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# Do Stimulant Medications for Attention-Deficit/Hyperactivity Disorder (ADHD) Enhance Cognition?

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## 1. Introduction

Characteristic symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD) have been recognized in the medical literature for over 200 years. The earliest known clinical description is found in the book by the Scottish physician Sir Alexander Crichton, entitled *An Inquiry into the Nature and Origins of Mental Derangement* (Crichton, 1798, as cited in Baumeister et al., 2011). In the chapter, "Attention, and its Diseases" (p. 254), Crichton notes that these conditions make people "incapable of attending with constancy to any one object of education" (p. 271), cause "mental restlessness", "walking up and down", and the "fidgets" (p. 272). Although Crichton was clearly describing disorders of attention, George Still, a British pediatrician, is usually credited with being the first person to describe the syndrome that has since been recognized as ADHD. Dr. Still gave a series of lectures on *Some Abnormal Psychical Conditions in Children* in 1902, in which he noted that even some children with normal intelligence may exhibit a "lack of attention which is very noticeable...[and which] no doubt accounts to a considerable extent for backwardness in school acquirements" (Still, 1902b, p. 1081 as cited in Baumeister et al., 2011).

Since those original descriptions, the diagnostic characterization of ADHD has been revised numerous times. The three core symptoms are presently considered to be Inattention, Impulsivity and Hyperactivity (Baumeister et al., 2011; Biederman & Faraone, 2005; Davidson, 2008). Current prevalence estimates in the United States are 6-9% for children and adolescents and 3-5% in adults (Dopheide & Plizka, 2009). In the most recent National Comorbidity Survey, in which nearly 3200 adults, 19 to 44 years of age, were screened, the prevalence was 4.4% (Kessler et al., 2006).

Unlike the childhood presentation, symptoms of hyperactivity and impulsivity are less prominent in ADHD-diagnosed adults than problems resulting from inattention, distractibility and disorganization (Dopheide & Plizka, 2009). The psychosocial difficulties caused by these symptoms have been well-documented, including marital and relationship problems, poor job performance and employment histories, and lower socioeconomic status (Biederman et al., 2011a; Fischer et al., 1990; Hechtman et al., 1984; Hechtman & Greenfield, 2003; Ingram et al., 1999; Mannuzza et al., 1993; Spencer et al., 2007). Many adults with ADHD report frequent employment changes, difficulty in organizing finances, and

household and parental management responsibilities, dangerous driving, and unstable social relationships or social isolation (Weiss & Murray, 2003). Adults with ADHD are less likely to attain the same educational (and occupational) level as those without the diagnosis relative to what would be predicted based on their IQ, even with pharmacotherapy (Biederman et al., 2006; Biederman et al., 2008a; Mannuzza et al., 1993). Moreover, cognitive deficits of adults with ADHD, relative to adults without the diagnosis, do not change across the lifespan (Biederman et al., 2010). For example, although 84% of ADHD-diagnosed adults were statistically expected to be college graduates, only 50% reached this level of education (Biederman et al., 2008a).

In adults, as with youth, first-line treatment options include the stimulant drugs, usually one of the many formulations of either methylphenidate (MPH) or amphetamine (AMPH) (Adler et al., 2007; Berman et al., 2009; Dopheide & Plizka, 2009; Dodson, 2005; Faraone et al., 2004; Paterson et al., 1999; Wender et al., 2011). These agents are the most efficacious drug treatments for ADHD, with large effect sizes, as measured by standardized rating scales in clinical trials. Methylphenidate and amphetamine formulations are considered similar in efficacy, with between 55 - 75 % of drug-treated patients (compared with 4 - 30% of placebo - treated patients) showing "clinically significant" improvement for up to 4 to 6 weeks (Berman et al., 2009; Dopheide & Plizka, 2009). Available information indicates that on standard efficacy measures, amphetamine is at least equivalent may be superior to methylphenidate, and, that individuals with ADHD who don't respond to methylphenidate will show significant improvement on amphetamine (Berman et al., 2009). When both drugs are tried, response rates may be as high as 85% (Dopheide & Plizka, 2009).

Given their substantial and reliable clinical benefit for treatment of attention disorders, it is not surprising that prescriptions for stimulants have increased dramatically in the last few years. Between 1998 and 2005, there was a 133% increase in amphetamine product prescriptions and a 52% increase in methylphenidate products, for teenagers and preteenagers in the US (Setlik et al., 2009). According to US government data, from 1998 to 2007, total amphetamine prescriptions increased by about 11.7 million, or 463% (Stix, 2009).

The increase in stimulant prescriptions has resulted in a corresponding escalation of illicit use, particularly in college students, confirmed by numerous survey results (Advokat et al., 2008; Arria & DuPont, 2010; Hall et al., 2005; McCabe et al., 2005; Rabiner et al., 2008; 2009a, 2009b; Rabiner et al., 2010; Teter et al., 2003; Teter et al., 2005; Teter et al., 2006; Weyandt et al., 2009; White et al., 2006; Wilens et al., 2008). Wilens and colleagues (2008) report lifetime rates of diversion ranging from 16 to 29%, with medical prescriptions being given, sold or traded by students. Studies consistently show that most students report using stimulant medications, legally or illicitly, to improve academic performance, specifically to increase concentration, organization, and the ability to stay up longer and study. Because the rationale for illicit stimulant use in undergraduates is usually stated to be improvement of academic performance, rather than recreational, it is not always considered to be as problematic as other types of drug abuse. Unfortunately, this is not necessarily the case, and the medical and legal consequences of illicit stimulant use may be underappreciated (Arria & DuPont, 2010; Arria et al., 2008; Arria et al., 2011).

The current escalation in stimulant diversion and misuse has initiated debate about the moral implications of using drugs to improve academic performance. Ethical discussions about taking drugs for 'cognitive enhancement,' have been the subject of several editorials

and commentaries (Farah et al., 2004; Greely et al., 2008; Harris, 2009; Monastersky, 2008), which confirmed the widespread use of these agents, especially among college students, professionals and academics. Often the term is used very broadly to include drugs "...that improve memory, concentration, planning and reduce impulsive behavior and risky decision-making..." (Sahakian & Morein-Zamir, 2007, p. 1157). Thoughtful proposals for the 'responsible use of cognitive-enhancing drugs' are espoused, calling for the scientific study of the expected risks and the benefits to be gained as well as the moral consequences of allowing broad access to pharmacological enhancement of mental capacities.

These developments led the Ethics, Law and Humanities Committee of the American Academy of Neurology (AAN) to release a special report, "Responding to requests from adult patients for neuroenhancements," (Larriviere et al., 2009). According to lead author, Dan Larriviere, "A growing number of patients without illness believe they can improve their memory, cognitive focus and attention span by taking neuroenhancement drugs and are asking for prescriptions." For the most part, these 'neuroenhancers' consist of stimulant drugs. "The drugs most commonly used for cognitive enhancement at present are stimulants, namely Ritalin (methylphenidate) and Adderall (mixed amphetamine salts), and are prescribed mainly for the treatment of attention deficit hyperactivity disorder (ADHD)." One of the strongest endorsements was expressed at the 60<sup>th</sup> Annual Conference of the Canadian Psychiatric Association in 2010 by Dr. Derryck Smith who presented a workshop on the subject and stated that psychiatrists should not hesitate to prescribe stimulants for neuroenhancement, if they wish. "We know they work....I think the effects of these medications are the same whether you have a medical diagnosis or not - they make everybody better" (Johnson, 2010).

These developments illustrate the fact that, because stimulants have been used effectively for decades to reduce hyperactivity, impulsivity and inattention in children, and now adults, with ADHD, it has understandably been assumed that the drugs enhance long-term intellectual performance. Although that would seem to be a reasonable conclusion, it turns out that the scientific evidence for this conclusion is less than compelling. Recent reviews (Advokat, 2010; de Jongh et al., 2008; Repantis et al., 2010; Smith & Farah, 2011) provide very little experimental support for stimulant-induced cognitive enhancement. deJongh (2008) cites a few research studies that found some improvement in acute memory task performance with amphetamine in individuals with a low memory baseline, "...while high-[memory]span subjects are either not affected or get worse" (p. 763). Similar results were summarized for methylphenidate, "With regard to MPH [methylphenidate], we were not able to provide sufficient evidence of positive effects in healthy individuals from objective tests" (Repantis et al., 2010, p. 204). A more detailed analysis of the scientific research on stimulant-induced cognitive effects in adults with and without ADHD (Advokat, 2010) also found little support for 'cognitive neuroenhancement' with these drugs. And recent articles in the *New Yorker* (Talbot, 2009) and *Scientific American* (Stix, 2009), describing the current resurgence of these agents confirm the modest intellectual benefit derived from their use in the 'real world.'

