ADHD, Amphetamines, Addiction, and the Amygdala

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Outline

• How to deal with ADHD and requests for ADHD medication in your SUD treatment program

• Adult ADHD reconsidered.

• Connections between ADHD, stimulant seeking and use, SUDs, and PTSD.
Meds with the Sirens’ Call

Opioids

Benzodiazepines

Cannabinoids

Stimulants
A.D.H.D. Nation

Children, Doctors, Big Pharma, and the Making of an American Epidemic

ALAN SCHWARZ

FINALIST FOR THE PULITZER PRIZE
Classes of ADHD Medications

• Amphetamines
  - Amphetamine salts
  - Lisdexamfetamine
  - Lisdexamfetamine (Vyvanse)
  - Adderall

Methylphenidate
  - Methylphenidate (Ritalin, Focalin)
  - OROS-methylphenidate (Concerta)

Nonstimulants
  - Atomoxetine (Strattera)
  - Bupropion (Wellbutrin)
  - Guanfacine (Intuniv)
  - Desipramine
Phenylethylamine
Chemical structures of some phenylethylamine stimulants and neurotransmitters.

- MDMA or ecstasy
- Cathinone
- Bupropion
- Cocaine
- Dopamine
- Norepinephrine
- Methamphetamine
- Amphetamine
Chemical structures of methylphenidate and related compounds

atomoxatine  fluoxetine  methylphenidate  thorazine

amitriptyline
Side Effects of Stimulants

• Increased pulse and blood pressure
• CV events
• seizures/aggravation of Tourettes
• Picking, formication
• Metabolic: poor appetite, weight loss, poor nutrition, poor growth in children
• Adverse fetal effects
• Delayed sleep onset and Circadian rhythm disruption, especially amphetamines
• Behavioral: agitation, irritability, psychosis, exacerbation of OCD
• Physical dependence, withdrawal syndrome, addiction
Warnings

Serious Cardiovascular Events

Sudden Death and Preexisting Structural Cardiac Abnormalities or Other Serious Heart Problems  Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs (see CONTRAINDICATIONS).

Hypertension and Other Cardiovascular Conditions  Stimulant medications cause a modest increase in average blood pressure (about 2 to 4 mmHg) and average heart rate (about 3 to 6 bpm) [see ADVERSE REACTIONS], and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with preexisting hypertension, heart failure, recent myocardial infarction, or ventricular.

Assessing Cardiovascular Status in Patients Being Treated With Stimulant Medications  Patients being considered for treatment stimulant medications should have a careful history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other
Schedule II Stimulant Rx’s in ME: Adult:---

Pediatric:-----

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The graph shows the increase in Schedule II Stimulant Rx’s in ME from 2005 to 2013, highlighting the growth in both Adult and Pediatric prescriptions.
CASE # 1

26 year-old enters your addiction treatment program for MAT with buprenorphine and IOP. Requests “to be put back on Adderall for my ADHD.” Was on it for 3 years from PCP until 6 months ago, when due to addiction issues, lost contact with PCP.

Has been using street buprenorphine. Presents not intoxicated or in withdrawal.

By hx and exam meets DSM V criteria for ADHD.

What do you want to know?
• Had ADHD a child, on stimulants only briefly—household too disordered to follow through. Abusive, alcoholic father. Diagnosed with conduct disorder in addition to ADHD.

• Has no confounding mental health or social issues— has a safe place to live, possibility of adequate sober supports.

• UDS shows buprenorphine, amphetamines, and cannabis. He claims use of cannabis is related to an unreliable supply of street buprenorphine.

• PMP search shows no ADHD medications for past year.
Can he be diagnosed with ADHD?

At what point would you consider starting medication or other treatment?
COCHRANE REVIEWS

- Amphetamines for ADHD in Adults. Castells, Cochrane Database Review, 2018
- Cognitive-behavioral Interventions for ADHD in Adults. Lopez, Cochrane Database Sys Rev Mar 2018
- The Cochrane Collaborative Withdraws a Review on Methylphenidate for Adults with ADHD. Evidence Based Medicine Boesen, K Aug 2017

OTHER REVIEWS OF RCTS


STUDIES OF NOTE

- RCT of OROS-methylphenidate with CBT in Adolescents with ADHD and SUDs. Riggs,P. J Am Acad Child Adolesc Psych Psych Sept 2011
- Is Adult ADHD a Childhood-onset Neurodevelopmental Disorder? Evidence from a 40-year Longitudinal Cohort Study. Moffitt TE, Am J Psych 2015 Oct
Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study

Terrie E. Moffitt, Ph.D., Renate Houts, Ph.D., Philip Asherson, M.D., Daniel W. Belsky, Ph.D., David L. Corcoran, Ph.D., Maggie Hamerlee, B.A., HonaLee Harrington, B.A., Sean Hogan, M.S.W., Madeline H. Meier, Ph.D., Guilherme V. Polanczyk, M.D., Richie Poulton, Ph.D., Sandhya Ramrakha, Ph.D., Karen Sugden, Ph.D., Benjamin Williams, B.A., Luis Augusto Rohde, M.D., Avshalom Caspi, Ph.D.

