Attention-Deficit/Hyperactivity Disorder and Substance Use Disorders in Adolescents

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There has been increasing interest in the overlap between attention-deficit/hyperactivity disorder and substance use disorders. Pharmacotherapeutic treatment of ADHD in children reduces the risk for later SUD in adolescence and adulthood. In contrast, medication treatment of substance-abusing adolescents with ADHD does not reduce the SUD. Diagnostic and treatment strategies for adults with ADHD plus SUDs are discussed.

The overlap between attention-deficit/ hyperactivity disorder and alcohol or drug abuse or dependence (referred to here as substance use disorders [SUDs]) in adolescents has been an area of increasing clinical, research and public health interest. Appearing in early childhood, ADHD affects from 6% to 9% of children and adolescents worldwide (Anderson et al., 1987) and up to 5% of adults (Kessler, in press). Longitudinal data suggest that childhood ADHD persists into adolescence in 75% of cases and into adulthood in approximately one-half of cases (for review, see Weiss, 1992).

Substance use disorders usually appear in adolescence or early adulthood and affect between 10% to 30% of U.S. adults and a less defined, but sizable, number of juveniles (Kessler, 2004). The study of comorbidity between SUDs and ADHD is relevant to both research and clinical practice in developmental pediatrics, psychology and psychiatry with implications for diagnosis, prognosis, treatment and health care delivery.

Overlap Between ADHD and SUD

Structured psychiatric diagnostic interviews assessing ADHD and other disorders in substance-abusing groups have indicated that from one-third to one-half of adolescents with SUDs have ADHD (DeMilio, 1989; Milin et al., 1991). For example, aggregate data from government-funded studies of mainly cannabis-abusing youth indicate that ADHD is the second most common comorbidity with from 40% to 50% of both girls and boys manifesting full criteria for ADHD. Data largely ascertained from adult groups with SUDs also show an earlier onset and more severe course of SUD associated with ADHD (Carroll and Rounsaville, 1993; Levin and Evans, 2001).

ADHD as a Risk Factor or Precursor for SUD

The association of ADHD and SUDs is particularly compelling from a developmental perspective as ADHD appears to manifest itself earlier than the SUD; therefore, the SUD is an unlikely risk factor for ADHD. Thus, it is important to evaluate to what extent ADHD is a precursor of SUDs. Prospective studies of children with ADHD have provided evidence that the group with conduct or bipolar disorders co-occurring with ADHD have the poorest outcome with respect to developing SUDs and major morbidity (Biederman et al., 1997; Mannuzza et al., 1993). As part of an ongoing prospective study of ADHD, it was found that differences in the risk for SUDs in adolescents with ADHD (mean age=15) compared to controls without ADHD were accounted for by comorbid conduct or bipolar disorders (Biederman et al., 1997). However, it also has been shown that the age of risk for SUD onset in adolescents without comorbid ADHD is approximately 17 years in girls and 19 years in boys (Biederman et al., in press-a; Milberger et al., 1997b). These findings were confirmed by Katusic and associates (2005) and Molina and Pelham (2003), who have shown elevated risk of SUDs in adolescents with ADHD.

ADHD treatment and SUD. Clarification of the critical influence of ADHD treatment in youth on later SUDs remains hampered by methodological issues. Since prospective studies in youth with ADHD 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 of the abuse liability and potential kindling of specific types of abuse (e.g., cocaine) secondary to early stimulant exposure in children with ADHD have been raised (Drug Enforcement Administration, 1995; Vitiello, 2001), the preponderance of clinical data do not appear to support such a contention.

To reconcile findings in this important area, my group completed a meta-analysis of the literature
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(Faraone and Wilens, 2003; Wilens et al., 2003). We included studies examining the later risk of SUDs in children exposed to stimulant pharmacotherapy, identifying two studies into adolescence and five studies into adulthood. We found that stimulant pharmacotherapy did not increase the risk for later SUDs. In fact, we found that stimulant pharmacotherapy protected against later SUDs (odds ratio of 1.9) and that the effect was stronger in adolescents relative to adults (Wilens et al., 2003). It is notable that the magnitude of risk reduction (e.g., 50% reduction in risk) indicated that the ultimate risk of SUDs in treated individuals with ADHD may approximate the level of risk in individuals without ADHD (general population).

**SUD Pathways Associated With ADHD**

An increasing body of literature shows an intriguing association between ADHD and cigarette smoking. It has been previously reported that ADHD is a significant predictor for early initiation of cigarette smoking (before age 15) and that conduct and mood disorders comorbid with ADHD put youth at particularly high risk for early-onset smoking (Milberger et al., 1997a) (Figure). Data also suggest that one-half of smokers with ADHD go on to later SUDs (Biederman et al., in press-b). This is not surprising given that not only does smoking lead to peer group pressures and availability of illicit substances, but that nicotine exposure may make the brain more susceptible to later behavioral disorders and SUDs (Trauth et al., 2000). Furthermore, nicotinic-modulating agents are increasingly being evaluated for the treatment of ADHD (Wilens et al., in press-b). Of interest, prospective data funded by the National Institute on Drug Abuse suggest that stimulant treatment of ADHD reduces not only the time to onset but also the incidence of cigarette smoking (Monuteaux, 2004).

