Stimulant medications for attention-deficit/hyperactivity disorder (ADHD) improve memory of emotional stimuli in ADHD-diagnosed college students

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**ABSTRACT**

Objective: Stimulant medications do not improve the academic achievement of ADHD diagnosed undergraduates. One reason may be that stimulant-induced sympathetic arousal might impair memory.

Participants and methods: To test this hypothesis, we conducted a study between September 2011 and March 2012, to compare medicated (n=12) and non-medicated (n=11) ADHD diagnosed undergraduates, with non-ADHD students (n=12). All participants were presented with an audiovisual narrative that included an emotional segment, and answered questions about the story one week later.

Results: All groups remembered the emotional segment significantly better than the neutral segments. Non-medicated ADHD students recalled less of both segments than the medicated ADHD or non-ADHD groups, which did not differ from each other.

Conclusion: Stimulants improved memory in ADHD students, and did not impair the relative retention of emotional, as opposed to neutral information. Stimulant-induced arousal cannot explain the academic deficit of ADHD undergraduates.

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1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a developmental disorder characterized by three main symptoms: inattention, hyperactivity, and impulsivity. Although more than 5 million children have been diagnosed with ADHD in the United States alone, it is not only a childhood disorder; approximately 4.5% of the adult population may also meet the diagnostic criteria for this condition (Advokat, 2010; Advokat and Vinci, 2012). The affected adult population exhibits a variety of impairments, such as more marital and relationship problems, poor job performance, and lower socioeconomic status than the normal population (Biederman et al., 2006). Many adults with ADHD are prescribed the same stimulant medications used to treat children with the disorder. The two main categories of stimulant drugs approved for the treatment of ADHD are amphetamine and methylphenidate. Amphetamine, marketed in formulations such as Vyvanse and Adderall, causes the release of catecholamines (primarily dopamine) from nerve terminals, and also blocks reuptake, whereas methylphenidate, such as Ritalin and Concerta, mainly blocks reuptake (Advokat and Vinci, 2012; Smith and Farah, 2011).

In spite of the well-established therapeutic benefit of stimulant drugs, several reviews of ADHD diagnosed children show that long-term stimulant use does not improve academic performance (Advokat, 2009). This is consistent with evidence that adults with ADHD are also less likely to reach predicted education levels, independent of medication use (Biederman et al., 2008). Among adults, college students with or without an ADHD diagnosis are especially likely to take stimulants to enhance memory, organization, and alertness (Advokat and Vinci, 2012). However, we have found that, regardless of stimulant use, the academic performance of ADHD-diagnosed undergraduates is still statistically worse than that of their non-ADHD cohort (Advokat et al., 2011). Considering the well-documented stimulant-induced improvement in attention, it is surprising that these drugs do not produce better academic outcomes.

One factor that might be relevant is that stimulants increase physiologically arousal (Advokat, 2010). Arousal is known to influence memory. As shown in a classic study by Cahill and McGaugh (1995) adult participants presented with an emotionally stimulating slideshow were more likely to remember the details of the 'emotional' story than participants presented with a neutral slideshow story. The classic view, derived from these types of studies is that modest levels of arousal will improve memory, while excessive levels of arousal will impair memory.

This generalization may be relevant to the fact that cognitive improvement is not seen in ADHD diagnosed undergraduates, even when they use stimulant medications. Academic environments are inherently anxiety provoking. It is possible that adding a physiologically
stimulating drug to the academically stressful situations that normally occur in college might not improve performance.

A study by Brignell et al. (2007) provides some evidence for this hypothesis. Using the emotionally arousing slideshow of Cahill and McGaugh (1995), this study compared the ‘emotional memory’ of normal, adult control groups, given either a placebo or methylphenidate. The control group responded as expected, with selectively increased memory for the ‘emotional’ material. The methylphenidate group did not show such an effect; the stimulant reduced the differential effect of ‘emotional’ and ‘neutral’ information on memory.

In the current study, we adopted this procedure to investigate if this type of emotional memory was affected in an undergraduate ADHD population, and, if so, whether it was reduced by stimulant medications.

