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Does Childhood Use of Stimulant Medication as a Treatment for ADHD Affect the Likelihood of Future Drug Abuse and Dependence? A Literature Review

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This article describes the disparate research findings regarding the effects of stimulant medication in subsequent substance abuse and dependence. A minimum of 4 to 5% of children in the United States will be diagnosed with ADHD; thus it is important for parents to be informed when making decisions about the use of stimulant medication to treat symptoms. Considering the inconsistencies in the literature, it is still difficult to determine the true effects of stimulant medication on drug abuse and dependence in adulthood.

KEYWORDS ADHD, medication, stimulants, substance abuse, substance dependence

INTRODUCTION

According to Wilens, Biederman, and Spencer (2002), Attention Deficit/Hyperactivity Disorder (ADHD) is "the most common emotional, cognitive, and behavioral disorder treated in youth" (p. 113). The prevalence of ADHD in the general population varies depending on study design, source of reporting, and the edition of *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) utilized. However, Wilens et al. (2002) indicated that 4 to 5% of children were diagnosed with ADHD. Furthermore, medication

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management was identified as an essential part of ADHD treatment, whether coupled with a behavioral modification plan or used in isolation.

The most common class of medication prescribed for ADHD symptom management is central nervous system (CNS) stimulants. The oldest yet still frequently prescribed CNS stimulant medication is methylphenidate, marketed as Ritalin, a schedule II controlled substance. A schedule II designation suggests that methylphenidate has potentially addictive properties. Considering the addictive potential of CNS stimulant medication, could its use to treat ADHD symptoms in children and adolescents be related to subsequent drug abuse and dependence?

The current literature appears to contain conflicting data and divergent opinions regarding the role of stimulant medication in later adolescent and adult substance abuse. Some authors have suggested that children prescribed CNS stimulant medication were, in fact, at greater risk for drug abuse and dependence (Brandon, Marinelli, Baker, & White, 2001; Lambert, 2005; Lambert & Hartsough, 1998; Schenk & Izenwasser, 2002). Others indicated that children taking stimulant medication were no more or less likely to abuse drugs than control groups (Barkley, Fischer, Smallish, & Fletcher, 2003; Wilens et al., 2005). Finally, another group of studies suggested that taking stimulant medication to treat symptoms of ADHD actually had a protective effect, reducing the propensity toward drug abuse and dependence (Faraone & Wilens, 2003; Upadhyaya et al., 2005; Wilens, Faraone, Biederman, & Gunawardene, 2003). Clearly, three such highly distinctive and conflicting models require further reflection and analysis.

ADHD DIAGNOSIS AND SUBSEQUENT DRUG ABUSE AND DEPENDENCE

It would be remiss to explore the connection between stimulant treatment and drug use/dependence without first exploring the relationship between an ADHD diagnosis and drug use/dependence. Biederman, Wilens, Mick, Faraone, and Spencer (1998) conducted a study whereby 239 participants with a clinically assigned diagnosis of ADHD were interviewed to determine the severity of their symptoms and nature of their drug use, if any. Based on these audio-taped interviews, three independent raters, blind to the study design, used DSM-III-R criteria to diagnose the interviewees with ADHD or another mental disorder, if present. These raters achieved high interrater reliability in diagnosing the participants, with a mean kappa coefficient of .90 across 115 interviews. Furthermore, participants were assessed using a structured clinical interview to determine if they met criteria for substance abuse or dependence based on DSM-III-R listings.

To be assigned a diagnosis of drug dependence, the participants must have met criteria at some point in their lives as indicated by historical

self-report. If assigned a diagnosis of substance abuse, the participants had to meet DSM-III-R criteria, without meeting the more stringent criteria for drug dependence. Specific data gathered regarding substance use history included level of impairment, age at onset of substance use, age at offset of substance use, the number of episodes, and history of treatment. The 239 participants were then compared to an existing sample of 268 adults not meeting criteria for ADHD diagnosis. The authors found that substance use disorder diagnoses were significantly higher in the ADHD group than in the comparison ($p < .001$). Furthermore, the age of onset of substance use was significantly lower in the ADHD group ($p < .014$). These finding suggested that ADHD symptoms affect not only a propensity toward drug and alcohol use, but also the earlier age of onset of substance use. The mean age of onset for the ADHD group was 19.2 years of age, while the mean for the control group was 21.8 years old (Biederman et al., 1998).