Accordingly, this selective review will discuss the evidence regarding cognitive effects of the two major stimulant medications, amphetamine (AMPH) and methylphenidate (MPH). We will emphasize information related to academic outcomes, incorporating some results of our own research on the neuropsychological and cognitive effects of stimulant medications

in college undergraduates, which show that these drugs do not reduce the academic disparity between ADHD-diagnosed and nonADHD-diagnosed students. We will discuss explanations proposed to account for the lack of cognitive improvement with stimulant drugs. Our goal is to shed some light on the apparent paradox of stimulant medications, namely: Why do drugs that acutely increase attention and concentration produce so little long-term intellectual benefit?

## 2. Academic achievement of children and adolescents with ADHD

The beneficial effect of stimulant drugs for classroom manageability of behavior-disordered children was first reported by Bradley (1937). During short, weekly, treatment periods he described increased productivity, comprehension and accuracy of the children, particularly in output of arithmetic problems. Since then, a vast literature has confirmed similar short-term benefits. These medications have been shown to acutely increase the quality of note-taking, scores on quizzes and worksheets, writing output and homework completion. The drugs "... reduce overactivity, restlessness and distractibility, enhance attention span or concentration and reduce impulsivity in responding to various tasks. Since a child who is attentive and better able to concentrate would presumably learn more from his classroom experiences, it should follow that these stimulant drugs would facilitate the scholastic performance of hyperkinetic children" (Barkley & Cunningham, 1978; p. 85). Nevertheless, it has been recognized for over 30 years that there is little evidence that these drugs improve the long-term academic achievement of ADHD diagnosed children.

Barkley and Cunningham (1978) reported in the first review of the topic, that in long term studies lasting at least one year (and as long as 5 to 10 years) the drugs had little impact on academic outcome. A substantial proportion of ADHD-diagnosed children were in special schools or classes, had failed one or more grades, had reading or arithmetic difficulty and were having problems sitting still and studying. The authors concluded that, in spite of various procedural differences among the published studies, the outcomes were the same – stimulant drugs had little impact on the "...long-term academic outcome or adjustment of hyperkinetic children. If the drugs contribute positively, they appear to reduce disruptive behavior rather than improve academic performance" (p. 89-90, italics added). The same conclusion was reached in a subsequent review by Gadow (1983) and almost 8 years later, another group (Swanson et al., 1991) acknowledged that "Even though it has been established that stimulants do improve *productivity*, it is still unclear whether stimulants alone improve long-term academic *achievement*, and, that... whether this widespread clinical practice has a long term beneficial effect on learning or academic achievement is still an open question" (p. 220). Carlson and Bunner (1993), incorporating the studies previously discussed by Gadow and Swanson concurred that stimulants facilitated acute academic *performance* of children with ADHD, but that long term treatment did not improve outcomes measured by the Wide Range Achievement Test (WRAT), the Peabody Individual Achievement Test (PIAT), the Stanford Achievement Test (SAT), and failed grades.

There is now substantial evidence for persistent academic underachievement and poor educational outcome in children and adolescents diagnosed with ADHD (Loe & Feldman, 2007). Children with ADHD have a consistently lower full-scale IQ than normal controls. They score significantly lower on reading and arithmetic achievement tests, use more remedial academic services, are more likely to be placed in special education classes, more

likely to be expelled, suspended or repeat a grade, compared with controls. By the time they reach adolescence, individuals with ADHD fail more grades have lower report card scores, lower class rankings, and worse scores on standardized achievement tests than “matched normal controls.” They take more years to complete high school, and have lower rates of college attendance and graduation. Subsequent investigations of long-term outcomes of children with ADHD have only confirmed these conclusions and verified the modest academic impact of stimulant medications (Advokat, 2009; Barbaresi et al., 2007a; 2007b; Galéra et al., 2009; Scheffler et al., 2009; Van der Oord et al., 2008).

Many investigators have considered possible reasons for this negative result, including the possibility that the stimulants might not affect the underlying cause of the academic dysfunction (Barkley & Cunningham, 1978). Gadow (1983) raised several issues in regard to the clinical use of the drugs. He discussed the possibility that doses required for behavioral control might be greater than needed to improve (and might actually worsen) cognition. He suggested that short-acting agents might wear off during a typical school day, such that information presented in the morning would be experienced while the child was under the influence of medication, while material presented in the afternoon might not be. He noted that the duration of treatment might not have been long enough to provide benefit for performance on achievement tests, because such tests assess concepts taught over several grade levels. He pointed out that previous studies did not take into account the contribution of co-morbid diagnoses, especially learning disabilities, the inclusion of different ADHD subtypes, or of non-responders. (However, as noted above, most patients do respond to stimulant medications if efforts are made to determine which drug would be most effective. A meta-analysis of the five studies in children that compared MPH to AMPH in blind crossover conditions found that about 37% of patients had a clearly better outcome on an amphetamine preparation, and 26% had a clearly better response to methylphenidate. The other 37% of stimulant responders could use either molecule with equal benefit, Greenhill et al., 1996).

### **3. Academic achievement of college students with ADHD**

During the last 30 years, special education and disability laws have been passed enabling a variety of qualified students with disabilities to graduate from college preparatory programs in high schools and enter colleges and universities. Specifically, the Americans with Disabilities Act (1990), the Individuals with Disabilities Education Act (1975) and Section 504 of the Rehabilitation Act (1973) mandated educational accommodation for students with disabilities, and more students with disabilities are now successfully completing high school and attending college. Students with “hidden disabilities,” which includes ADHD, have represented the greatest increase. Because these students don’t have to report to disability offices it is difficult to determine the prevalence of ADHD, but the best estimate is that 25% of students getting disability services do so because of ADHD and that 2% to 8% of the undergraduate population “self-report” ADHD symptoms (Weyandt & DuPaul, 2006; Wolf, 2001).

Because most ADHD-diagnosed adults do not obtain a college degree, it is possible that those who do successfully progress through a college curriculum might differ from those who do not attend, or do not complete college. In other words, adults with ADHD who meet admission criteria for postsecondary education might be less cognitively impaired

than those who don't. As noted by Frazier et al., (2007), not all ADHD-diagnosed individuals have academic deficits. Moreover, college students with ADHD might have more intellectual ability, better academic preparation and be able to compensate better than their non-collegiate cohort (Frazier et al., 2007). Such students might have developed a way to use stimulant medications more effectively, or to apply successful learning strategies, or both. If these individuals were able to benefit academically from stimulants it would be important to know how they did it. On the other hand, if the drugs are no more effective for this population than they were for elementary and high school students, it would be important to try to understand why they don't provide the expected intellectual advantage.

Moreover, the undergraduate population provides an excellent opportunity to evaluate some of the pharmacological explanations offered, in the past, for why stimulants did not improve academic outcome in children and adolescents. As noted above, one hypothesis was that the stimulant doses required to control the hyperactivity of ADHD-diagnosed children might be greater than doses that are most effective for improving cognition. However, unlike children, college students are less likely to be characterized as hyperactive, and more commonly diagnosed with, or to self-report, the symptom of inattention (Frazier et al., 2007; Norwalk et al., 2009; Rabiner et al., 2008; Schwanz et al., 2007) even without a specific diagnosis of ADHD (Lewandowski et al., 2008). Therefore, undergraduates should be able to determine the amount of stimulant medication that would presumably improve their attention and concentration without having to control hyperactivity as well.

Previous reviews of children had also speculated that perhaps the short-acting agents didn't provide sufficient coverage during a standard school day, and that daily variability in blood levels made it difficult to benefit from the intellectual advantages of the drugs. But duration of coverage is also less of a problem in undergraduate populations since long-acting formulations are now available, and regardless, college classes are usually not scheduled all day long. These considerations make arguments about dosage and variability of blood levels less persuasive, and would predict greater efficacy in the college population.

Furthermore, therapeutic use of stimulants in children usually involves administration primarily during the school day, so that drug effects wear off in the evening, perhaps while homework is being done, to allow for sufficient sleep. This is not necessarily how college students, or other adults, routinely use stimulants. Surveys report that undergraduates often use the drugs to stay up at night to study or complete other projects. That is, adults are able to choose when they take the drugs, which might also promote more effective cognitive outcomes.

The first review to describe the general academic functioning of college students with ADHD appeared only a few years ago and summarized results from 23 studies (Weyandt & DuPaul, 2006). They found that ADHD-diagnosed college students did not differ in IQ from those without ADHD, and were able to meet the demands of college courses. Nevertheless, they had significantly lower grade point averages (GPAs), reported more "academic problems," and were less likely to graduate from college. Students who self-reported high levels of ADHD symptoms used significantly fewer coping strategies compared with those who did not (see also Reaser et al., 2007). They were less organized and 'methodical,' they had less self-control and discipline, and they procrastinated more. On laboratory

administered neuropsychological tests they showed significant deficits in attention, but were not different from normal students on other measures, such as the ability to be flexible and to maintain performance as task demands were varied. There was also no difference between those with and without ADHD on computerized tasks that assessed divided attention. However, the role of medications in these outcomes was not determined "...it is unclear what effects medications have on academic, interpersonal and psychological outcomes among college students" (Weyandt & DuPaul, 2006, p. 14).

