Published in final edited form as:

J Child Adolesc Subst Abuse. 2011 ; 20(4): 314–329. doi:10.1080/1067828X.2011.598834.

A Prospective Examination of the Association of Stimulant Medication History and Drug Use Outcomes among Community Samples of ADHD Youths

KEN C. WINTERS, SUSANNE LEE, ANDRIA BOTZET, TAMARA FAHNHORST, GEORGE M. REALMUTO, and GERALD J. AUGUST

University of Minnesota, Twin Cities, MN, USA

Abstract

A continuing debate in the child psychopathology literature is the extent to which pharmacotherapy for children with attention-deficit/hyperactivity disorder (ADHD), in particular stimulant treatment, confers a risk of subsequent drug abuse. If stimulant treatment for ADHD contributes to drug abuse, then the risk versus therapeutic benefits of such treatment is greatly affected. We have prospectively followed an ADHD sample (N = 149; 81% males) for approximately 15 years, beginning at childhood (ages 8 to 10 years) and continuing until the sample has reached young adulthood (ages 22 to 24 years). The sample was originally recruited via an epidemiologically derived community procedure, and all youths were diagnosed with ADHD during childhood. We report on the association of childhood psychostimulant medication and subsequent substance use disorders and tobacco use. The substance use outcomes were based on data collected at three time points when the sample was in late adolescence and young adulthood (age range approximately 18 to 22 years old). We did not find evidence to support that childhood treatment with stimulant medication, including the course of stimulant medication, was associated with any change in risk for adolescent or young adulthood substance use disorders and tobacco use. These results from a community-based sample extend the growing body of literature based on clinically derived samples indicating that stimulant treatment does not create a significant risk for subsequent substance use disorders.

Keywords

ADHD; drug abuse; stimulant medication; tobacco use

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a childhood-onset behavioral disorder that is estimated to affect approximately 3% to 8% of children (Biederman, 2005). This disorder contributes to a wide range of impairments in social, school, and emotional domains (August et al., 2006; Smith, Barkley, & Shapiro, 2007).

A continuing debate in the child psychopathology literature is the extent to which pharmacotherapy for children with ADHD, in particular stimulant treatment, confers a risk of subsequent drug abuse. If stimulant treatment for ADHD contributes to drug abuse, then the risk versus therapeutic benefits of such treatment is greatly affected.

A significant body of work supports the argument that childhood stimulant treatment does not increase the risk for later development of drug abuse (e.g., Barkley, Fischer, Smallish, & Fletcher, 2004; Faraone & Wilens, 2003; Mannuzza, Klein, & Moulton, 2003; Paternite, Loney, Salisbury, & Whaley, 1999). In addition, some studies have shown that stimulant treatment may contribute to protective effects against drug abuse risk (Biederman, Wilens, Mick, Spencer, & Faraone, 1999; Molina, Pelham, & Roth, 1999; Whalen, Jamner, Henker, Gehricke, & King, 2003). In contrast, Lambert and Hartsough (1998) found in their large prospective study of a community sample of ADHD youths that abuse of cocaine and nicotine (two stimulant-like drugs) in adulthood was associated with previous stimulant treatment during childhood ADHD.

An important contribution to the debate is provided by Wilens and colleagues (Wilens, Faraone, Biederman, & Gunawardene, 2003) in which they conducted a meta-analysis on prospective or retrospective studies in the literature that had information relating childhood exposure to stimulant therapy and later substance use outcomes in either adolescence or adulthood. Six studies were identified. The pooled estimates for risk for subsequent substance use disorders during adolescence and adulthood showed reductions in risk.

The mixed findings in the literature regarding the link of stimulant therapy and subsequent drug abuse may be due to methodological differences and limitations across studies (Biederman et al., 2008). Some studies report only adolescent outcomes and not drug abuse behaviors during young adulthood. Another issue is that some studies do not control for the presence of comorbid externalizing disorders such as conduct disorder and oppositional defiant disorder. For example, this point has been raised in the explanation of Lambert's finding of increased risk for later drug use in the medicated- ADHD group; significant differences on baseline characteristics between medicated and unmedicated youths may have contributed to the results (Wilens et al., 2003).

Other methodological concerns are that studies vary to the extent to which they describe a wide range of substances of abuse, such as alcohol, nicotine, and illicit drugs, and some studies do not use DSM-defined attention deficit disorder when identifying or recruiting children into the longitudinal study (August et al., 2006; Weinberg, Rahdert, Collier, & Glantz, 1998). Finally, there is the issue of the source of the samples of children with ADHD studied in these investigations. With one exception in the published literature (i.e., Hartsough, Babinski, & Lambert, 1996), samples of ADHD youths are recruited from clinical sites. Because community-based ADHD youths are likely to reveal a less-severe form of ADHD (August, Realmuto, Crosby, & MacDonald, 1995), the association between childhood stimulant medication and later drug abuse may not be the same as among clinic-referred ADHD youths.

We have sought to contribute to this literature by reporting on our prospective follow-up study of ADHD youths recruited from a community sample. This study, the Minnesota Competence Enhancement Project (MNCEP), is a longitudinal follow-up study of an epidemiologically derived community sample diagnosed with ADHD during childhood. This sample has been followed for six assessment points since childhood (T1–T6), and DSM-IV substance use criteria and tobacco use have been measured for the last three assessments (T4–T6), which cover the participants' late adolescence and young adulthood. In this report we describe the relationship of psychostimulant medication during childhood and subsequent substance use disorders and tobacco use reported at the T4–T6 assessments.