Objective: Despite a prevailing assumption that adult ADHD is a childhood-onset neurodevelopmental disorder, no prospective longitudinal study has described the childhoods of the adult ADHD population. The authors report follow-back analyses of ADHD cases diagnosed in adulthood, alongside follow-forward analyses of ADHD cases diagnosed in childhood, in one cohort.

Method: Participants belonged to a representative birth cohort of 1,037 individuals born in Dunedin, New Zealand, in 1972 and 1973 and followed to age 38, with 95% retention. Symptoms of ADHD, associated clinical features, comorbid disorders, neuropsychological deficits, genome-wide association study-derived polygenic risk, and life impairment indicators were assessed. Data sources were participants, parents, teachers, informants, neuropsychological test results, and administrative records. Adult ADHD diagnoses used DSM-5 criteria, apart from onset age and cross-setting corroboration, which were study outcome measures.

Results: As expected, childhood ADHD had a prevalence of 6% (predominantly male) and was associated with childhood comorbid disorders, neurocognitive deficits, polygenic risk, and residual adult life impairment. Also as expected, adult ADHD had a prevalence of 3% (gender balanced) and was associated with adult substance dependence, adult life impairment, and treatment contact. Unexpectedly, the childhood ADHD and adult ADHD groups comprised virtually nonoverlapping 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.

Conclusions: The 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.

Findings of Moffitt NZ Study

• No correlation between child and adult ADHD
• Although adults with history of child-onset ADHD didn’t meet criteria for ADHD they carried some of their problem behaviors and poor function into adulthood.
• Few patients in either group treated were treated with medication.
• 48.4% of adults with ADHD also had a SUD diagnosis.
What we know about Adult ADHD and its Treatment

• Poor correlation between child and adult ADHD
• Most controlled studies of ADHD treatment are in children.
• Robust benefits for treatment of adult ADHD at least for a month, but these are attenuated when other diagnoses are present, including SUD.
• The majority of controlled studies involve methylphenidate—there is a lack of studies supporting amphetamine for treatment of adult ADHD.
• Few adults continue ADHD medication long-term. Why?
• Behavioral treatments have equal or greater benefit than medication, but there are no head-to-head studies addressing which approach is more effective and for whom.
• The quality of evidence for any medication for adult ADHD is poor.
So...what IS Adult ADHD?

- ADHD as a personality trait/lifelong neurobehavioral disorder needs to be reconsidered.
- Adult ADHD diagnosis may include several different categories:
  - ADHD without SUD
  - ADHD with SUD
  - Persistence of impairments of childhood ADHD into adulthood
  - Over-diagnosis of ADHD to legally obtain performance-enhancing drugs
  - ADHD symptoms as part of a different mental health disorder—autism, learning disability, conduct disorder, mood disorders (depression, bipolar), PTSD. To get payment for medication ADHD dx is often required.
What we know about ADHD and SUD

• ADHD medication in SUD provides subjective, but not objective, benefit.
• CBT is superior to medication for treating ADHD in a SUD treatment setting.
• In the aggregate, there is neither benefit nor harm to recovery from SUD when a stimulant is prescribed for ADHD.
• Those who use illicit stimulants are more likely to have addiction issues around stimulants or to have other SUDs then those who use stimulants by prescription.
• Corollary: treating use of nonprescribed stimulants with prescription stimulants rarely results in discontinuation of stimulant misuse—in spite of promises and good intentions.
Adult ADHD with SUD--Continued

• Many SUD patients meet criteria for ADHD on entry into treatment.
• Sequelae of Attachment Disorder, ACE, childhood trauma
• Most effective treatment is behavioral: medication of limited benefit.
• Amphetamines are often sought to relieve symptoms of anxiety associated with trauma history and attachment disorder—including situational anxiety, depression, poor self esteem, social phobias, low motivation. And as an addictive drug to replace the former drug of choice.
Bolby and Ainsworth’s Attachment Theory

• The bonds a child forms with parent figures up to age 3 form the basis for both future connections with others and a healthy internal state.