2. Methods

2.1. Participants

Undergraduate college students, at least 18 years old, were recruited through on-campus flyers and the psychology department extra-credit system. All participants were screened through email correspondence to verify that they had a diagnosis of ADHD and had a current prescription for stimulant medication. At that time, respondents with ADHD chose whether or not they wanted to participate before (Off medication) or after (On medication) taking their medication. Participants without ADHD were eligible to be enrolled in the Control group. All participants received the same number of extra credit points and a total of $10.00 if they completed the study. All procedures were reviewed and approved by the university’s Institutional Review Board. All data were collected between September 2011 and March 2012.

2.2. Procedure

ADHD participants were asked not to take their medication for at least 12 h prior to arriving at their sessions. During the first session, all ADHD participants had to provide proof of the diagnosis, which, in every case consisted of the presentation of their prescription vial. Then the experimenter presented the consent form, discussed the experimental procedures with the participant, and explained that they would be able to stop the experiment at any time and still receive credit and compensation. Participants with ADHD were asked when they last took their medication. Those who chose to take their medication for the study then did so in the presence of the experimenter. Each participant then completed a short demographic questionnaire.

All participants, Control or ADHD (whether on medication or not) waited for approximately 1 h after signing the consent form, before beginning the experiment. This was done to allow the drug to take effect in the On medication group. Participants were told ahead of time about this interval and that they could bring some other work or game with which to occupy themselves during this period.

After an hour each participant was shown the series of slides on a computer, with the accompanying pre-recorded story. The slideshow story and subsequent quiz questions were taken from Brignell et al. (2007), as originally used in Cahill and McGaugh (1995). A total of eleven slides were shown for 20 s each, accompanied by a pre-recorded narrative. The story was shown on a Dell laptop in a darkened room. The first four and final three slides consisted of emotionally neutral stimuli, such as a mother and son going on a walk. The four middle slides described an incident in which the boy was hit by a car, had his legs mangled in the crash and was taken to surgery. Slide 8 was particularly ‘emotional,’ as it was a close image of the child’s re-attached legs after surgery. After the slideshow was presented, participants were asked to rate on a 10-point Likert scale how emotional they found the story to be, with 0 = not emotional at all and 10 = extremely emotional.

Participants were asked to return a week later, for a second session. At that time, they repeated the process of taking or not taking medication, depending on their previous group assignment. They waited for an hour and then took a computer-based quiz about the slides on the same computer on which the slide show was viewed. The quiz was administered using Class Marker, an online testing resource. Although participants could not go back and change any previous answers, they were given unlimited time to complete the quiz. There were a total of 70 multiple-choice questions about the content on the slides, regarding both verbal and visual components of the story. Each question had four possible answers. For example, ‘who was pictured in slide 1’ (a) a mother and her son, (b) a father and his son, (c) a mother and father, and (d) no one is pictured. The score consisted of the percent of questions correctly answered on each of the three phases, the two neutral and one emotional phase of the slides, as well as on individual slides. During the quiz, the experimenter remained in the room with the participant so that they could ask any questions regarding the test itself.

Each session took approximately 2 h. Statistical analyses were performed with the SPSS program, version 19 (SPSS Inc., Chicago, IL). All comparisons were considered significant at $p<.05$.

3. Results

Data were obtained from 35 participants whose respective sessions were scheduled during the same time of day (approximately 1 to 3 pm in the afternoon): 12 without ADHD (Control group), 12 with ADHD in the On medication group, and 11 with ADHD in the Off medication group. Demographic information for these participants is shown in Table 1.

The average age of the three groups did not differ, ranging from 20.7 to 21.4 years.

The two ADHD groups were prescribed stimulant medications for a comparable period of time, between an average of 3.5 and 3.9 years. There were also no differences between the two ADHD groups with regard to the category of ADHD medications, in that a statistically equal number of participants were prescribed either an amphetamine formulation or a methylphenidate agent. The respective doses were in the approved range.