Since that review, numerous studies have reached similar conclusions. Some (Advokat et al., 2008; Advokat et al., 2011; Blase et al., 2009) have found significantly lower GPAs in ADHD-diagnosed college students relative to non-ADHD controls. Not surprisingly, higher levels of ADHD symptomatology are consistently associated with poor study habits, skills and academic adjustment, and greater self-reports of attention deficits (Norwalk et al., 2009; Schwanz et al., 2007). Recent surveys (Rabiner et al., 2008; 2009a; 2009b) show no difference between the ADHD-diagnosed undergraduates who used stimulant medications and those who didn't, in regard to self-reported concerns with their academic performance, problems of inattentiveness, hyperactivity, depression or their social life. In other words medication had no discernible effect in the transition to college of students with ADHD (Blase et al., 2009).

For the last several years, our laboratory has been conducting research in undergraduates with ADHD to try to understand the cognitive effects of stimulant medications (Advokat et al., 2007; Advokat et al., 2008; Advokat et al., 2011; Advokat & Luo, unpublished; Barrilleaux & Advokat, 2009). Given evidence that suggests there is a positive relationship between the Grade Point Average of undergraduates and their working memory (Gropper & Tannock, 2009) our efforts to clarify the cognitive actions of these drugs include studies of both, neuropsychological and academic performance of adult ADHD-diagnosed undergraduates.

### 3.1 Neuropsychological assessment of ADHD-diagnosed college students

Because inattention is a core symptom of ADHD, Barrilleaux and Advokat (2009) tested the effect of stimulant medications on attention with a repeated measures design, using the computerized, "Standard" version of the Conner's Continuous Performance Test (CPT). In this version, letters of the alphabet are presented one at a time for 250 ms and the respondent is instructed to press the space bar for every letter *except* the letter X. ADHD-diagnosed undergraduates ( $n = 13$ ), and those without ADHD ( $n = 17$ ), were tested twice on the CPT. For the ADHD-diagnosed participants one test was administered after they had taken their medication and the other when they were not on their medication.

The results are summarized in Figure 1, which shows the average number of commission errors, that is, responses made when they should not have been (when the letter X appeared). This kind of mistake is often viewed as a measure of impulsivity. The left side of the figure shows the mean number of commission errors for the Control Group, on the first session (open bar), second session (dark bar) and the average of the two sessions (light bar). The right side of the figure shows the mean number of commission errors for the ADHD Group when they were Medicated (dark bar) and Non-Medicated (light bar). Non-medicated ADHD-diagnosed adults made significantly more commission errors than

## Commission Errors

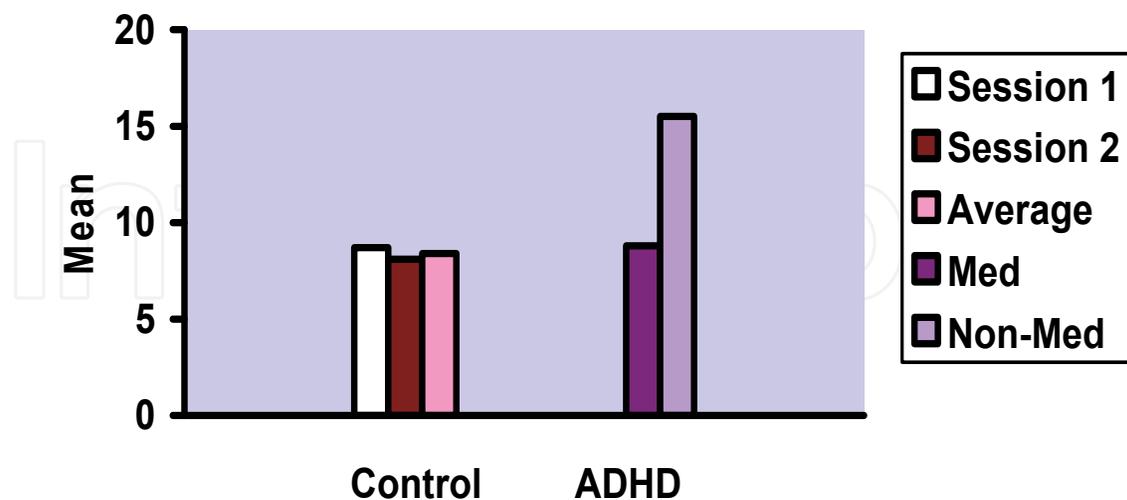


Fig. 1. Mean number of Commission Errors of Non-ADHD (Control) and ADHD-diagnosed undergraduates on the Continuous Performance Test (CPT).

controls; when medicated, they performed as well as controls and significantly better than when they were unmedicated. These data illustrate the typical, classic impairment of attention found in numerous studies of ADHD diagnosed individuals, and the improvement produced by stimulant medications.

In subsequent studies we assessed the effect of stimulant medications on several other neuropsychological tests. Unlike the CPT, performance on these tasks is influenced by practice; therefore, all of our other studies used a between-subject procedure. That is, in each experiment, three groups of undergraduate students were tested, one group without an ADHD diagnosis (Control), one group of ADHD-diagnosed students tested without medication (Off Meds) and one group of ADHD-diagnosed students tested while on their medication (On Meds). Several types of tests were administered, ranging from assessments of motor dexterity, verbal fluency, acquisition and retention of word lists, distractibility and problem-solving.

Motor dexterity was tested with a mirror-tracing task. Each participant was asked to trace the outline of a star shape, which was presented on a computer screen. Tracing direction was set to mirror-reversed, such that the participant had to move the cursor in the opposite direction to that of the pattern lines in order to trace the pattern. That is, the participants had to learn over successive trials to trace the star shape as if it was being shown in a mirror.

The results, summarized in Figure 2 below, showed no overall difference in latency among the three groups; all participants completed the task in the same amount of time. However, while the control group showed a significant decrease in latency across the five trials ( $p = .002$ ) the two ADHD groups did not (Advokat & Vinci, unpublished data). That is, unlike nonADHD students, the performance of ADHD-diagnosed students did not improve significantly regardless of whether or not they were on stimulant medication.

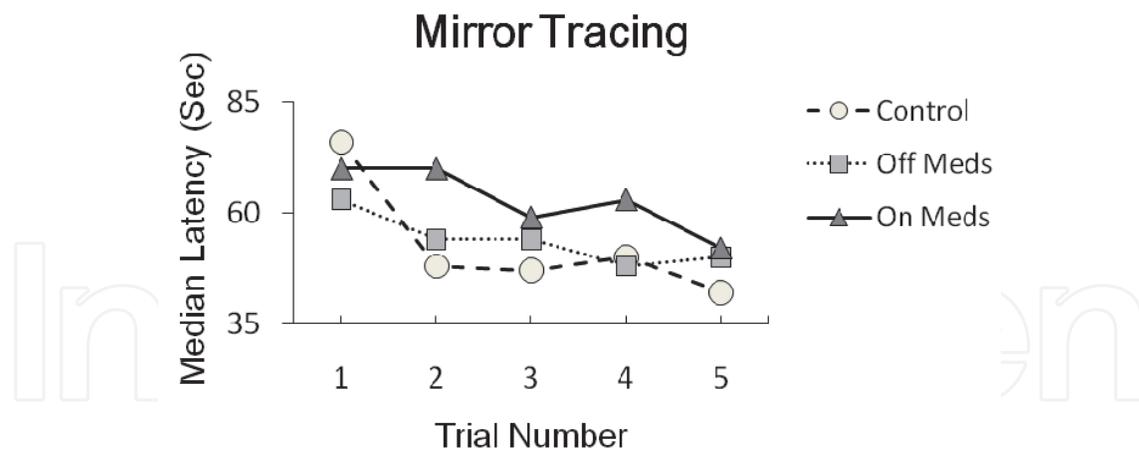


Fig. 2. Median latency of mirror-tracing across 5 successive trials, in 3 groups of college students: nonADHD (Controls) ( $n = 19$ ), ADHD-diagnosed students, tested without medication (Off Meds;  $n = 22$ ) and ADHD-diagnosed students tested when on their medication (On Meds;  $n = 22$ ).

Our result is reminiscent of a report by Tucha & Lange (2004) that medication worsened some aspects of handwriting in ADHD-diagnosed children. In that situation, the handwriting impairment was attributed to a drug-induced *enhancement* of attention. That is, the results were interpreted to mean that, when they were on their medication, children with ADHD paid so much attention to the writing process that it impaired the fluency of their handwriting movements. It is tempting to speculate that a similar phenomenon occurred in our ADHD-diagnosed undergraduates.

