Non-specific effects of Methylphenidate (Ritalin) on cognitive ability and decision-making of ADHD and healthy adults

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Abstract

The effect of a single dose of Methylphenidate (MPH) on cognitive measures and decision-making processes was assessed in a sample of adults with ADHD and in a control sample. Thirty-two adults satisfying DSM-IV criteria for ADHD and 26 healthy controls performed several cognitive tasks. Half the participants received MPH prior to performing the tasks and the other half received placebo in a randomized, double-blind manner. The average digit-span test score was higher in the groups receiving MPH compared to the groups receiving placebo, while diagnosis did not have an effect upon scores. In decision-making tasks however, MPH did not have an effect upon performance, whereas in one of the tasks the average proportion of risky choices was higher in ADHD adults compared to controls. Our data therefore demonstrates that a) MPH is capable of enhancing specific aspects of cognitive performance and b) this enhancement is not specific to ADHD.

Keywords: developmental disorder; behavioral assessment; decision making; memory; attention.

Ever since approved by the FDA in 1968, Methylphenidate (MPH) has been increasingly used in the treatment of Attention Deficit/Hyperactivity Disorder (ADHD) in children and adults. It has also been used in the treatment of apathy (Marin et al. 1995) and narcolepsy (Mitler 1994). Nevertheless, several studies have demonstrated its cognitive-enhancing effects on healthy individuals as well, effects which are a source of controversy (e.g., Sahakian and Morien-Zamir 2007; Swanson and Volkow 2008). Questions concerning who can- and should -benefit from the drug are still left open. Surprisingly, none of the various studies done so far has compared an adult ADHD group with a healthy control group. In this study, we therefore examined the effect of MPH on the performance of ADHD and non-ADHD adults, in a double blind placebo-controlled experiment, using a battery of tasks measuring sustained attention, executive functioning, and decision-making. Our aim was to identify whether indeed MPH improves performance in the domains that are relatively impaired in ADHD adults, thus testing the hypothesis that the effect of MPH is ADHD-specific.

MPH's mechanism of action has been previously explained (Volkow et al. 2004, 2008): it increases extra-cellular levels of Dopamine (DA) and Norepinephrine by blocking their respective transporters. Dopamine and Norepinephrine reduce background firing rate of neuronal cells, thus decreasing non-task related activity and improving signal to noise ratio. Volkow et al. (2002) postulated that this increase in DA improves attention and reduces distractibility. Their conclusion is based on a PET imaging study where healthy volunteers performed a mathematical task and a neutral task (viewing cards passively with no reward) both under MPH and placebo conditions. MPH enhanced dopaminergic activity during the mathematical task, but not during the neutral task – an evidence that MPH's action is context specific. Also,

participants' self-reports of interest and motivation in the mathematical task were greater with MPH than with placebo, hence demonstrating that by increasing dopamine MPH also enhances the saliency of the task, and can improve performance in this manner.

Imaging studies further showed that MPH causes a reduction in prefrontal cortex activation (Schweitzer et al. 2004; Mehta et al. 2000) and in glucose metabolism in the brain (Volkow et al. 2008) during the performance of cognitive tasks. These studies may provide a hint why some people benefit from MPH while others do not (Volkow et al. 2008): for people who activate task-unrelated neural networks while accomplishing a task (e.g., mind-wander or have an attention disorder) - MPH will reduce this unwanted activity, causing a more focused activation pattern. However, when activation is already relatively focused - MPH will make no difference.

While previous studies focused initially on MPH's effect upon vigilance and reaction time tasks, then later on more complex cognitive components such as spatial working memory, few studies have examined its effect on decision making processes. Sevy et al. (2006) have shown that reduced levels of dopamine resulted in disadvantageous decision-making, so it might be expected that MPH, by increasing dopamine levels, will cause the opposite result. Indeed, in two studies involving dementia patients (Rahman et al. 2006) and children with ADHD (DeVito et al. 2008), administration of MPH caused participants to make more advantageous choices. However, no study aimed at assessing the effect of MPH upon risk-taking behavior of ADHD adults.