As is typical of this experimental population, the participants were mostly Caucasian females, who were all single (not shown). In fact, all Control group participants were female, while the two ADHD groups included a few male participants. We have consistently found in several studies that, although the ADHD college population has a more equal distribution of males and females than the distribution seen in this study, more females sign up for the Extra Credit. We have heard, anecdotally from our colleagues, that this is true for many of the undergraduate courses, not just in regard to our study, or specifically with ADHD-diagnosed students. In our experience, female undergraduates are more likely than males to earn extra credit when that option is offered. As discussed below, this did not alter the results; all outcomes were the same, regardless of whether the data from all participants were analyzed, or only the data from the female participants.

A one-way ANOVA indicated a trend among the groups in time taken to complete the quiz $F(2, 32) = 3.1, p = .058$. Post-hoc Tukey HSD tests showed that the mean time to complete (in whole seconds) for the On medication ADHD group (784 ± 84) was statistically longer than the time to complete for the Off medication ADHD group (576 ± 21), $p = .046$. The control group’s time to complete (696 ± 47) was not different from either of the ADHD groups.

There was no difference among the groups in the emotional score given immediately after viewing the slideshow. On a scale of 0 to 10 the group averages were 5.8 ± 0.7 (Control), 6.25 ± 0.8 (On medication), and 5.6 ± 0.7 (Off medication). This shows that the subjective affective reaction to the narrative was the same across the 3 conditions.
Fig. 1 shows the percent of correctly answered questions in each group as a function of the story phase. The first phase, Neutral 1, consisted of questions about the first 4 slides; Neutral 2 consisted of questions about the last 3 slides, and the data for the Emotional Slide consisted of 6 questions about slide 8, which was a picture of the child’s re-attached, severed legs.

3.1. Within group analyses

As seen in Fig. 1, there was a significant main effect of story phase for all 3 groups.

For the Control group, the percent correct for the 3 phases was 55.4, 95.8 and 57.9; $F = 60.7; df = 11$, $p < .001$. Pairwise comparisons showed that the score on slide 8 was significantly higher than the score on the 2 neutral phases, which did not differ from each other.

For the ADHD group On medication, the percent correct for the 3 phases was 60.1, 98.6, and 61; $F = 63.6, df = 11$, $p < .001$. Pairwise comparisons showed that the score on slide 8 was significantly higher than the score on the 2 neutral phases, which did not differ from each other. This outcome was the same when only the female participants were included in the analyses.

For the ADHD Off medication, the percent correct for the 3 phases was 44.4, 81.8, and 53.6; $F = 44.8, df = 10$, $p < .001$. In this case, pairwise comparisons showed not only that the score on slide 8 was significantly higher than the score on the 2 neutral phases ($p < .01$ in each case), but that the score on the second neutral phase was significantly higher than that of the first neutral phase ($p = .047$). The same outcome was obtained when only the 9 scores of the female participants were used. The scores on the first and second neutral phases were 44.4 and 55.5, respectively, $t = 2.4$, $df = 8, p = .043$.

3.2. Between group analyses

Fig. 1 also indicates the results of the comparisons made among the groups. For the first neutral phase, there was a statistical difference among the 3 conditions ($F [2,32] = 4.0; p = .028$). Post-hoc Tukey HSD tests showed a significant difference between the On (60.1) and Off (44.3) Medication groups ($p = .025$), but that neither differed from the Control (55.4) condition. Again, this outcome was the same when only the female participants were included in the analyses.

There was also a significant difference among the 3 groups on the scores for the emotional slide 8 ($F [2,32] = 8.76, p = .001$). In this case, post-hoc Tukey HSD tests showed that both the Control (95.8) and the On (98.6) Medication groups had significantly higher scores than the Off (81.8) Medication group ($p = .007$ and .001, respectively), and did not differ from each other. Using only data from the female participants, the results were the same: $F [2,27] = 7.36, p = .0028$, and the Off medication group had significantly lower scores than the Control and On medication groups ($p = .011$ and $p = .008$, respectively).

In contrast to the first 2 phases, there was no difference among the groups on the last phase, the second neutral phase. Control, On medication and Off medication groups scored 57.9, 61 and 53.6, respectively, $F [2,32] = 1.2, ns$.

