ARTICLE

Association Between Attention-Deficit/Hyperactivity Disorder in Adolescence and Substance Use Disorders in Adulthood

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Objectives: To determine whether attention-deficit/hyperactivity disorder (ADHD) in adolescence is related to substance use disorders (SUDs) in adulthood and whether conduct disorder (CD) mediates this relationship.

Design: A prospective design incorporating 5 assessments in participants spanning the mean ages of 14 to 37 years. Two baseline assessments were taken at ages 14 and 16 years, and 3 outcome assessments were taken between ages 27 and 37 years.

Setting: United States.

Participants: A community sample of individuals initially drawn from upstate New York in 1975 and observed to a mean age of 37 years.

Interventions: The Diagnostic Interview Schedule for Children was used to assess ADHD and CD and the University of Michigan Composite International Diagnostic Interview was used to assess SUDs.

Main Outcome Measure: A diagnosis of SUDs given to participants in adulthood.

Results: The odds ratios for ADHD and CD in adolescence as related to SUDs in adulthood were 1.9 and 3.5, respectively. The association between ADHD and SUDs, however, was indirect because CD served as a mediator between ADHD and SUDs.

Conclusions: Pediatricians should focus on adolescent ADHD when it progresses to CD because CD is a major predictor of SUDs in adulthood.

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Substance use disorders (SUDs) are associated with psychiatric disorders and with low educational levels, unemployment, and risky sexual behavior.[1-3] Given the negative consequences of SUDs, it is important to identify its predictors. One factor that researchers have identified as being related to the development of SUDs is the presence of attention-deficit/hyperactivity disorder (ADHD). Cross-sectional and longitudinal research[4-10] indicate that ADHD in childhood or adolescence is associated with an increased risk of substance use or dependence later in adolescence or in early adulthood. Another factor shown to be related to SUDs is conduct disorder (CD).[11] In addition to their relationship to SUDs, ADHD and CD are strongly correlated with one another.[12,13] Researchers have attempted to identify the independent association of ADHD with the onset of SUDs, most often by statistically controlling for the presence of CD or other psychiatric disorders.[7-10]

These attempts to link diagnoses of ADHD to SUDs have generally not found an independent prospective association between ADHD and SUDs. For example, Elkins et al[9] examined the relationship between diagnoses of ADHD on the one hand and 3 types of SUDs (nicotine dependence, alcohol abuse/dependence, and cannabis abuse/dependence) on the other. Diagnoses of ADHD were unrelated to the diagnosis of SUDs at age 18 years, once analyses were adjusted to control for childhood CD. Similarly, after controlling for other psychiatric disorders, including CD, Biederman et al[8] found that ADHD in childhood and adolescence was related to lifetime and 1-year prevalences of nicotine dependence at 10-year follow-up but not of drug or alcohol dependence.

To our knowledge, only 1 study[10] has found that a diagnosis of ADHD is independently, prospectively linked to the subsequent development of SUDs. Gau et al[10] found that a diagnosis of ADHD at age 12 years was related to the development of SUDs in the next 3 years, even after controlling for other psychiatric disorders, including CD. One possible explanation for the discrepancy between the findings of

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Gau et al and those of other researchers noted previously herein is that Gau et al used a shorter longitudinal timeframe than did other studies, and their outcome assessment occurred at a younger age. Because ADHD is most prevalent in childhood and early adolescence,[14,15] it may be that the disorder exerts a direct effect on SUDs at these early ages, but the effect is mediated with time.

Given that the literature suggests a stronger relationship between CD and SUDs than between ADHD and SUDs, we hypothesized a mediational model.[16] To test the mediational hypothesis, we applied the 3 conditions of Baron and Kenny[16] for a possible mediational pathway: (1) the independent variable (ADHD) is related to the potential mediator (CD), (2) the mediator (CD) is related to the dependent variable (SUDs) despite controlling for the independent variable, and (3) the relationship between the independent and dependent variables is rendered nonsignificant once there is statistical control for the effect of the mediator.

After the mediational model, we tested the following hypotheses: (1) ADHD is related to CD; (2) CD in adolescence is associated with SUDs in adulthood, even after controlling for ADHD; and (3) ADHD in adolescence is associated with SUDs in adulthood, but this effect no longer holds after controlling for CD.

