

The Nature of the Relationship Between Attention-Deficit/Hyperactivity Disorder and Substance Use

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This report examines the developmental relationship between attention-deficit/hyperactivity disorder (ADHD) and substance use disorders (SUD) and associated concurrent disorders relative to adolescents and adults. ADHD is a risk factor for the development of SUD in adulthood, and it is particularly of concern with conduct and bipolar disorder comorbidities. Conversely, approximately one fifth of adults with SUD have ADHD. Individuals with SUD and ADHD have a more severe and complicated course of SUD. Pharmacotherapeutic treatment of ADHD in children reduces the risk for later cigarette smoking and SUD in adulthood. (*J Clin Psychiatry* 2007;68[suppl 11]:4–8)

An area of increasing clinical, research, and public health interest is the relationship between attention-deficit/hyperactivity disorder (ADHD) and alcohol or drug abuse or dependence (substance use disorders [SUD]) in adolescents and adults. ADHD (the term *ADHD* here includes previous definitions of the disorder) has an onset in early childhood and affects from 6% to 9% of children and adolescents and up to 5% of adults.¹ Longitudinal data suggest that childhood ADHD persists into adolescence in 75% of cases and into adulthood in approximately one half of cases.² Substance use disorders usually have an onset in adolescence or early adulthood and affect between 10% to 30% of U.S. adults, as well as a less defined, but sizable number of juveniles.³ In the following sections, data relevant to understanding the overlap between ADHD and SUD with an emphasis on tangible factors mediating this association are addressed.

OVERLAP BETWEEN ADHD AND SUBSTANCE USE DISORDERS

Studies in adults with SUD indicate an overrepresentation of ADHD. Studies have found that between 35% and 71% of adult alcoholics had childhood-onset and persistent ADHD (for review, see Wilens⁴). Furthermore, from 15% to 25% of adult addicts and alcoholics have current ADHD.⁵ For example, Schubiner et al.⁶ found that 24% of 201 inpatients in a substance abuse treatment facility had ADHD and two thirds of them also had conduct disorder. The importance of careful diagnosis, however, has been demonstrated by Levin et al.,⁷ who found that while 10% of cocaine-dependent adults met strict criteria for ADHD (clear childhood and adult ADHD), another, equal amount (11%) were found to have ADHD symptoms only as adults (ADHD not otherwise specified).

The characteristics of the SUD are related to the presence of ADHD. Adults with ADHD and SUD have been reported to have earlier onset of substance abuse relative to adults without ADHD.⁸ Additionally, more severe SUD has been reported in adults with ADHD compared with adults without ADHD.^{6,9} For example, Carroll and Rounsaville⁹ showed that, compared with cocaine abusers without ADHD, those with ADHD were younger at presentation for treatment, manifested earlier onset, and engaged in more frequent and more severe cocaine use. Similarly, Schubiner et al.⁶ reported higher numbers of motor vehicle accidents and prior treatments for SUD in adults with comorbid ADHD relative to those without ADHD.

An overrepresentation of SUD has also been consistently observed in studies of ADHD adults: 17% to 45% of ADHD adults have alcohol abuse or dependence, and 9% to 30% have drug abuse or dependence (for review, see Wilens et al.¹⁰). One study¹¹ in never-treated adults with ADHD has reported that the risk of the development of SUD over the lifespan of an individual with ADHD is

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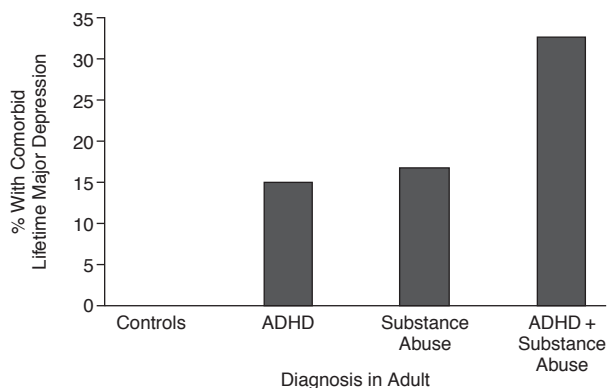
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Figure 1. Lifetime Major Depression Comorbidity in Adults With Attention-Deficit/Hyperactivity Disorder (ADHD) Plus Substance Abuse^a



^aData from Wilens et al.¹⁶ N = 78 for all groups combined.