These observations show that although a decrease in behavioral activity is the most reliable effect of stimulant medications in ADHD, all types of behavioral activity are not reduced or improved by these drugs. ADHD-diagnosed children often show impairment in rudimentary motor function, including postural stability (Jacobi-Polishook et al., 2009), gait (Leitner et al., 2007), motor timing (Rubia et al., 2003) and other neurological reflexes (Stray et al., 2009), which is generally alleviated by stimulants. However, improvement is not always complete, or evident under all conditions. For example, Pelham et al., (1990) evaluated methylphenidate in boys with ADHD while they were playing a series of softball games. Although the drug improved the children's attention during the games, it did not affect their actual performance or skill.

There is a vast literature describing experimental efforts to determine the neurocognitive deficits associated with ADHD, and how they might be affected by stimulant drugs. While the technology and the conceptual models have become more sophisticated, progress has been modest. Recent analyses of stimulant effects on neurocognitive impairments in ADHD children (Doyle, 2006; Gualtieri & Johnson, 2008; Swanson et al., 2011) have essentially confirmed early observations (Robbins & Sahakian, 1979): stimulants are most likely to improve performance of ADHD diagnosed individuals in the domains of reaction time and processing speed, rather than in more complex functions requiring "...inhibition, working memory, strategy formation, planning and set-shifting" (Swanson et al., 2011, p. 211).

Several reviews have assessed neuropsychological functions in the adult population with ADHD (Frazier et al., 2004; Hervey et al., 2004; Schoechlin & Engel, 2005; Woods et al., 2002)

and shown modest, but inconsistent impairment. Furthermore, these deficits are also not always eliminated by stimulant drugs. Turner et al., (2005) tested ADHD adults, before and after methylphenidate, on attention tests and one memory task, and did not find improvement. Müller et al., (2007) reported that medicated ADHD adults were still impaired, relative to controls, on several neuropsychological measures such as the Tower of London test of 'planning ability,' and the Stroop test of 'distractibility.' Kurscheidt et al., (2008) reported retrospective results of 34 patients on chronic methylphenidate. Compared to baseline, the drug significantly improved attention and 'verbal memory performance' after months of treatment - while other tasks were not affected. Tucha et al., (2011) reported differences between nonADHD and ADHD-diagnosed adults on the Tower of London task and one that measured verbal fluency. In this case, MPH did improve performance of ADHD adults on the Tower of London, but not on the verbal fluency task. Biederman et al., (2008b) administered a battery of tests to non-ADHD subjects and separate groups of ADHD patients who were either on or off medication. They found the largest beneficial effects on sustained attention (vigilance) and verbal learning, whereas stimulants did not significantly improve measures of interference (i.e. distractibility) or processing speed (on the Stroop test).

We recently conducted a study of the most commonly used neuropsychological tasks in our undergraduate population, including a verbal fluency measure, the Tower of London planning task and the 'distractibility task,' the Stroop test. The only significant difference among the groups was on the Stroop test. This test involved three sets of stimuli, presented on a computer screen. The word reading stimuli consisted of three color words (blue, red, and green) in black ink, which the participant read aloud. In the color naming test, the stimuli were a series of five Xs (i.e., XXXXX) in all blue, all red, or all green ink, and the participant read aloud the ink color. Finally, in the incongruent color naming stimulus set (interference condition), stimuli consisted of the color words blue, red, and green printed in an incongruent color. The participant had to name the color of the *ink* in which the word is printed, not the word color.

We found modest, but statistically significant differences on two measures of the Stroop test. As shown in the top half of Figure 3, below, on the Stroop Interference test, the Control (n=35) and ADHD (On Med) groups (n=36) reacted significantly faster than the ADHD (Off Med) group (n=33). Part B shows that the Control group made slightly, but significantly, fewer mistakes (was more accurate) than the ADHD (Off Med) group, while the ADHD (On Med) group did not differ from the other two groups.

These data are consistent with other studies showing first, that adults (Johnson et al., 2001; King et al., 2007; Murphy et al., 2001; Rapport et al., 2001) as well as children with ADHD (Bedard et al., 2002; Prehn-Kristensen et al., 2011), are impaired on the Stroop interference measure compared to control populations. Second, Biederman et al., (2008b) showed that medication did not normalize Stroop interference control in young adults with ADHD. In our study, the Interference RT of the On Med group *was* normalized. Yet, the Interference *accuracy* of the On Med group, although improved, was still not significantly different from either of the other two groups. Considering the small absolute difference in magnitude, it is surprising that the drugs did not fully eliminate the accuracy deficit along with the RT deficit. One possibility is that the reduction in RT increased impulsivity, which might have impaired a corresponding improvement in accuracy.

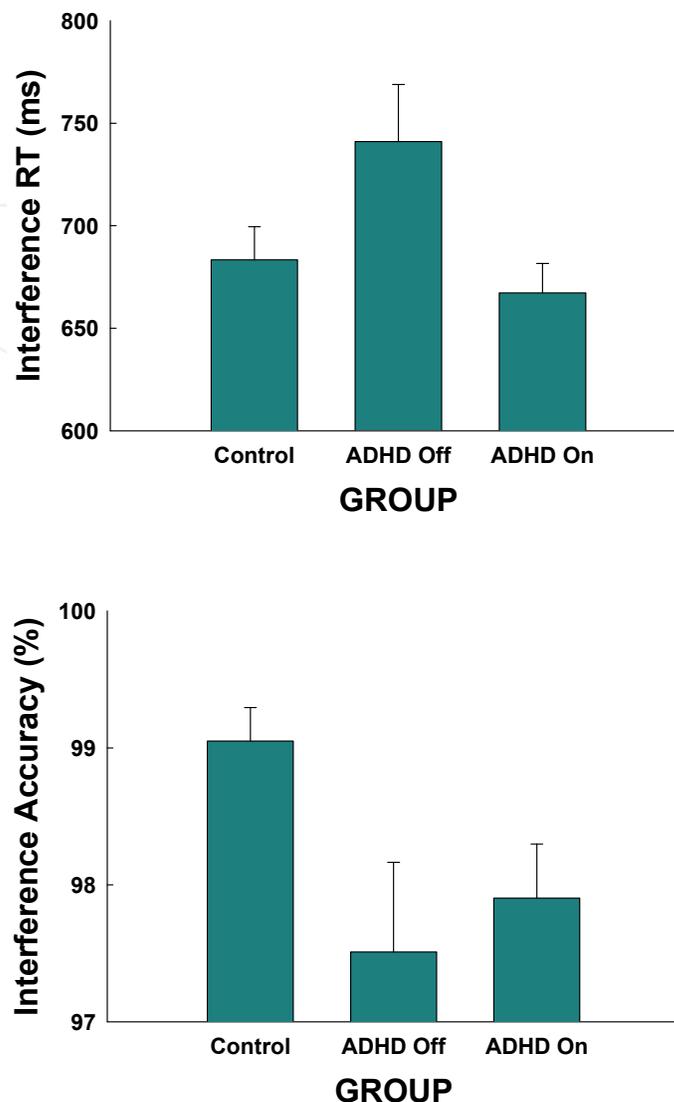


Fig. 3. Top: Stroop Interference Reaction Time (RT - milliseconds). The Control group (n=35) and ADHD (On Med) group (n=36) reacted faster than the ADHD Off Med group,  $p < 0.05$  (n=33). Bottom: Stroop Interference Accuracy. The Control group made fewer mistakes than the ADHD (Off Med) group in interference,  $p < 0.05$ , and the ADHD On Med group did not differ from the other two groups. Bars represent standard error of the mean.

In brief, our results showed that undergraduate students with ADHD did not show significant deficits in verbal fluency or planning ability, compared to normal students. The only statistical effects occurred in the Stroop test, and the absolute differences were extremely small. Even so, while medications improved the performance of ADHD students they did not eliminate the deficit, nor did they help ADHD students perform better than normal students in domains of functions where no deficits were found. It is possible that more differences might have been seen in measures other than the Stroop test, if the groups were larger. However, our group sizes were comparable to those typically used. A more likely possibility is that our ADHD population may have had less severe symptomatology than participants in other studies, cited above, who appeared to be clinic patients.

Although research shows practically no cognitive benefit of either methylphenidate or amphetamine on acquisition (Advokat, 2010), there is some evidence that stimulants might improve *retention* of previously acquired information (Izquierdo et al., 2008; Soetens et al., 1993; 1995; Zeeuws & Soetens, 2007). In a series of experiments by Soetens and colleagues, nonADHD adult males received placebo and amphetamine, in a within-subject experimental procedure. After each drug, participants were asked to study word lists and were tested at various times afterward to assess how many words they could recall. The first test took place immediately after presentation of each of 10 word lists, the next test was given at the end of each daily session (after all the lists), and other tests were given after 1 hour, after 1 day, and after 3 days.

There was no drug effect after immediate recall or at the end of the daily session, that is, no effect of amphetamine on *acquisition* of the words. But there was a significant effect of amphetamine on recall 1 hour after the end of the session, and at 1 and 3 days later. These results were interpreted to mean that although amphetamine did not improve learning (acquisition), it facilitated the *consolidation* of information that had already been learned, and that the beneficial effect on consolidation was responsible for the improved retention of the words at 1 hour and 1 and 3 days later. The term 'consolidation' refers to the process by which memory undergoes a change from the short-term, labile, form to a long-term, stable form.

