Adolescents With ADHD and Substance Use Disorders: A Primer

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You are evaluating a 16-year-old boy referred for mandated substance use treatment by his high school, where he was found drinking alcohol and smoking cannabis with a friend in the restroom. As you gather his history, he says, “One doctor told me I have ADHD. That’s why I smoke pot—it helps me focus. But I think I’d do better with some Adderall.”

You are fairly skeptical, but you make an effort to elicit symptoms of ADHD during the interview. He endorses most criteria. Yet at the end of the session, you’re not sure how to handle the situation. If he really has ADHD, it’s important to treat him, since improved focus on constructive activities might help him cut down on illicit substances. On the other hand, you wonder if he memorized the symptoms of ADHD to get a prescription for Adderall.

Treatment quandaries like the one above are common for any clinician who sees patients with substance use disorders (SUDs). For many years, we’ve seen research studies

describing connections between ADHD and substance use, but the findings are inconsistent and difficult to incorporate into our practices.

Recently, a group of international experts published an excellent review of this important topic. Called the "International Consensus Statement on Screening, Diagnosis and Treatment of Substance Use Disorder Patients With Comorbid Attention Deficit/Hyperactivity Disorder," it collects the latest research and has some practical suggestions. Let's use this paper as a jumping-off point for a deep dive into the issue.

How common is ADHD in substance users?

Studies show that ADHD is much more likely to be diagnosed in substance-using youth than in community samples. Among adolescents receiving substance use treatment, 25%–66% have ADHD (Hogue A et al, J Child Adolesc Sub Abuse 2017;26(4):277–292), higher than the overall prevalence of about 10% in children and adolescents. It's not clear whether this means that substance use leads to ADHD, or that ADHD leads to substance use, but regardless of the direction of causality, you need to be extra vigilant in asking about ADHD symptoms in this population.

Overdiagnosis or underdiagnosis—both can occur

Many of us are concerned about ADHD overdiagnosis in substance-using patients. We know that adolescents often divert stimulants to friends and often use them for purposes other than ADHD, such as for fueling all-night study sessions or parties. But the consensus statement reminds us that it's possible to miss an ADHD diagnosis in substance users. After all, many ADHD-related consequences, such as poor school performance or job loss, can be erroneously blamed on the substance use.

Why are SUDs so common in adolescents with ADHD?

Patients with ADHD are typically impulsive and hyperactive—traits that may reduce their ability to judge whether it's a good idea to try substances when offered by friends. And since ADHD can cause significant life problems, like failing out of school, getting speeding tickets, or forgetting crucial tasks, the disorder can lead teens to turn to substances to cope with disappointments and frustrations.

Of course, the developing brain during adolescence primes teens to be vulnerable to substance use, whether they have ADHD or not. The maturation of the brain's motivation and reward system (MRS) and cognitive control system (CCS) occur at different rates. The MRS network originates primarily in the midbrain (in the limbic structures), while the CCS refers primarily to the forebrain (especially the prefrontal cortex).

In a healthy adult brain, the CCS essentially applies the brakes to the MRS, regulating the brain's desire for pleasure. But in an adolescent, these brain structures are less developed. Because of this, the adolescent brain is primed for risky behaviors, such as substance use.

It is hypersensitive to drug-related cues and less responsive to any negative consequences, particularly in the presence of peers.

Can prescribing stimulants for ADHD lead to substance use?

A long-standing question, and one that parents may ask you, is whether prescribing stimulants for ADHD can somehow sensitize children to developing a SUD in later life. The few studies that have looked at this question indicate that this is probably not a concern for most kids. Participants in the multimodal treatment study (MTA) of children with ADHD, who received medication, did not have higher rates of substance use over a 3-year follow-up (Molina BSG et al, *J Am Acad Child Adolesc Psychiatry* 2007;46(8):1028–1040). Although the ADHD children in the MTA study had higher rates of substance use than a non-ADHD control group, medication had no adverse effects on the development of later substance use.

The jury is still out on whether treating ADHD actually prevents SUDs. One recent study hints that stimulants might protect against substance use, but this was an open study without a robust control group (Hammerness P et al, *J Attention Disorders* 2017; 21(1):71–77), so the question remains unanswered.

