Stohler R, Rössler W (eds): Dual Diagnosis. The Evolving Conceptual Framework.
Bibl Psychiatr. Basel, Karger, 2005, No 172, pp 92–104

Having Attention-Deficit/Hyperactivity Disorder and Substance Use Disorder: A Review of the Literature

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The co-occurence of attention-deficit/hyperactivity disorder (ADHD) and substance use disorders (SUDs) is a relatively new topic in the field of psychiatric comorbidity. Accordingly, the ADHD syndrome is a relatively new diagnostic category: the category was first introduced in ICD-8 (1968) [1] as Hyperkinetic Syndrome and then in DSM-III (1980) [2] as Attention-Deficit Disorder and subsequently changed from revision to revision until it was called Attention-Deficit/Hyperactivity Disorder in DSM-IV [3]. As of now, there is no diagnostic entity regarding adult ADHD in the diagnostic manual ICD-10 of the World Health Organization [4]. Despite these diagnostic deficiencies, comorbidity of ADHD and SUD has received considerable attention in the scientific community in the recent years. This is not surprising given the diverse close connections between the two disorders (for an overview, see Sullivan and Rudnik-Levin [5]): symptoms of ADHD and SUDs can be very similar, making it difficult to diagnostically differentiate between the two disorders and to assess ADHD in the presence of a known SUD. Another concern is that the treatment of ADHD needs special considerations in persons with a SUD. And – coming to the main issue of this article – persons with ADHD seem to be at increased risk for developing a SUD: studies [6] have shown that individuals with ADHD have an earlier onset of substance abuse and exhibit a pattern of more frequent or more intense substance use than persons with SUDs without comorbid ADHD.

Diagnostics of ADHD

According to ICD-10 [4] and DSM-IV [3], the core symptoms of ADHD are inattention, hyperactivity, and impulsivity. These symptoms have to be

present before the age of 7. Since there is no diagnostic category for adult ADHD, criteria for childhood ADHD have to be used. This is problematic, as there seems to be a developmental shift in the symptoms from childhood to adulthood. Moreover, symptoms can vary according to the different social environment adults live in and the challenges they face, and symptoms have to be present at least in two different domains.

The predominating symptoms in adult ADHD comprise the following: attention deficits, impulsivity, susceptibility to stress, chaotic organization in occupation and private life, lowered self-esteem, lower frustration tolerance, propensity to dangerous activities (risky sport, traffic), nicotine abuse, illicit drugs, and alcohol [7–9]. The diagnosis of ADHD in the presence of a SUD poses particular clinical challenges because of several reasons, as for example, impaired memory in the substance abuser, undiagnosed childhood ADHD, failure to determine the degree of impairment caused by ADHD symptoms. Other criteria for ADHD as onset of ADHD symptoms in childhood cannot always validly be assessed in persons with a SUD. Childhood reports by significant others such as parents, teachers, school psychologists etc. are also not always accessible. Therefore, diagnosis of adult ADHD in presence of a SUD should be made especially thoroughly and validated by different clinical and psychological methods such as interviews and tests.

Epidemiology of ADHD

ADHD is the most common behavioral disorder of childhood: estimated prevalence rates in the general population of school-aged children vary from 3 to 9%. In contrast to earlier assumptions, long-term controlled follow-up studies have shown the persistence of full ADHD syndrome from childhood to adulthood [10–13]. Derived from studies showing that about 3–70% of these children have persistent symptoms in adulthood, a prevalence rate of approximately 1–6% can be assumed [13–20]. Looking at the syndrome more specifically, longitudinal studies in ADHD youths seem to indicate that the symptom clusters of hyperactivity and impulsivity decay over time, whereas the symptoms of inattention persist [11, 14, 21, 22].

Epidemiology of Concurrent ADHD and SUD

The co-occurence of ADHD and SUDs has been examined over the past decade and been consistently observed by several groups [23–25]. Wilens et al.

[25] found that ADHD was associated with earlier onset of SUDs independent of psychiatric comorbidity. Several investigators [18, 26] found that ADHD represents a broad vulnerability to substance abuse in general and Clure et al. [27] examined the issue of drug choice in ADHD population and concluded that there were no significant differences in ADHD prevalence by substance of choice. Biedermann et al. [28] demonstrated that ADHD represents an independent risk factor for SUDs while psychiatric comorbidity is known to increase the risk for SUDs.