Adults with ADHD are considered impaired in a variety of cognitive domains such as sustained attention, executive functioning, working memory, and response

inhibition. In addition, they are prone to making decisions that lead to unfavorable consequences, and show increased risk for substance abuse, dangerous driving, and frequent change of jobs, as well as difficulties in sustaining stable relationships (Weiss and Murray 2003; Asherson 2005). The decision-making deficits of ADHD adults have also been demonstrated in laboratory decision-making tasks such as the Iowa Gambling Task (Toplak et al. 2005; Malloy-Diniz et al. 2007). Considering that MPH is the most commonly prescribed drug for the treatment of adults with ADHD, it seems important to assess its effect upon people's decision-making patterns as manifested in such decision-making tasks; tasks which, to a certain extent, mirror everyday behavior more than purely cognitive tasks. To our knowledge, no study compared the effect of MPH upon decision-making in ADHD and non-ADHD adults.[1] Our study aims at comparing the effect of MPH upon ADHD adults with its effect upon non-ADHD adults in the decision-making domain as well as in executive functions.

The battery of tasks we used for evaluating the effects of MPH on cognitive processes included the Test of Variables of Attention (TOVA) (Greenberg and Kindschi 1996); and the Forward and Backward digit-span task (Wechsler 1981). As several reports demonstrate that adults with ADHD show impairments in sustained attention and working memory (Hervey et al. 2004; Seidman 2006), we predicted that without MPH, the ADHD group will achieve lower scores than the non-ADHD group. Based on evidence showing that these impairments can be ameliorated by MPH treatment (Tucha et al. 2006; Kurscheidt et al. 2008; Turner et al. 2005), and that healthy adult may also benefit from MPH (Elliot et al. 1997; Cooper et al. 2005), we

[1] Concerning childhood ADHD however, an imaging study (Vaidya et al. 1998) compared the effect of MPH on children with and without ADHD and found that MPH improved performance of both ADHD and control groups on a go/no-go task.

predicted that performance will be positively affected by MPH in both ADHD and non-ADHD groups. However, we expected the improvement to be more significant in the ADHD group, as the effectiveness of MPH is greatly determined by baseline capacities (Mehta et al. 1999). Additionally, in order to rule out group differences in intelligence, we employed the Raven Progressive Matrices Test (Raven 1989) which assesses non-verbal intelligence.

For decision processes evaluation, a computerized version of the Iowa Gambling Task (Bechara et al. 1994) was used along with a new version of this task that was especially developed for the purpose of this study. The new task, referred to as the Foregone Payoff Gambling Task (FPGT) includes foregone payoffs; that is, it provides outcomes for non-selected alternatives, which act as distracters (Yechiam et al. 2005). Given the fact that reward learning tasks are highly sensitive to task repetition (see e.g., Sevy et al. 2006), we used a between-subject design for assessing the effect of MPH on task performance. Based on the fact that ADHD is associated with frontal-lobe dysfunction (McLean et al. 2004) and that the IGT was originally designed to capture this behavioral profile, we expected the ADHD-placebo group to perform worse than controls on the IGT (as was found by Malloy-Diniz et al. 2007, and by Toplak et al. 2005 with adolescents). We predicted that group differences would be larger on the FPGT, which involves additional distracting information. Finally, we predicted that in both decision tasks MPH would improve decision making performance for the ADHD group, as MPH has previously been shown to reduce excessive risk-taking tendencies in clinical samples whose performance was impaired in this domain (Rahman et al. 2006; De Vito et al. 2008).

Method

Participants

Fifty-Eight participants were recruited from the “Shalvata” Mental Health Center (MHC) outpatient clinic, and from surrounding community. Recruitment was achieved through advertisement both within the Medical Center facilities (branched to the Tel-Aviv University school of medicine), and in the community. The final participants included four patients of the outpatient clinic (see details below), and the rest were community or staff members who responded to the advertisement.

