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Attention Deficit Hyperactivity Disorder, Conduct Disorder, Substance Use Disorder, and Nonprescription Stimulant Use

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Abstract

Objective—To assess whether the relationship of an Attention Deficit Hyperactivity Disorder (ADHD) diagnosis by adolescence to nonprescription stimulant use in adulthood is direct or indirect, via Conduct Disorder (CD) and/or Substance Use Disorder (SUD).

Method—Data was obtained from multiple waves of interviews and questionnaires completed by 551 community based participants when they were between the mean ages of 14.1 and 36.6 years.

Results—The results of the Structural equation model (SEM) supported both a direct association between early ADHD and later nonprescription stimulant use ($B=.18$, $z=2.74$) and the relationship from ADHD to later nonprescription stimulant use ($B=.01$, $z=1.72$) via CD and SUD.

Conclusion—The longitudinal data supporting these paths suggests that efforts to prevent and treat the misuse of nonprescription stimulants may be more effective if attention is paid to those with a history of ADHD, as well as to those who also had CD and SUD.

Keywords

ADHD; CD; SUD; Nonprescription stimulants

Introduction

Use of over-the-counter (OTC) drugs without medical advice, and misuse of prescribed medicines, both of which have deleterious health consequences, has become sufficiently widespread to become a public health concern (Pomeranz, Taylor, & Austin, 2013; Spoth et al., 2013). Specifically, considerable research has focused on assessing whether or not young adults with Attention Deficit Hyperactivity Disorder (ADHD) or a history of ADHD are more likely to misuse OTC or prescription medicines than those who have not manifested ADHD symptoms (Wilens et al., 2008). Comparatively few studies have examined whether the relationship of ADHD to nonprescription stimulant use is direct or indirect, via conduct disorder (CD) and/or substance use disorder (SUD) (Flory & Lynam, 2003).

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Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Several investigators have focused specifically on the direct association of ADHD to the nonmedical use (NMU) of stimulants (Arria et al., 2011; Cassidy et al., 2012; Dussault & Weyandt, 2013; Poulin, 2007; van Eck, Markle, & Flory, 2012; Wilens et al., 2008; Wilens, Gignac, Swezey, Monuteek, & Biederman, 2006). These investigations indicate that individuals manifesting ADHD symptoms are at higher risk for the NMU of stimulants (Arria et al., 2011; Cassidy et al., 2012; Dussault & Weyandt, 2013; Poulin, 2007; Wilens et al., 2006; Wilens et al., 2008).

Only two investigator teams have assessed the role of conduct problems or CD in the relationship of ADHD to the NMU of stimulants (van Eck et al., 2012; Wilens et al., 2006; Wilens et al., 2008). Van Eck et al. (2012) found that ADHD symptoms and conduct problems were each directly related to the NMU of OTC stimulants. Wilens and his colleagues (2006) found that among those with ADHD symptoms, those also having SUD or CD were at the highest risk for stimulant misuse.

Several investigators have found a positive relationship between ADHD and substance use or SUDs (Frodl, 2010; Katusic et al., 2005; Barbaresi et al., 2013; Upadhyaya et al., 2005; Baker, Prevatt, & Proctor, 2012). Other investigators have considered the role of CD in the association of ADHD with substance use (Charach, Yeung, Climans, & Lillie, 2011; Flory & Lynam, 2005; Harty, 2012; Rooney, Chronis-Tuscano, & Yoon, 2012; Ross, 2008). Flory and Lynam's (2005) literature review concluded that ADHD alone is not a major risk factor for substance use (apart from nicotine use/dependence). At best, ADHD is a distal predictor, while CD is a more proximal risk for substance use. Similarly, Ross (2008) concluded that, while ADHD is a risk for SUD, most of the relationship was mediated by CD. Moreover, recent research reports that CD, not ADHD, is associated with substance use severity and impairment (Harty, 2012). The present study uses longitudinal data to assess the relationship between childhood ADHD and CD and subsequent substance use disorder in the path to nonprescription stimulant use in the late thirties.

To our knowledge, few investigators have addressed the direction of the relationship between illicit drug use and the nonmedical use (NMU) of stimulants. Cassidy and her co-authors (2012) could not demonstrate which came first: the use of illicit drugs or the NMU of stimulants. However, they concurred that the National Survey of Drug Use and Health data suggested that the NMU of stimulants rarely was the entry point into drug use (Sweeney, Sembower, Ertischek, Shiffman, & Schnoll, 2013).