ADHD and Opiates

As to the comorbidity of ADHD and opioid addiction, studies from Ornoy [29], Ornoy et al. [30], and Weissmann et al. [31] demonstrate that children of heroin-dependent parents (both mothers and fathers) have an increased risk of developing ADHD – even if adopted early by families without heroin-dependent members. On the other hand, Eyre et al. [32] found that 22% of opiate addicts had childhood ADHD with many of them showing sequelae of childhood ADHD symptoms. King et al. [26] assessed ADHD in patients entering methadone maintenance treatment: 19% of the patients had a history of ADHD and of these, 88% had current symptoms. This again, indicates an association of ADHD with an increased risk for opioid use, abuse, or dependence.

ADHD and Cocaine

There are many studies investigating different aspects of the association of ADHD and cocaine use and abuse: Weissmann et al. [31] found elevated rates of ADHD in children of mothers with heroin and/or cocaine dependence in two studies: 13% of the children in study 1 and 8% in study 2 were assessed to have ADHD. The other way around, Chronis et al. [33] investigated children with ADHD and found elevated rates of cocaine and stimulants dependence in their mothers. According to the findings of Bandstra et al. [34] and Richardson et al. [35], prenatal cocaine exposure leads to deficits in sustained attention in children. Thus, mothers' cocaine and stimulants abuse seems to be a risk factor for ADHD in their offspring. Vice versa, ADHD seems to be a risk factor for the development of a SUD. According to Davids and Gastpar [36], up to 50% of adult patients with continuing ADHD symptoms from childhood suffered from a SUD; especially cocaine and nicotine abuse. Compared to other persons with a SUD, those with comorbid symptoms of ADHD had an earlier onset, a higher frequency, a longer duration, and a more probable transition from alcohol to other SUDs. Converging findings are reported by other authors: Rounsaville et al. [37] found increased rates of childhood ADHD in cocaine abusers seeking treatment. Levin et al. [18] found childhood ADHD

in 12% of 281 cocaine abusers in treatment; of those, 79% had adult ADHD. Similarly, Carroll and Rounsaville [38] found that of 298 treatment-seeking cocaine abusers, 35% had childhood ADHD. Furthermore, those cocaine abusers with childhood ADHD differed from abusers without childhood ADHD in the following characteristics: abusers with childhood ADHD were younger at presentation for treatment, had more severe cocaine abuse, an earlier onset of cocaine abuse, more frequent and more intense cocaine use, intranasal rather than freebase or intravenous cocaine use, higher rates of alcoholism, and more previous treatments. According to the authors, this pattern of use is consistent with clinical descriptions of self-medication of residual symptoms of ADHD in cocaine abusers. Therefore, it seems to be important to identify and treat residual symptoms of ADHD in cocaine abusers as concluded by Weiss and Mirin [39]. They identified 5 subtypes of cocaine abusers, one of which appears to self-medicate ADHD symptoms with cocaine. Further support for the self-medication hypothesis [40, 41] is given by Castaneda et al. [42], Khantzian et al. [43], and Levin et al. [44], who successfully treated cocaine abuse in patients with comorbid ADHD with long-acting stimulants such as methylphenidate. Schubiner et al. [45] conducted a double-blind, placebo-controlled trial and found that methylphenidate alleviated symptoms of ADHD in adult patients with concurrent cocaine dependence without worsening cocaine use.

The role of methylphenidate in the treatment of ADHD is still controversial as there are studies raising concern about potential unwanted effects of methylphenidate on the brain: Morton and Stockton [46] reported that intranasal use of methylphenidate produces effects rapidly that are similar to the effects of cocaine in both onset and type. Volkow and Swanson [47] have found strikingly similar neurophysiological mechanisms of action of cocaine and methylphenidate and claimed that reinforcing effects of methylphenidate consumed intravenously and intranasally are very similar to intravenous cocaine use. Kollins et al. [48] reviewed several studies with human and nonhuman subjects and came to the conclusion that methylphenidate has similar abuse potential as other psychostimulants such as cocaine or amphetamine.

In experiments with rats, Schenk and Izenwasser [49] found an increased vulnerability to cocaine abuse when rats were pretreated with methylphenidate. Similarly, Andersen et al. [50] found increased sensitivity to aversive effects of cocaine in rats pretreated with methylphenidate. Given these findings, one could assume that methylphenidate given to children as treatment for ADHD could increase their risk for later developing a cocaine abuse disorder: Lambert and Hartsough [51] report a linear trend for increased rates of smoking and cocaine dependence, the longer children were treated with CNS stimulants. In contrast, both Barkley et al. [52] and

Biederman [53] found no such association: Barkley et al. [52] found that stimulant treatment in children with ADHD did not lead to an increased risk for substance experimentation, use, dependence or abuse by adulthood. Biederman [53] investigated 140 persons with ADHD and 120 persons without ADHD and found that children with ADHD treated with stimulants had *lower* rates of SUD compared to untreated people with ADHD. The rates for developing a SUD when suffering from ADHD were 3–4 times greater for persons *without* stimulant treatment. Thus following these findings, stimulant medication seems to have a protective effect in persons with ADHD. This effect possibly cannot be generalized to all cocaine users. Gawin et al. [54] reported 5 cases of cocaine dependence without diagnoses of ADHD: since treatment with methylphenidate did not result in a decrease of cocaine consumption, it seems possible that treatment with stimulants as methylphenidate might help only in cocaine abusers with ADHD.