The study was approved by the local and national IRB, and all participants consented and signed an informed consent. Exclusion criteria were age below 21 or above 50; pregnant or nursing women; people suffering from a disorder other than ADHD which might affect the studied parameters; people who cannot be given MPH due to medical reasons; and people incapable of performing the computerized tasks due to motor or sensory disabilities. Prior to their participation, participants were screened for ADHD using three standard self-report rating scales: the ASRS-18 rating scale, whose items correspond to the DSM-IV criterions for ADHD diagnosis, the Conners Adult ADHD Rating Scale, and the Wender-Utah rating scale. Classification into ADHD and non-ADHD groups was done by a senior psychiatrist or a clinical expert, based primarily on the participant's self-reports as follows: those who demonstrated at least 6 inattention symptoms and/or at least 6 hyperactivity-impulsivity symptoms in their ASRS-18 self-report were included in the ADHD group, according to DSM-IV criteria. In addition, on the basis of recent publications in the clinical literature (McGough and Barkley 2004), we also included those who scored only 4 or 5 symptoms in the ASRS-18 but scored above the clinical cut-offs in

at least one of the other two self-reports – a score above 46 in Wender-Utah or a score above 65 in the CAARS. [2]

Additionally, each participant was interviewed by the psychiatrist or clinical expert who confirmed the diagnosis, and screened the participants for axis-1 psychiatric disorders using the Hebrew version of SCID-2 - a DSM-based structured interview. Most of the participants had no current axis-I diagnosis. Exceptions were the four outpatients who had past diagnoses of anxiety disorder, depression, substance abuse and cluster-B personality disorder. All were in complete remission as assessed by a senior psychiatrist.

Participants' demographic data is presented in Table 1. A two by two ANOVA was conducted for each item with diagnosis (ADHD versus non-ADHD) and medication group as independent variables. The ADHD and non-ADHD groups did not significantly differ in age, gender, and years of education. They significantly differed in the number of inattention symptoms ($F(1,54) = 34.32$, $p < 0.001$) and number of hyperactivity/impulsivity symptoms ($F(1,54) = 48.58$, $p < 0.001$) on the ASRS self-report, as well as in the Wender-Utah score ($F(1,51) = 62.94$, $p < 0.001$), and in the CAARS ADHD score ($F(1,33) = 48.72$, $p < 0.001$). In each group, half the participants received a capsule containing 10-20 mg[3] of MPH prior to performing the battery of tasks (specified below), and the other half received a placebo capsule in a randomized double-blind manner. These conditions were labeled as MPH and Placebo. Sub-grouping was done while carefully matching for gender, age and

[2] The participants were also asked if they had been previously diagnosed with ADHD. Of the 26 participants categorized in this way into the ADHD group, 18 participants had a previous ADHD diagnosis. Of the 32 participants allocated into the control (non-ADHD) group, only one had a previous diagnosis, which was not confirmed either in the three self-reports or in the interview with the psychiatrist. Thus, she was classified into the non-ADHD group.

[3] Participants received 15 mg MPH, unless high or low in body weight (according to Body Mass Index categories) in which case they received 20 or 10 mg respectively.

education level as follows: in each group (ADHD/Non-ADHD), each participant in the MPH condition belonging to a distinct combination of gender (M/F), age (21-30, 31-40, 41-50) and education level (high-school/academic) was matched with another participant in the Placebo condition who belonged to these same categories (using a linear matching procedure; Lovasz and Plummer 1986). As indicated in Table 1 there were no significant difference between the MPH and Placebo group in any of the demographic or ADHD-related measures.

Eleven participants in the ADHD group have been treated with MPH in their adult life. Of these, 5 were in the Placebo condition and 6 were in the MPH condition. Participants did not take their medication on the morning of testing. Any participants taking other kinds of medication that might affect attention (e.g., medication for Tourette syndrome) were excluded from the study. A senior psychiatrist confirmed that any other medication taken by participants did not have a significant interaction with MPH.

Participants were all rewarded for their participation, and in addition they were paid 1% of their earnings in the gambling tasks.

Measures

Digit-span tasks. For assessing executive functioning we used a computerized version of the digit-span Forward and Backward tasks (Wechsler 1981). In these tasks participants are presented with increasingly longer sequences of digits, which they are required to type on the screen right after the series have been presented. In the Forward version they are required to memorize the digits in the original order, while in the Backward version they are required to memorize each sequence in the opposite

order. The scores in these two task versions were combined to a total digit-span score, which served as an index of executive ability, specifically working-memory.

