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CLINICAL REVIEW

Stimulant Treatment and the Comorbid Nature of ADHD and SUD

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Clinicians diagnosing adult attention-deficit/hyperactivity disorder (ADHD) are faced with several challenges, including understanding how to interpret ADHD symptoms in adults having a history of substance use disorders (SUDs). To assist in the assessment, treatment, and counseling of ADHD patients and families, this article, as part of the newsletter series, the ADHD Practice Guide—ADULT ADHD EDITION, addresses the following questions:

1. How strong is the link between ADHD and SUDs?
2. Is ADHD a precursor to SUDs?
3. What explains the association between ADHD and SUDs?
4. Does the stimulant treatment of ADHD teach ADHD youth to abuse psychoactive (mood-altering) drugs?

How Strong Is the Link Between ADHD and SUDs?

The link between ADHD and SUDs has been examined by assessing the prevalence of ADHD among SUD patients and by assessing the prevalence of SUD among ADHD patients. Studies of alcohol abusers report the prevalence of ADHD to range between 35% and 71%.¹ Studies of substance-dependent populations report the prevalence of ADHD to range between 15% and 25%.¹ Schubiner et al found that 24% of 201 inpatients in a substance abuse treatment facility had ADHD.² Levin et al found that 10% of cocaine-dependent adults met strict criteria for ADHD.³

Adults with both ADHD and SUD have been reported to have earlier onset of substance abuse relative to adults without

ADHD, and a greater severity of SUD has been reported in ADHD adults compared with non-ADHD adults.^{2,4,5} Carroll and Rounsaville showed that compared to cocaine abusers without ADHD, those with ADHD had an earlier onset of cocaine use and a more severe history of cocaine use.⁵ Another study similarly reported higher numbers of prior treatments for SUD in SUD adults with ADHD relative to those without ADHD.² Among adult ADHD patients with alcohol use disorders, ADHD increased the risk for subsequent drug abuse or dependence. Also, compared with non-ADHD controls, ADHD patients had a higher lifetime risk for SUD.⁶

As reviewed by Wilens et al, studies of ADHD adults have consistently found an elevated prevalence of SUDs.⁷ Histories of alcohol abuse or dependence were found in 17% to 45% of ADHD adults, and 9% to 30% have histories of drug abuse or dependence. The study by Biederman et al of untreated adults with ADHD found that the risk of an SUD developing over the lifespan in an ADHD individual is 2-fold compared to non-ADHD individuals (52% vs 27%, respectively).⁶ Although a history of conduct or bipolar disorders increases that risk, ADHD is an independent risk factor for later SUD.^{6,8} Comparisons of ADHD adults

with SUDs and non-ADHD adults with SUDs show no differences in the preference for specific substances.⁷ Another study found higher rates of psychiatric comorbidity in adult patients having both SUD and ADHD compared with those having only SUD or only ADHD.⁹ This finding suggests that ADHD and SUD are each independent risk factors for psychiatric

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“The risk of an SUD developing over the lifespan in an ADHD individual is 2-fold compared to non-ADHD individuals.”

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Statement of Need

One of the challenges in managing adult attention-deficit/hyperactivity disorder (ADHD) is the propensity for comorbidities—75% of adults with ADHD have a comorbid condition. Substance use disorder (SUD) is a common comorbidity with ADHD, with new data currently emerging on its role and impact in ADHD. It is important for optimal outcomes in ADHD management that clinicians be informed on ADHD and SUD through a review of current and emerging study results on the relationship between the two.

Learning Objectives

Upon completion of this educational activity, participants should be able to:

- Describe the prevalence of comorbid ADHD and SUD
- List the possible causes for the connection between ADHD and SUD
- Articulate the data regarding stimulant treatment in childhood and its effect on the risk of SUD later in life

Release Date: June 1, 2006; Expiration Date: June 1, 2007

There is no fee associated with this activity.

Target Audience

This educational activity is designed for primary care physicians and psychiatrists.