We extend the literature in 2 important respects. First, to our knowledge, this study is the first to formally test for CD as a mediator between ADHD and SUDs. As noted previously herein, we proposed that CD is the mediator because its relationship with SUDs is more powerful than is the relationship between ADHD and adult SUDs.[9] Second, we observed the sample to a much later age than have other researchers who studied the relationship between ADHD and SUDs. Thus, these data allow us to investigate the association between ADHD in adolescence and SUDs in adulthood.

METHODS

PARTICIPANTS AND PROCEDURE

Data for the participants in this study came from a community-based random sample residing in 2 upstate New York counties (Albany and Saratoga) first assessed for drug use in 1983. The sample was taken from an earlier study using maternal interviews in 1975 (T1). The original maternal/youth study assessed problem behavior in youngsters. The sampled families were generally representative of the population of families in Albany and Saratoga for sex, family intactness, family income, and education. Interviews of mothers and youths were conducted in 1983 (T2, n=756), 1985-1986 (T3, n=739), and 1992 (T4, n=750). Three more interviews of the second generation were conducted in 1997 (T5, n=749), 2002 (T6, n=673), and 2005-2006 (T7, n=607). Some participants who were not interviewed in previous years were interviewed in later waves of data collection.

The mean (SD) ages of participants at the interviews were 14.1 (2.8) years at T2, 16.3 (2.8) years at T3, 22.3 (2.8) years at T4, 27 (2.8) years at T5, 31.9 (2.8) years at T6, and 36.6 (2.8) years at T7. In the present analyses, we included 485 participants whose measurements of SUDs at T5 through T7 and of ADHD and CD at T2 and T3 were available and who had no history of SUDs assessed in adolescence (T2). Excluding the 30 participants who were diagnosed as having SUDs at T2 helped us identify adolescent ADHD and CD in a cohort that was free of the outcome (SUD) at the outset of the study. Using the T2 sample (n=756) as the baseline, there was a significantly higher percentage of female participants in the group of 485 individuals included in this study than in the 271 not included (57.5% and 38.0%, $\chi^2_1=27.2$, $P<.001$). There was a significantly lower percentage of participants with ADHD at T2 in the 485 included individuals than in the 271 not included (9.1% and 18.4%, $\chi^2_1=12.8$, $P<.001$). There was a significantly lower percentage of participants with CD at T2 in the 485 included individuals than in the 271 not included (7.1% and 21.3%, $\chi^2_1=31.4$, $P<.001$).

Extensively trained and supervised lay interviewers administered interviews in private. Written informed consent was obtained from participants and their mothers in 1983, 1986, and 1992 and from participants only in 1997, 2002, and 2007. The institutional review board of New York University School of Medicine authorized the use of human subjects in this research study. Additional information regarding the study methods is available in previous publications.[17]

MEASURES

ADHD and CD at T2 and T3

The parent and youth versions of the Diagnostic Interview Schedule for Children were administered in 1983 (T2) and again in 1985-1986 (T3) to assess psychiatric disorders, including ADHD and CD. Symptoms of ADHD include an unusually high and long-term level of inattention, hyperactivity, or both. Some items were added to the Diagnostic Interview Schedule for Children to make the diagnosis of ADHD consistent with that of the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) (*DSM-IV*).[18] Criteria from the *DSM-IV* were used to classify the participants for ADHD. According to the *DSM-IV*, CD is a repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms are violated, as manifested by the presence of 3 (or more) of several criteria in the past 12 months, with at least 1 criterion present in the past 6 months.

Major Depressive Disorder at T2

Adolescent major depressive disorder (MDD) at T2 was diagnosed if participants had a change in functioning reflected by 5 or more of the following *DSM-IV* criteria during the same 2-week period: (1) depressed mood most of the day, nearly every day, or (2) markedly diminished interest or pleasure in all, or almost all, activities (1 must be present); (3) significant weight loss or gain when not dieting; (4) hypersomnia or insomnia nearly every day; (5) psychomotor agitation or retardation; (6) feeling tired nearly every day; (7) feeling worthless or inappropriate guilt; (8) problems concentrating; and (9) recurrent thoughts about death.