Raven's (1989) Progressive Matrices. This computerized test was used for assessing non-verbal intelligence. In each item, participants are presented with a 3×3 matrix of shapes, with one shape missing. They are asked to choose, out of 8 options, the shape which best completes the matrix. The task consisted of ten items (Set 1), and the score was the number of right answers.

Test Of Variables of Attention (TOVA). This test, devised by Greenberg and Kindschi (1996), is one of many continuous performance tests (CPTs), rapid reaction-time tasks in which participants have to discriminate predetermined target stimuli from distracting non-targets. CPTs, and TOVA among them, are widely used both by practitioners and investigators as an objective tool for assessing ADHD and determining beneficial medical effects (Llorente et al. 2001).

The TOVA used here is a standardized, fixed-interval (21.6 ± 1.1 min), visual CPT. Successful performance on the TOVA requires sustained attention and an ability to discriminate between correct and incorrect responses with relatively few other neurocognitive domain contaminations (Greenberg and Kindschi 1996). An electronic micro-switch is used to distinguish between two identical large outlined rectangles, each containing either the target stimulus (smaller color square at the top) or the non-target stimulus (smaller color square at the bottom). The target to-non-target presentation ratio is constant in each half of the test but different for each half. The task is set so that 22.5% of the trials include targets during the first half (infrequent stimulus condition) and 77.5% include targets in the second half (frequent stimulus condition).

The score provided by the TOVA (labeled “TOVA score”) is a weighted average of several measures of response time, response errors, and performance quality over time (lower scores are suggestive of an attentional disorder). Hence, this overall score can be viewed as a general performance measure of sustained attention, while its components may provide more specific measures of different dimensions. Thus, in our main analysis apart from analyzing TOVA score we focused on two of the measures constructing it: omission errors - which are trials where the target was presented but the participant failed to respond, and commission errors - which are trials where the participant responded to a non-target. The former is considered a measure of inattention, and the latter a measure of motor impulsivity (Llorente et al. 2001).

Participants performed the TOVA twice: Before self-administration of 10-20 mg of MPH, or placebo; and 40 minutes after. Peak plasma concentration of methylphenidate is reached approximately 2 hours after ingestion and the half life of the drug in plasma is 1.2 hours (Gilman et al. 1980). Testing was started 40 minutes after ingestion of the drug to maximize drug levels during the decision-making tasks.

The first TOVA session (i.e., before taking a pill) confirmed our classification of the participants into ADHD and Non-ADHD groups: scores in the ADHD group were significantly lower on average than those in the non-ADHD group (-4.3 versus -0.73, $t(43) = 2.58$, $p = 0.01$, Cohen’s $d = 0.66$). This is hardly surprising, considering that this task is designed to measure sustained attention and motor impulsivity, both of which are believed to be impaired in ADHD. In order to estimate the specificity of the TOVA, we considered the percentage of participants whose scores were considered by the TOVA as suggestive of attentional problems (score below -1.8). Specificity

was poor: TOVA scores were suggestive of an ADHD diagnosis in 53% of the ADHD cases, compared to 34% of the non-ADHD cases ($\chi^2(1) = 1.98$, p = 0.16).

Decision-making tasks. Decision-making ability was assessed by two gambling tasks. The first was a computerized version of the Iowa Gambling Task (Bechara et al. 1994), which assesses reward learning. In this task the participant is presented with four decks of cards on the computer screen. Each card yields a reward, but might also cast a loss. In each trial, the participant selects a card out of one of the four decks by clicking on it. Consequently, the card is exposed, displaying the gain and the loss for that trial. The accumulated total amount is presented at the bottom of the screen all along, and is updated after every trial. Through contingent feedback, participants are expected to learn that decks A and B yield constant large gains but also larger losses, so that their net loss across trials is 2,500 tokens, whereas decks C and D yield smaller gains but also smaller losses, leading to a net gain across trials of 2,500 tokens (the complete task outcomes are detailed in Table 2).