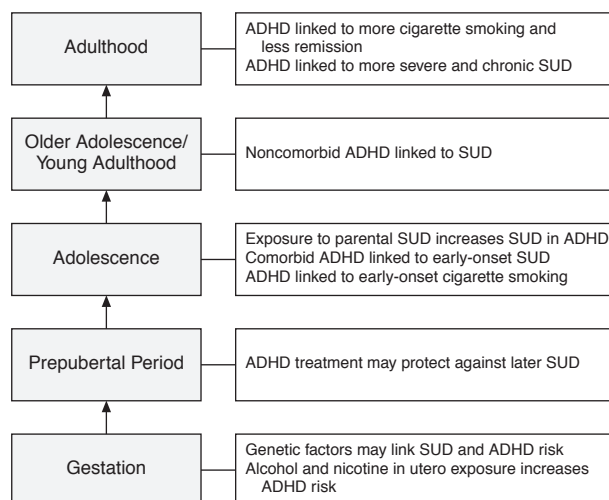
2-fold compared with non-ADHD adults (52% vs. 27%, respectively). While psychiatric comorbidity with juvenile conduct or bipolar disorder increases that risk,^{12,13} ADHD itself appears to be a risk factor for later SUD.^{11,14,15} Adults with ADHD plus SUD also have the added burden of increased risk for other psychiatric disorders compared with either condition alone (Figure 1).¹⁶ Hence, the literature strongly indicates that a bidirectional overrepresentation of SUD and ADHD exists among subjects with these disorders and that adults with ADHD plus SUD are at risk for other psychiatric comorbidity and a longer course of SUD.

ADHD as a Risk Factor for Substance Use Disorders

The association of ADHD and SUD is particularly compelling from a developmental perspective since ADHD manifests itself earlier than SUD; therefore, SUD as a risk factor for ADHD is unlikely. Thus, it is important to evaluate the extent to which ADHD is a precursor of SUD. Moreover, SUD-related risks increase ADHD risk. For example, in utero exposure to alcohol and cigarettes increases the risk of ADHD in an unborn child.¹⁷⁻¹⁹ Longitudinal studies of children with ADHD and children who develop SUD provide the most compelling data on this developmental hypothesis (Figure 2).²⁰

Prospective studies^{12,14,21} of children with ADHD have provided evidence that the group with conduct or bipolar disorders co-occurring with ADHD has the poorest outcome with respect to developing SUD and major morbidity. For example, in 5- and 8-year follow-up studies, more alcohol use was shown among hyperactive and largely conduct disordered ADHD adolescents compared with non-ADHD controls.²² Moreover, as part of an ongoing prospective study²¹ of ADHD, my colleagues and I found differences in the risk for SUD in ADHD adolescents (mean age = 15 years) compared with non-ADHD controls that were accounted for by comorbid conduct or bipolar disorders. These findings were confirmed recently by

Figure 2. Developmental Timeline of Substance Use Disorder (SUD) Risk in Attention-Deficit/Hyperactivity Disorder (ADHD)^a



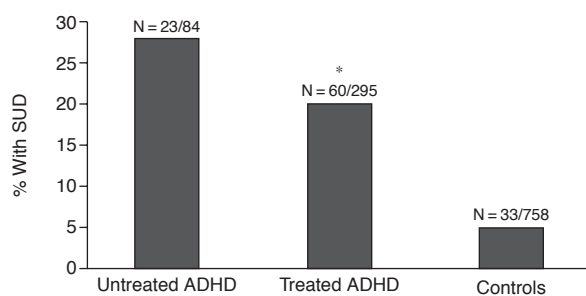
^aBased on Wilens.²⁰

Katusic and associates,¹⁵ who completed a large case controlled study of 363 youth with ADHD compared with 726 matched controls followed from age 5 years to mid-adolescence. They reported that ADHD was associated with a 3-fold risk for SUD and that there was an earlier onset of SUD in the ADHD group. Molina and Pelham,¹⁴ in a longitudinal study of drug use in 142 adolescents and 100 controls, also recently found that ADHD was associated with an increased risk for SUD. These authors reported that the severity of ADHD and the severity of the inattentive symptoms of ADHD were specifically associated with increased SUD risk. This is particularly of concern given the persistence of attentional symptoms into young adulthood, which is the time of risk for developing SUD. Conversely, the hyperactive/impulsive symptoms are most prominent in adolescence.²³ These data support retrospectively derived data from untreated adults with ADHD, indicating a higher risk for SUD and an earlier age at SUD onset in adults with ADHD (mean age of full SUD at 19 years) compared with non-ADHD controls (mean age = 22 years, $p < .01$); these associations were more marked in the presence of comorbid conduct or bipolar disorder.⁸

ADHD Treatment and Substance Use Disorders

Since prospective studies in ADHD youth are naturalistic, and hence not randomized for treatment, attempts to disentangle positive or deleterious effects of treatment from the severity of the underlying condition(s) are hampered by serious confounds. Whereas concerns about the abuse liability and potential kindling of specific types of abuse (i.e., cocaine) secondary to early stimulant exposure in ADHD children have been raised,²⁴ the preponderance of clinical data do not appear to support such a contention.