Several limitations to this study should be considered, including a concern for self-reported ADHD symptoms in adult participants. The adult participants were diagnosed for the purposes of this study based on retrospective self-report of childhood experiences. In addition, substance abuse and dependence was diagnosed based on self-report. When relying solely on self-report, the researchers run a risk of engaging participants that report inaccurately; thus it would be difficult to ascertain the reliability of the substance use reporting as well. Perhaps consulting with parents or other pertinent third parties known to these participants would further enhance the reliability of the self-report.

In a separate study, Biederman et al. (2006) assessed data gathered from 300 participants over the age of 12 years old, 97 diagnosed with ADHD and 203 not meeting criteria for an ADHD diagnosis based on the DSM-III-R. The purpose of this study was to confirm the significance of nicotine use as a gateway to other drug use in youths diagnosed with ADHD. Assessments administered included the Schedule for Affective Disorders and Schizophrenia for School-Age Children: Epidemiologic Version (K-SADS-E). Participants over the age of 18 were assessed using a structured clinical interview. Diagnosis was also informed by interviews with mothers of the participants and direct interviews with the participants under the age of 18. If, based on the interviews and assessments, participants met criteria for ADHD, the diagnosis was assigned. In any questionable cases whereby diagnosis could not be clearly labeled, the diagnostic facts were presented to a committee of psychiatrists who remained blind to the study and they were charged with formulating the diagnosis. The interviewer also gathered data regarding a history of substance use including, but not limited to, alcohol, nicotine, marijuana, cocaine, and amphetamines.

Information such as types of substances used, age of onset of each, and diagnosis of substance abuse or dependence was collected. Among the participants with and without an ADHD diagnosis, 22% and 12% respectively

were identified cigarette smokers ($\chi^2_{(1)} = 4.4, p = .036$). In addition, the mean age of onset in participants experiencing ADHD was 12.5 years old, while that of participants without ADHD was 15.1 years old ($t_{(44)} = 4.0, p < .001$). The authors also found that smoking was a significant predictor of subsequent alcohol or drug abuse or dependence, alcohol use, drug use, and marijuana use ($p < .001$ for each variable). This study indicated that cigarette smoking acted as a predictor of subsequent alcohol use ($\chi^2_{(1)} = 13.4$, $p < .001$), drug use ($\chi^2_{(1)} = 15.5, p < .001$), and marijuana use ($\chi^2_{(1)} = 15.8, p <$ .001), specifically in participants experiencing ADHD (Biederman et al., 2006).

While this study was sound, there were some procedural limitations that should be highlighted. Foremost, the study participants were predominately Caucasian and female, not an adequate representation of the general population. In addition, characteristics of substance use were based on participant historical self-report, and therefore may be inaccurate. Despite these limitations, the results were quite provocative.

In a similar study, Lambert and Hartsough (1998) also gathered data about tobacco and other substance use in adults diagnosed with ADHD in childhood. This study, beginning in 1974, was longitudinal in nature and assessed 492 participants in childhood. These participants were placed, based on diagnostic symptom presentation as indicated by the parent and teacher ratings of the Children's Attention and Adjustment Survey (CAAS), into one of the following five groups: (1) primary ADHD participants ($n = 175$), (2) secondary ADHD participants ($n = 39$), (3) ADHD control participants ($n = 68$), (4) behavioral problem controls ($n = 51$), and (5) age-mate controls ($n = 159$). The primary ADHD group met the following criteria: situational or pervasive ADHD based on CAAS ratings, medical diagnosis of hyperactivity, and/or central nervous system (CNS) stimulant treatment, no prescription of anticonvulsant medication, and parent report of hyperactivity symptoms present prior to eight years of age. Participants in the secondary ADHD group had situational or pervasive ADHD on the CAAS, medical diagnosis of organic factors attributing to hyperactivity, use of anticonvulsant medication, and parent report of hyperactivity prior to age eight. ADHD control participants met criteria for situational or pervasive ADHD on the CAAS, rated as hyperactive by two of three reporters (teacher, parent, and physician), appearance of hyperactive symptoms prior to age eight, and no medical diagnosis or CNS treatment. Behavior problem controls were rated high on ADHD symptoms, conduct problems, and affective behaviors on the CAAS, but there were not enough reporting sources to indicate an ADHD diagnosis, no medical diagnosis had been established, and there was no evidence of symptoms in early childhood. Finally, the age-mate controls were selected from the same class in which the ADHD participants were enrolled. Participants were queried on a number of occasions in childhood, adolescence, and adulthood regarding their substance use, specifically tobacco.