The precise mechanism(s) mediating the expression of SUDs in ADHD remains to be seen. The self-medication hypothesis is compelling in ADHD considering that the disorder is chronic and often associated with demoralization and failure, factors frequently associated with SUDs in adolescents. Moreover, it has been found that among substance-abusing adolescents with and without ADHD, adolescents with ADHD reported using substances more frequently to attenuate their mood and to help them sleep. No evidence of differences in types of substances has emerged between substance-abusing teen-agers with or without ADHD (Biederman et al., 1997). In addition, the potential importance of self-medication needs to be tempered against more systematic data showing the strongest association between ADHD and SUDs is comorbidity and familial contributions, such as exposure to parental SUDs during vulnerable developmental phases.

**Diagnosis and Treatment Guidelines**

Evaluation and treatment of comorbid ADHD and SUDs should be part of a plan in which consideration is given to all aspects of the teen-ager's life. Any intervention in this group should follow a careful evaluation of the adolescent including psychiatric, addiction, social, cognitive, educational and family evaluations. A thorough history of substance use should be obtained that includes past and current usage and treatments. Although no specific guidelines exist for evaluating the patient with an active SUD, in my experience at least one month of abstinence is useful in accurately and reliably assessing for ADHD symptoms. Semi-structured psychiatric interviews or validated rating scales of ADHD are invaluable aids for the systematic diagnostic assessments of this group.

The treatment needs of individuals with SUDs and ADHD need to be considered simultaneously; however, the SUD needs to be addressed initially (Riggs, 1998). If the SUD is active, immediate attention needs to be paid to stabilization of the addiction(s). Depending on the severity and duration of the SUD, adolescents may require inpatient treatment. Self-help groups offer a helpful treatment modality for many with SUDs. In tandem with addiction treatment, adolescents with co-occurring SUDs and ADHD require intervention(s) for the ADHD as well as other co-occurring psychiatric disorders.

Medication serves an important role in reducing the symptoms of ADHD and other concurrent psychiatric disorders. Effective agents for adolescents with ADHD include the stimulants, noradrenergic agents and catecholaminergic antidepressants (Wilens et al., 2002). Findings from a meta-analysis of 10 studies of open and controlled trials suggest that medications used in adolescents and adults with ADHD plus SUDs have only a meager effect on the ADHD, but have little effect on substance use or cravings (Riggs et al., 2004; Schubiner et al., 2002; Wilens et al., 2005). Of interest, no evidence exists that treating ADHD pharmacologically through an active SUD exacerbates the SUD. This is consistent with the work of Grabowski et al. (2004), who used stimulants to block cocaine and amphetamine abuse. Also consistent with these findings, earlier work by Volkow et al. (1998) demonstrated significant differences between binding at the dopamine transporter between methylphenidate and cocaine, suggesting a much smaller abuse risk for...
methylphenidate in contrast to cocaine. In ADHD adults with SUDs, the nonstimulant agents (atomoxetine [Strattera]), antidepressants (bupropion [Wellbutrin]), and extended-release or longer-acting stimulants with lower abuse liability and diversion potential are preferable (Riggs, 1998). While of particular interest because of the drug's broad spectrum of activity in ADHD and lack of abuse liability (Heil et al., 2002), results from ongoing trials of atomoxetine in SUDs are not yet available. In individuals with SUDs and ADHD, frequent monitoring of pharmacotherapy should be undertaken— including evaluation of compliance with treatment, use of questionnaires (Gignac et al., 2005), random toxicology screens as indicated, and coordination of care with addiction counselors and other caregivers.

**Issues of diversion.** Surprisingly, limited information is available on the inappropriate use of stimulants in terms of the magnitude of the problem and the characteristics of misuse in individuals for whom they are prescribed. Musser et al. (1998) surveyed 161 children with ADHD responding to methylphenidate in order to assess diversion. The authors reported that 16% of children had been approached to sell or give away their prescribed medication; however, the actual rates of diversion were not reported. Marsh et al. (2000), using a retrospective review of the medical charts of 240 adolescents with ADHD, reported that 12% had misused their methylphenidate, although the characteristics of those youth were not reported. Poulin (2001) surveyed 13,549 students in grades 7 through 12 and found that 8.5% had used nonprescribed stimulants in the year prior to the survey. Of those students who were receiving prescribed stimulants, 14.7% had given their medications and 7.3% had sold their medication to other students. Similar to other studies, those to whom the stimulants were diverted misused the stimulants in context with other substances of abuse. Similarly, we recently found that 11% of adolescents and young adults with ADHD diverted (sold) and 22% had misused their stimulants (e.g., escalated dose, used with other substances, became euphoric) (Wilens et al., in press-a). We also found that ADHD individuals with conduct disorder or SUDs accounted for the misuse and diversion and that there appeared to be more misuse and diversion of immediate-release compared to extended-release stimulants (Wilens et al., in press-a).

**Summary**

There is a strong literature supporting a relationship between ADHD and SUDs. Both family/genetic and self-medication influences may be operational in the development and continuation of SUDs in ADHD. Adolescents with ADHD and SUDs require multimodal interventions incorporating addiction and mental health treatment. Pharmacotherapy in individuals with ADHD and SUDs needs to take into consideration timing, misuse and diversion liability, potential drug interactions, and compliance concerns. While the existing literature has provided important information on the relationship of ADHD and SUDs, it also points to a number of areas in need of further study. The mechanism by which untreated ADHD leads to SUDs, as well as the risk reduction of ADHD treatment on cigarette smoking and SUDs, needs to be better understood. Given the prevalence and major morbidity and impairment caused by SUDs and ADHD, prevention and treatment strategies for these adolescents need to be further developed and evaluated.

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