The second gambling task is a version of the IGT developed for the purpose of the current study. Two differences distinguish it from the original version – a different payoff distribution as detailed in Table 3, and a feedback method called *foregone payoffs*: following each choice made by the participants, they get to see not only the card chosen but also the other three cards from the three decks not chosen. This provides more information, but can also cause temptation, and may distract participants from the advantageous decks (see e.g., Yechiam et al. 2005; Yechiam and Busemeyer 2006). Specifically, when decision-makers select the advantageous decks, they still have to face peripheral feedbacks from the unselected disadvantageous decks as well. Given the difficulty of individuals with ADHD to deal with distracting information (Tucha et al. 2008; Arnsten 2006), it was expected that this Foregone

Payoff Gambling Task (FPGT) would present a more difficult challenge to ADHD adults than the standard IGT.

Preceding each gambling task participants were given verbal instructions (similar to those used in Bechara et al. 1994). In addition, they were told that they are given 20 Shekels (1 Shekel = $0.26) in advance, and that by the end of the task they would receive 1% of their earnings in real money.

Results

Digit-span tasks

The overall scores in the digits span task for the four experimental conditions are shown in Figure 1. As the figure shows, performance was better for the participants who received MPH compared to those who received placebo, regardless of their diagnosis. A multivariate analysis of variance (MANOVA) with Forward and Backward digit span scores as dependent variables, and diagnosis (ADHD/Non-ADHD) and condition (MPH/Placebo) as independent variables revealed a significant main effect of condition (F (2, 53) = 3.77, p = 0.03) and no interaction effect (F (2, 53) = 1.23, p = 0.30) or an effect of diagnosis (F (2, 53) = 0.10, p = 0.90). Thus, the beneficial effect of MPH that we observed was not specific to ADHD adults.

We also analyzed separately the results of the Forward and Backward versions of the digit span task. The results showed a significant difference between the MPH and Placebo conditions in the Backward version (F (1, 54) = 7.16, p = 0.01, Cohen's d = 0.74) and a marginally significant difference in the same direction in the Forward version (F (1, 54) = 3.58, p = 0.06, Cohen's d = 0.53). Again, no significant interactions or main effects of diagnosis were observed.

TOVA

A two-way ANOVA of TOVA score by diagnosis (ADHD/Non-ADHD) and condition (MPH/Placebo) revealed no main effect of diagnosis (F (1, 54) = 1.48, p = 0.23) and no main effect of condition (F (1, 54) = 0.02, p = 0.89), as well as no interaction (F (1, 54) = 0.002, p = 0.96). No effect of MPH on TOVA scores was also found for the specific measures of commission and omission errors.

Raven's Progressive Matrices

A two-way ANOVA of the Raven's test score by diagnosis (ADHD/Non-ADHD) and condition (MPH/Placebo) revealed no significant effect of diagnosis (F (1, 54) = 0.39, p = 0.54) or condition (F (1, 54) = 2.18, p = 0.15), and no interaction (F (1, 54) = 1.01, p = 0.32).

Decision-making tasks

The main results from the IGT and FPGT are shown in Figure 2. Statistical analyses for the IGT showed no significant differences between the MPH and Placebo conditions, no effect of diagnosis, and no interaction in any of the four decks (this was conducted for the two disadvantageous decks together using multivariate analysis, as well as for each individual deck). We also analyzed the net score on the IGT (total number of disadvantageous choices minus total number of advantageous choices). This produced identical findings: No significant differences among the four groups.

In contrast, a multivariate analysis for the choices of the two disadvantageous decks for the FPGT revealed a significant main effect of diagnosis, with ADHD adults making more choices from the disadvantageous decks (F (2, 53) = 3.62, p = 0.03).

Specifically, participants in the ADHD group made significantly more choices from deck D compared to controls (t (56) = 2.12, p = 0.04, Cohen's d = 0.58).

In order to examine differences in trial-by-trial adaptations in the two tasks, we modeled participants' choice behavior using the Expectancy-Valence model (Busemeyer and Stout 2002), which for each participant extracts three parameters characterizing his or her performance (see supporting online information). No significant group differences were found in this analysis for the IGT (while for the FPGT the model was found to be inadequate).