We attempted to replicate this phenomenon in our undergraduates. Although we could not administer stimulant drugs to nonADHD participants, it was possible that ADHD students might have a memory impairment that could be reduced by stimulants. In our study, participants from each of the three experimental groups viewed five sets of ten words. After each list of 10 words the participants were asked to write down as many words as they could remember (Test 1). After the fifth set of words was presented, participants were 'distracted' by performing a second behavioral task (the mirror tracing task, discussed above). Following the mirror tracing task, participants were asked to write down as many of the 50 words as they could remember (Test 2). Last, participants were contacted on the next day and asked a third time to recall as many words as they could remember from the word lists (Test 3). As shown in Figure 4, below, there was no difference among the groups. ADHD students did not differ from nonADHD students in regard to acquisition or retention of the word lists at any time point, regardless of whether or not they were on medication during the test.

In summary, our assessment of neuropsychological function in undergraduates with ADHD showed the expected impairment on the classic, CPT test of attention, which was normalized with stimulants. We also observed a previously unreported motor deficit (on the mirror tracing task), which was not improved by stimulants. We saw two types of deficit in the Stroop test of 'distractibility,' namely, a slower reaction time, corrected by stimulants, and a very slight impairment in accuracy, which was not eliminated by stimulants. These results are consistent with the literature, and illustrate the counterintuitive nature of stimulant effects in ADHD. That is, although cognitive processing speed and basic aspects of attention are normalized, even slight deficits in 'distractibility' are not eliminated. Finally, although we did not replicate the memory improvement that had been shown in nonADHD adults with amphetamine, we also did not see any deficits in that task in our ADHD students. It is appreciated that because they were college students, our ADHD population might have had very mild symptoms and were perhaps not representative of the typical ADHD adult. We could not confirm their diagnoses. However, if that was the case, we would not expect them to

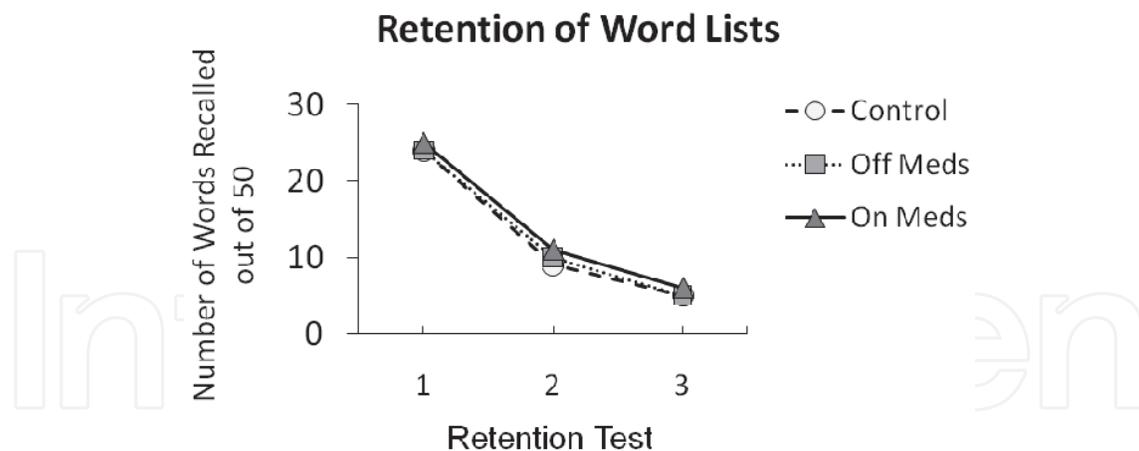


Fig. 4. Retention of word lists in nonADHD students (Control), ADHD students, who were tested when they were not on medication (Off Meds) and ADHD students who were tested when they were on their medication (On Meds). Retention was tested immediately after each list of 10 words (Test 1), about 20 minutes after the 5 lists (Test 2) and 1 day after the 5 lists (Test 3). There was no difference among the groups in the number of words recalled on any test.

be academically impaired, relative to their nonADHD counterparts, especially considering that the stimulants exert the same types of effects in those with or without the diagnosis. The data obtained regarding academic performance, discussed below, show that that is not the case.

### 3.2 Academic performance of ADHD-diagnosed college students

The ADHD-diagnosed undergraduates we tested showed very little neurocognitive impairment. Perhaps the fact that they had successfully entered college meant either that they had less severe symptomatology or that they were able to gain some academic benefit from the stimulants (or both). If the latter, it would be important to find out how, so that their strategies could be broadly implemented. On the other hand, in view of growing concerns about escalating abuse and diversion of stimulant drugs, it would be equally important to know if these medications did not provide any academic advantage for ADHD-diagnosed undergraduates.

In these investigations we compared the self-reported drug use (both licit and illicit), study habits and strategies of ADHD-diagnosed and non-diagnosed undergraduates. We administered questionnaires to find out if there was a substantial difference in how these two groups approached their schoolwork, and, if there was any corresponding difference in their respective Grade Point Averages (GPA) and other measures of academic achievement.

In the first study (Advokat et al., 2008) we asked about the legal use of prescription stimulants by undergraduates diagnosed with ADHD, and compared that with illicit use by students without the diagnosis.

A total of 1550 undergraduate students completed at least part of the survey, with 163 (10.5%) of these students reporting a diagnosis of ADHD (the ADHD Group). Among the remaining 1387 respondents, 591 (43%) reported that they used stimulant medications without a prescription (the No ADHD, Illicit Use group) while 794 (57%) stated they did not use stimulant medications illicitly (the No ADHD, No Illicit Use group).

As shown in Figure 5, the three groups differed significantly in response to the question: “Do ADHD medications help academic performance,” in that a significantly greater proportion of the ADHD, and No ADHD Illicit Use groups, endorsed this statement compared with the No ADHD No Illicit Use group. The fact that a majority of illicit users endorsed this statement supports the conclusion that the drugs were primarily used as study aids. For that matter, a surprising 12% of illicit users in that study reported that they believed they also had ADHD. That might even be true, but we have no way of verifying that assumption.

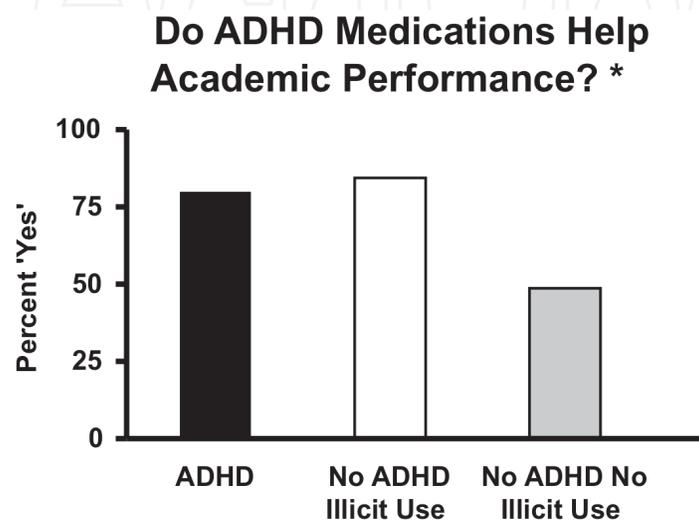


Fig. 5. Percent of undergraduates who agreed with the statement “Do ADHD Medications Help Academic Performance.” \*Significantly fewer students in the No ADHD No Illicit Use group endorsed this statement compared to each of the other two groups.

Figure 6 shows that the same groups also differed significantly in GPA, in that the GPA of the ADHD group (3.05, out of a possible 4.0) was significantly lower than that of the No ADHD Illicit Use group (3.15) and the No ADHD No Illicit group (3.19).

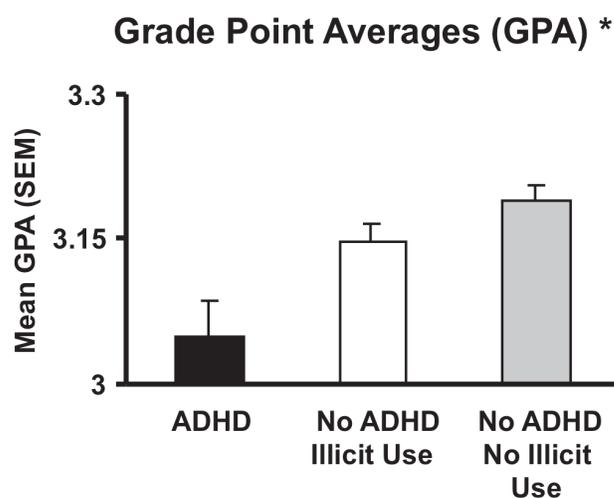


Fig. 6. Mean Grade Point Average (GPA) of each of the three groups. \* The GPA of the ADHD group (3.05, out of a possible 4.0) was significantly lower than that of the No ADHD Illicit Use group (3.15) and the No ADHD No Illicit group (3.19).