METHODS

Participants

Individuals in this study are part of an ongoing longitudinal study of ADHD that began in 1991 as part of the Minnesota Competence Enhancement Project (MNCEP). That project identified samples of disruptive and control children drawn from 22 suburban elementary schools using a multiple-gate screening procedure (see August et al., 1995). To accomplish this, a total of 7,231 students in grades 1 through 4 (ranging in age from 7 to 11 years) were screened. Of these, 318 (ages 7 to 9) were identified as having cross-setting disruptive behavior based on scores derived from the teacher and parent Conners' Hyperactivity Index (HI-T, HI-P; Goyette, Conners, & Ulrich, 1978) that exceeded 1.75 standard deviation (*SD*) units above the normative mean. The ratio of boys to girls was 4.1:1. In addition, stratified random sampling was used to obtain a normal control sample of 144 children that resulted in a group proportionately equivalent by demographic characteristics (school, age, and gender) to the 318 children identified as disruptive, with the requirement of a HI-T score below 1.1 *SD* above the normal mean. This cut point was chosen in order to identify a heterogeneous group of control children; too narrow or homogeneous a control group could contribute to difference between the control and disruptive groups that lacked external validity. Mean raw scores (range for each 0–30) for the two groups on the HI-T and HI-P were as follows: disruptive, 22 and 21; controls, 2 and 5, respectively. All participants at baseline (T1) had an IQ score of ≥ 80 (Kaufman Brief Intelligence Test (K-BIT); Kaufman & Kaufman, 1990), did not have a pervasive developmental disorder, came from predominantly middle socioeconomic status families (Hollingshead, 1975), and were predominantly Caucasian. All of these disruptive children participated in a two year psycho-educational intervention during the initial two years of the project. The results of the intervention were insubstantial (Braswell et al., 1997), and therefore, the possible impact on the long-term outcomes of these children is deemed to be insignificant.

To further assess diagnostic status, the parents of the 318 children who screened positive for cross-setting disruptiveness were interviewed using the Revised Parent Version of the Diagnostic Interview for Children and Adolescents (DICA-R; Reich, Shayla, & Taibelson, 1992) by two technicians who were rigorously trained in administering the DICA (e.g., required to reach high concordance with independent ratings of taped interviews). The interview was modified to include all symptoms related to the *Diagnostic and Statistical Manual of Mental Disorders (3rd ed., rev.) (DSM-III-R; American Psychiatric Association, 1987)* diagnoses of ADHD, oppositional defiant disorder (ODD), conduct disorder (CD), separation anxiety disorder, avoidant anxiety disorder, overanxious disorder, major depressive disorder (MDD), and dysthymia. In accord with the hierarchical rule provided in *DSM-III-R*, ODD was not diagnosed in the presence of CD. As stipulated in *DSM-III-R*, the diagnosis of ADHD required endorsement of any 8 of 14 symptoms with an age of onset prior to age 7 for a majority of symptoms. Of the initial 318 children identified with cross-setting disruptive behavior at T1, 205 (64%) met ADHD criteria. (For a breakdown of the frequencies of ADHD and comorbid disorders, see August, Realmuto, MacDonald, Nugent, and Crosby, 1996.)

The project reassessed these children with disruptive behaviors in 1995 (T2), at which time all were between 11 and 15 years old, and again in 1996 (T3) when children ranged in age from 12 to 16 years old. At the outset of the most recent assessment, T4, a decision was made to not attempt to contact and seek an assessment among families recruited at T1 who had subsequently dropped out of the study and had not been assessed at both T2 and T3. These families (representing 37 ADHD and 28 control youths) had already expressed disinterest in continuing with the research, and our current grant was budgeted to only focus on drug abuse outcomes in youths for which we already had multiple data points (i.e., T1–

T3). Thus, these attrition cases were not approached for assessment at T4, which gave us an eligible ADHD sample for the present study of 168 youths ($205 - 37 = 168$).

Assessments at T4 were timed to coincide with participants' status as either a senior in high school or one-year post-graduate, thus the age range at T4 is narrower than the age range at T1. Subsequent assessments (T5 and T6) were approximately 1.5 years apart. After attrition at T4 (discussed below) the final ADHD sample size was 149 and the final control sample was 93. We further subdivided the ADHD group according to the presence or absence of an externalizing disorder (either conduct disorder or oppositional defiant disorder; procedures described below), thus resulting in these two subgroups: ADHD–no externalizing disorder, $N = 59$; ADHD–externalizing disorder, $N = 90$. The ADHD samples had mean ages at these time points: T4 (“adolescence”), 18.4 years; T5 (“young adult”), 20.4 years; T6 (“young adult”), 22.0 years. The sample demographics of the ADHD subject groups for the present study are provided in Table 1. The normal control participants are included in the outcome analyses in order to provide context for the results in the ADHD samples.

Measures

Socioeconomic status (SES)—The Four Factor Index of Social Status (Hollingshead, 1975) was administered to parents at T1. A score of 8 (low SES) to 66 (high SES) was derived based on parent occupation and education, which correlate with five levels of SES (unskilled to major business/professionals).