• Failure to achieve healthy attachment can lead to issues of trust, inability to maintain healthy relationships, inability to “self-soothe”, chronic anxiety and stress, behavior problems in children, myriad of problems in adults including addiction.

• Pathology, presentation, and treatment overlap with a number of conditions common in our recovering patients: ADHD, PTSD, borderline personality disorder, fibromyalgia, panic disorder, other chronic anxiety and mood disorders.
Recommendations

• Initial treatment is directed at substance abuse, any underlying serious mental health conditions, and coping strategies for ADHD and PTSD symptoms.

• For persons not on stimulants, these should be withheld until early recovery is past—6 months. Those presenting on rx stimulants should be assessed individually.

• Some treatment programs proscribe controlled stimulant use.

• Don’t get caught in the trap that an ADHD diagnosis requires medication.

• Don’t prescribe abusable stimulants to those who are abusing stimulants.

• Set goals for treatment. Value of CBT and other behavioral therapies: note VA group-based approach.

• Value of direct observation: what’s seen in IOP, reports from family members.
Insisting that amphetamine (Adderall) is ‘the only thing that works.”

Avoiding the “upper-downer cycle”: the need to re-establish Circadian Rhythm in early recovery. Cannabis, benzos, Zdrugs, alcohol.

The role of stimulants in perpetuating craving and addiction.

Rx stimulants in the patient with Stimulant Use Disorder. Should you prescribe stimulants to someone actively abusing them?

Difficulty of patients with SUDs in taking IR stimulants as prescribed.

Use of stimulants for nonapproved indications

Immediate release forms are abuse-prone: Amphetamine by insufflation, methylphenidate by injection, both taken PRN to quash uncomfortable feelings, both diverted.

To minimize the above issues, consider using non-stimulants—bupropion, atomoxetine, tricyclics, guanfacine---if scheduled stimulants are prescribed, use longacting preparations: Lisdexamfetamine, OROS-methylphenidate (Vyvanse, Concerta)
A Link Between Sleep and ADHD

COULD ADHD be a problem caused by a disruption in circadian rhythms?

It's an area of research that some experts say holds promise for developing new treatments for attention-deficit hyperactivity disorder.

Many adults and children diagnosed with ADHD report sleep problems. Some have difficulty falling asleep, staying asleep, and some develop sleep apnea.

Sandra Kooij, an associate professor of psychiatry at VU University Medical Centre in Amsterdam, says ADHD and sleep may be more intertwined than previously thought. She proposed a theory at a conference in September that ADHD may be caused by a lack of regular circadian sleep.

Her research has found that 78% of adults diagnosed with ADHD have a delayed-sleep phase or circadian rhythm, which means they are night owls and don’t get sleepy or tired enough to fall asleep until 2 or 3 a.m. In the normal adult population about 20 to 25% have such a chronotype, or sleep-wake rhythm, she says.

“Everyone who treats people with ADHD recognizes the day and night cycle,” she says.
Treatment-associated Insomnia

- Amphetamine salts 40-45%
- Vyvanse 10-19%
- Concerta 11%
- Methylphenidate IR 10%
Case 3-easy to start, hard to stop

• 32 yearold mother of 3 in treatment for opioid use disorder complicated by frequent relapses to other drug families—alcohol, benzos, cannabis, less often cocaine.
  
  Difficult relationships and other stressors.
  
  Did poorly in IOP settings due to conflict with other clients (question BPD). ADHD dx and on methylphenidate in past but during 4 years of treatment with me, no ADHD symptoms or complaints noted.

  cannabis Picked her up again 2016 after a year with a different treatment provider, now using cannabis and rx Vyvanse 70 mg. In DEEP counseling with us. Due to cannabis use, UDS + for cocaine, possible amphetamine side effects I started a taper. As it progressed, became increasingly focused on the Vyvanse—’I need it to survive’, “I need it to manage my OCD.” Tapered down to 40 mg at which point she had completed DEEP and promptly left the practice for another provider.
CASE 4--ADHD, PTSD, and the Amygdala

• 55 yearold female with PTSD, verbal and physical abuse history from male partners and adult son, often homeless, on buprenorphine for opioid use, fluoxetine. Moderate, disabling COPD, continues to use tobacco.