It should be noted that we cannot tell from these data how many students in the ADHD group actually used stimulant medications. Nor can we tell if the GPA of both groups that used stimulant drugs would be even lower if those students didn't use the drugs. That is, we can't tell if the drugs were effective, either because they worked or because the students believed the drugs worked.

Last, Figure 7, below, summarizes reported recreational drug use of Tobacco, Alcohol, and Marijuana of these same groups. In each case there was a significant difference among the groups in frequency of drug use. For each drug, post-hoc comparisons indicated that a greater percent of the No ADHD Illicit Use and ADHD groups used these drugs compared with the No ADHD No Illicit Use group. Only in the case of alcohol did the ADHD group use less than the illicit stimulant users, although they still drank significantly more frequently than those who didn't use stimulants illicitly.

Overall, recreational drug use in our student sample was very modest. Nevertheless, the significant difference between ADHD-diagnosed and Non-diagnosed-non-stimulant users was unexpected, and we can only speculate about the reasons for this result. First, perhaps, believing that their symptoms are effectively controlled by stimulant medications, these students feel they are able to use other drugs responsibly. Second, because of the impulsiveness that often characterizes ADHD, these young adults might not be able to inhibit other drug use, especially if the drugs are offered in the social context of a party, or other nonacademic environment, when students might not be using their stimulants "medically." Third, considering that alcohol and marijuana are sedating, ADHD students might use them to counteract the stimulatory effect of the medications, that is, to help them relax or go to sleep. It is also possible that those with ADHD (and nonADHD, illicit users) have comorbid conditions (such as conduct disorder) or other risk factors that increase use.

These data show that, although the GPA of the ADHD students was significantly lower than that of the nonADHD-Illicit users, both groups endorsed significantly greater recreational drug use than students who did not use stimulant drugs illicitly. Unfortunately, we can't tell from these data if perhaps ADHD students were more vulnerable than nonADHD students to a detrimental effect of recreational drugs on academic performance, or if both groups might have had a better GPA without such use.

Our results showed that a majority of ADHD diagnosed students (and many without the diagnosis) believed that stimulants improved academic performance. And although the GPAs of ADHD students were statistically lower than those of nonADHD students that did not mean the stimulants didn't help. The aim of our next study was to find out more about the influence of stimulant medications on academic outcome. We surveyed the self-reported study habits and strategies of ADHD-diagnosed and non-diagnosed undergraduates, to determine if they differed in response to the academic demands of the college curriculum (Advokat et al., 2011).

A total of 143 students without ADHD (Control group) and 92 students with an ADHD diagnosis (ADHD group) completed the survey. The average age of the two groups, approximately 21 years, did not differ, and most participants in each group were Caucasian (81.8% and 89.1% for Control and ADHD, respectively), although there were significantly more males in the ADHD group (38% compared to 17.5%).

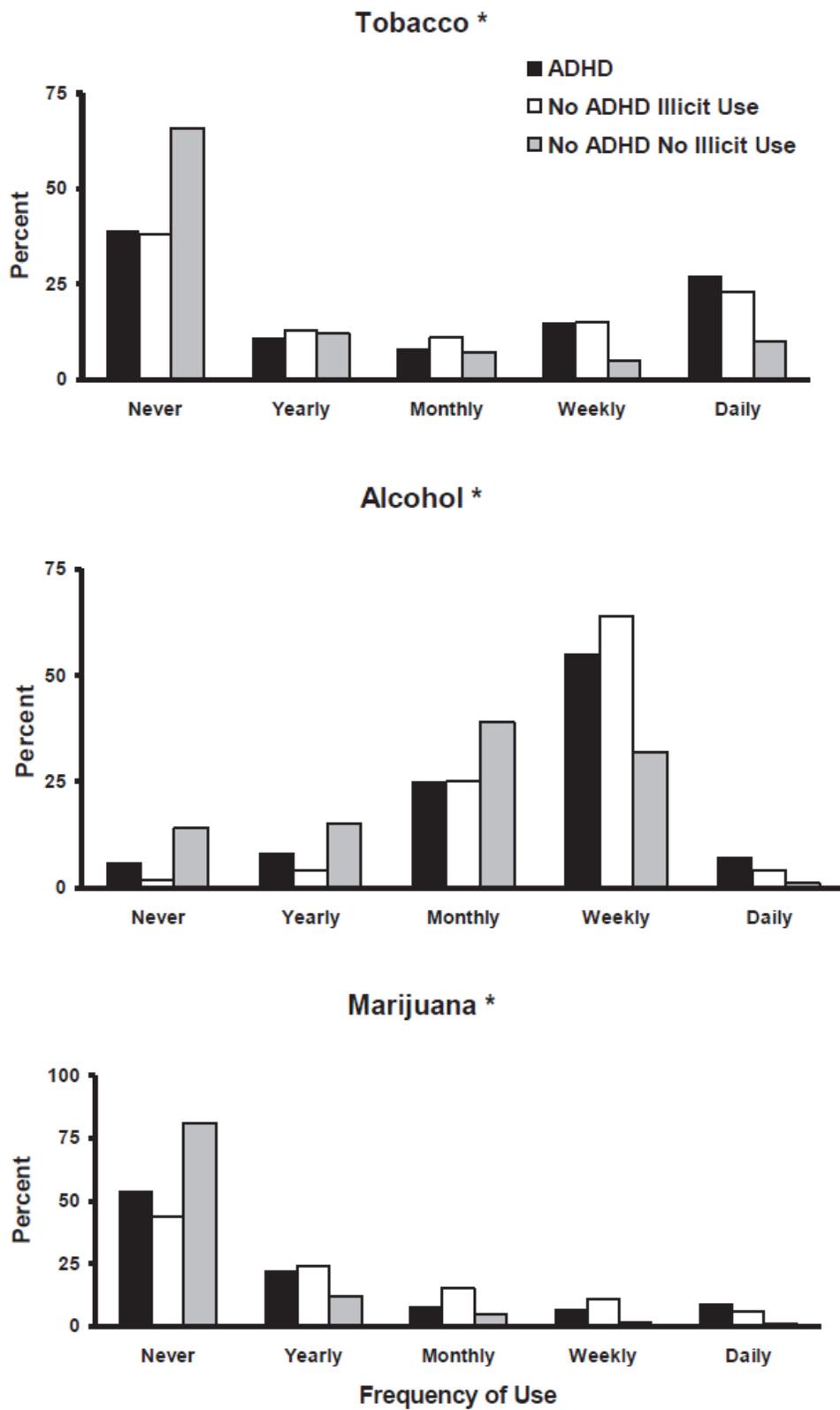


Fig. 7. Percent of respondents in each group as a function of the frequency with which they used tobacco, alcohol and marijuana. \*In each case, the ADHD and the No ADHD Illicit Use groups endorsed significantly more use than the No ADHD, No Illicit Use group. The ADHD group also used alcohol significantly less than the No ADHD Illicit Use group.

The average age at which the ADHD participants received the diagnosis was between 15 and 16 years, about 5 years before entering college. While nearly 98% of this group had taken ADHD medication, only 78.3% (72 respondents) were currently using the drugs, while 19.6% (18 respondents) stated that they were not currently taking the medications. When asked why they might not be taking stimulant medications, the majority cited the problem of side effects. Although specific side effects were not always mentioned ("I did not like the way it made me feel; ...make me feel crappy; the negative side effects outweigh the positives"), some individuals cited headaches, irritability, temporary heart rate elevation, nausea, sleep interference and 'antisocial' feelings as examples of undesirable reactions. Five in this subgroup also stated that they either didn't need the drugs anymore, or, they wanted to see if they didn't need them anymore.

Similar to the previous study, more than 90% of the students with ADHD endorsed the statement that medications helped them academically. Most of them stated that the drugs helped them to focus or to concentrate better i.e. pay attention, stay awake, and organize their studying. However, relatively few students ( $n = 6$ ) with ADHD specifically stated that they took medication to avoid distractions.

With regard to academic performance, Control and ADHD students took the same amount of Advanced Placement Credits (an average of 8.1 for the Controls and 6.7 for ADHD students). For those few in each group who took the SAT (Scholastic Aptitude Test, a national exam sometimes required for college admission), there was no difference in their self-reported SAT scores. They did not differ in the number of scholarships awarded, were enrolled for the same number of semesters (between 6 and 7), took the same number of credits per semester (about 14.5), and studied the same number of hours per week (about 9.5 to 10.5).

These two groups also did not differ statistically on many of their answers to questions about study habits. The same proportion of both groups believed that they studied "about the same as" other students and that the quality of their class notes was either "better" or "the same" as those of other students. The same proportion in each group did not review their notes either before or after class, and only "sometimes" read assigned reading before class. About three-quarters of each group stated that they were "somewhat accurate" at predicting how well they did after exams. The fact that there was no statistical difference between nonADHD-diagnosed students, and those with ADHD in response to these questions suggests that the diagnosis did not seem to promote better study habits in the ADHD group.