IQ—The Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) was individually administered to child participants at T1 to assess expressive and receptive vocabulary and nonverbal problem solving (matrices). Age-based standard scores with a mean of 100 and a standard deviation of 15 were derived.

Diagnosis—Diagnostic Interview for Children and Adolescents–Revised (DICA-R; Reich et al., 1992) was used to assess childhood ADHD and other psychiatric disorders. It was administered to one parent (usually mother) via telephone by trained assessors at the three follow-up assessment points (T4, T5, and T6). Structured diagnostic interviews administered to parents over the telephone have been shown to be valid (Holmes et al., 2004; Todd, Joyner, Heath, Neuman, & Reich, 2003). The DICA-R generates standardized diagnoses as reflected by the *DSM-III-R*. Each item was scored *yes* if the behavior was definitely endorsed or *no* if the respondent indicated “sometimes,” “rarely,” or “never.” A data sheet was prepared for each child and the number of symptoms endorsed was tallied and entered. Specific diagnostic parameters, including age of onset, duration of symptoms, and frequency, were recorded. Diagnostic scoring algorithms were adopted from the DICA-R by which categorical diagnoses were made. Twenty percent (every fifth interview completed) of the interviews were independently rated by an assessment technician via an extension phone, in order to obtain interrater reliability on item scoring and to prevent interviewer drift. Kappas for symptoms were derived for each disorder; average symptom kappas ranged from 0.88 for conduct disorder at T1 to 1.00 for ADHD at T2 (see August et al., 1995).

Medication history—Using a semistructured format, the parent provided at each time point (T1 to T3) a record of their child's psychostimulant medication history. Based on these data, youths were categorized into three psychostimulant medication groups: (1) never used; (2) medication prescribed and used up to age 12 but not later; and (3) medication prescribed and used after age 12 (includes both childhood and later prescription).

Drug use measures—Our outcome drug use variables were measured at T4–T6 and for this article focused on substance use disorders (SUD) diagnoses. *DSM-IV* SUDs were

measured with the substance use disorders module of an updated structured interview, the Adolescent Diagnostic Interview (ADI; Winters & Henly, 1993). The ADI has established reliability and validity in adolescent clinical and nonclinical populations (Winters & Henly, 1993). With respect to SUDs for adolescents, there is a controversy as to whether the distinction between abuse and dependence is valid for adolescents (Martin & Winters, 1998). Thus we chose to analyze the general SUD category and not make a distinction between abuse and dependence. For the data analysis, a SUD refers to the presence of either an abuse or dependence diagnosis. The assessment at T4 (late adolescence) covered the youth's entire adolescent years; T5 and T6 time points assessed the prior year. Base rate considerations limited our analysis to alcohol, marijuana, and any other SUD. For the latter, this meant the presence of an abuse or dependence diagnosis for at least one of these drugs: amphetamines, cocaine, hallucinogens, barbiturates, heroin, inhalants, or club drugs. We also created a "two or more SUDs" variable given that this poly-SUD variable has been linked to a higher likelihood of continued drug use problems compared to adolescents with a single SUD (Winters, Stinchfield, Latimer, & Lee, 2007). A composite variable of "any SUD" was created that reflected if a participant had any of the three SUDs (alcohol, marijuana, or other SUD) at a certain time point.

Finally, we included regular tobacco use (defined as weekly or daily use of any tobacco product during prior 12 months) as the final substance use variable. Tobacco use is very common among ADHD youths (Milberger, Biederman, Faraone, Chen, & Jones, 1997). We measured this variable with the tobacco use items from the Cigarette Use Questionnaire (CUQ; Winters, 2006). A wide range of reliability (internal consistency) and validity evidence (concurrent and criterion) has been reported on the CUQ (Winters, 2006), including the items we used in our tobacco questionnaire. For each of the drug use variables we included an "ever" variable that indicated if a particular SUD had ever occurred to a participant over the three time points.

Procedures

Adolescent participants and their parents at T4–T6 completed an assessment battery that focused on the youth's substance use disorder criteria, tobacco use, psychosocial adjustment, and health history. The majority of the adolescent participants were interviewed in person during a one-time session by two highly trained research technicians; a majority of parents were interviewed via telephone. All participant recruitment, informed consent, and study methodology met ethical guidelines according to the Institutional Review Board at the University of Minnesota. Technicians were not blind to ADHD versus control status but were blind as to the ADHD person's psychostimulant medication history and comorbidity status. Due to relocation, some of the participants had to be interviewed via telephone. Adolescents were paid a stipend of \$75.00 for their participation.