Figure 3. Effect of Attention-Deficit/Hyperactivity Disorder (ADHD) Treatment on Later Substance Use Disorder (SUD)^a



^aData from Katusic et al.²⁶ The rate of SUD in those with untreated ADHD and conduct disorder was 100%. The effect of treatment was more protective in boys versus girls.

* $p < .05$ vs. untreated ADHD and vs. controls.

To reconcile findings in this important area, my colleagues and I completed a meta-analysis of the literature.²⁵ We reviewed studies examining the later risk of SUD in children exposed to stimulant pharmacotherapy. We identified 2 studies into adolescence and 5 studies into adulthood. We found that stimulant pharmacotherapy did not increase the risk for later SUD. In fact, we found that stimulant pharmacotherapy protected against later SUD (odds ratio = 1.9) and that the effect was stronger in adolescents relative to adults,²⁵ with this finding probably related to the proximity of treatment. Subsequent studies²⁶ have found similarly reduced risk for SUD associated with ADHD treatment (Figure 3). One recent survey study²⁷ in college students found that current ADHD symptoms (e.g., adequacy of treatment) were directly related to cigarette, alcohol, and drug use and abuse.

Longitudinal Studies of Substance Use Disorders

If ADHD is a risk factor for SUD, then ADHD should be overrepresented in those adolescents and young adults who develop an SUD. Similar to data from studies of ADHD children, longitudinal research in children who later develop SUD also indicates that ADHD (plus conduct disorder) may be an important antecedent in some individuals that develop SUD.^{28,29} For instance, in the classic Chicago-based "Woodlawn Study,"³⁰ children who were rated aggressive, impulsive, and inattentive as first graders had higher rates of substance use 10 years later as adolescents (and in young adult years). Although not clearly articulated in these studies, the patterns of behavior described are consistent with ADHD and other comorbidity commonly associated with ADHD.

Substance Use Disorder Pathways Associated With ADHD

An increasing body of literature shows an intriguing association between ADHD and cigarette smoking. Higher rates of ADHD in adult smokers have been reported,^{31,32}

and adults with ADHD are less likely to quit smoking than those adult smokers without ADHD.³¹ Preliminary work indicates that half of adolescents with ADHD who smoke will develop an SUD in young adulthood,³³ which is twice the risk compared with non-ADHD controls. The effect of smoking cessation treatment on ultimate SUD risk in this group remains unclear; however, recent findings suggest that ADHD pharmacotherapy may prevent the onset of cigarette smoking. In a study³⁴ of 56 high-risk youth with ADHD treated naturalistically for the disorder, bupropion had no effect on smoking outcomes compared with placebo. However, on secondary analyses, higher stimulant doses (e.g., 1 mg/kg/day) relative to lower stimulant doses (0.3 mg/kg/day) resulted in a delayed onset and lower risk for cigarette smoking.³⁴

The presence of ADHD also appears to influence the transition into and out of SUD. Research indicates that ADHD and related comorbidities accelerate the transition from less severe drug or alcohol abuse to more severe dependence (1.2 years in ADHD vs. 3 years in non-ADHD controls),⁸ reflecting recent work demonstrating a linear trend toward more psychiatric comorbidity in adults with ADHD or SUD alone (compared with controls) or ADHD plus SUD (compared with ADHD or SUD alone and controls).¹⁶

Moreover, ADHD may affect remission from SUD. In a study of 130 referred adults with ADHD plus SUD and 71 SUD adults without ADHD, the rate of remission and duration of SUD differed between ADHD subjects and controls.³⁵ The median time to SUD remission was more than twice as long in ADHD than in control subjects, with SUD lasting more than 3 years longer in the ADHD adults compared with their non-ADHD peers.³⁵ Hence, the aggregate data indicate that ADHD and associated conditions developmentally influence the initiation of, transitions within, severity of, and recovery from SUD.

Familial Relationships Between ADHD and Substance Use Disorders

Family studies are highly informative to help examine the nature of the association between 2 co-occurring disorders. For instance, if ADHD and SUD are related in a familial/genetic nature, then family members of individuals with SUD or ADHD (probands) should be at elevated risk for the other disorder. The link between ADHD in children and SUD in relatives has been noted for many years to aggregate in families.³⁶ Offspring of parents with SUD have been reported in controlled studies to have not only higher rates of ADHD but also cognitive and behavioral traits including lower attention spans; higher impulsivity, aggressiveness, and hyperactivity; and elevated rates of ADHD compared with nonaffected children.³⁷ For example, in a classic study, Earls and associates³⁸ found elevated rates of ADHD in children of alcoholics compared with children of controls that were more robust in families

in which both parents were affected by SUD. My colleagues and I³⁹ reported that the risk for ADHD in children of parents with SUD was elevated relative to controls. Moreover, we found that approximately half of the school-aged offspring of parents with SUD plus ADHD had ADHD, thus necessitating screening for ADHD in the children of parents with SUD plus ADHD.

