



## Correlates of co-occurring ADHD in drug-dependent subjects: Prevalence and features of substance dependence and psychiatric disorders

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### ABSTRACT

We examined the prevalence and course of psychiatric and substance dependence (SD) disorders in subjects with SD and attention deficit hyperactivity disorder (ADHD).

**Method:** We interviewed 1761 adults with a lifetime diagnosis of cocaine and/or opioid dependence using the Semi-Structured Assessment for Drug Dependence and Alcoholism. Generalized linear regression with generalized estimating equation analysis was used to examine the associations between a lifetime diagnosis of ADHD and indicators of clinical course, and to identify unique correlates of ADHD.

**Results:** Lifetime ADHD prevalence in the SD sample was 5.22% (vs. 0.85% in a group of individuals without SD). ADHD was associated with an earlier age of first substance use, more SD and psychiatric diagnoses, a greater likelihood of attempted suicide, and more hospitalizations. After controlling for conduct disorder, there were unique effects of ADHD on age of first substance use and number of SD diagnoses.

**Conclusion:** In subjects with cocaine or opioid dependence, ADHD is associated with greater SD and psychiatric comorbidity and a more severe course of illness.

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### 1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a common, highly heritable, neurobehavioral disorder, beginning in childhood but often persisting into adulthood, which is associated with significant impairment in psychosocial function (Biederman, 2005). Estimates of the worldwide lifetime prevalence of childhood ADHD in the general population usually range from less than 5%, to 12% (Kessler, Adler, et al., 2005; Fayyad et al., 2007; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007; Faraone et al., 2003). The prevalence of ADHD is thought to be considerably higher among individuals with a substance use disorder (SUD) than in the general population (see Kalbag and Levin, 2005 for a review). The prevalence of childhood and adult ADHD in substance-abusing populations has been estimated to be three times that in the general population (Rounsaville et al., 1991; Levin, Evans, & Kleber, 1998; King, Brooner, Kidorf, Stoller, & Mirsky, 1999; Clure et al., 1999). Similarly, rates of SUDs among individuals with adult ADHD, which are as high as 40% (Kalbag and Levin, 2005; Biederman et al., 1995), are substantially higher

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than those in the general population, estimated to be 14.6% for any SUD (Kessler, Adler, et al., 2005). Examination of non-treatment-seeking ADHD samples reveals findings similar to those obtained in clinical samples (Biederman et al., 1995).

The National Comorbidity Survey Replication study (NCS-R) is the only study to date that reports on the co-occurrence of SUD and ADHD in a general, non-treatment-seeking SUD population (Kessler, Adler, et al., 2005; Kessler, Berglund, 2005; Kessler et al., 2006). This national survey yielded overall prevalence rates of 8.1% and 4.4% for childhood (i.e., lifetime) ADHD and adult ADHD, respectively. Although the prevalence of childhood ADHD among individuals with a lifetime SUD was not reported, the prevalence of adult ADHD in this subgroup was 10.8%, compared to 3.8% among individual without a lifetime SUD.

Adults with a history of ADHD (including those with adult ADHD) have double the risk of developing a SUD as adults without ADHD (Biederman, Wilens, Mick, Faraone, & Spencer, 1998). A co-occurring ADHD diagnosis is also associated with an earlier onset and more severe course of a SUD, poorer treatment adherence, more difficulty achieving treatment goals and progress in treatment, and higher rates of relapse (Carroll and Rounsaville, 1993; Wise, Cuffe, & Fischer, 2001; Levin et al., 2004; Wilens, Biederman, Mick, Faraone, & Spencer, 1997). In a study by Kolpe and Carlson (2007), the presence of clinically significant ADHD symptoms just prior to admission to a methadone program was associated with a poorer outcome in that program. Despite these associations, the specific nature of the relationship between ADHD and SUDs is unclear, and there are few data on their co-occurrence in non-treatment-seeking SUD populations. Prior studies have also linked ADHD to increased suicidal behaviors and/or self-mutilation, though the nature of this relationship remains unclear (Kelly, Cornelius, & Clark, 2004; Fulwiler, Forbes, Santangelo, & Folstein, 1997).