Data Analysis

An attrition analysis was performed to test whether there were significant differences in characteristic variables between those who were included in the present study and those who attrited. One-way ANOVAs and chi-square tests were conducted to compare the two groups on characteristic variables for the ADHD sample. Next we examined the relationship between stimulant medication usage and substance use outcomes. The SUD outcome variables were coded as 1 versus 0, with 1 indicating having the disorder at the time of assessment (T4, T5, T6). Regular use of tobacco was also coded as 1 versus 0, with 1 indicating weekly or daily use of any tobacco product in the past year. Chi-square test was used to examine group differences in substance use outcomes at each time point and across the three time points ("ever"). Generalized linear models were used to evaluate whether ADHD externalizer versus non-externalizer subtypes moderated the relationship between

medication group and change in probability (slope) of having a substance use outcome over time (alcohol, marijuana, other, two or more SUDs, any SUD, tobacco). Analyses were conducted to incorporate the structure of within-individual correlations (i.e., repeatedly measured outcome) by using the generalized estimating equations (GEE; Liang & Zeger, 1986). The GEE method appropriately models dependencies in repeatedly measured categorical data (MacKinnon & Lockwood, 2003). In the analyses, age and gender were included to control for their effects on the outcome. To test the moderating effect of ADHD externalizer versus non-externalizer subtypes on the relationship between medication group and change in probability of having a substance use outcome over time, we included a three-way interaction of Time $\times$ Medication $\times$ ADHD in the model. The GEE method was applied using PROC GENMOD in SAS (1999). Bonferroni corrections were used for multiple tests.

RESULTS

Attrition Analysis

To test for attrition-related effects, two sets of analyses were conducted. First, we compared T1 ADHD cases whom were “ineligible” for a T4 assessment because of early attrition and had no T2 and T3 data versus ADHD cases that were “eligible” for a T4 assessment (i.e., cases for whom T2 and T3 data were available and other inclusion criteria were met) ($N = 167$). Separate one-way ANOVAs (attrition status) for continuous variables, and a separate chi-square analysis for categorical data, were conducted within the disruptive and control groups across several demographic (age, gender, ethnicity, IQ, and SES) and T1 measures (HI-T, HI-P, and number of ADHD symptoms). For the ADHD group, we found only two significant group differences: the eligible ADHD group had a higher ADHD symptom count at T1 and a higher HI-P score at T1 when compared to the ineligible ADHD group ($p < .05$). (This finding may seem to be counterintuitive. However, it is possible that families with youths who did not want to be recontacted after T1 had children with fewer ADHD symptoms.)

Next we examined the T4 eligible sample to examine differences between the consenters and non-consenters. We again compared T1 data between these two respective samples within the ADHD sample. None of the T1 variables showed a group difference between the non-consenting ADHD group ($N = 18$) and the consenting ADHD group ($N = 149$).

In general, ADHD youths who were not eligible for the present study due to only being assessed at T1 were quite similar to those who were eligible. Also, eligible ADHD youths who could not be located or who refused to participate at T4 were similar on nearly all variables compared to eligible cases that received a T4–T6 assessment.

Outcomes as a Function of Group

Prevalence of substance use within the past year assessed at T4, T5, and T6 for the combined ADHD group and the normal control group is presented in Table 2. For the two groups, the prevalence of alcohol use disorder ranged from 26% to 41%, and marijuana use disorder from 17% to 44%. Prevalence of other substance use disorder ranged from 5% to 10%; the prevalence of having any of the three SUDs ranged from 38% to 52%. Prevalence of regular tobacco use ranged from 42% to 61%. Chi-square tests showed that there were significant group differences in marijuana use at T4, and in two or more SUDs at T4 and “ever” (Bonferroni correction for multiple tests, $\alpha .05/4 = .013$). In all instances of statistical significance, the ADHD group prevalence rate was higher than the control group rate. Group difference in prevalence approached significance for alcohol use at T4 and regular tobacco use at T4.

Outcomes as a Function of Medication History Groups

Table 3 presents the prevalence of substance use within the past year assessed at T4, T5, and T6 for total sample, ADHD–non-externalizers and ADHD–externalizers. In the total sample, prevalence of alcohol use disorder ranged from 27% to 50%, marijuana use disorder ranged from 24% to 48%, and other substance use disorder ranged from 0% to 16%. Prevalence for the presence of two or more substance use disorders ranged from 13% to 37%. The prevalence of having any SUDs ranged from 39% to 58%. Prevalence of regular use of tobacco ranged from 53% to 71%. Chi-square tests revealed that there were no significant group differences among the three medication groups in any outcome variables measured at T4, T5, and T6 (Table 3) (Bonferroni correction for multiple tests, $\alpha .05/12 = .0042$). There were also no significant group differences in “ever” having an SUD across the three time points. When medication groups were broken down further by ADHD externalizer status (non-externalizers versus externalizers), there were no significant medication group differences in the outcome variables (Table 3).

Analyses of medication group differences in slopes (change in probability) of having a substance use problem over time for each of the six substance use outcomes detected no significant three-way interactions (Time $\times$ Medication $\times$ ADHD) or two-way interactions (Time $\times$ Medication, Time $\times$ ADHD, Medication $\times$ ADHD), except for “any SUD” outcome (Bonferroni correction for a three group test, $\alpha .05/3 = .017$). There was a significant Time $\times$ Medication $\times$ ADHD interaction effect on the “any SUD” variable ($Z = 3.31, p = .0009$), which indicated that ADHD externalizers with no medication history showed a significant reduction in probability of having a SUD over time compared to other groups. The nonsignificant three-way interaction effects on the five substance use outcomes indicated that there were no significant moderating effects of ADHD externalizer status on the relationship between medication groups and rates of change in substance use problems. The nonsignificant two-way interaction of Time $\times$ Medication indicated that there were no significant medication group differences in rates of change in probability of having a substance use problem. Gender and age had no significant effects on the outcome variables.