SUDs at T5 Through T7

At T5 through T7, SUDs (dependence or abuse) was assessed using the University of Michigan Composite International Diagnostic Interview SUDs measure.[19] We adapted this measure to make it consistent with the criteria used in the *DSM-IV*. We ascertained substance dependence by the presence of 3 or more of the following criteria for each substance (marijuana or other illicit drug, eg, cocaine/crack, heroin, LSD [lysergic acid diethylamide], ecstasy, and amphetamines) used during the 12 months before the interviews at T5 through T7: (1) use of more of the substance than usual to get the same effect, or the same amount has less of an effect than it used to; (2) the presence of withdrawal symptoms or the use of the substance to avoid with-

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Table. Adolescent ADHD, Adolescent CD, and Adult SUDs by Characteristics of the 485 Participants

Variable	Adolescent ADHD (11.6%)		Adolescent CD (12.0%)		Adult SUDs (11.1%)	
	Participants, %	OR (95% CI)	Participants, %	OR (95% CI)	Participants, %	OR (95% CI)
Adolescent ADHD						
Yes (11.6%)			37.5	6.4 (3.4-12.0)[a]	17.9	1.9 (0.9-4.0)[b]
No (88.4%)			8.6		10.3	
Adolescent CD						
Yes (12.0%)	36.2	6.4 (3.4-12.0)[a]			25.7	3.5 (1.8-6.8)[a]
No (88.0%)	8.2				9.1	
Sex						
Male (42.5%)	12.1	1.1 (0.6-1.9)	15.1	1.7 (1.0-2.9)[b]	16.5	2.6 (1.4-4.6)[a]
Female (57.5%)	11.1		9.7		7.2	
Age group						
<36 y at T7 (47.6%)	14.7	1.8 (1.0-3.2)[b]	11.8	1.0 (0.6-1.8)	11.7	1.1 (0.6-2.0)
≥36 y at T7 (52.4%)	8.7		12.1		10.6	
Adolescent MDD						
Yes (2.5%)	66.7	17.7 (5.1-6.1.0)[a]	58.3	11.6 (3.5-37.8)[a]	8.3	0.7 (0.1-5.7)
No (97.5%)	10.2		10.8		11.2	

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CD, conduct disorder; CI, confidence interval; MDD, major depressive disorder; OR, odds ratio; SUDs, substance use disorders; T7, 2005-2006.

[a] $P<.001$ (1-tailed test).

[b] $P<.05$.

drawal symptoms; (3) the use of much larger amounts of the substance than intended, or use for a longer period than intended; (4) the presence of such a strong desire or urge to use the substance that the person could not resist using it; (5) a period of 1 month or more in which the person spent a great deal of time using the substance or getting over its effects; (6) the person gave up activities because of use of the substance; or (7) emotional or psychological problems resulting from using the substance, such as feeling uninterested in things, depressed, suspicious of people, or paranoid or having strange ideas. If a participant did not meet the criteria for substance dependence, substance abuse was ascertained by the presence of at least 1 of the following 4 criteria during the same 12-month period: (1) being under the effects of the substance or experiencing its after-effects while at work or at school or while taking care of children, (2) being under the effects of the substance or feeling its after-effects in a situation that increased the user's chances of getting hurt (ie, when driving a car or boat, using knives or guns or machinery, crossing against traffic, climbing, or swimming), (3) having legal problems because of use of the substance, or (4) having problems getting along with other people because of use of the substance.

Analytic Plans

χ^2 Tests were used to test whether sex, age, and adolescent MDD were associated with adolescent ADHD, adolescent CD, and adult SUDs and whether adolescent ADHD and CD were associated with adult SUDs. We then conducted 3 separate logistic regression analyses to examine the association between earlier adolescent ADHD (at T2 or T3) and later adult SUDs (at T5, T6, or T7): (1) without any controls (ie, sex, age, adolescent CD, and adolescent MDD), (2) controlling only for earlier adolescent CD, and (3) controlling for earlier adolescent CD, sex, age, and adolescent MDD. We also conducted 3 separate logistic regression analyses to examine the association between earlier adolescent CD (at T2 or T3) and later adult SUDs (at T5, T6, or T7): (1) without any controls (ie, sex, age, adolescent ADHD, and adolescent MDD), (2) controlling only for earlier adolescent ADHD, and (3) controlling for earlier adolescent ADHD, sex, age, and adolescent MDD. Next, we conducted a logistic regression analysis to examine the relationship between adolescent ADHD and CD, with CD as the dependent variable and ADHD as the independent variable. To calculate the mediational effect of earlier adolescent CD, which operated between earlier adolescent ADHD and later adult SUDs, we used the SAS macro[20] based on the formula of MacKinnon and Dwyer[21] and selected the option that the mediator and the outcome are binary. We used 1-tailed tests throughout the analyses.