However, the Control and ADHD groups did differ on several academic variables, as shown in Table 1. (Although the values of ADHD students who stated that they did not take stimulant medications are shown for some of the variables, the statistical results are based on a comparison between Control and all ADHD students).

As in our previous report, the college GPAs of ADHD students were statistically lower than that of the Controls. In this study we also found that ADHD students had a significantly lower high school GPA and ACT score than Controls. Although small, this difference was detected in spite of the fact that a minimum high school GPA and ACT score were required for admission to the university. The table also shows that ADHD students were significantly more likely to withdraw from a class, to say that they were worse than other students at planning for and completing class assignments, frequently taking class notes, studying ahead of time for exams and avoiding distractions.

	Control (n) (N = 143)	ADHD (n) (N = 92)	ADHD No Meds (n = 18)	P **
High School GPA	3.55 ± 0.47 (141)	3.38 ± 0.43 (89)		0.006
College GPA	3.12 ± 0.49 (142)	2.94 ± 0.44 (91)	2.90 ± 0.46	0.006
ACT Score	25.45 ± 5.2 (124)	24.1 ± 3.0 (80)	24.6 ± 2.61 (16)	0.032
Times Withdrawn from a Class	1.6 ± 1.7 (139)	2.3 ± 2.4 (89)	3.28 ± 3.89 (18)	0.008
Planning for class assignment				<0.001
Better	32.9 (47)	26.1 (24)	27.8 (5)	
Worse	13.3 (19)	35.9 (33)	38.9 (7)	
About the same	53.8 (77)	38.0 (35)	33.3 (6)	
				<0.001
Completing class assignment				
Better	33.6 (48)	30.4 (28)	33.3 (6)	
Worse	2.1 (3)	19.6 (18)	22.2 (4)	
About the same	62.9 (90)	47.8 (44)	44.4 (8)	
Frequency of note-taking				0.002
Nearly every lecture	82.5 (118)	63.0 (58)		
Sometimes	16.1 (23)	27.2 (25)		
Read someone else's notes	1.4 (2)	5.4 (5)		
Neither take notes nor read other's notes	0	4.3 (4)		
				0.011
When you study for an exam do you				
Study well before the exam	39.2 (56)	25 (23)	16.7 (3)	
Study in the day or two before the exam	60.1 (86)	69.6 (64)	83.3 (15)	
Both situations could happen	0.7 (1)	5.4 (5)		
Avoiding distractions while studying				<0.001
Better	16.8 (24)	16.3 (15)	11.1 (2)	
Worse	33.6 (48)	64.1 (59)	66.7 (12)	
About the same	49.0 (70)	18.5 (17)	22.2 (4)	

\* Unless otherwise indicated, scores are percent; \*\* p values are for Control vs all ADHD respondents  
GPA and ACT scores are all self-reported

**Table 1. Academic Variables That Differed Between Controls and ADHD-Diagnosed College Students \***

These results show that Control and ADHD-diagnosed students differ in some of their self-reported study habits. But these data alone don't tell us if these endorsements are relevant to the academic achievement of either group. In other words, we didn't know if the statistically significant differences in professed study habits were related to the respective GPAs. We

therefore analyzed the answers to some of the questions on which the two groups differed as a function of GPA. The results are summarized in Table 2.

There were significant differences within the groups on several measures. Control students who stated they were 'better' at planning and completing assignments, took 'frequent' notes in class and 'avoided distractions,' had higher GPAs than those who said they weren't, suggesting that their judgments were accurate. However, the GPA of Control students did not differ as a function of whether or not they said that they studied 'ahead of time' or just days before an exam. In other words, Control students did not 'pay a price' in GPA for waiting until a few days before exams to study. In contrast, the GPA of ADHD students who stated that they studied 'well before' an exam, was significantly higher than the GPA of those (the majority of this group) who said they studied in the 'day or two' before an exam. Unlike Control students, ADHD students did 'pay a price' for waiting until the exam was imminent before they began to study. This difference seemed to epitomize a fundamental behavioral impairment in ADHD, so we examined it further.

Variables	Control	ADHD
Planning for class assignment	*	*
Better	3.26 ± 0.43 (46)	3.09 ± 0.39 (23)
Worse	2.92 ± 0.52 (19)	2.79 ± 0.41 (33)
About the same	3.06 ± 0.50 (77)	2.93 ± 0.48 (35)
Completing class assignment	*	*
Better	3.30 ± 0.44 (48)	3.04 ± 0.42 (28)
Worse	2.49 ± 0.82 (3)	2.67 ± 0.39 (18)
About the same	3.02 ± 0.47 (90)	2.97 ± 0.46 (43)
Frequency of note-taking	*	NS
Nearly every lecture	3.13 ± 0.46 (117)	3.0 ± 0.46 (57)
Sometimes	3.06 ± 0.57 (23)	2.86 ± 0.42 (24)
Read someone else's notes	2.25 ± 0.35 (2)	2.76 ± 0.39 (5)
When you study for an exam do you	NS	*
Study well before the exam	3.12 ± 0.48 (56)	3.16 ± 0.35 (22)
Study in the day or two before the exam	3.10 ± 0.50 (86)	2.86 ± 0.47 (64)
Avoiding distractions while studying	*	NS
Better	3.30 ± 0.51 (24)	3.0 ± 0.44 (15)
Worse	2.91 ± 0.50 (48)	2.88 ± 0.46 (58)
About the same	3.18 ± 0.69 (69)	3.07 ± 0.40 (17)

\*  $p < 0.05$ , for GPAs within each of the 2 groups, as a function of their answers to each question

Table 2. Factors Affecting College GPA ± SD (n) of Control and ADHD-Diagnosed Students

Because we had asked the students if they were taking ADHD medications, we could distinguish between those ADHD students who said they did ( $n = 72$ ) from the smaller group, who said they didn't ( $n = 18$ ). The existence of these subgroups allowed us to compare the GPA of ADHD students who did or did not take the drugs, as a function of

whether or not they studied ahead of time for exams. This resulted in 4 groups, with the following GPAs ( $\pm$  Standard Errors): Those who took the medications, and did not study ahead of time ( $n = 47$ ),  $2.88 \pm 0.48$ ; those who used the drugs and did study early ( $n = 19$ )  $3.15 \pm 0.35$ ; those who did not take the medications, and did not study ahead of time ( $n = 15$ ),  $2.84 \pm 0.47$ ; and those few who did not take the drugs but did study early ( $n=3$ )  $3.19 \pm 0.36$ . A two-way analysis of these GPAs found no effect of medication, but a statistically significant effect of study interval, ( $F = 4.06$ ,  $p = .047$ ).

This preliminary analysis showed that, if ADHD students utilized the well-known strategy of studying ahead of time for exams, they could overcome their achievement deficit, *even if they didn't take stimulant medications*. In spite of the fact that only 3 students 'studied ahead of time' without using the drugs, their GPA was comparable to that of the 19 undergraduates who did take the drugs in addition to using good study habits. Obviously this outcome needs to be validated in a larger group of individuals. But, the data suggest the optimistic implication that the GPA disparity between ADHD and nonADHD students could be eliminated if ADHD students were able to develop well-established study habits.

Unfortunately, it is not clear from these data alone if taking stimulant medications actually helps ADHD students to develop beneficial study habits. That is, do the stimulant drugs help students to plan ahead, e.g., to begin studying ahead of time so that they can compensate for their cognitive deficit? If so, why didn't this behavior occur in more of the ADHD students?

These data provide preliminary empirical evidence that, as with elementary and high school students, adult college students with ADHD are less likely to reach the same academic level as their non-ADHD counterparts, even when they use stimulant medications. Stimulants do not necessarily normalize academic achievement, even when they can be administered at the most appropriate doses and durations for maximum efficacy, and, even in a population that is considered to be less intellectually impaired than the typical adult with ADHD.

It should be noted that even those ADHD students who did not engage in good study habits were not failing. Their average GPA was just above a 'C,' which means they were able to progress towards graduation at a normal pace. On the other hand, the absolute difference between the GPAs of ADHD students and Control students was not very large, only about a third of a grade. Yet this difference was consistent, and it is surprising that the stimulants were not more effective in narrowing the gap. Why aren't the stimulant medications more cognitively effective?

#### 4. Discussion

In their consideration of this question, Barkley and Cunningham (1978) raised the possibility that the problem with stimulant medication might be that it made hyperactive children less aware of their environment, perhaps more intellectually 'constricted' and rigid and less inquisitive or interested in learning. Similarly, Gadow noted that stimulant drugs might produce 'cognitive perseveration,' akin to amphetamine-induced stereotypies (that is, the repetitive performance of an invariant behavioral sequence). Subsequently, Carlson and Bunner (1993) proposed the term 'cognitive toxicity' to describe this same hypothesized phenomenon.