DISCUSSION

We found no evidence that childhood treatment with stimulant medication was significantly associated with change in risk for adolescent or young adulthood drug use. This finding held up for substance use disorders (alcohol, marijuana, other illicit drugs, and 2 + substance use disorders) and regular (weekly or more) tobacco use. Our results were observed for outcome data at the adolescent (mean age = 18.4) and the young adult (mean age = 20.4 and 22.0) time points.

It is noteworthy to comment on the pattern of prevalence rates, which suggests some interesting trends. An inspection of these rates showed a trend toward lower alcohol and marijuana substance use disorders in only the younger medication group (age 12) compared to the unmedicated group at one time point—late adolescence (T4). But this pattern was not observed in the younger medication group for the prevalence rates at the two subsequent assessments (young adulthood), nor was it observed for any time point for the older medication group (age > 13). This pattern may support the view that the optimal protective effect for stimulant therapy is for youths who receive psychostimulant therapy only during childhood and do not continue the course of medication during the teenage years. Also, our pattern of prevalence rates is consistent with the general finding in the Wilens and colleagues (2003) meta-analysis that there is less protective effect of stimulant pharmacotherapy in reducing drug abuse in adulthood compared to adolescence.

It is also relevant to comment on our result in light of Lambert and Hartsough's (1998) findings given that both that study and ours identified the ADHD sample from the community. Unlike their study, we did not find a significant increase in tobacco use between the medication and unmedicated groups (we did not have enough cocaine abusers in the sample to compare groups on this drug). It is possible that the difference in the two studies is because Lambert and Hartsough (1998) did not control for conduct disorder and we did. In fact, if you compare medicated and unmedicated ADHD youths and disregard externalizing status, tobacco use rates are higher in the medication group compared to the unmedicated group at each time point.

The study results also provide a picture of the rates of substance use disorders and tobacco use among ADHD youths as they age into young adulthood. Whereas prospective studies have been characterized by inconsistencies (see August et al., 2006), our outcomes are generally consistent with a large body of literature supporting the view that ADHD status during childhood is associated with an elevated risk for subsequent drug use (American Academy of Child and Adolescent Psychiatry, 2002). The ADHD group reported higher rates of substance use disorders and regular tobacco use for most of the data points, and in all instances of statistical significance, the ADHD group prevalence rate was higher than the control group rate. Also, an inspection of our observed rates of substance use disorders shows that ADHD youths with an externalizing disorder generally reported higher rates than those without an externalizing disorder. For example, the average prevalence rates of alcohol use disorders across T4–T6 for those in the ADHD–externalizing group versus those in the ADHD–non-externalizing group were 65.6% and 45.8%, respectively [$X^2(1, N = 149) = 5.7, p < .05$]. A similar pattern of average prevalence rates disorders was found for marijuana use (61.1% for ADHD–externalizers and 30.5% for ADHD–non-externalizers) [$X^2(1, N = 149) = 13.4, p < .001$]. This pattern of results is part of a growing body of literature that points to the significant liability to future drug use when an externalizing disorder is comorbid with ADHD (Barkley et al., 2004; Biederman, Wilens, Mick, & Faraone, 1997; Brook, Whiteman, Finch, & Cohen, 1996; Chilcoat & Breslau, 1999; Lynskey & Fergusson, 1995).

From a clinical perspective, our results are in line with the viewpoint that the discussion of the risks and benefits of treating ADHD with stimulant medication should not be greatly affected by concerns about the link between early stimulant exposure and future drug use problems. However, given the inconsistencies in the literature regarding the link between drug abuse and stimulant medication, this issue still merits continued research and monitoring. Also, because of the relative high risk of developing substance use disorders among ADHD youths, particularly those with an externalizing disorder, there is still a public health need to educate parents of children with ADHD about the importance of parenting behaviors that serve to prevent drug use.

Our findings must be considered in light of several study limitations. This is a naturalistic study; youths were not randomized to medication groups. Thus, confounds could have affected the results (e.g., parents with a history of drug problems may have been reluctant to pursue medication options for their child because of concerns that a link existed between stimulant medication and drug abuse). We did not collect highly rigorous data regarding medication history, including detailed dosage amounts and how many months medication was taken by youths within each of the medication groups. Our screening tool, which was the 10-item Conners' Hyperactivity Index (CRPS-R; Goyette et al., 1978), while a logical choice for mass screening at the time the study was initiated in 1990, likely identified primarily children who would be diagnosed as ADHD-combined type using *DSM-IV* criteria and excluded many children with only attention problems (ADHD predominantly inattentive type). Thus, our screening procedure may have produced a sample with a

relatively small number of children diagnosed as ADHD-only and larger number of ADHD youths comorbid with ODD. The results may not generalize to non-white populations given that the vast majority of research participants were of Caucasian descent. Also, our sample of girls is relatively small and thus one should cautiously interpret our finding of no gender effects. The relatively small group sizes restricted the statistical power for detecting small to moderate effect sizes. Last, our study did suffer from some sample attrition, although the attrition analyses indicated that ineligible cases and non-ascertained cases were similar on most baseline variables compared to the non-attrition cases.

In summary, there are several studies that have investigated the possible link between childhood stimulant medication for ADHD and the risk for subsequent drug abuse. This study is consistent with the large group of research findings indicating that psychostimulant use in childhood does not increase the risk for drug abuse during adolescence or young adulthood.

Acknowledgments

Support for this manuscript comes from NIDA grants DA12995 and K02 DA15347.