Of the 492 original participants, 400 (81%) were able to be tracked through adulthood for interviews. After further assessment of group characteristics, the authors decided to collapse the three ADHD groups, identified previously, into one group identified as the ADHD group. The authors reported that the age at which participants began smoking regularly was significantly different in the ADHD group and behavioral control group as compared to the age-mate controls ($p < .02$), indicating that the ADHD and behavioral control groups started smoking earlier in adolescence than age-mate controls. In addition, by adulthood, 42% of ADHD participants, 26% of behavioral controls, and 26% of age-mate controls were regular, current smokers ($p < .02$). Significant differences also existed between the ADHD group and the two control groups on tobacco, stimulant, and cocaine dependence. Most important, the authors examined whether prior exposure to stimulant medication was related to the use of tobacco, cocaine, and stimulants in adolescence or adulthood. It was determined that 48% of the ADHD group had used stimulant medication in childhood for six months or longer. CNS stimulant medication history was significantly related to rates of smoking in adulthood. Among ADHD participants never using stimulant medication, 44.7% of smokers smoked daily, while 71% of those using stimulants for more than one year were daily smokers. Finally, the authors indicated a linear relationship between the measure of stimulant medication and the likelihood of tobacco ($p < .03$) or cocaine ($p < .05$) dependence diagnosis in adulthood. The purpose of the study was to assess the relationship between ADHD and drug use. However, with the unexpected finding related to stimulant treatment and drug use, a follow-up study was necessitated. Limitations of the study are provided in the next section (Lambert & Hartsough, 1998).

STIMULANT MEDICATION INCREASES LIKELIHOOD OF SUBSEQUENT DRUG ABUSE AND DEPENDENCE

The previous study initiated an exploration of the relationship between childhood stimulant medication used and adult substance use, specifically related to tobacco use. Evidence from additional sources also supported the notion that use of stimulant medication would increase the likelihood of substance abuse or dependence (Brandon et al., 2001; Lambert, 2005; Schenk & Izenwasser, 2002). Lambert (2005) utilized the same data set (in addition to further data gathered) to conduct a study more specific to the relationship between stimulant treatment and adult drug use. The participants were followed through childhood, adolescence, and into adulthood for 28 years, making this, to date, the only long-term longitudinal study investigating licit and illicit drug use in children who were prescribed stimulant medication. Less detail will be provided, as the study was previously described in great depth. The 40 classrooms

in which participant recruitment was conducted were randomly selected in the San Francisco area and three referral resources (parents, teachers, and physicians) were informed of the criteria.

Following the initial diagnostic phase, the researchers contacted the participants one time per year to gather data related to health and medical history, education level, family interactions, peer relationships, school performance, activities, and treatment (if any). In early adolescence and continuing into adulthood, the author began interviewing participants about substance use, including age of onset of substance use and use of each substance at the time of the interview.

When comparing participants who had received stimulant treatment in childhood to those receiving no stimulant treatment, Lambert (2005) found that the percentage of participants who did not smoke regularly was lower in those having received stimulant medication (42% as compared to 56%). In other words, the stimulant-treated group contained more regular smokers than the group not treated with stimulant medication. Participants receiving stimulant treatment were grouped based on age of discontinuation of stimulant medication (age 10, between age 11 and 13, and age 14). The author noted that regular smoking began when stimulant treatment ended ($p < .01$). Furthermore, a significant chi square indicated a relationship between ADHD diagnosis and tobacco dependence, cocaine dependence, and amphetamine dependence, but not alcohol or marijuana dependence. The non-significant relationship between stimulant treatment and alcohol/marijuana could have occurred because the chemical composition and physiological responses are vastly different compared to tobacco, cocaine, and amphetamine (whereby the biological activity closely resembles that of CNS stimulants).