  Misuse of benzos in past, has been on welbutrin and trazadone, currently abusing street amphetamine. Has been off it at times, does have a physical withdrawal syndrome when she stops it.

  Refuses groups, reluctantly participates in individual counseling.

  In her view she suffers from iatrogenic addiction to both opioids and stimulants. “If my doctor hadn’t cut back on my oxycodone I wouldn’t have had to go to the street to treat my pain and wouldn’t have been labelled an addict. Similarly, if I was prescribed the Adderall I need to feel right, I wouldn’t have to buy it off the street.”

  She has little interest in addressing her PTSD at this stage of her life, just wants to be on the medications that make her feel euthymic and function at her present level.

QUESTION: What role is the amphetamine playing here?
Amygdala hijack - fear caused by optical stimulus.
The Amygdala in ADHD and PTSD

- The amygdala is the seat of the “fight or flight” response to a stressful situation.
- In ADHD, lack of cortical suppression leads to an overactive amygdala accounting for impulsiveness.
- In PTSD, an overactive amygdala, fed by memories of traumatic events stored in the hippocampus, leads to inappropriate stress responses to everyday situations.
- In ADHD, stimulants improve inhibition of the amygdala by the prefrontal cortex.
- In PTSD the amygdala is hypertrophied and the hippocampus shrunken; in ADHD these changes are not observed.
A Party Drug’s Path to Prescribable Medicine

MDMA—aka ecstasy—has been illegal for 36 years. But in August, the FDA designated it a breakthrough therapy for PTSD, putting it on the fast track for potential approval.

Josh Dean investigates the decades-long campaign to change the government’s mind.

Photographs by MILES ALDRIDGE

THE FUTURE OF EVERYTHING

THE WALL STREET JOURNAL
How MDMA Went From Club Drug to ‘Breakthrough Therapy’
Better known as ‘ecstasy,’ it’s emerging as one of the most promising treatments for PTSD

As the director of addiction psychiatry at NYU Langone Medical Center, Stephen Ross spends most of his time helping people quit drugs. But early next year, he will begin administering MDMA in his “dosing room,” a chamber in Dr. Ross’s medical research lab that resembles a comfortable living room, with a gong on the wall and ceramic mushrooms...
Conclusions Regarding Stimulants and PTSD

• When prescribing stimulants in recovery settings assess what you are treating: PTSD vs ADHD.

• Patients using street stimulants—amphetamine, methamphetamine, cocaine—are unlikely to benefit from prescribed stimulants with addictive potential despite their pleas.

• Treatment of PTSD by any number of modalities may be integrated into behavioral therapy in early recovery. Treatment that improves PTSD decreases stimulant misuse.

• In heavy stimulant users treatment of addiction without specific attention to PTSD may exacerbate stimulant use.

• Medications that in the past were thought beneficial for PTSD have turned out to be anything but—namely, benzos.
Literature Regarding Stimulants and PTSD

• Rat studies of stimulants to treat PTSD models: many
• Alpha 1 and alpha 2 agonists/inverse agonists/antagonists and norepinephrine reuptake inhibitors to treat PTSD symptoms: many. These include guanfacine, clonidine, desipramine, prazosin.
• McAlister T et al. RCT of MPH or galantamine for PTSD and/or TBI. Neuropsychopharm 41: 1191-8, Apr 2016
• Amoroso T and Workman M. Treating PTSD with MDMA-assisted Psychotherapy: a preliminary metanalysis and comparison to prolonged exposure therapy. J Psychopharm 2016 July: 30
• Ruglass L: Association between PTSD symptoms, stimulant use, and Treatment Outcomes: a Secondary Analysis of the NIDA Women and Trauma Trial; Am J Addiction 2014 Jan; 23(1)
Take-homes

• Caution with prescribed stimulants in early recovery especially schedule IIs.
• Treatment of ADHD does not imply prescribing medication.
• Avoid “upper-downer cycle”—stimulants with benzos, cannabis, alcohol, Zdrugs, multiple sedatives.
• Avoid stimulants for life-enhancement purposes.
• Stimulant use disorder rarely responds to prescribed schedule II stimulants.
• Use long-acting preparations: OROS MPH, lisdexamfetamine.
• Are you treating ADHD or PTSD?
NON-ADHD PERSON ON FIRST DATE:

ADHD PERSON ON FIRST DATE:

FOCUSED

SOMEONE'S FOOD!

OMG A MOUSE

WHO'S IN THERE?

WTF IS A FISH FORK EVEN?

COOL SHIRT

CRUMBS!