References

- American Academy of Child & Adolescent Psychiatry. Practice parameters for the use of stimulant medications in the treatment of children, adolescents and adults. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2002; 41:26S–49S. [PubMed: 11833633]
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3. Washington, DC: Author; 1987. rev
- August GJ, Realmuto GM, Crosby RD, MacDonald AW. Community-based multi-gate screening procedure of children at-risk for conduct disorder. *Journal of Abnormal Child Psychology*. 1995; 23:521–544. [PubMed: 7560560]
- August GJ, Realmuto GM, MacDonald A, Nugent SM, Crosby RD. Prevalence of ADHD and comorbid disorders among elementary school children screened for disruptive behavior. *Journal of Abnormal Child Psychology*. 1996; 24:571–595. [PubMed: 8956085]
- August GJ, Winters KC, Realmuto G, Fahnhorst T, Botzet A, Lee S. Prospective study of adolescent drug abuse among community samples of ADHD and non-ADHD participants. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2006; 45:824–832. [PubMed: 16832319]
- Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult follow-up of hyperactive children: Antisocial activities and drug use. *Journal of Child Psychology and Psychiatry*. 2004; 45:195–211. [PubMed: 14982236]
- Biederman J. Attention-deficit/hyperactivity disorder: A selective overview. *Biological Psychiatry*. 2005; 57:1215–1220. [PubMed: 15949990]
- Biederman J, Monuteaux MC, Spencer T, Wilens TE, MacPherson HA, Faraone SV. Stimulant therapy and risk for subsequent substance use disorders in male adults with ADHD: A naturalistic controlled 10-year follow-up study. *American Journal of Psychiatry*. 2008; 165:597–603. [PubMed: 18316421]
- Biederman J, Wilens T, Mick B, Faraone SV. Is ADHD a risk factor for psychoactive substance use disorders? Findings from a four-year prospective follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:21–29. [PubMed: 9000777]
- Biederman J, Wilens T, Mick E, Spencer T, Faraone SV. Pharmacotherapy of attention-deficit/hyperactivity disorder reduces risk for substance use disorder. *Pediatrics Electronic Pages*. 1999; 104:e20. Retrieved from www.pediatrics.org/cgi/content/full/104/2/e20.
- Braswell L, August GJ, Bloomquist ML, Realmuto GM, Skare SS, Crosby RD. School-based secondary prevention for children with disruptive behavior: Initial outcomes. *Journal of Abnormal Child Psychology*. 1997; 25:197–208. [PubMed: 9212372]

- Brook JS, Whiteman M, Finch SJ, Cohen P. Young adult drug use and delinquency: Childhood antecedents and adolescent mediators. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1996; 35:1584–1592. [PubMed: 8973064]
- Chilcoat HD, Breslau N. Pathways from ADHD to early drug use. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1999; 38:1347–1354. [PubMed: 10560220]
- Faraone SV, Wilens T. Does stimulant treatment lead to substance use disorders? *Journal of Clinical Psychiatry*. 2003; 64(Suppl 11):9–13. [PubMed: 14529324]
- Goyette CH, Conners CK, Ulrich RF. Normative data on Revised Conners Parent and Teacher Rating Scales. *Journal of Abnormal Child Psychology*. 1978; 6:221–236. [PubMed: 670589]
- Hartsough CS, Babinski LM, Lambert NM. Tracking procedures and attrition containment in a long-term follow-up of a community-based ADHD sample. *Journal of Child Psychology and Psychiatry*. 1996; 37:705–713. [PubMed: 8894951]
- Hollingshead, AB. Four factor index of social status. New Haven, CT: Yale University Department of Sociology; 1975.
- Holmes J, Lawson D, Langley K, Fitzpatrick H, Trumper A, Pay H, Thapar A. The Child Attention-Deficit Hyperactivity Disorder Teacher Telephone Interview (CHATTI): Reliability and validity. *British Journal of Psychiatry*. 2004; 184:74–78. [PubMed: 14702231]
- Kaufman, AS.; Kaufman, NL. Kaufman Brief Intelligence Test (K-BIT). Circle Pines, MN: American Guidance Services, Inc; 1990.
- Lambert NM, Hartsough CS. Prospective study of tobacco smoking and substance dependencies among samples of ADHD and non-ADHD participants. *Journal of Learning Disabilities*. 1998; 31:533–544.
- Liang K, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986; 73:13–22.
- Lynskey MT, Fergusson DM. Childhood conduct problems, attention deficit behaviors, and adolescent alcohol, tobacco, and illicit drug use. *Journal of Abnormal Child Psychology*. 1995; 23:281–302. [PubMed: 7642838]
- MacKinnon DP, Lockwood CM. Advances in statistical methods for substance abuse prevention research. *Prevention Science*. 2003; 4:155–171. [PubMed: 12940467]
- Mannuzza S, Klein RG, Moulton JJ. Does stimulant treatment place children at risk for adult substance abuse?: A controlled, prospective follow-up study. *Journal of Child and Adolescent Psychopharmacology*. 2003; 13:273–282. [PubMed: 14642015]
- Martin CS, Winters KC. Diagnosis and assessment of alcohol use disorders among adolescents. *Alcohol Research and Health*. 1998; 22:95–105.
- Milberger S, Biederman J, Faraone S, Chen L, Jones J. ADHD is associated with early initiation of cigarette smoking in children and adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1997; 36:37–44. [PubMed: 9000779]
- Molina, B.; Pelham, W.; Roth, J. Stimulant medication and substance use by adolescents with a childhood history of ADHD. Poster presented at the Biennial Meeting of the International Society for Research in Child and Adolescent Psychopathology; Barcelona, Spain. 1999 Jun.
- Paternite CE, Loney J, Salisbury H, Whaley MA. Childhood inattention-overactivity, aggression, and stimulant medication history as predictors of young adult outcomes. *Journal of Child and Adolescent Psychopharmacology*. 1999; 9:169–184. [PubMed: 10521010]
- Reich, W.; Shayla, JJ.; Taibelson, C. The Diagnostic Interview for Children and Adolescents-Revised (DICA-R) (structured psychiatric interview). St. Louis, MO: Washington University; 1992.
- Smith, BH.; Barkley, RA.; Shapiro, CJ. Attention-deficit/hyperactivity disorder. In: Mash, E.; Barkley, R., editors. *Assessment of childhood disorders*. New York, NY: Guilford; 2007. p. 53–131.
- Todd RD, Joyner CA, Heath AC, Neuman RJ, Reich W. Reliability and stability of a semi-structured DSM-IV interview designed for family studies. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2003; 42:1460–1468. [PubMed: 14627881]
- Weinberg NZ, Rahdert E, Collier JD, Glantz MD. Adolescent substance abuse: A review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1998; 37:252–261. [PubMed: 9519629]