4. Comment

This study was prompted by our recent results, showing that ADHD stimulant medications do not eliminate the academic disparity between ADHD diagnosed college students and their non-ADHD diagnosed counterparts. As with children and adolescents, these drugs did not improve the academic performance of the undergraduates with ADHD (Advokat et al., 2011). We suggested that one possible reason for this lack of efficacy was the physiological arousal elicited by stimulant drugs. We proposed that stimulant medications might increase sympathetic arousal, which, in conjunction with the anxiety engendered by academic demands, could interfere with the drugs’ cognitive benefits (Advokat, 2010). The current study tested this hypothesis by comparing the cognitive performance of medicated and non-medicated ADHD diagnosed undergraduates with their non-ADHD counterparts, on the relative retention of emotional and neutral information. An audiovisual narrative that included an emotional segment was presented to all
participants, and they were asked to recall details about the story one week later.

The results of this study replicated the expected facilitation of emotional memory in the non-ADHD control group (Cahill and McGaugh, 1995). In addition, however, the differential retention of emotional memory was also replicated in ADHD diagnosed participants regardless of whether they were tested while on or off their medication. Stimulant medication did not eliminate the contrast between emotional memory and neutral memory; rather, it produced the same inverted U-shaped function as in the non-ADHD Control group. To our knowledge, this is the first report of this phenomenon in ADHD diagnosed individuals; we are not aware of any prior study of emotional memory retention in this population.

However, we hypothesized the opposite outcome, that stimulant medication, combined with the arousing nature of the narrative, would diminish the differential recall between neutral and emotional information. Our prediction was based on the results of Brignell et al. (2007), who found that methylphenidate administration did reduce the differential effect of emotional stimuli on memory. There are at least a couple of explanations for this difference between the two studies. First, stimulant-induced cognitive improvement most often occurs in situations where there is a deficit (Advokat, 2010) whereas all participants in the Brignell et al. study were ‘healthy volunteers,’ who did not have ADHD, and whose baseline performance would presumably be normal (in our situation, the administration of stimulant drugs to non-diagnosed participants was not legally permissible). Second, the ADHD participants in our study were familiar with the drugs, whereas the participants in Brignell et al.’s study were not. We suggest that the ADHD participants in our study had habituated to the physiological effects of their stimulant medications, which they had been using for several years. Of course, without corresponding physiological confirmation, this interpretation is highly speculative. In contrast, the participants in Brignell et al.’s study may not have been familiar with the drugs’ physiological effects, and this novelty might have interfered with their cognitive performance. In fact, Brignell et al. provided evidence that the stimulants were physiologically active, by measuring heart rate and blood pressure in their participants. Although we did not collect such data, the fact that our ADHD participants in the On medication group took significantly longer to complete the test than those in the Off medication group, suggests that the drugs were pharmacologically active. On the other hand, the fact that there was no difference on the emotional rating scale suggests that the stimulants no longer produced a significantly different subjective state (one prediction from this interpretation is that the initial novelty of stimulant-induced physiological effects might impair cognitive performance in individuals without such deficits or, perhaps in ADHD-diagnosed persons as well at the beginning of treatment).

Nevertheless, although all groups showed the classic ‘inverted U’ function for the recall of emotional information, the non-medicated ADHD participants answered fewer questions correctly than Controls and medicated ADHD participants. Although this difference only reached statistical significance for the first neutral segment, it was statistically significant for the emotional memory segment, and was retained even when only data from females was analyzed. While the finding of a cognitive impairment in non-medicated ADHD adults is consistent with the literature, the magnitude of the deficit seen here is greater than reported in most other paradigms and is especially striking when considering that all participants were college students. It remains to be seen if the difference would be even larger in a non-college community population (Frazier et al., 2007).

It may be worth noting that the performance of the non-medicated ADHD group improved on the second neutral phase. The score on that segment was the same as that of the other two groups and was significantly better than on the first neutral phase. Even with such a modest amount of data, it is tempting to speculate that questions about the emotional story segment may have increased arousal or alertness in non-medicated ADHD students sufficiently to improve subsequent recall. This speculation is consistent with the generalization that a modest amount of arousal improves memory.