Discussion

In this study we aimed at detecting whether MPH-induced cognitive enhancement is specific to ADHD. By comparing ADHD adults with healthy adults in a randomized controlled trial we were able to determine whether this effect is specific to ADHD adults.

Our results are surprising in two aspects: First, on average, participants who received MPH performed better in the Working-Memory (WM) task, regardless of whether they had ADHD or not. Moreover, the ADHD group did not demonstrate impairment in this domain compared to controls. Second, there was no effect of MPH on risk-taking in both groups. The ADHD group performed worse than controls (that is, made more selections from risky alternatives that were disadvantageous) in the Foregone Payoff Gambling Task (FPGT), regardless of the drug they had received (MPH/Placebo). Similarly, MPH did not have an effect on sustained attention as assessed by the TOVA in either group. Hence, we suggest that the cognitive-enhancing features of MPH are 1) not specific to ADHD, and 2) do not apply to executive functions in general but specifically to WM performance, which is not

necessarily impaired in ADHD. In domains that are considered impaired in ADHD (sustained attention, risk-taking) MPH did not provide the expected improvement.

In the WM task, participants who received MPH did better than those who received placebo, a finding which is consistent with existing literature on the cognitive-enhancing features of MPH on healthy adults (Elliot et al. 1997) and adults with ADHD (Schweitzer et al. 2004; Tucha et al. 2006; Turner et al. 2005). However, these features are apparently not diagnosis-specific; no significant difference was found when comparing ADHD adults and controls. This is inconsistent with some studies of neuropsychological functioning in adults with ADHD, which demonstrated WM deficits (e.g., Hervey et al. 2004; Seidman 2006; Biederman et al. 2008), although most of these studies inspected spatial working memory. Other studies failed to find WM deficits in ADHD adults compared to controls (Rapport et al. 2001). Indeed, WM might be a secondary deficit in ADHD; recent theories consider inhibitory control as the core deficit in ADHD, deficit which can intrude into WM capacity (Seidman 2006), but not necessarily.

In contrast to its effect on WM, MPH did not cause a significant improvement in the sustained attention task. Prior to taking a pill, the TOVA succeeded in differentiating ADHD from non-ADHD adults (see method section), as expected from Continuous Performance Tests (see Seidman 2006, though Weyandt et al. 1998 reports otherwise concerning the TOVA). However, after receiving a MPH/placebo pill, the average performance was improved in each one of the four groups, regardless of what was inside that pill. Analysis of the difference between scores (before and after the pill) revealed a trend towards a greater improvement in the ADHD group compared to the control group ($F(1, 54) = 3.09$, $p = 0.08$), but this can be attributed to a regression to the mean and in any respect was not affected by MPH administration.

Although this finding is inconsistent with existing literature regarding the effect of MPH on CPT performance both in healthy participants (Koelega 1993; Cooper et al. 2005) and in participants with ADHD (Riccio et al. 2001; Barkley, Murphy, O'Connell, and Connor 2005; Tucha et al. 2006; Boonstra, Kooij, Oosterlaan, Sergeant, and Buitelaar 2005), none of these studies employed the TOVA.

A possible interpretation of our findings can be that in the TOVA, a substantial practice effect masks the effect of medication; hence while the TOVA had moderate success in discriminating the ADHD group from the non-ADHD group, it might not be useful in assessing the beneficial effect of MPH as a treatment for ADHD patients. Clearly, more research is needed in order to validate this clinically important finding. Indeed, the dosage usually used in clinical assessment sessions of the TOVA is slightly higher than the sub-therapeutic dosage we used in this study. Nevertheless, this dosage was high enough to inflict significant differences in the WM task.

Furthermore, MPH did not manage to alter the typically increased tendency towards risky and long-term-disadvantageous choices, as demonstrated by the ADHD group in the FPGT. Participants in the ADHD group made significantly more selections from the risky decks compared to controls, regardless of the drug they had received (MPH/placebo). Similarly, MPH did not have an effect on performance in the first gambling task, the classic IGT. In this task diagnosis did not have an effect as well; the average proportion of disadvantageous choices was approximately the same in all four groups (about 40%).[4] These gambling tasks surely place demands on

[4] This finding is inconsistent with a study showing relatively impaired IGT performance in adults with ADHD (Malloy-Diniz et al. 2007). In this study Both ADHD and control groups learned to select advantageously but the rate of convergence to the advantageous alternative in the second half of the task was lower in ADHD adults. However, Malloy-Diniz et al.'s (2007) study used the dynamic version of the IGT, where the differences between decks change with time (Bechara et al. 1999).

working-memory to some extent, but our results indicate that they capture an additional ability essential to this sort of decision-making, which is dissociated from WM and unaffected by MPH.