- Whalen CK, Jamner LD, Henker B, Gehricke JG, King PS. Is there a link between adolescent cigarette smoking and pharmacotherapy for ADHD? *Psychology of Addictive Behaviors*. 2003; 17:332–335.
- Wilens TE, Faraone SV, Biederman J, Gunawardene S. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics*. 2003; 111:179–185. [PubMed: 12509574]
- Winters, KC. Cigarette use questionnaire. Los Angeles, CA: Western Psychological Services; 2006.
- Winters, KC.; Henly, GA. Adolescent diagnostic interview schedule and manual. Los Angeles, CA: Western Psychological Services; 1993.
- Winters KC, Stinchfield RD, Latimer WW, Lee S. Long-term outcome of substance dependent youth following 12-step treatment. *Journal of Substance Abuse Treatment*. 2007; 33:61–69. [PubMed: 17588490]

TABLE 1

Demographics of the Study Groups

Variable	Total ADHD <i>N</i> = 149	ADHD–Non-Externalizers <i>N</i> = 59	ADHD–Externalizers <i>N</i> = 90
Percent male	81	83	80
Percent white	93	97	91
Mean (<i>SD</i>) age at T4	18.36 (1.10)	18.37 (1.13)	18.36 (1.08)
Mean (<i>SD</i>) age at T5	20.44 (1.51)	20.37 (1.57)	20.47 (1.48)
Mean (<i>SD</i>) age at T6	21.97 (1.27)	21.91 (1.21)	22.00 (1.31)
Percent high school graduate	82	86	79
Baseline mean (<i>SD</i>) IQ	104.56 (11.51)	106.22 (12.35)	103.47 (10.85)
Baseline mean (<i>SD</i>) SES ^a	46.08 (11.14)	46.19 (11.98)	46.01 (10.61)

^aHollingshead, 1975; range 17–66.

TABLE 2

Frequency, Cell Size, and Proportion (%) of Drug Use for ADHD versus Normal Comparison Groups

Variable	ADHD (N = 149)	Normal (N = 93)	p
Alcohol ^a			
T4	61/149 (41)	24/93 (26)	.016
T5	52/141 (37)	32/91 (35)	.79
T6	48/120 (40)	31/84 (37)	.66
Ever	86/149 (58)	46/93 (49)	.21
Marijuana ^a			
T4	66/149 (44)	23/93 (25)	.002
T5	39/141 (28)	22/91 (24)	.56
T6	29/120 (24)	14/84 (17)	.20
Ever	73/149 (49)	33/93 (35)	.039
Other drug ^a			
T4	15/149 (10)	5/93 (5)	.20
T5	11/141 (8)	5/91 (5)	.50
T6	10/120 (8)	4/84 (5)	.32
Ever	24/149 (16)	10/93 (11)	.24
2 + SUD ^a			
T4	51/149 (34)	13/93 (14)	.001
T5	32/141 (23)	15/91 (16)	.25
T6	27/120 (23)	13/84 (15)	.21
Ever	66/149 (44)	24/93 (26)	.004
Any SUD			
T4	78/149 (52)	35/93 (38)	.026
T5	66/141 (47)	40/91 (44)	.67
T6	56/120 (47)	35/84 (42)	.48
Ever	96/149 (64)	55/93 (59)	.41
Tobacco ^b			
T4	86/149 (58)	39/93 (42)	.017
T5	81/141 (57)	39/91 (43)	.030
T6	72/119 (61)	37/84 (44)	.021
Ever	101/149 (68)	54/93 (58)	.13

^aRefers to either abuse or dependence substance use disorder, *DSM-IV*.

^bRefers to weekly or daily use.