To our knowledge, Sweeney et al. (2013) are the only researchers to have investigated the sequential relationship between illegal drug use and stimulant use. While Sweeney et al.'s (2013) cross-sectional data relied on participant recall, the present study's longitudinal data will permit the time ordering of SUD and nonprescription stimulant use and will compare this pattern in those with and without ADHD.

Following the recommendation of Charach et al. (2011), this study controls for several of the variables (e.g., family drug use) that might mediate or moderate the relationship of ADHD to the nonprescription use of stimulants, in order to more clearly assess the role of CD and SUD. This study's longitudinal data will permit us to clarify the relationship between

ADHD, CD, and SUD on the path to stimulant use in the fourth decade of life. To date, cross-sectional studies have not yielded consistent results. Using longitudinal data, this study hypothesizes that 1) there is a direct path between a childhood diagnosis of ADHD and stimulant use 25 years later; 2) there also is an indirect path from having ADHD to a concurrent diagnosis of CD to a diagnosis of SUD in adulthood; and 3) SUD in adulthood, in turn, predicts subsequent stimulant misuse. This study extends the literature by predicting nonprescription stimulant use over a 25-year period beginning in adolescence and extending into the fourth decade of life, rather than just to the more customary adolescent/young adult period.

METHOD

Participants and Procedure

Data for the participants in this study came from a community-based, random sample residing in two upstate New York counties 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 among youngsters. The sampled families were generally representative of the population of families in Albany and Saratoga counties, with respect to gender, family intactness, family income, and education. Interviews of both 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). The mean ages (SDs) of participants at the interviews were 14.1 (2.8) at T2, 16.3 (2.8) at T3, 22.3 (2.8) at T4, 27 (2.8) at T5, 31.9 (2.8) at T6, and 36.6 (2.8) at T7, respectively. In the current analyses, we included the participants (N=551) whose measurements of ADHD and CD at T2 and T3 and of nonprescription stimulant use at T7 were available. Using the T2 sample (N = 756) as the baseline, there was a significantly higher percentage of female participants among those who met the inclusion criteria (N=551) than among those who did not meet the inclusion criteria (N=205) (55.4% and 37.9%, respectively; $\chi^2(1) = 18.6$, p-value < 0.001). There was a significantly lower percentage of participants with ADHD at T2 in the 551 sample as compared with the 205 sample (10.1% and 17.1%, respectively; $\chi^2(1) = 7.0$, p-value < 0.01). There was also a significantly lower percentage of participants with CD at T2 in the 551 sample as compared with the 205 sample (9.4% and 17.1%, respectively; $\chi^2(1) = 8.9$, p-value < 0.01).

Extensively trained and supervised lay interviewers administered the 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 2005–2006. The Institutional Review Boards of the Mount Sinai Medical Center, New York Medical College, and New York University School of Medicine authorized the use of human subjects in this research study. Additional information regarding the study methodology is available from prior publications (*name deleted to maintain the integrity of the review process*).

Measures

ADHD and CD at T2-T3—The parent and youth versions of the Diagnostic Interview Schedule for Children (DISC-I) (Costello, Edelbrock, Dulcan, Kalas, & Klaric, 1984) were administered in 1983 (T2), and again in 1985–1986 (T3) to assess psychiatric disorders including ADHD and CD (Anderson, Cohen, & Naumova, 2006). Symptoms of ADHD include an unusually high and chronic level of inattention, hyperactivity, or both. Some items from other parts of the questionnaire were added to the DISC-I to make the diagnosis of ADHD consistent with the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994). Criteria from DSM-IV were used to classify the participants with respect to ADHD. The proportion of participants (N=551) who met the DSM-IV criteria for ADHD at T2 or T3 or both was 13.1%.

According to the DSM-IV, conduct disorder 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 three (or more) of several criteria in the past 12 months, with at least one criterion present in the past six months. The proportion of participants who met the DSM-IV criteria for CD at T2 or T3 or both was 14.2%.

Substance Use Disorder at T5-T6—At T5 and T6, substance use disorder (dependence or abuse) was assessed by use of the University of Michigan Composite International Diagnostic Interview (UM-CIDI) substance use disorder measure (Kessler, Nelson, McGonagle, Edlund, Frank, & Leaf, 1996). We adapted this measure to make it consistent with the criteria used in the DSM-IV (American Psychiatric Association, 1994). We ascertained substance dependence by the presence of three or more of the following criteria for each substance (marijuana or other illicit drug, e.g., cocaine/crack, heroin, LSD, ecstasy, and amphetamines) used during the 12-month period before the interviews at both T5 and T6: (1) use of more of the substance than usual to get the same effect, or the same amount has less of an effect than before; (2) the presence of withdrawal symptoms or the use of the substance to avoid withdrawal symptoms; (3) the use of much larger amounts of the substance than intended, or use for a longer period of time 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 a 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, feeling depressed, suspicious of people, 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 one of the following four criteria during the 12-month period before the interviews: (1) being under the effects of the substance or suffering its after-effects while at work or school or while taking care of children; (2) being under the effects of the substance or feeling its after-effects in a situation which increased the user's chances of getting hurt – i.e., 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. The proportion of participants who met the DSM-IV criteria for SUD at T5 or T6 or both was 12.7%.