Clinical Review

This activity was peer reviewed by Kevin R. Murphy, PhD, President, Adult ADHD Clinic of Central Massachusetts, Research Associate Professor, Department of Psychiatry, SUNY Upstate Medical Center.

Disclosure Information

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The faculty reported the following:

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comorbidity. Because the prevalence of SUD and other psychiatric comorbidities among ADHD adults is substantial, the assessment of SUD and common psychiatric comorbidities should be a standard part of all adult ADHD evaluations.

Is ADHD a Precursor to SUDs?

Because ADHD typically onsets prior to SUDs, it is reasonable to suggest that ADHD is a risk factor for SUDs rather than SUDs being a risk factor for ADHD. Longitudinal studies of children with ADHD, or children who develop SUD, have addressed this issue from an empirical perspective.

Prospective studies of ADHD children show that those with comorbid conduct or bipolar disorders are most likely to develop an SUD.¹⁰⁻¹² For example, in a 5- to 8-year follow-up study, more alcohol use was shown among hyperactive and largely conduct-disordered ADHD adolescents compared to non-ADHD controls.¹¹ Katusic et al followed 363 youths with ADHD and 726 matched controls from age 5 to mid-adolescence and found that ADHD resulted in a 3-fold increased risk for SUD and an earlier onset of SUD.¹² A longitudinal study of 142 ADHD adolescents and 100 controls also found ADHD was associated with an increased risk for SUD.¹⁰

If ADHD were a risk for SUD, then ADHD should be common among adolescents and young adults who later develop an SUD. This idea has been confirmed by longitudinal studies of children and adolescents with SUD.^{13,14} Kellam et al found aggression, inattention, and impulsivity in children in the first grade predicted an increased risk for substance use in adolescence and young adulthood.¹⁴

In the drug abuse literature, self-medication for symptoms of anxiety, depression, and aggression has been suggested to be an important pathway to SUDs.¹⁵ Although there is substantial evidence that patients with ADHD are at high risk for subsequent SUDs, comparatively little is known about the effects of ADHD on the developmental pathway from drug abuse to drug dependence and on pathways from use of licit substances (eg, nicotine and alcohol) to illicit substances. Glantz and Pickens suggested that there are specific neuropsychological developmental pathways that prime youths for a worsening course of substance use, abuse, and dependence.¹⁶

This work has huge implications for treatment and prevention efforts. If the specific factors that lead some to develop comorbid SUD and the protective factors that allow others to avoid comorbid SUD could be identified, this would be enormously helpful and might lead to improved primary prevention, which could reduce the risk for SUD in ADHD subjects. Such data could also be used to justify secondary prevention efforts to stop or mitigate transitions from milder to more severe SUDs.

What Explains the Association Between ADHD and SUDs?

Although there is strong evidence that ADHD is associated with an increased risk for SUDs, we know relatively little about the causes of the association. It is possible that some ADHD patients self-medicate by abusing licit or illicit drugs to control their ADHD symptoms. Although drug-abusing ADHD patients do not selectively abuse stimulants, they are heavy users of nicotine, which is known to have modest therapeutic effects on ADHD symptoms.¹⁷ The symptoms of ADHD may be a direct cause of associated SUD. For example, impulsivity could lead ADHD youth to try drugs they would not otherwise have tried. Also, chronic ADHD and its associated social and school failure could create demoralization, negative peer group interactions and influences, low self-esteem, and a sense of learned helplessness, which in turn might fuel substance use.¹⁸

It is also possible that ADHD and SUDs share biological risk factors. Family studies have shown that there is a strong familial association between ADHD and SUD, which suggests that the 2 disorders may share genetic or other familial risk factors.^{19,20} The offspring of substance-abusing parents are at increased risk not only for SUDs, but also for inattention, impulsivity, aggressiveness, hyperactivity, and ADHD.^{21,22} Wilens et al studied children with an opioid-dependent parent, and these children had Child Behavior Checklist scores consistent with the diagnoses of ADHD and conduct disorder.²³ Another study found an elevated risk for ADHD in the children of alcoholics, but not in a matched control group.²⁴ Roizen et al compared

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“Family studies have shown that there is a strong familial association between ADHD and SUD, which suggests that the 2 disorders may share genetic or other familial risk factors.”