Childhood conduct problems were significantly related to only tobacco dependence. The research also found a significant relationship between stimulant use in childhood and tobacco dependence ($p < .001$), and cocaine dependence ($p < .01$) in adulthood. Use of substances (tobacco, cocaine, amphetamines, marijuana, and alcohol) over a lifetime was also assessed. It was found that ADHD was significantly related to daily smoking ($p < .001$), while conduct problems were significantly associated with marijuana use ($p < .05$). Those treated with stimulant medication were significantly more likely to be daily smokers ($p < .000$) and exhibit increased use of amphetamines throughout their lifetime ($p < .05$). According to Lambert (2005),

> ADHD did not increase the odds of becoming a heavy lifetime user of any of the substances at an average age of 26, but those treated with stimulants for more than 1 year were 2.9 times more likely to become daily smokers in adulthood, and those treated for less than 1 year were 4.0 times more likely to become daily smokers; therefore, these results indicate that any stimulant treatment increases the odds of becoming a daily smoker. (p. 215)

This study was of sound design and interpretation. Many of the limitations of studies previously reviewed here were addressed in the current study by the longitudinal design and multiple reporting sources. The final sample size was adequate considering the participants were tracked for 28 years and attrition was likely to occur. The study design was distinctive, in that participants did not have to rely on memory recall to determine their pattern of drug use. Instead, they were queried one time per year about their current drug use. A major limitation of this study was a lack of consideration for confounding variables. For example, Lambert (2005) did consider the severity of the ADHD symptoms as a contributing factor to substance use, but did not consider the influence of conduct problems. In addition, the author did not assess the effectiveness of the stimulant medication in treating the ADHD symptoms of participants. These are some vexing limitations of this study, as they may impact subsequent drug use.

To further support the proposition that stimulant treatment increased the likelihood of subsequent drug abuse and dependence, several studies based on animal models were reviewed. Schenk and Izenwasser (2002) conducted a study designed to measure the effects of pretreatment with methylphenidate on the acquisition of self-administration of cocaine in rats. Male rats (all approximately 12 weeks old) were surgically implanted with a catheter in the right jugular vein. After 5 days of recovery time, the rats underwent a 9-day pretreatment phase before being placed in operant chambers equipped with two levers for 10 days of self-administration training. Depressing the active lever resulted in the delivery (via the catheter) of a dose of cocaine dissolved in sterile physiological saline and heparin, as well as the illumination of a "house light" above the active lever. No programmed consequence resulted with the depression of the inactive lever.

The rats were divided into three groups to be given three different pretreatments for nine consecutive days leading up to the self-administration testing. On each pretreatment day, rats were injected with either saline ($N = 18$), 5.0-mg/kg methylphenidate ($N = 17$), or 20.0-mg/kg methylphenidate ($N = 14$). Early days of self-administration testing, after the nine-day treatment, showed comparable responses on both levers for all groups (saline, 5.0-mg/kg methylphenidate, and 20.0-mg/kg methylphenidate), while later testing days showed a decrease in inactive lever depressions and an increase in active lever responses (Schenk & Izenwasser, 2002).

The total number of active lever responses recorded on each testing day for the saline and each of the methylphenidate groups was compared utilizing separate repeated measures ANOVAs (Days × Pretreatment). There was a significant difference in cocaine administration between the saline control group and the experimental group receiving 20.0-mg/kg of methylphenidate ($p < .001$). According to Schenk and Izenwasser (2002), there was no significant difference between the control group and the experimental group receiving 5.0-mg/kg of methylphenidate. Rats treated with 20.0-mg/kg

methylphenidate showed more active lever responses on days, 5, 6, and 10 than those treated with saline ($p < .05$). Thus, while pretreatment with just 5.0-mg/kg of methylphenidate showed no significant effect on the advent of cocaine self-administration or the amount of cocaine used each day, pretreatment with 20.0-mg/kg of methylphenidate resulted in statistically significant increases in the amount of cocaine used, as well as a statistically significant decrease in the latency period for the onset of self-administration of cocaine. Simply stated, the 20.0-mg/kg of methylphenidate resulted in a more rapid onset of active bar compressions. The rats receiving 20.0-mg/kg of methylphenidate had a significant increase in active bar depressions around day 4 of the self-administration training, while the control group responses increased around day 7.