Nonprescription Stimulant Use at T7—At T7, the scale of nonprescription stimulant use during the past 12 months consisted of three items: A) diet pills (such as Dexatrim and Dietic), B) stay-awake pills (such as No-Doz, Vivarin, and Caffedrine), and C) other nonprescription stimulants and pep pills. Each item was scored on a 7 point scale indicating the frequency of use: 0 (1), 1–2 (2), 3–5 (3), 6–9 (4), 10–19 (5), 20–39 (6), and 40+ (7). The Cronbach's alpha of the scale was .67. The proportion of participants who ever used nonprescription stimulants in the past 12 months at T7 was 9.6% (6% used nonprescription diet pill; 4.6% used stay-awake pills; and 2% used other nonprescription stimulants and pep pills).

Data Analysis

We conducted t-test analyses and χ^2 test analyses to compare the participants with/without T7 nonprescription stimulant use. We used a structural equation model (SEM) to examine the empirical validity of the hypothesized pathways. To account for the influences of the participants' age, gender, T2 stimulant use, T2 depressive mood, T2 delinquency, T2 self-esteem, T2 time spent with friends, T2 maternal marijuana use, T2 parental educational level, T2 family income, and T7 neighborhood cohesion (see Table 1 for the details on these control variables) on these pathways, we created residual variables by statistically partialing out the effects of the above variables from each of the manifest variables. We then used the residual variables in the Mplus software (Muthén & Muthén, 2010) to estimate the proposed model. We used the full information maximum likelihood (FIML) option in Mplus (Muthén & Muthén, 2010) to impute any missing data. The advantage of FIML is that the results are less likely to be biased even if the data are not missing completely at random (Muthén, Kaplan, & Hollis, 1987). The correlation matrix of the resulting data is called the partial correlation matrix and is used for the SEM analysis. We chose three fit indices to assess the fit of the model: (1) the root mean square error of approximation (RMSEA), (2) Bentler's comparative fit index (CFI) (Bentler, 1990) and (3) the standardized root mean square residual (SRMR). Values between .90 and 1.0 on Bentler's CFI indicate that the model provides a good fit to the data (Kelloway, 1998). Values for the RMSEA and the SRMR below .10 indicate a good fit. To account for the non-normal distribution of the model variables (e.g., smoking and drinking measures), we used Mplus's maximum likelihood with robust standard errors (MLR) as the estimator. In order to test for mediational effects (Baron & Kenny, 1986; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002), we calculated the standardized total effects and total indirect effects by using the Model Indirect command in Mplus. The standardized total effect equals the sum of the direct and the indirect effects of each earlier latent variable (estimated in the analysis) on nonprescription stimulant use at T7. The total indirect effect of a latent construct on nonprescription stimulant use is the mediated effect via the intermediate variables that are depicted in the model (see Figure 1).

Results

Table 2 presents the means (or percentages when appropriate) of the variables with/without T7 nonprescription stimulant use. We also present the results of the t-test analyses and χ^2 test analyses for each of the variables with/without T7 nonprescription stimulant use. Compared to those participants who did not use nonprescription stimulants at T7, those who

did use them at T7 had a significantly greater likelihood of having ADHD at T2-T3, CD at T2-T3, and SUD at T5-T6, and had a significantly higher mean score on T2 delinquency and a lower mean score on T7 neighborhood cohesion.

The three fit indices of the SEM model were obtained. The RMSEA was 0.00. Bentler's CFI was 1.00. The SRMR was .016. These results reflect a satisfactory model fit. The obtained path diagram along with the standardized regression coefficients and z-statistics are depicted in Figure 1.

As shown in Figure 1, the results supported the following major hypothesized pathways ($p < 0.05$; one-tailed test): First, ADHD (T2-T3) was associated with CD (T2-T3) ($B = .26$; $z = 4.55$), which, in turn, was associated with SUD (T5-T6) ($B = .14$; $z = 2.45$). Second, SUD (T5-T6) was associated with T7 nonprescription stimulant use ($B = .14$; $z = 1.96$). Third, ADHD (T2-T3) was also directly associated with T7 nonprescription stimulant use ($B = .18$, $z = 2.74$).