RESULTS

At T5, T6, or T7, 11.1% of the adults were diagnosed as having SUDs according to *DSM-IV* criteria; at T2 or T3, 11.6% of the adolescents were diagnosed as having ADHD and 12.0% were diagnosed as having CD (**Table**). In total, 19.1% of the adolescents were diagnosed as having either ADHD alone (7.2%), CD alone (7.6%), or both ADHD and CD (4.3%). The percentage of adult SUDs was significantly higher in those who had adolescent ADHD (17.9%) than in those who did not (10.3%) (odds ratio [OR], 1.9; 95% confidence interval [CI], 0.9-4.0). The percentage of adult SUDs was significantly higher in those who had adolescent CD (25.7%) than in those who did not (9.1%) (OR, 3.5; 95% CI, 1.8-6.8). The percentage of adolescent CD was significantly higher in those who had adolescent ADHD (37.5%) than in those who did not (8.6%) (OR, 6.4; 95% CI, 3.4-12.0). The Table also provides the percentages of adolescent ADHD, adolescent CD, and adult SUDs by sex, age group, and adolescent MDD.

The logistic regression analyses revealed that without any controls, adolescents who had earlier ADHD at T2 or T3 were 1.9 times (95% CI, 0.9-4.0 times; $P=.047$) more likely to have later adult SUDs than were those who did not have earlier ADHD. However, the association between earlier ADHD and later SUDs was no longer significant with earlier CD controlled for (adjusted OR, 1.3; 95% CI, 0.6-2.9; $P=.27$). The relationship between ADHD in adolescence and later SUDs in adulthood was also no longer significant when controlling for CD at T2 or T3, sex, age, and earlier MDD (adjusted OR, 1.4; 95% CI, 0.6-3.2; $P=.22$).

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The logistic regression analyses revealed that without any controls, adolescents who had earlier CD at T2 or T3 were 3.5 times (95% CI, 1.8-6.8 times; $P<.001$) more likely to have later adult SUDs than were those who did not have earlier CD. Participants who had earlier CD remained significantly more likely to have later SUDs with earlier ADHD controlled for (adjusted OR, 3.2; 95% CI, 1.6-6.6; $P<.001$). In addition, earlier adolescent CD remained significantly associated with later adult SUDs when controlling for ADHD at T2 or T3, sex, age, and earlier MDD (adjusted OR, 3.1; 95% CI, 1.5-6.4; $P=.001$).

In addition, males were 2.3 times (95% CI, 1.3-4.2 times; $P<.01$) more likely to have later adult SUDs than were females after adjusting for other factors, that is, earlier ADHD, earlier CD, age, and earlier MDD. The adjusted ORs for age (0.96, $P=.23$) and earlier MDD (0.41, $P=.27$) were not significantly different from 1.

We then conducted logistic regression analyses to examine the association between ADHD (at T2 or T3) and CD (at T2 or T3). The results indicated that adolescents with ADHD were 6.4 times more likely to have CD ($P<.001$) than were those who did not have ADHD. Therefore, the findings suggest a mediational effect of ADHD on adult SUDs via CD. The mediational effect was 0.6 on a scale from 0 to 1 and significant (SE=0.2, $t=2.8$, $P=.005$).

COMMENT

These findings support the hypotheses. First, ADHD is related to CD. Second, CD is highly related to SUDs, even after controlling for ADHD. Third, ADHD is related to SUDs, but this effect is not maintained after controlling for CD. Thus, these findings support a meditational model: the association between ADHD and SUDs is mediated by CD.