The study did not account for the possibility that cocaine was self-administered more rapidly in the 20.0-mg/kg methylphenidate group because of its ability to alleviate withdrawal effects from the methylphenidate administered during the 9-day pretreatment regimen. Likewise, the study does not address whether cocaine may be counteracting more severe side effects of exposure to the higher dosages of methylphenidate, nor does it examine how different delivery methods of the drugs may affect sensitivity to cocaine use. The rats in this study were administered both drugs intravenously, while humans generally ingest methylphenidate through the stomach in its pill form and deliver cocaine to their systems in a variety of manners. Speed of chemical delivery, relevant to human drug self-administration behaviors, should be explored for their effects on sensitivity to cocaine.

The authors also note that children treated with methylphenidate were generally administered maximum doses of 0.5 mg/kg, twice per day. This was a significantly lower dose than the 20.0 mg/kg pretreatment dosage shown to increase sensitivity to cocaine in the rat study. Further studies of children given regimens of prescribed drugs, used over various lengths of time, should be considered.

Brandon and colleagues (2001) conducted a study to, in part, assess whether treatment with low doses of methylphenidate in rats during adolescence increases the likelihood of cocaine self-administration in adulthood. Four-week-old rats were surgically implanted with catheters in their external jugular veins. Separated into two groups, the rats underwent a 7-day pretreatment period, during which they were administered either low doses (2.0 mg/kg) of methylphenidate or saline. The lower dosage of methylphenidate was intended to more closely emulate the average doses given to human children.

Two weeks after the pretreatment with methylphenidate concluded, the rats were placed in operant chambers, which were fitted with two "nose-poke holes." Poking its nose in the active hole caused a subject to receive a dose of cocaine (via the catheter). Nose-poking in the inactive hole had no programmed consequence. Results of the experiment showed that

self-administration of cocaine was significantly greater in rats pretreated with methylphenidate ($N = 12$) compared to rats pretreated with saline ($N = 10$, $p = .007$). No significant variation was shown between the groups for the inactive hole. Furthermore, there was no evidence of nonselective behavior since no significant difference existed between the saline and methylphenidate groups for poking the inactive hole on day one of the self-administration. In summary, low-dose regimens of methylphenidate in adolescent rats resulted in a greater sensitivity to cocaine self-administration in adulthood. It is curious that this study yielded different results from those of Schenk and Izenwasser (2002), whereby high-dose rats were more likely to self-administer cocaine as compared to the control group, but the low-dose rats did not differ from the control group in cocaine self-administration.

The only notable differences between these two studies that could account for these disparate results include the age of the rats and the latency of onset of self-administration. In the Schenk and Izenwasser (2002) study, after the nine-day pretreatment was completed, the rats began the self-administration training the following day. However, in the Brandon et al. (2001) study, the rats were given a two-week washout period, prior to self-administration training, where they received no saline or methylphenidate. Finally, Schenk and Izenwasser (2002) used 12-week-old, adult rats, while Brandon and colleagues (2001) used 4-week-old, adolescent rats. Schenk and Izenwasser (2002) suggested this discrepancy could indicate that "younger subjects might be particularly susceptible to the effect of methylphenidate preexposure" (p. 655). One could speculate that human children and adolescents are more susceptible to stimulant treatment as well.

STIMULANT MEDICATION DOES NOT INCREASE LIKELIHOOD OF SUBSEQUENT DRUG ABUSE AND DEPENDENCE

Barkley and colleagues (2003) achieved slightly different results from those reported previously. The authors conducted a study whereby children diagnosed with ADHD in childhood ($N = 119$) and a control group ($N = 81$) were tracked through adolescence and adulthood. Initial data about the participants was gathered using the Conners Parent Rating Scale Revised (CPRS-R) and the Werry-Weiss-Peters Activity Rating Scale (WWPARS) to evaluate symptoms of ADHD. During this longitudinal study, assessment of current ADHD and Conduct Disorder (CD) symptoms and substance use information was gathered from two follow-up sessions. During the adolescent follow-up, the inquiry about adolescent drug use was binary (had used or had not used), and no frequency information was collected. However, during the adult follow-up, frequency data were gathered. All of the follow-up data were gathered via a structured interview with the participant and a parent over the telephone.