In addition, T2-T3 ADHD, T2-T3 CD, and T5-T6 SUD each had a significant total effect ($p < 0.05$, one-tailed test) on T7 nonprescription stimulant use. Among them, ADHD (T2-T3) ($B = .18$; $z = 2.81$; $p < .01$) had the greatest total effect on T7 nonprescription stimulant use. The test of the indirect effect of T2-T3 ADHD on T5-T6 SUD, as mediated by T2-T3 CD, was statistically significant ($B = .04$; $z = 2.26$; $p < .05$; one-tailed test). The test of the indirect effect of T2-T3 ADHD on T7 nonprescription stimulant use, as mediated by T2-T3 CD and T5-T6 SUD, was also statistically significant ($B = .01$; $z = 1.72$; $p < .05$; one-tailed test).

Discussion

All three of this study's hypotheses were supported, despite controlling for several potential mediating variables. An ADHD diagnosis at T2-T3 was directly associated with nonprescription stimulant use twenty-five years later at T7. ADHD was also indirectly related to T7 nonprescription stimulant use via its association with T2-T3 CD, which in turn was associated with T5-T6 SUD. SUD was directly related to T7 nonprescription stimulant use. It is noteworthy that having a diagnosis of ADHD at T2-T3 had the strongest total effect on T7 nonprescription stimulant use. Consequently, the results support both an independent and a mediational model; more specifically, the relation between ADHD and nonprescription stimulant use is partially mediated by both CD and SUD.

Our findings are in accord with several investigators who have found a direct association between having ADHD symptoms and using nonprescription stimulants (Arria et al., 2011; Cassidy et al., 2012; Dussault & Weyandt, 2013; Poulin, 2007; van Eck, Markle, & Flory, 2012; Wilens et al., 2006; Wilens et al., 2008). Cassidy and her colleagues noted that the NMU of stimulants was twice as high among 18–25 year olds as among those 26 years old and older, possibly, reflecting student use to enhance academic performance. Still, we found a direct association between early ADHD symptoms and later stimulant use by age 37.

Volkow et al. (2009) suggest an explanation for the use of nonprescription stimulants without a physician's advice for those with ADHD. In ADHD, certain neurotransmitters, such as dopamine and norepinephrine, are reabsorbed back into neurons prematurely, and

unavailable for the efficient transmission of messages within the brain. Stimulant drugs increase the availability of these neurotransmitters, and people with ADHD may engage in self-medication to enhance their attention and executive abilities.

Our findings are also in accord with several investigators who have studied the relationship of ADHD, CD, and SUD. More specifically, they found that the relationship between ADHD and SUD is mediated by CD (August, Winters, Realmuto, Fahnhorst, Botzet, & Lee, 2006; Gau, Chong, Yang, Yen, Liang, & Cheng, 2007). Based on a meta-analysis, Charach and her colleagues (2011) reported that childhood ADHD is related to alcohol and drug dependence. As noted by Molina and her colleagues (2013), these results suggest the need for further research on psychosocial factors that contribute to the relation of ADHD and stimulant use. Such knowledge will inform the most beneficial treatment. The present study's findings extend the literature regarding ADHD's relationship to the nonmedical use of prescription stimulants to nonprescription stimulants (Arria et al., 2010; Cassidy et al., 2012; Dussault & Weyant, 2013; Poulin, 2007).

In addition, this study's longitudinal results were consistent with Sweeney et al.'s (2013) conclusion, based on cross-sectional data, regarding the direction of the relationship between illegal substance use and the nonmedical use of prescription stimulants. Illegal substance use generally preceded the nonmedical use of prescription stimulants. This study's results, based on longitudinal data that permitted the time ordering of variables, suggests that the direction is similar when the stimulants include nonprescription drugs.