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children with developmental disabilities to those with ADHD, and found the ADHD youth to be significantly more likely to have a parent with drug abuse (excluding alcohol), ADHD, learning disabilities, depression, delinquency ($P < .001$ for all) and alcoholism ($P = .007$).²⁵ Two community-based epidemiologic studies are consistent with these findings. Zucker and Noll and Rubio-Stipec et al found more evidence of ADHD symptoms in children of parents with an SUD compared to those with parents without an SUD.^{26,27}

Does the Stimulant Treatment of ADHD Teach ADHD Youth to Abuse Psychoactive Drugs?

Although the data reviewed above suggest that ADHD is a risk factor for SUD and that both may share genetic risk factors, some have postulated that the stimulant treatment of ADHD may increase the risk for SUD among ADHD patients.²⁸ This claim is not supported by the most recent study data.

To make sense of the contradictory findings, Wilens et al conducted a meta-analysis in 2003, which used statistical methods to determine the most rational conclusion to be drawn from a group of studies.²⁹ The meta-analysis identified 2 studies that followed ADHD youth into adolescence and 4 studies that followed ADHD youth into adulthood. The analysis showed that stimulant-treated ADHD youths were half as likely to develop SUD as those who had not been treated with pharmacotherapy. The magnitude of risk reduction was such that the ultimate risk of SUD in the stimulant-treated group was similar to the risk in individuals without ADHD. These data clearly show that stimulant treatment of ADHD, rather than causing SUDs, protects ADHD youth from developing an SUD.

“Stimulant-treated ADHD youths were half as likely to develop SUD as those who had not been treated with pharmacotherapy.”

Some ADHD symptoms may increase the risk for using substances, and by reducing those symptoms, youths would be protected from SUD. Also, treatment of ADHD reduces the possibility of the social and school failure that is often a precursor to substance use. Another possibility is that, compared with other ADHD youths, ADHD youths who are treated with stimulants may have parents who are more involved in their lives and provide more supervision. Additionally, stimulant treatment may directly affect the reward circuits of the brain to reduce the risk for SUD, but this theory must remain speculative in the absence of studies addressing that issue.

Conclusion

The research reviewed above provides clear answers to the questions posed at the outset of this clinical review. As ADHD adults are at high risk for having SUD and those who have both disorders are at highest risk for additional psychiatric comorbidity, this group is of special concern to clinicians. Moreover, because the retrospectively derived data from clinically referred adults with ADHD are consistent with the longitudinal studies, it seems reasonable to conclude that the findings about ADHD and SUD are constant across different populations.

While ADHD can be a precursor to SUD, the stimulant medications associated with treatment of ADHD in childhood are not clearly linked to an increased risk of SUD. While some studies indicate that stimulants may in fact decrease the risk of SUD later in life, more studies are necessary to confirm the long-term effects of stimulant use both in childhood ADHD, as well as in ADHD in adults, as they relate to comorbid SUDs. ■

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CASE STUDY

Assessing ADHD in Young Adults with Substance Use Disorder

Himanshu P. Upadhyaya, MBBS, MS, Associate Professor, Director, Adolescent Substance Abuse Training/Education, Director, Addiction Psychiatry Fellowship Program, Medical University of South Carolina

Case Description A 22-year-old male college student presents to the clinic after reading an article on attention-deficit/hyperactivity disorder (ADHD). The patient reports being “a little hyper” since elementary school, which did not present much of a problem, but he did have trouble focusing and day-dreamed a lot during class. The patient reports that he had variable grades in elementary school and high school, rarely did homework, had poor study habits, and was viewed by his teachers as an underachiever. Since starting college, he has had a lot of difficulty studying, has generally poor grades, and is struggling just to get by academically. On assessment, besides meeting all 9 criteria for ADHD, Predominantly Inattentive Type, he reports smoking half a pack of cigarettes per day since age 16, drinking “socially,” and using marijuana 2 to 3 times per week.