Treating ADHD in adolescent substance users

Non-stimulants

Generally, you should start by trying non-stimulants in substance users, even though they are significantly less effective agents. Atomoxetine is a good first choice; a typical dosing regimen in an adolescent is to start at 40 mg QAM, increase to 80 mg after 3 days, and then look for a response, which may take 2–4 weeks. While atomoxetine is clearly not as effective nor as rapid-acting as stimulants, it has the advantage of causing neither insomnia nor anxiety.

For adolescents with prominent insomnia, the alpha agonists, such as guanfacine or clonidine, are good choices. Of the two, guanfacine might be a better choice, simply because the extended release version has long been generic and thus is more affordable (the ER version of clonidine is newly generic, and its price will gradually come down). Start at 1 mg QHS, then increase by 1 mg/day at weekly intervals; the maximum recommended dose is 4 mg/day.

Finally, for adolescent ADHD patients who are smokers, bupropion can be a good two-fer, since it's fairly effective for both conditions. Bupropion XL is the most convenient since it can be taken once in the morning; start with 150 mg QAM and titrate up to either 300 mg or 450 mg, depending on response.

Stimulants

Who are we fooling? Given how much more effective stimulants are for ADHD than non-stimulants, chances are good that you're going to try them, even for substance-using adolescents. The American Academy of Pediatrics' (AAP) committee on substance abuse in fact recommends the cautious use of stimulants in such patients (Harstad E et al, *Pediatrics* 2014;134(1):e293–e301). The AAP also encourages doctors to carefully confirm the diagnosis ahead of time, and they recommend the following interventions:

- Psychoeducation for patients and parents
- Anticipatory guidance for parents and guardians
- Contracting with caregivers and teens for pill monitoring
- Prescription tracking through state drug monitoring programs

Which stimulants should you choose?

When selecting an agent, start with a long-acting stimulant that has low risk of misuse or diversion. The main methylphenidate options in this category are Concerta and Ritalin LA. A clever choice for kids who are highly likely to divert is to prescribe orally disintegrating tablets (ODTs). If teens put one of these tablets in their mouth, parents can feel reassured that it will dissolve and not be "cheeked" to sell to friends later. ODTs are available in both methylphenidate form (Cotempla XR-ODT) and amphetamine form (Adzenys XR-ODT).

Vyvanse (lisdexamfetamine) is a reasonable choice for patients who can afford what is often a steep co-pay. Because it's a prodrug that is converted to its active form in the gut, Vyvanse can't be snorted. It also scores low on "drug-liking effects" when given to known substance users on the Drug Rating Questionnaire.

Do the world a favor and don't prescribe substance users Adderall (mixed amphetamine salts, or MAS), whether immediate or extended release. It's just too popular on high school and college campuses, and it's a recipe for diversion. However, there is a new very-long-acting version of MAS called Mydayis, which uses a fancy triple-beaded delivery system and lasts up to 16 hours. Being new, it's expensive and unlikely to be covered by insurance companies. It's approved for ages 13 and up.

Making stimulants less addictive: An intriguing study

A little-known aspect of stimulants is that they activate mu-opioid receptors in the brain, which may be the cause of their euphoriant effect in some users. So, what would happen if we prescribed stimulants along with naltrexone, which blocks opioid receptors? Would the stimulant still be effective for ADHD while conferring less risk of abuse?

This combined approach was recently studied in a 6-week, double-blind, placebo-controlled randomized clinical trial of adults with ADHD (Spencer TJ et al, *J Clin Psychiatry* 2018;79(1):19–25). The 37 participants (ages 18–30) were screened as having experienced euphoria with a test dose of immediate release methylphenidate. They were

then randomly assigned to methylphenidate with naltrexone 50 mg or placebo. After 6 weeks, there was no difference between the groups—ADHD symptoms improved significantly in both. Unfortunately, the study did not measure whether adding naltrexone to methylphenidate eliminated the feeling of euphoria, but the results are intriguing nonetheless.

CATR Verdict: Don't neglect treatment of ADHD in substance users, since untreated ADHD can interfere with substance use treatment. While you should give non-stimulants a good try, stimulants can be safely used, especially if you choose extended release or ODT medications. Future options to minimize abuse potential may include co-administration with naltrexone.

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