ADHD and Cannabis

Data on the association of ADHD with cannabis use and dependence are not unequivocal: some studies found an association and some did not. Lambert and Hartsough [51] conducted a longitudinal study and followed both ADHD diagnosed children and children without ADHD into adulthood. They reported that adulthood rates of cannabis dependence did not differ between the ADHD and the non-ADHD group (27 vs. 29% in the samples that consisted about 2/3 to 3/4 boys). Likewise, Fergusson et al. [55] found no association between childhood ADHD and cannabis use by age 15 when controlling for the association between conduct problems and ADHD. In contrast, Flory et al. [56] found in 481 young adults that ADHD and conduct disorder together predicted the highest levels of cannabis dependence as well as hard drug use and dependence symptoms. The report of Murphy et al. [57] had converging findings: they compared 96 young adults with ADHD to a control group of 64 young adults without ADHD. The group with ADHD had increased rates of both cannabis and alcohol dependence and abuse. Fried et al. [58] investigated the influence of prenatal exposure of cannabis, cigarettes, and alcohol in 126 children at age 6. They found that prenatal cannabis exposure was related both to deficits in sustained attention and higher ratings on impulsiveness and hyperactivity scales. Similar results were found in other studies by Fried and colleagues [59–62]: prenatal cannabis exposure was found to be associated with childhood deficits in attentional behavior and executive functioning.

ADHD and Nicotine

Associations of ADHD with smoking and nicotine dependence are reported by Lambert and Hartsough [51] from their longitudinal study. They

found significant differences in age of beginning to smoke regularly between persons with and without ADHD. At age 17, 46% of the ADHD group reported smoking daily, compared to 24% of the non-ADHD group. At adulthood, 42% of the ADHD group were current smokers compared to 26% of the non-ADHD group. Lifetime tobacco dependence rates were 40% in the ADHD group and 19% in the non-ADHD group indicating that ADHD seems to be a clear risk factor for nicotine use, abuse, and dependence. Furthermore, tobacco use and dependence varied whether children were treated with stimulant medication or not: there was a linear trend for increased rates of smoking the longer children were treated with CNS stimulants. Molina and Pelham [63] also conducted a longitudinal study and compared 142 persons with ADHD to 100 persons without ADHD. They found that the ADHD group had higher use of tobacco, alcohol and illicit drug use. In addition, persistence of ADHD symptoms in adolescence was associated with elevated substance use. Converging findings are reported by several other investigators [28, 36, 64–68]: ADHD was found to be associated with increased rates of tobacco use, higher frequency of smoking, earlier initiation of smoking, and more intense symptoms of nicotine withdrawal. Moreover, individuals with ADHD seemed to quit smoking less frequently compared to the general population of smokers. Some studies [63, 69–71] investigated the association of different subtypes of ADHD with nicotine dependence and found evidence that the ADHD subtype of inattention had a stronger association with nicotine abuse than other subtypes.

ADHD and Alcohol

There are different approaches to investigating associations between ADHD and alcohol use disorders. All in all, there seems to be a clear association between ADHD and alcohol use disorders. For example, Kuperman et al. [72] interviewed 463 children and their biological parents and found that parental alcoholism was associated with increased risk for ADHD in their offspring: the same was true for conduct disorder and overanxious disorder. Clark et al. [73] compared two groups of 14–18-year-old adolescents – one group with ($n = 133$) and one group without ($n = 86$) alcohol dependence: the alcohol dependence group exhibited increased rates of ADHD. Johann et al. [74] found in a genetic study that comorbidity of alcoholism and ADHD seemed to form a distinct phenotype of alcohol dependence (related to Cloninger's type 2) that showed an increased severity of the substance disorder. Molina and Pelham [63] found in their longitudinal study, higher use of alcohol and other substances in their ADHD group of 142 persons compared to the non-ADHD control group of 100 persons. Furthermore, persistence of ADHD symptoms in adolescence was associated with elevated substance use. In contrast,

Lambert and Hartsough [51] found no statistically significant differences in their prospective longitudinal study when they compared adulthood rates of alcohol dependence between the ADHD and the non-ADHD group (38 vs. 30%). Similarly, Schuckit et al. [75] investigated 162 children in alcoholic and nonalcoholic families and found no association between ADHD and family history of alcoholism after controlling for conduct disorder and socioeconomic status.