This study contributes to the literature as the first investigation to longitudinally study a sample of adolescents with and without ADHD, CD, and SUDs observed to a later stage of development, namely, their 30s.[7-10] In following the sample to a later stage of development than have previous investigators,[7-10] we confirmed that the relationship between adolescent ADHD and SUDs is indirect at this developmental stage (ie, adulthood). The present findings related to the mediational model are consistent with those of several researchers who have emphasized the importance of CD in predicting SUDs.[7,22,23] For example, Fergusson et al[22] maintained that after allowing for their high intercorrelation, attentional problems and conduct problems have differential consequences for later development. Specifically, conduct problems are directly related to later substance abuse, whereas attentional problems are not.

Although ADHD and CD are separate dimensions, they are significantly correlated.[12,13] Several factors may contribute to this association. Family and peer factors may mediate the relationship between ADHD and CD.[24] More specifically, individuals with ADHD may have difficulty in relating to family members and may associate with deviant peers, which, in turn, may be related to the development of CD.[25] Shared genetic influences are probably a contributing factor.[26] For example, Nadder et al[27] noted that twin studies suggest a common genetic component underlying ADHD and CD. Perinatal complications,[28] temperament,[29] and impaired cognitive functioning[30] have also been shown to be associated with ADHD and CD.

The present findings have important implications for the risk factors that predict SUDs. Given the symptom profile that characterizes CD, it is perhaps not surprising that adolescent CD is independently associated with the development of SUDs. That is, CD is typified by aggression (eg, showing physical cruelty to people or using a dangerous weapon) or delinquent behavior (eg, destroying property, lying, or stealing), both of which are reliable predictors of the development of SUDs.[31,32] The association between aggressive and delinquent behavior on the one hand and SUDs on the other may also be accounted for by problem behavior theory,[33] which posits that problem behaviors cluster within individuals. In the present study, it is particularly striking that the interval between the first baseline assessment and the final outcome assessment spanned more than 20 years. Therefore, the adverse effects of CD on the risk of SUDs are not temporally limited but persist across a considerable length of time.

Several factors may serve to mediate the relationship between CD and SUDs. Adolescents with CD may seek out peers who are delinquent and use drugs.[34] The peer group may then supply the individuals with drugs or otherwise reinforce their drug use. In adolescents, CD may evoke difficulty in the mutual attachment relationship between parent and child. A distant parent-child mutual attachment relationship has been found to predict substance use.[35]

This study has several limitations. First, the sample was predominantly white. The results, therefore, may not be generalizable to samples of ethnic minorities. Second, we are limited to self-report measures of substance abuse and dependence. Self-report measures of substance use, however, have generally been found to be reasonably accurate.[36] In the present study, the prevalences of adolescents with ADHD and CD are higher than those in some other national samples.[37] However, note that in the present study, we focused on relationships among the variables. Furthermore, measures that involved assessments at 2 time points might be more valid assessments of ADHD and CD than those that assessed these diagnoses only at 1 time point. Further research might be necessary to address this important issue. Third, there was a differential attrition rate between those (eg, males) who may have been more likely to incur adult SUDs and those (eg, females) with a lower risk. Fourth, we did not address how ADHD and CD can be handled in school and clinical programs without the negative label assigned to adolescents with these disorders.

These findings hold relevance for pediatricians because they demonstrate that the presence of adolescent ADHD, CD, or both is related to SUDs in one's 20s and 30s. However, where CD has a direct effect in predicting the development of substance abuse and dependence by adulthood, the effect of ADHD is mediated through CD. In sum, adolescents with ADHD remain at risk for SUDs, particularly if there are indicators of CD. For CD, a diagnosis indicates that the individual may be at risk for SUDs not only in the several years after diagnosis but for more than 20 years. Furthermore, for pediatricians, because ADHD generally develops earlier than

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CD,[37] ADHD may be an important diagnostic cue for later CD and perhaps, ultimately, SUDs. At the same time, CD, because of its proximal effect on SUDs, serves as a major risk factor for SUDs. Given the clinical and public health importance of the progression of ADHD, CD, and SUDs, further research about the specific mechanisms explaining this developmental pattern is indicated. From a clinical perspective, early interventions should focus on CD, particularly in children with ADHD, because this may put the youngsters at risk for later SUDs.

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