Barkley and colleagues (2003) reported extensive results that were also somewhat inconsistent. Foremost, the group of children exhibiting ADHD symptoms was subdivided into two groups: stimulant treated ($N = 98$) and non-stimulant treated ($N = 21$). No significant differences existed between these two groups in the following areas of adolescent drug use: cigarettes, alcohol, marijuana, hashish, cocaine, heroin, hallucinogens, unprescribed stimulants, unprescribed sedatives, and unprescribed tranquilizers. Though they did not meet statistical significance, the percentage of drug use in each category was typically higher for ADHD symptomatic participants treated with stimulants as compared to those not treated: 52% versus 30% for cigarettes, 41% versus 35% for alcohol, 20% versus 6% for marijuana, 7% versus 6% for hashish, 5% versus 0% for cocaine, 3% versus 0% for hallucinogens, 6% versus 6% for unprescribed stimulants, 3% versus 0% for unprescribed sedatives, and 1% versus 0% for unprescribed tranquilizers.

The study found no significant differences between the stimulant-treated and non-stimulant-treated groups in adult substance abuse. The authors reported a "marginally significant finding" for a higher frequency of cocaine use in those treated with stimulant medication in childhood ($p = .059$). The degree of substance use in adulthood was also examined based on stimulant treatment in childhood. It was determined that lifetime reporting of cocaine use in adulthood was significantly higher in the stimulant-treated participants than in those not treated with stimulant medication ($p = .037$). The authors also reported that participants diagnosed with ADHD and treated with stimulant medication for less than one year had a significantly greater propensity toward cocaine abuse disorder ($p = .05$) than those treated for more than one year. This could indicate that stimulant treatment added a protective effect to reduce the likelihood of subsequent substance abuse in those treated for a more extensive period of time.

This study was interesting in that most reported statistics indicated no difference between the stimulant-treated groups as compared to those not treated. However, some statistics supported an increased likelihood of subsequent drug abuse based on stimulant medication treatment, while others suggested a protective factor to reduce the penchant toward substance use. A question of interpretative bias was raised based on the authors' approach in explaining their findings. For instance, regarding the significant relationship between stimulant treatment and cocaine use, the authors wrote, "we believe that there are good reasons from other results in this study to pose strong reservations about that conclusion" (p. 105). However, they make no such statements when the results supported the protective factors of stimulant treatment. The study included a disproportionate sample grouping between stimulant-treated and non-stimulant-treated participants (98 versus 21, respectively), which raises concerns about sample bias. Furthermore, there was a reported control group not diagnosed with ADHD; however, none of the reported statistics included that group. All findings

were based on comparisons between the ADHD groups. As a result, the validity of this study is drawn into question.

STIMULANT MEDICATION REDUCES THE LIKELIHOOD OF SUBSEQUENT DRUG ABUSE AND DEPENDENCE

A separate body of literature suggests stimulant treatment actually reduces the likelihood of subsequent substance use. Lambert (2005) was previously reviewed in depth and most of the findings indicated an increased likelihood of drug use if treated with stimulants in childhood; however, some of the data gathered demonstrated some protective factors. For instance, children ceasing stimulant treatment at 14 years old or later demonstrated a decreased likelihood of smoking regularly compared to those treated with stimulants until age 10 ($p \leq .01$). Therefore, children who maintained stimulant treatment beyond the age of 10 were less likely to smoke cigarettes.

Faraone and Wilens (2003) conducted a random effects meta-analysis to reconcile the conflicting findings of ADHD studies attempting to answer the question of whether stimulant treatment is related to substance abuse. The authors examined seven long-term studies that aimed to measure the potential role, if any, childhood stimulant treatment played in the onset of substance abuse disorders in adolescence or adulthood. Each study contained a 2×2 table, dividing subjects into two categories for treatment status (exposure to stimulant therapy or no exposure) and two categories for onset of substance abuse disorders (present or not). These tables were used to calculate odds ratios, which were intended to estimate the increase in "the odds of *not* developing substance abuse disorders" (p. 10). This was referred to as the "protective effect" of stimulant treatment in childhood.