Case Discussion This case is challenging due to the complexity of the comorbid ADHD and substance use disorder (SUD). Besides a *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)*-based clinical interview, a thorough assessment should include a review of current and early childhood ADHD symptoms, a review of systems (eg, cardiovascular, neurological, and endocrine) to establish a baseline for comparison for any future adverse events, and an assessment of medical and psychiatric history, social history (eg, academic functioning, family functioning, peer drug use), and family psychiatric history. Collateral information from previous mental health providers

(if applicable) and a parent, significant other, or friend, who has known the patient for a significant period, should be gathered, if possible, since patients with an externalizing disorder, such as ADHD, may have impaired insight. Patients with a possible SUD may also deny or minimize their use of substances. For these reasons, obtaining information from multiple sources and informants is always advisable as part of a thorough assessment. The patient should also be assessed for nicotine dependence and other drugs, as well as for high-risk behaviors, such as unprotected sex. Based on the initial case description, at the minimum the patient meets criteria for marijuana abuse. When

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CASE STUDY**Assessing ADHD in Young Adults with Substance Use Disorder**

considering treatment, due to current active marijuana use and possible alcohol abuse, use of medications for ADHD with abuse potential should be carefully evaluated and closely monitored.

Screening instruments for SUD are helpful in situations where a *DSM-IV*-based clinical interview is not practical for all patients. In those situations, using a screening instrument with reasonable psychometric properties (eg, CAGE questionnaire for alcohol, Drug Abuse Screening Test, Fagerstrom Test for Nicotine Dependence) may be helpful.^{1,2} The Addiction Severity Index (ASI) is a comprehensive structured assessment instrument that assesses for impairments in multiple domains besides SUD and takes about 1 hour to administer.³ Hence, the ASI may not be practical in a standard office-based psychiatric or primary care practice, but it is valuable in situations where physician extenders, such as therapists, nurse practitioners, or physician assistants, are available.

Substance use rarely occurs in isolation. It is frequently linked with complications related to 1 or more associated domains, such as impaired family relationships, peer relations, and access to and use of leisure time activities, poor academics, psychiatric comorbidities, access to and use of other drugs, and participation in other high-risk behaviors (eg, unprotected sex). Random toxicology tests (eg, urine drug test) are a useful component in the assessment and treatment of SUD. Ideally, random toxicology tests should be observed to prevent any possible sample tampering. A urine drug test and an alcohol breathalyzer test should be performed at the initial visit (unless results are available from hospitalization or an emergency department visit) and randomly during treatment. A urine drug test can now be performed in

the office using one of the several instant testing cups available in the market. Lastly, in light of high-risk behaviors common in substance-using young adults, the patient should be counseled on safer sex, including assessment of birth control in female patients, if appropriate.



Since regular alcohol, nicotine, and marijuana use can cause withdrawal symptoms, assessment should include a history of withdrawal and need for detoxification (most notably for alcohol). The need for detoxification would be unlikely in this patient since he reports being a social drinker. In addition, comorbidity of ADHD and SUD has implications for decisions around when and if medications should be prescribed for ADHD. Current rec-

ommendations indicate that ADHD and SUD should ideally be treated concurrently.⁴ In cases where there is a clear pattern of substance dependence with loss of control, pharmacotherapy of ADHD with medications with low abuse potential should be considered first. Ideally, the addiction(s) should be treated and stabilized before considering stimulants. After gaining better control of the addiction (not a well-defined period, but usually a few months depending on individual progress), it becomes safer and more appropriate to begin stimulant treatment for the ADHD. On the other hand, in cases where there is only episodic use of a substance (and not an SUD, ie, abuse or dependence), it may be appropriate to use stimulants. The decision to prescribe a medication with abuse potential for a patient with a comorbid SUD should be made only after a thorough assessment of the potential risks, benefits, and safety issues. In all cases of ADHD with comorbid SUD, frequent follow-up and close monitoring of progress are essential so any necessary changes or other interventions can be made as needed. ■

“Substance use rarely occurs in isolation. It is frequently linked with complications related to 1 or more associated domains.”