It also appears that ADHD creates a vulnerability to development of SUD. In support of this, it has been found that familial risk is important in mediating ADHD and SUD. In particular, exposure of adolescents with ADHD to active parental SUD during certain developmental periods (e.g., young adolescence) specifically increased the risk for subsequent SUD.⁴⁰ Similarly, youth with ADHD who were from a relatively high or low social class were at high risk for SUD; however, such a relationship was not operant in non-ADHD controls.⁴¹

Self-Medication Hypothesis

The precise mechanism(s) mediating the expression of SUD in ADHD remain to be seen. In studies of drug- and alcohol-dependent populations, the self-medication of anxiety, depressive, and aggressive symptoms has been forwarded as a plausible explanation for SUD.⁴² Limited data exist in ADHD. One study⁴³ has suggested a progression from ADHD to conduct disorder and eventually to SUD that is speculated to be related to demoralization and failure. Other evidence of self-medication includes data indicating preference of drugs over alcohol in both ADHD adolescents and adults; however, no differences in the selection of specific drugs have been found.¹¹

Of interest, adults with nicotine dependence often describe improved attention and executive functioning, consistent with the literature on nicotinic agents,⁴⁴ and more recently, nicotinic agents have been used for ADHD.^{45,46} Recent research examined both young adults with ADHD and controls in order to determine their motivation for use of their preferred drug.⁴⁷ To our surprise, strong evidence of self-medication was seen: a minority noted using their preferred drug to “get high,” whereas a majority reported using the drug for the purpose of “attenuating their mood,” for other unknown reasons (individual either could not identify or was not queried), or for sleep. No differences were noted between ADHD and controls, and those using to get high had higher problem scores associated with their substance use. Anecdotally, young adult marijuana users often describe a calming of internal restlessness (possibly the decay of hyperactive symptoms) or improved attention and focus with marijuana, perhaps related to endocannabinoid signaling and precognitive effects in the CNS.⁴⁸

DIAGNOSIS

Any intervention in adults with ADHD and SUD should follow a careful evaluation of the patient including psychi-

atric, addiction, social, cognitive, educational, and family evaluations. A thorough history of substance use should be obtained, including past and current usage and treatments. Although no specific guidelines exist for evaluating the patient with active SUD, in our experience, 1 week to 1 month of abstinence is useful in accurately and reliably assessing for ADHD symptoms. In the clinical setting, the diagnosis of ADHD is established using the DSM-IV criteria for ADHD. While determining whether the patient fulfills full criteria for ADHD is preferable, often patients have difficulty with the accurate retrospective recall of symptoms back into childhood. Recent work indicates that ADHD not otherwise specified, defined by relaxing the full age-at-onset criteria for the disorder, is a valid and reliable subtype of ADHD⁴⁹ and may be of particular importance in adults with SUD.^{7,50}

Semistructured psychiatric interviews and validated rating scales for ADHD are invaluable aids for the systematic diagnostic assessments of this group. In evaluating for ADHD, it is necessary to also examine other learning and psychiatric comorbidities including anxiety, mood, and disruptive disorders. Neuropsychological examinations may be useful when learning disorders are suspected or when prominent executive function deficits appear operant.

CONCLUSION

A review of the literature indicates important associations between ADHD and SUD, namely (1) there is a clinical and statistical bidirectional overlap of ADHD and SUD; (2) ADHD is a risk factor for earlier onset cigarette smoking and SUD; however, co-occurring conduct and bipolar disorders confer a much greater risk of very early onset SUD, both independently and when comorbid with ADHD⁸; (3) stimulant treatment of ADHD reduces the risk for cigarette smoking and SUD to that in the general population^{25,34}; and (4) adults with ADHD have a more severe and prolonged course of SUD. Thus, while a robust relationship between ADHD and SUD is supported in the literature, the nature of this association remains unclear. Emerging data support that ADHD makes youth vulnerable to developing SUD that may be unmasked under various conditions such as exposure to parental SUD or certain social classes.

While the existing literature has provided important information on the relationship of ADHD and SUD, it also points to a number of areas in need of further study. The mechanism by which untreated ADHD leads to SUD, as well as the risk reduction of ADHD treatment on later SUD, needs to be better understood. The influence of adequateness of treatment of ADHD on later SUD needs to be delineated. Given the prevalence of and major morbidity and impairment caused by SUD and ADHD, prevention and treatment strategies for these patients need to be further developed and evaluated.

Drug name: bupropion (Zyban and others).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, bupropion is not approved by the U.S. Food and Drug Administration for the treatment of attention-deficit/hyperactivity disorder (ADHD). In addition, medications approved for the treatment of ADHD are not approved for the treatment of substance abuse.

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