The influence of other psychiatric disorders that frequently co-occur with ADHD [e.g., oppositional defiant disorder, conduct disorder (CD), and antisocial personality disorder (ASPD)] on risk for the development of a SUD further complicates the picture. The co-occurrence of ADHD with CD, in particular, is of interest, since in a number of studies showing them to be associated, results for ADHD are not significant when comorbid CD is taken into account, raising the question of whether it is CD rather than ADHD that accounts for the increased risk of a SUD (Flory and Lynam, 2003). However, other studies have provided evidence for a direct link between ADHD and risk for the age of onset and presence of a SUD, after controlling for CD (Biederman et al., 1995; Wilens et al., 1997; Milberger, Biederman, Faraone, Chen, & Jones, 1997). The co-occurrence and effects of ADHD and CD on a child's development, including the impact on the risk and features of SUDs, require further research. ADHD and CD could make unique contributions to the risk of a SUD; these disorders could also interact developmentally with social difficulties faced by ADHD, increasing the risk of the individual affiliating with deviant peer groups and thereby modify the phenotypic expression of a SUD (Marshal and Molina, 2006).

It has been proposed that ADHD and SUDs may share common genetic risk factors, as well as similar etiologies based in personality factors or psychosocial environmental factors, or that co-occurrence of SUDs may stem from "self-medication" of ADHD (Kalbag and Levin, 2005). To date, however, there is little evidence to support a shared genetic etiology, possibly because the complex relationship between ADHD and SUDs complicates etiologic and pathophysiological analysis (Johann, Bobbe, Putzhammer, & Wodarz, 2003; Kim et al., 2006; Lasky-Su et al., 2006). A recent study by Wilens et al. (2007), reported no difference in rates of drug use for self-medication or for getting high between ADHD subjects and controls, when motivations for drug use were examined, arguing against a strong role for self-medication in the link between ADHD and SD.

Because there are few published studies examining the impact of ADHD on the course of SD course and on its outcome, despite a comparatively high rate of co-occurrence, studies in the population of patients with these co-occurring disorders are clinically important. This study explores the association with ADHD of a number of psychiatric and SD-related variables, some of which serve as proxy measures of course and outcome, while others are descriptive and serve to characterize this population more fully. Of particular interest is whether ADHD itself (and not co-occurring disorders or other associated factors) is associated with a more severe phenotypic expression of psychiatric and substance use disorders, as is suggested by the literature reviewed above. The population studied here is unique in that it contains subjects recruited largely from the community, as opposed to a primary treatment sample.

To examine the correlates of co-occurring ADHD with regard to substance dependence (SD), psychiatric disorders, and related features, we studied a sample of subjects recruited as small nuclear families, ascertained on the basis of sibling pairs affected with cocaine and/or opioid dependence to participate in linkage studies of cocaine and opioid dependence (Gelernter et al., 2005, 2006). We predicted that the prevalence of ADHD in this population of SD subjects would be elevated relative to a comparison group screened to exclude individuals with a lifetime SUD. We hypothesized that a lifetime history of ADHD would be associated with a more severe course of SUD and more co-occurring SD and psychiatric disorders, including outcomes associated with impulsivity (often a prominent feature of ADHD), such as suicidal behaviors. We also hypothesized that ADHD would be associated with these indicators of more severe substance use and psychiatric disorders even when the particularly important confounding effect of CD is taken into account. As an exploratory analysis, we also examined whether there is a preference for certain types of drugs in drug-dependent individuals with ADHD, as such information could inform further studies designed to understand the link between ADHD and substance use disorders.

## 2. Methods

### 2.1. Study sample

A total of 2047 individuals from 984 small nuclear families were ascertained on the basis of a sibling pair, in which both individuals were affected with cocaine and/or opioid dependence. Subjects were recruited to participate in one of two multi-site

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