There is clear evidence that fetal alcohol syndrome incurs a significantly elevated risk for later development of ADHD: Burd and colleagues [76, 77] reported high rates of ADHD in children with fetal alcohol syndrome; 73 and 40% of children with fetal alcohol syndrome later developed ADHD.

The Role of Conduct Disorder and Antisocial Personality Disorder

Lynskey and Hall [78] as well as Modestin et al. [79] doubt the causal link between ADHD and SUDs. They recount several reasons: first, early studies on the association between ADHD and SUDs retrospectively investigated symptoms of ADHD in persons seeking treatment for opiate, cocaine and other SUDs. The problem of such methodology includes the unclear validity and accuracy of retrospective assessment of ADHD symptoms. The retrospective reporting of ADHD symptoms could be correlated with current psychiatric status. Thus, persons currently seeking treatment for SUD could potentially report their childhood behavior in a distorted way. Another problem is potential lack of representativeness: since SUD comorbid with ADHD could be more severe than SUD alone, the comorbid group could be overrepresented in the treatment-seeking population. The same is true for other types of studies investigating the association of ADHD and SUD: most longitudinal prospective studies compared clinic-referred children with ADHD to community control samples. Again, clinic-referred children potentially are not representative for children with ADHD in general since there are studies showing that those who receive treatment are more likely to experience comorbid psychiatric conditions and other social adjustment problems [80–82]. In a longitudinal study of their own, Lynskey and Hall [78] investigated a representative sample of 1,265 children. They assessed attentional difficulties (including restless, inattentive, and hyperactive behaviors) at age 8 and illicit drug use (principally cannabis use) at age 15. The simple association showed a moderate and approximately linear association between ADHD symptomatology at age 8 and rates of illicit drug use at age 15. However, further analysis indicated that this association was explained by the

fact that attentional difficulties were highly associated with conduct problems that were, in turn, causally related to later drug use. Thus, Lynskey and Hall [78] claim that the observed association between ADHD and SUD is an illusory correlation stemming from the correlations of ADHD and conduct disorder on one hand and conduct disorder and SUD on the other hand. From their review of the existing literature and their own study, they conclude that the role of ADHD in the etiology of substance use problems has been overemphasized. They claim that much of the association between ADHD and later substance abuse can be explained by the associations between ADHD and conduct problems, which have been shown to influence later propensities to substance use and misuse [83–85].

Conclusions

There is clear evidence that there are notably strong associations between ADHD and SUDs: among persons with SUD, more than could be expected suffer from comorbid ADHD; vice versa, persons with ADHD seem to be at greater risk for developing a SUD. The patterns of substance use and abuse of individuals with comorbid ADHD and SUD are characterized by the earlier onset, more intense use, faster progression from use to abuse and dependency, faster transition from alcohol to other substances, longer duration of the SUD, and more therapy failures compared to persons with SUD without comorbid ADHD.

The largely converging evidence regarding the association of ADHD and SUD stems from studies using quite different methodological and theoretical approaches, enhancing their validity. Still, the question remains unclear whether the observed association is an artifact stemming from two independent associations between ADHD and conduct disorder/antisocial personality disorder on the one hand and conduct disorder/antisocial personality disorder and SUD on the other [78, 79]. However, the co-occurrence of ADHD and SUD poses special challenges both to the correct diagnosis and the treatment of these persons. Therefore, the investigation of optimal diagnosis and treatment for this group of persons may be better investigated independently of the more academic question regarding the nature of the association between these two disorders. Treatment strategies for persons with SUDs and ADHD can be resumed as treating one disorder may have beneficial effects upon the other. Both, pharmacological and nonpharmacological treatments require closer considerations, but will not be discussed here.

Another point that still is not answered unequivocally is the question of whether the presence of ADHD incorporates a risk factor for the development

of the abuse of certain substances rather than others; i.e. whether there is a 'drug of choice' for persons with ADHD. Some studies found no evidence that there is a 'drug of choice', while the other studies seem to indicate a special risk for substances as nicotine and cocaine while for opiates the risk seems to be smaller.

Acknowledgment

We thank Victoria Reed for her help in preparing the manuscript.

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