The results of the meta-analysis demonstrated an overall statistically significant protective effect of stimulant psychopharmacological treatment for children ($p = .02$). In other words, the authors suggested that children treated with stimulant medication were less likely to develop substance use disorders. The authors also conducted a study to assess for overestimation of results in the studies used, and the results were not significant, thus indicating that the studies utilized did not overestimate the protective effects of stimulant treatment (Faraone & Wilens, 2003).

Wilens and colleagues (2003) conducted a similar meta-analysis utilizing a total of six studies. Five of those studies were used in the previously reviewed meta-analysis; thus, similar results would be expected. Overall the study included 674 stimulant-treated and 360 unmedicated participants. Four of the studies indicated a protective effect of stimulant treatment in childhood, while two of them suggested an adverse effect. Overall, the meta-analysis estimate of the odds ratio was 1.9, which was statistically significant ($p = .037$), suggesting a reduction in the risk of developing

substance use disorders in participants receiving stimulant medication (as ADHD treatment). The authors also found that studies whereby the stimulant-treated and non-stimulant-treated groups displayed similar severity of ADHD symptoms demonstrated a more pronounced protective effect of stimulant medication. The publication bias statistic was not significant in this meta-analysis, suggesting that the individual study results were not overestimated.

One of the limitations of the two meta-analytic studies was the paucity of research available for review in this particular area. As a result, the sample size reviewed was relatively small and weighted with male participants. Generalization to the female population would be questionable, as there were so few female participants. In addition, the studies reviewed in the meta-analysis relied solely on naturalistic data gathered. Due to ethical concerns, researchers were not able to conduct long-term, randomized, placebo-controlled trials.

In another study, Upadhyaya and colleagues (2005) examined ADHD symptoms, stimulant treatment, and drug use in 334 college-aged students. The data were collected utilizing several instruments including the Core Alcohol and Drug Survey, the Current Symptoms Scale—Self Report (CSS) for ADHD, and a self-report form of medication treatment. Of the 334 participants, 19 had current ADHD symptoms (11 of which were medicated). In addition, 71 participants reported a previous diagnosis of ADHD, but were not currently experiencing diagnostically significant symptoms. A total of 76 participants (including those currently taking medication) had been prescribed stimulant medication to treat ADHD symptoms sometime throughout their development. Tobacco use was significantly higher in those experiencing current ADHD symptoms than in controls not experiencing ADHD and those with ADHD symptoms controlled by stimulant medication. Students currently experiencing ADHD, regardless of medication status, were also more likely to use marijuana and "other" drugs, but not alcohol.

The authors concluded that college students currently experiencing ADHD symptoms had increased tobacco (OR (CI) = 3.21) and "other drug" use (OR (CI) = 6.68) as compared to those with effective symptom management using stimulant medication. It seemed that the results of this study illuminated the fact that ADHD symptoms increased the risk of substance abuse in college students; however, effective symptom management with stimulant medication reduced the likelihood of substance use. This study supported other studies indicating that ADHD medication management may provide some protective factors against substance abuse (Upadhyaya et al., 2005).

While the unique quality of this study is intriguing (i.e., examining differences between students receiving effective ADHD stimulant treatment with those receiving ineffective treatment), several limitations are worthy of recognition. The ADHD symptoms were self-reported, thus susceptible to inaccurate reporting. Furthermore, previous stimulant treatment in

adolescence and childhood was not assessed. This information might have provided the authors additional information regarding the effects of stimulant treatment on subsequent substance use.

Wilens and colleagues (2005) conducted a meta-analysis examining the effects of stimulant treatment in adolescents and adults diagnosed comorbidly with ADHD and Substance Use Disorders (SUD). The authors utilized four treatment studies conducted with adolescent participants and five with adults. The studies varied in length from four weeks to six months. In the open trials evaluated in the meta-analysis, there was a significant reduction in the ADHD symptoms of participants treated with stimulants. Furthermore, there was a significant decrease in SUD symptoms for those participants placed on stimulant medication. When evaluating the placebo-controlled studies, no significant reductions in ADHD or SUD existed in those treated with stimulants as compared to those treated with placebo. The authors also examined the possibility of increased SUD symptoms based on initiation of a stimulant regimen to treat ADHD symptoms. No significant increase occurred. The limitation noted in previous meta-analyses examined applied to this study as well. Few empirical studies examined the effect of stimulant treatment in participants with ADHD and SUD. In addition, according to the authors, the methodology of the studies varied greatly, making them difficult to compare.