Most important, this study shows a substantial improvement, essentially normalization, of long-term memory in ADHD diagnosed adults who were on medication when exposed to the narrative and the subsequent recall test one week later. This provides striking evidence of cognitive benefit from stimulant drugs, and is one of the most dramatic examples of memory improvement demonstrated by stimulants.

One of the few other examples of such clear-cut stimulant-induced memory enhancement comes from Soetens and colleagues (Soetens et al., 1993, 1995; Zeeuws and Soetens, 2007). In their within-subject studies, non-ADHD adult males received both placebo and amphetamine injections during the different phases of the experiment. All participants were shown lists of unrelated words and asked to recall them at different times after presentation. There was no effect of the drug on word recall immediately after each list or at the end of the daily session. But, amphetamine significantly improved recall at 1 h, 1 day and 3 days after the session. This result is consistent with our findings because even though none of the participants in the Soetens studies had ADHD, the placebo retention baseline was low (around 25%) and there was substantial room for improvement.

This perspective is supported by Izquierdo et al. (2008), who also showed that methylphenidate promoted recall at longer time intervals, and only in situations where performance was already impaired. Specifically, those studies found that subjects over 35–40 years old were significantly less likely to remember information they had received seven days before, relative to younger subjects. After methylphenidate, only older subjects showed improvement: their age-related memory deficit was reversed, and they remembered as much information as the younger subjects.

4.1. Limitations

There are several limitations of this study. First, our participants were all undergraduates, which limits generalizability. Most of them were single, young, white, females (which is common in studies of college students) so these results may not apply to older, minority, or male populations. Of course, this is also the population whose academic performance was the basis for the investigation (Frazier et al., 2007; Weyandt and DuPaul, 2006).

Second, the students themselves chose whether to participate in the study before or after taking their respective medication. This was an unavoidable design weakness, in that we were not authorized to impose these conditions on our participants. However, this is not an uncommon experimental constraint when conducting naturalistic research. Although the choices appeared to be related to the participants’ respective academic schedules, rather than any systematic confound, it is possible that this self-selection might have affected the outcome.

For example, expectations about the drugs’ effects might have influenced the ADHD results. That is, if ADHD-diagnosed students thought that the drugs promote memory, then the non-medicated group might have done poorly, in part, because they believed they would not do as well as they would if they were medicated. Similarly, the medicated group might think that they would do well because they had taken their medications. All of these considerations are worth investigating further, perhaps with non-collegiate, community populations.

It is worth noting, however, that all our previous studies have suffered from the same defect. Yet those studies did not show much cognitive improvement from the stimulants. The lack of substantial cognitive improvement that we previously found on many laboratory tasks was consistent with most of the literature, including studies that used counterbalanced group designs. In other words, no matter
how the studies are designed, the stimulants do not seem to improve performance on certain types of cognitive tasks, i.e. those most commonly used in experimental investigations. Yet, this study shows that a robust memory enhancement is easily seen under ‘real world’ conditions. A more rigorous replication, to confirm the phenomenon, would certainly be welcome.

5. Conclusions

This study was prompted by the question: why don’t students with ADHD do as well as their cohorts in school, regardless of medication use? A logical answer was that the stimulants simply do not improve cognitive performance. Our results, however, have shown that the medications may, in fact, improve memory in ADHD-diagnosed adults. One potential contributing factor to this result is that we closely regulated when participants took their medication, ensuring that they were exposed to the narrative and tested during the drugs’ peak duration of effect. Perhaps students who are regulating their own medication do not administer the drugs to their best advantage, that is, they may not take the drugs to increase their ability to focus on salient cognitive information.

Of course, another possibility is that the persistent underachievement in ADHD undergraduates may be due to a non-cognitive factor, which is either not ameliorated by, or may even be worsened by, stimulant drugs (Bidwell et al., 2011; Swanson et al., 2011). This is an important issue for further research.

References