TABLE 3
Frequency, Cell Size, and Proportion (%) of Drug Use by ADHD Group, Psychostimulant Medication History, and Assessment Time Point

Variables	Total (N = 149)				ADHD-Non-Externalizers (N = 59)				ADHD-Externalizers (N = 90)			
	No Medication	Medication	Age 12	Medication	Age 13	p	No Medication	Medication	Age 12	Medication	Age 13	p
Alcohol ^a												
T4	34/83 (41)	4/15 (27)		23/51 (45)	.44		12/41 (29)	1/5 (20)	5/13 (38)	22/42 (52)	3/10 (30)	.71
T5	27/78 (33)	7/15 (47)		19/48 (40)	.55		11/38 (29)	2/5 (40)	4/12 (33)	15/40 (38)	5/10 (50)	.86
T6	26/67 (33)	6/12 (50)		20/41 (49)	.20		10/33 (30)	2/4 (50)	3/10 (30)	12/34 (35)	4/8 (50)	.72
Ever	48/83 (52)	9/15 (60)		34/51 (67)	.24		18/41 (44)	2/5 (40)	7/13 (54)	25/42 (60)	7/10 (70)	.79
Marijuana ^a												
T4	48/83 (48)	4/15 (27)		22/51 (43)	.30		10/41 (24)	1/5 (20)	5/13 (38)	30/42 (71)	3/10 (30)	.57
T5	16/78 (24)	5/15 (33)		15/48 (31)	.61		7/38 (18)	2/5 (40)	3/12 (25)	12/40 (30)	3/10 (30)	.52
T6	16/67 (24)	3/12 (25)		10/41 (24)	.99		6/33 (18)	0/4 (0)	2/10 (20)	10/34 (29)	3/8 (38)	.63
Ever	48/83 (51)	6/15 (40)		25/51 (49)	.75		11/41 (27)	2/5 (40)	5/13 (38)	31/42 (74)	4/10 (40)	.65
Other drug ^a												
T4	6/83 (8)	0/15 (0)		8/51 (16)	.16		3/41 (7)	0/5 (0)	1/13 (8)	4/42 (10)	0/10 (0)	.82
T5	7/78 (6)	1/15 (7)		5/48 (10)	.71		0/38 (0)	0/5 (0)	0/12 (0)	5/40 (13)	1/10 (10)	–
T6	6/67 (6)	1/12 (8)		5/41 (12)	.52		2/33 (6)	0/4 (0)	0/10 (0)	2/34 (6)	1/8 (13)	.64
Ever	16/83 (12)	2/15 (13)		12/51 (24)	.20		3/41 (7)	0/5 (0)	1/13 (8)	7/42 (17)	2/10 (20)	.82
2 + SUD ^a												
T4	30/83 (37)	2/15 (13)		18/51 (35)	.19		9/41 (22)	1/5 (20)	3/13 (23)	22/42 (52)	1/10 (10)	.99
T5	13/78 (22)	4/15 (27)		11/48 (23)	.92		4/38 (11)	2/5 (40)	2/12 (17)	13/40 (33)	2/10 (20)	.21
T6	13/67 (19)	3/12 (25)		11/41 (27)	.65		5/33 (15)	0/4 (0)	2/10 (20)	8/34 (24)	3/8 (38)	.64
Ever	36/83 (42)	6/15 (40)		25/51 (49)	.70		11/41 (27)	2/5 (40)	5/13 (38)	24/42 (57)	4/10 (40)	.65
Any SUD												
T4	44/83 (53)	6/15 (40)		28/51 (55)	.59		13/41 (32)	1/5 (20)	7/13 (54)	31/42 (74)	5/10 (50)	.26
T5	32/78 (41)	8/15 (53)		26/48 (54)	.31		14/38 (37)	2/5 (40)	5/12 (42)	18/40 (45)	6/10 (60)	.95
T6	26/67 (39)	7/12 (58)		23/41 (56)	.15		12/33 (36)	2/4 (50)	3/10 (30)	14/34 (41)	5/8 (63)	.78
Ever	51/83 (61)	10/15 (67)		35/51 (69)	.69		18/41 (44)	2/5 (40)	7/13 (54)	33/42 (79)	8/10 (80)	.79
Tobacco ^b												
T4	46/83 (55)	8/15 (53)		32/51 (63)	.66		18/41 (44)	1/5 (20)	6/13 (46)	28/42 (67)	7/10 (70)	.56

Child Adolesc Subst Abuse. Author manuscript; available in PMC 2016 May 8.

Variables	Total (N = 149)				ADHD-Non-Externalizers (N = 59)				ADHD-Externalizers (N = 90)			
	No Medication	Medication	Age 12	Medication	Age 13	p	No Medication	Medication	Age 12	Medication	Age 13	p
T5	42/78 (54)	10/14 (71)		29/49 (59)	.45		17/38 (45)	2/4 (50)		7/12 (58)	.71	
T6	36/66 (54)	8/12 (67)		28/41 (68)	.33		16/32 (50)	2/4 (50)		6/10 (60)	.85	
Ever	53/83 (64)	10/15 (67)		38/51 (75)	.44		22/41 (54)	2/5 (40)		8/13 (62)	.71	
										8/10 (80)	22/37 (60)	.49
										6/8 (75)	22/31 (71)	.50
										8/10 (80)	30/38 (79)	.83

^aRefers to either abuse or dependence substance use disorder, *DSM-IV*.

^bRefers to weekly or daily use.