CONCLUSIONS

Based on the reviewed studies and literature, it could be confidently asserted that this is a complex body of literature to examine. Four studies indicated that stimulant medication increased the likelihood of substance use (Brandon et al., 2001; Lambert, 2005; Lambert & Hartsough, 1998; Schenk & Izenwasser, 2002), while one indicated no risk (Barkley et al., 2003), and four suggested decreased risk (Faraone & Wilens, 2003; Upadhyaya et al., 2005; Wilens et al., 2003; Wilens et al., 2005).

A question of interpretation biased toward one's own research and critical of those with disparate outcomes and opinions was raised. For example, in Hresko (2000), Mick, Biederman, and Faraone wrote a letter appearing in the *Journal of Learning Disabilities* debunking the results of Lambert and Hartsough's (1998) study. They wrote

> we were puzzled by these findings because they are not consistent with our own published work.... Although Lambert and Hartsough's outstanding follow-up study has provided the field with many useful findings, it may mislead readers about a very important public health issue because, for the purpose of addressing the link between stimulant treatment and substance abuse, their study lacked an appropriate comparison group and did not use an appropriate method of statistical analysis. (p. 314)

Lambert and Hartsough responded with the following:

> rather than making claims that pharmacotherapy "protects" against substance dependence based on findings with marijuana and alcohol, and dismissing a possible link between stimulant treatment and adult stimulant (tobacco and cocaine) involvement, it seems prudent to us not to foreclose on studies of possible important risk factors for adult abuse of tobacco and stimulants. (p. 316)

Jackson (2006) also included an opinion claiming "according to several recent publications prepared by corporately sponsored clinicians, ADHD medications (predominately stimulants) 'do not increase, but appear to decrease the risk for substance abuse.' It would be difficult to imagine a more misleading or distorted presentation of the pertinent facts" (p. 1). This author proceeded to summarize several of the studies included in this paper, offering very positive comments about Lambert (2005) and highly critical remarks about Barkley and colleagues (2003). It appeared as though many in the medical or helping professions had already formed opinions about stimulant treatment for ADHD, specifically the effects it had on subsequent substance abuse.

Regardless of opinions, relationships with pharmaceutical companies and researchers, etc., it is pertinent to follow these studies with an unbiased eye. The most significant consideration is the health and safety of the children, adolescents, and adults receiving stimulant medications. It is important for consumers to examine the risks and benefits to make an informed decision about medication consumption. At this time, it cannot be unequivocally stated that ADHD stimulant medication increases or decreases the risk of substance use. How is a consumer to make an informed decision on the basis of such divergent evidence?

Further studies need to be conducted with an eye toward minimizing bias. From the body of literature reviewed, several factors can be noted to influence substance use and stimulant treatment. They are as follows:

1. a potential comorbid diagnosis of ADHD and conduct disorder, oppositional defiant disorder, anxiety, etc.,
2. the severity of ADHD symptoms based on multiple reporting sources,
3. the effectiveness of current stimulant medication (if the participant is taking medication),
4. the length of time taking the stimulant medication, and
5. the point in development at which the stimulant medication was initiated.

Further research should be considered and account for these variables. In addition, this writer noted a deficit in literature delineating differences in substance abuse and dependence as related to stimulant use and type of

ADHD. For instance, does the propensity toward substance use after stimulant exposure appear differently in children with ADHD combined type, as compared to those with inattentive type? While an extensive review of the inappropriate stimulant-prescribing practices of psychiatrists and physicians is beyond the scope of this literature review, it will be important to consider in future publications.

Clients present to helpers with a need, sometimes a need for medication. These clients entrust the helper to guide them in the right direction so that their symptoms (ADHD) will be alleviated. A betrayal of that trust would ensue if a client developed another set of symptoms (SUD) from the medication intended to treat the original symptoms. It is important to become further informed in this area, considering the previously listed variables, so clients can be provided with optimal information and maintain a trusting relationship.

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