Robbins and Sahakian (Robbins & Sahakian 1979; Sahakian & Robbins, 1977) provided an insightful discussion of this point, proposing that stimulant-induced stereotypy might play a role in the behavioral effect of the stimulants. They noted that, "...although stereotypy may improve performance in certain situations, perhaps by focusing or channeling "attention," it may also lead to impairments when behavioral flexibility is required" (p. 944). Their review summarized results of numerous studies in ADHD-diagnosed children, including activity measures and complex motor tasks, cognitive tasks, intelligence tests, verbal fluency and language tests, and attention and vigilance tests. Across all these categories, the greatest improvement from stimulants was seen in activity tests (measured with photo cells, actometers and stabilimetric apparatus') and the least amount of improvement occurred in the problem-solving test category.

Subsequently, these researchers obtained evidence for stimulant-induced 'cognitive perseveration'. They conducted a study in children who had been on methylphenidate for 4 to 29 months (Dyme et al., 1982). Each child was tested 3 times, first, under a 'no drug' practice condition, then on two trials of either placebo or drug (1 mg/kg). The tasks included a test of 'flexibility of thinking,' the Wisconsin Card Sort Test (WCST), involving a set of response cards which could be sorted according to color form or number. Subjects were not told which variable was correct for sorting, only when the choice was right or wrong; they had to figure it out for themselves. After 10 cards were sorted correctly the examiner changed the sorting variable without telling the subject who then had to determine the new 'correct' sort. Subjects were scored on the number of errors as well as correct cards sorted. 'Perseverative Errors' were mistakes in which the subjects sorted according to a prior category after they had already been told that sort was "wrong."

The results showed that although all children improved their speed or performance on measures of attention, none improved on this flexibility measure and most got worse. This result has since been replicated (Tannock & Schachar, 1992), although not in all cases (Swartwood et al., 2003). Moreover, Tannock and Schachar (1992) found that this impairment recovered rapidly (that is, tolerance developed).

Nevertheless, consistent with the WCST data, Schroeder et al., (1987) found that methylphenidate impaired performance of 15 normal male volunteers, 18 - 40 years old, on a unique procedure. "The task was an arcade-like game called Telekinesis Star Wars, which was highly engaging., as opposed to the more monotonous tasks commonly used in these neuropsychological studies." Several measures were obtained from the subject's performance in this game, which reflected the strategies used by each player, and indicated if they were improving or not. In each case, the data showed that subjects given methylphenidate, at doses of 0.15 or 0.30 mg/kg, were *poorer* than controls at improving their performance throughout the test session. Drug-treated subjects did not develop "adaptive problem-solving strategies selected by controls."

Similarly, Burns et al., (1967) also described a learning task that was worsened by amphetamine. Subjects were seated in front of 8 lights, each placed above a key that controlled one of the lights. The subjects "had to learn which single key was the correct response to each [of 8] light[s] when the keys were randomly assigned, except that the correct button was never in front of the light associated with it." The session consisted of 840 trials balanced for frequency of light/key pairings. In this situation, the d-amphetamine group showed a significantly *slower* rate of learning than the placebo group. Such results

suggest that, due to their profound effects on attention, stimulants may impair adaptive problem-solving ability, perhaps by inducing perseverative behavior.

Similarly, because attentional 'overfocusing' and creativity may be inversely related, there has been concern that stimulants might decrease creativity in people using the drugs for cognitive enhancement. Several studies have explored this possibility, mostly in children, with mixed results. Swartwood et al., (2003) found that MPH actually worsened the scores of ADHD-diagnosed children on a battery of tests assessing 'divergent thinking,' relative to their nondrug tests. Funk et al., (1993) saw no effect of methylphenidate on a test battery of 'creative thinking,' in young boys, relative to a nonADHD comparison group. Solanto and Wender (1989) also reported that methylphenidate maintained 'divergent thinking' in ADHD-diagnosed children when the children were tested over several days, relative to the decline that occurred on nondrug days. And Douglas et al., (1995) found that "... MPH doses up to 0.9 mg/kg had an increasingly positive effect on measures of mental flexibility and other cognitive processes" in 17 ADHD children.

To our knowledge, there are no studies of stimulant effects on creativity in ADHD adults. However, Farah et al., (2008) examined the effect of amphetamine in 16 nonADHD adults on four tests of creativity, "two tasks requiring divergent thought and two requiring convergent thought (p. 542)." Only performance on the convergent tasks was affected, and the effect depended on baseline performance. The results suggested that people who are already very creative might be unaffected or even impaired, whereas those who were not very creative to begin with might improve with stimulants. It remains to be seen however whether ADHD-diagnosed adults (or even children for that matter) are actually less 'creative' than their nonADHD cohorts.

Stimulant-induced perseveration and impairment of cognitive flexibility (creativity) have been the most commonly proposed reasons for why these drugs produce so little long-term cognitive benefit. But, stimulants are also sympathomimetics, that is, they produce the same effects as the sympathetic transmitters that mediate arousal and alertness. This physiological action is rarely discussed in regard to ADHD, perhaps because stimulants are used therapeutically to decrease rather than increase behavioral activity. But arousal is known to have significant effects on memory; moderate levels of arousal enhance memory while too much arousal impairs memory.

Recent studies of Brignell and colleagues (Brignell et al., 2006; 2007) illustrate the possible relevance of this approach. In one study, separate groups of subjects were given either placebo or methylphenidate while undergoing classical conditioning of a skin conductance response. Methylphenidate did not impair conditioning; the subjects who received the drug did acquire the conditioned response. However, the drug increased the number of responses to both, the non-conditioned stimulus and conditioned stimulus, compared to the placebo group. This was described as a "general pattern of methylphenidate-induced arousal increasing propensity to respond." It was concluded "methylphenidate decreased responses to highly arousing stimuli and increased responses to the less arousing stimuli (512)."

A second study suggests that this phenomenon might be relevant to the issue of stimulants and cognition. In this case, subjects were presented with a series of slides that were designed to tell a story that included a very 'emotional' component. One week later the participants

returned to answer multiple choice questions about the story. Placebo-treated subjects showed the expected enhancement of memory for the emotional slides, relative to the neutral slides. But methylphenidate-treated subjects did *not* show this increase in memory of emotional material, even though the drug had increased their pulse and blood pressure. Unlike placebo-treated subjects, those given the drug showed comparable retention across all phases of the story. In other words, methylphenidate eliminated the preferential retention of the information on the emotional slides. These data suggest that the physiological arousal produced by stimulant drugs may be relevant to the fact that they do not seem to provide lasting cognitive benefit.

## 5. Conclusion

There is a paradox in regard to the use of stimulant medications indicated for the treatment of ADHD. On the one hand, there is much recent medical, legal and ethical concern about escalating use of these drugs, both licit and illicit, primarily to enhance cognition. On the other hand, there is surprisingly little evidence that the stimulant drugs truly are 'cognitive enhancers.' Results from neuropsychological studies confirm that while stimulants apparently increase attention in adults diagnosed with ADHD, the drugs produce very modest and inconsistent improvement on a variety of other neuropsychological tasks. Although responses may be faster, inaccuracy and errors persist, especially on tests of 'distractibility.' Intuitively, it would seem logical that drugs that improve attention and concentration should promote learning and academic achievement. Yet, for more than 30 years data have shown that this is not the case in regard to children and adolescents. Evidence presented here supports the same conclusion for adult college students. Whether this lack of effectiveness is due to drug-induced perseveration, inflexibility, arousal or some other factor(s) remains to be determined.

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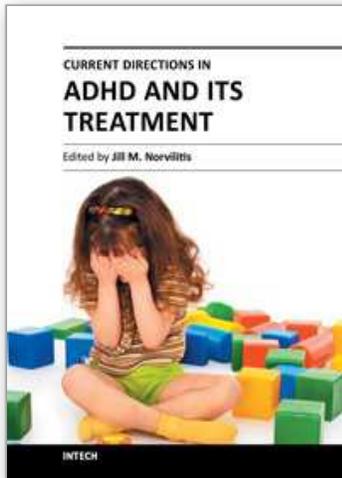
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## **Current Directions in ADHD and Its Treatment**

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The treatment of Attention Deficit Hyperactivity Disorder is a matter of ongoing research and debate, with considerable data supporting both psychopharmacological and behavioral approaches. Researchers continue to search for new interventions to be used in conjunction with or in place of the more traditional approaches. These interventions run the gamut from social skills training to cognitive behavioral interventions to meditation to neuropsychologically-based techniques. The goal of this volume is to explore the state-of-the-art in considerations in the treatment of ADHD around the world. This broad survey covers issues related to comorbidity that affect the treatment choices that are made, the effects of psychopharmacology, and non-medication treatments, with a special section devoted to the controversial new treatment, neurofeedback. There is something in this volume for everyone interested in the treatment of ADHD, from students examining the topic for the first time to researchers and practitioners looking for inspiration for new research questions or potential interventions.

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