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Post-Test

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Participants should select the single most appropriate answer to each of the following questions.

1. The prevalence of ADHD in adults who abuse alcohol is between ____, and between ____ in patients with substance dependence.
 - a) 15% and 25%, 35% and 71%
 - b) 15% and 35%, 25% and 71%
 - c) 25% and 71%, 15% and 35%
 - d) 35% and 71%, 15% and 25%
2. Adults with both ADHD and SUD exhibit ____ compared with non-ADHD adults.
 - a) Earlier onset of substance abuse
 - b) Greater severity of SUD
 - c) A and B
 - d) None of the above
3. While ADHD is an independent risk factor for later SUD, a history of ____ increases that risk.
 - a) Conduct or bipolar disorder
 - b) Conduct disorder or depression
 - c) Verbal abuse or bipolar disorder
 - d) Personality disorder
4. Adults with comorbid ADHD and SUD had higher ____ rates compared with adults having only ADHD or only SUD.
 - a) Medical complication
 - b) Psychiatric comorbidity
 - c) Stimulant treatment
 - d) Hospitalization
5. Katusic et al, in a study following children with and without ADHD from age 5 to mid-adolescence, found that:
 - a) ADHD had no effect on the risk for SUD.
 - b) ADHD children were at a lower risk for SUD.
 - c) The risk for SUD was largely affected by gender.
 - d) ADHD resulted in a 3-fold increased risk for SUD.
6. A study by Kellam et al found that ____ predicted an increased risk for substance use in adolescence and young adulthood.
 - a) Aggression, inattention, and impulsivity in children in the first grade
 - b) Poor home relationships in childhood
 - c) A lack of interaction with other children
 - d) None of the above
7. According to drug abuse literature, ____ has been suggested to be an important pathway to SUDs.
 - a) Treatment of ADHD with stimulants
 - b) Psychological counseling
 - c) Self-medication for symptoms of anxiety, depression, and aggression
 - d) All of the above
8. ____ is a possible cause of the association between ADHD and SUDs.
 - a) Self-medication of ADHD symptoms
 - b) Demoralization caused by social and school failure
 - c) Shared biological risk factors
 - d) All of the above
9. A meta-analysis by Wilens et al found that the risk of developing an SUD was ____ in youths treated with a stimulant compared to those not receiving ADHD pharmacotherapy.
 - a) Increased by 50%
 - b) Reduced by half
 - c) Unchanged
 - d) Varying depending on the type of stimulant used
10. Which of the following is a possible reason that stimulant therapy may reduce the risk of SUD development?
 - a) Reduction of symptoms and social and school failure
 - b) Parents who are more involved and provide more supervision
 - c) A and B
 - d) The kindling effect of stimulant medications

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ACTIVITY EVALUATION

The University of Cincinnati College of Medicine would appreciate your comments on the quality of this educational activity. Please answer the following 7 questions—I through 5 using a 5-point grading system, with 1 being the lowest rating (strongly disagree/poor) and 5 being the highest rating (strongly agree/excellent).

1. Upon completion of this educational activity, the participant was able to:

Describe the prevalence of comorbid ADHD and SUD

1	2	3	4	5
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List the possible causes for the connection between ADHD and SUD

1	2	3	4	5
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Articulate the data regarding stimulant treatment in childhood and its effect on the risk of SUD later in life

1	2	3	4	5
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2. How current was the information presented in this activity?

1	2	3	4	5
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3. This educational activity was objective, balanced, and free of commercial bias.

1	2	3	4	5
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4. Please indicate your overall evaluation of this activity.

1	2	3	4	5
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5. Do you intend to make changes to your practice as a result of this activity?

1	2	3	4	5
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6. What aspects of this activity were of most interest to you?

7. Do you have any comments or suggestions for this or future activities?

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