There are several limitations to this study's sample and methodology. First, the results are based on self-report measures of ADHD, CD, SUD, and nonprescription stimulant use. However, self reports of substance use are reasonably reliable (Harrison, Martin, Enev, & Harrington, 2007). Second, since the participants in this study were predominantly white males and females, generalization of the results to more ethnically diverse samples may not be warranted. Third, we did not have data on several important factors which may mediate the relationship between ADHD and nonprescription stimulant use. Such mediating factors may include early trauma and maltreatment, family history of violence, violence in the neighborhood, school drop-out, and earlier nonprescription stimulant use (e.g., ages 18–25). Nevertheless, several potential mediating factors between ADHD in adolescence and nonprescription stimulant use at age 37 were examined. These factors include demographic factors (e.g., gender), earlier stimulant use, childhood personal attributes (e.g., depressive mood), childhood family factors (e.g., maternal marijuana use), and concurrent neighborhood factors (i.e., neighborhood cohesion). These psychosocial factors do not appear to serve as mediating factors between ADHD and nonprescription stimulant use. Fourth, the findings would be strengthened if data regarding ADHD diagnoses subsequent to T2-T3 and information regarding physician involvement were available (Barkley et al., 2002).

Despite the limitations, the findings have implications for prevention, treatment, and public health. Educators should be aware of their students' risk for misusing nonprescription stimulants and adapt prevention programs for these individuals. Physicians and other health care providers should advise individuals, particularly those adolescents and young adults

with ADHD, of the pitfalls of the misuse of nonprescription drugs as well as of illegal drug use. Research that identifies characteristics of adolescents and adults at risk for misusing nonprescription stimulants will contribute to prevention and treatment programs. Empirical data on the best treatment for individuals with ADHD and the risk of nonprescription drug use is essential.

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Figure 1.

Obtained model: standardized pathways (t-statistic) to nonprescription stimulant use (N=551).

Note:

- a. * $p < .05$; ** $p < .01$; *** $p < .001$ (one-tailed test);
- b. CFI=1.00; RMSEA=0.00; SRMR=0.016;
- c. The participants' age, gender, T2 stimulant use, T2 depressive mood, T2 delinquency, T2 self-esteem, T2 time-spent with friend, T2 maternal marijuana use, T2 parental educational level, T2 family income, and T7 neighborhood cohesion were statistically controlled.

Table 1

Details on Control Variables.

Variables	Sample Item and Source	Alpha	N. of Items
Gender	What is your gender?	N.A.	1
Age	How old are you?	N.A.	1
Nonprescription Stimulant Use (T2)	Do you ever take amphetamines, diet pills uppers, or speed?	N.A.	1
Depression (T2)	How much were you bothered by feeling low in energy or slowed down? (Derogatis et al., 1974)	0.75	5
Delinquency (T2)	How often have you cheated on tests at work or school? (Jackson, 1974)	0.65	5
Self-esteem (T2)	I feel that my life is very useful (Original)	0.72	4
Time-spent with Friends (T2)	How often do you hang out with other kids/spend time with friends? (Original)	0.69	7
Parental Educational Level (T2)	What is the highest grade or year of school you or the child's father completed?	N.A.	1
Family income (T2)	How much was your family's income (the amount before taxes) for last year?	N.A.	1
Maternal Marijuana Use (T2)	How often have you ever-used marijuana?	N.A.	1
Neighborhood Cohesion (T7)	Overall, I like living in my neighborhood very much. (Buckner, J.C., 1988)	0.81	7

Table 2

Descriptive statistics with/without nonprescription stimulant use (N=551).

Variables	With nonprescription stimulant use Mean (SD)	Without nonprescription stimulant use Mean (SD)	t-statistic or χ^2 test
ADHD (T2–T3)	37.7%	10.4%	$\chi^2=31.4^{***}$
CD (T2–T3)	22.6%	13.3%	$\chi^2=3.5^*$
SUD (T5–T6)	18.9%	5.0%	$\chi^2=15.4^{***}$
Gender (male)	41.5%	45.4%	$\chi^2=0.29$
AGE	36.4 (2.7)	36.6 (2.9)	0.59
T2 Nonprescription Stimulant Use	3.8%	1.4%	$\chi^2=1.67$
T2 Depressive Mood	10.7 (0.5)	10.4 (0.2)	$t=-0.5$
T2 Delinquency	9.4 (0.5)	8.3 (0.2)	$t=-2.01^*$
T2 Self-esteem	13.0 (2.3)	13.3 (2.1)	$t=0.80$
T2 Time-spent with Friends	16.0 (3.8)	15.5 (3.1)	$t=-0.82$
T2 Parental Educational Level	13.3 (2.3)	13.7 (2.4)	$t=1.1$
T2 Family Income	8.2 (3.1)	8.8 (2.4)	$t=1.34$
T2 Maternal Marijuana Use	1.3 (1.1)	1.2 (1.1)	$t=-1.16$
T7 Neighborhood Cohesion	20.7 (19.5)	22.0 (21.6)	$t=2.16^*$

Note:

*
p<0.05;***
p<0.001 (one-tailed test)