxetine hydrochloride, capsules
- It increases noradrenaline and dopamine within the prefrontal cortex, but not in the nucleus accumbens or striatum
- This is beneficial in the treatment of ADHD as dopamine activation in the subcortical nucleus accumbens and striatum is associated with many stimulant-associated side effects and an increase in abuse potential, which is a limiting factor in the use of stimulant medications

NON-STIMULANT MEDICATIONS, continued

- Dopamine – Norepinephrine reuptake inhibitors

Wellbutrin, Wellbutrin SR, Wellbutrin XL – bupropion hydrochloride, tablets, off label use

- NEUROPSYCHIATRIC REACTIONS IN PATIENTS TAKING BUPROPION FOR SMOKING CESSATION
- Serious neuropsychiatric reactions have occurred in patients taking bupropion for smoking cessation. Most of these reactions occurred during bupropion treatment, but some occurred in the context of discontinuing treatment. In many cases, a causal relationship to bupropion treatment is not certain, because depressed mood may be a symptom of nicotine withdrawal. However, some of the cases occurred in patients taking bupropion who continued to smoke. Although Wellbutrin® is not approved for smoking cessation, observe all patients for neuropsychiatric reactions. Instruct the patient to contact a healthcare provider if such reactions occur.

NON-STIMULANT MEDICATIONS, continued

- Serotonin – norepinephrine reuptake inhibitors
- Cymbalta – duloxetine hydrochloride, delayed release, capsules, off label use
- Effexor and Effexor XR – venlafaxine hydrochloride, capsules, off label use

- Serotonin -Norepinephrine Modulating Agents
- Qelbree (FDA approved in 2021) - viloxazine hydrochloride, extended release, capsule
- Viibryd - vilazodone hydrochloride, tablet – off label use
- Trintellix – vortioxetine, tablet, off label use

NON-STIMULANT MEDICATIONS, continued

- Tricyclic antidepressants

- Norpramin – desipramine hydrochloride, tablet, off label use
- Tofranil – imipramine hydrochloride, tablet, off label use
- Pamelor - nortriptyline hydrochloride, tablets, off label use

NON-STIMULANT MEDICATIONS, continued

- Wakefulness promoting agents (eugeroics)
- Provigil - modafinil – tablets, off label use
- Nuvigil - armodafinil (isomer of modafinil)– tablets, off label use
- Both are weak inhibitor of dopamine reuptake that also increase the concentrations of norepinephrine and serotonin in the prefrontal cortex and hypothalamus
- Serious rash requiring hospitalization and discontinuation of treatment has been reported in association with the use of both

PSYCHOTHERAPY FOR ADHD

- Psychotherapies address the negative cognitive, emotional and behavioral aspects of living with ADHD
- They help patients improve motivation, decrease perfectionism and procrastination, strengthen self-esteem and self-confidence, and develop effective emotion regulation and interpersonal skills
- Psychotherapies found beneficial for patients with adult ADHD include
  - Cognitive Behavioral Therapy
  - Dialectical Behavioral Therapy
  - Mindfulness Based Cognitive Therapy

VITAMINS AND SUPPLEMENTS

- A lot of research has also been dedicated to finding effective complementary therapies for ADHD in children and adults
- So far studies have produced mixed results

<u>Multivitamins and minerals</u>

- Vitamin D
- Iron
- Zinc supplementation
- Magnesium supplementation

VITAMINS AND SUPPLEMENTS

Omega Fatty Acids - The U.S. Food and Drug Administration (FDA) has deemed omega-3 fatty acids safe up to 3 grams a day

Broad-Spectrum Micronutrients

- Daily Essential Nutrients - https://www.hardynutritionals.com/
- EMPower+ - https://www.truehope.com/empowerplus
- Brillia - https://discoverbrillia.com/pages/inattention

OTHER NON – PHARMACOLOGICAL TREATMENTS FOR ADHD

The evidence is nonconclusive

Certain patients may benefit more than others

Diet modifications

- Gluten free diet
- Sugar free diet
- Diet free of artificial food coloring

OTHER NON – PHARMACOLOGICAL TREATMENTS FOR ADHD

Brain training

- Cognitive Remediation and Rehabilitation – computerized or therapist delivered, focusing on improving working memory, organizational skills, etc.
- Study skills training and self-monitoring
- Neurofeedback - neurofeedback protocols are considered "Efficacious and Specific, Level V" in the treatment of ADHD by Association for Applied Psychophysiology and Biofeedback Guidelines

OTHER NON – PHARMACOLOGICAL TREATMENTS FOR ADHD

- Video game brain training – EndeavorRx - by Akili Interactive – FDA approved in June 2010, requires a prescription - EndeavorRx® - ADHD on the App Store (apple.com)
- Yoga - Studies found that practicing yoga regularly (at least twice a week) may reduce ADHD symptoms. Several small imaging studies showed an increase in the activity of the prefrontal cortex and other brain areas
- Regular physical exercise elevates the release of fronto-striatal dopamine and norepinephrine leading to reduced impulsivity and hyperactivity, improved attention, and enhanced performance on executive functioning tasks