A major difference between the two gambling tasks used in the current study is in the level of distraction, or peripheral information, that each one casts upon the decision-maker; in the FPGT participants are faced in each trial with the payoffs of all four decks – compared to only a single payoff in the IGT. This extra-information can help in making the right distinction between decks but it can also be a distraction for making the "right" choice, as it continually conveys information that is inconsistent with the right preference (along with information that is consistent with it). Therefore, a possible conclusion from our data may be that an environment where information is abundant and distracting leads to suboptimal decision-making in ADHD. Indeed, distractibility and deficits in divided attention and selective attention have been well documented in ADHD (Hervey et al. 2004; Seidman 2006; Tucha et al. 2008).

A limitation of the current study is the procedure used for classification of participants into the ADHD and non-ADHD groups, which was based on self-reports rather than on a multi-pronged assessment incorporating more sources of information. Nevertheless, the classification was confirmed by a senior psychiatrist and was accompanied by a clinical interview. Another limitation involves the heterogeneity of our ADHD sample: we have not controlled for routine MPH treatment or for ADHD subtypes. Controlling for this may elicit more specific results. Another important issue for future research would be examining the long-term effects of MPH treatment. Regardless of these limitations, the current study points out to the beneficial but non-selective effect of MPH on working memory; and to the lack of effect of MPH on

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Similar to the current FPGT, this task possibly taxes sustained attention resources to a greater extent than the original IGT.

decision making, despite the fact that ADHD adults do show differences in this domain.

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Table 1. Demographic and self-report data by group. The table denotes group means and standard deviations (in parenthesis).

	ADHD		**Non-ADHD**	
	Placebo	**MPH**	**Placebo**	**MPH**
N (males)	16 (8)	16 (10)	13 (5)	13 (6)
Age	32.9 (6.9)	32.4 (7.7)	31.7 (7.9)	33.2 (8.6)
Education	14.3 (2.3)	14.5 (2.8)	13.9 (2.6)	14.7 (2.9)
ASRS-innatention *	4.5 (2.7)	4.6 (2.3)	1.3 (1.6)	1.2 (1.4)
ASRS-hyperactivity/impulsivity *	4.8 (2.5)	5.1 (2.3)	1.2 (1.2)	1.2 (1.5)
Wender-Utah *	53.3 (15.3)	48.7 (13.6)	22.8 (10.1)	22.4 (12.9)
CAARS *	70.7 (6.5)	68.7 (9.3)	49.3 (8.3)	50.4 (8.9)

* Effects of diagnosis: $p<0.001$

Table 2. Payoff structure for the Iowa Gambling Task (IGT).

Deck	Wins	Losses	Description
A	100 every card	In each card, 50% chance of losing 200, 250, or 300	Disadvantageous, risky
B	100 every card	In each card, 10% chance of losing 1250	Disadvantageous, risky
C	50 every card	In each card, 50% chance of losing 25,50 or 75	Advantageous, safe
D	50 every card	In each card, 10% chance of losing 250	Advantageous, safe

Table 3. Payoff structure for the Foregone Payoff Gambling Task (FPGT).

Deck	Wins	Losses	Description
A,B	20 every card	0	Advantageous, safe
C,D	In each card, 50% chance of gaining 25, 50, 75, or 100	In each card, 50% chance of losing 25, 50, 75, or 100 *	Disadvantageous, risky

* The likelihood of losses and gains was dependent such that outcomes entailed either gains or losses.

Figure 1. Digit-span total score (Forward + Backward) by condition (MPH versus Placebo) and diagnosis (ADHD versus Non-ADHD). Each bar indicates the average score on a scale of 0-100 %. Error bars indicate standard errors.

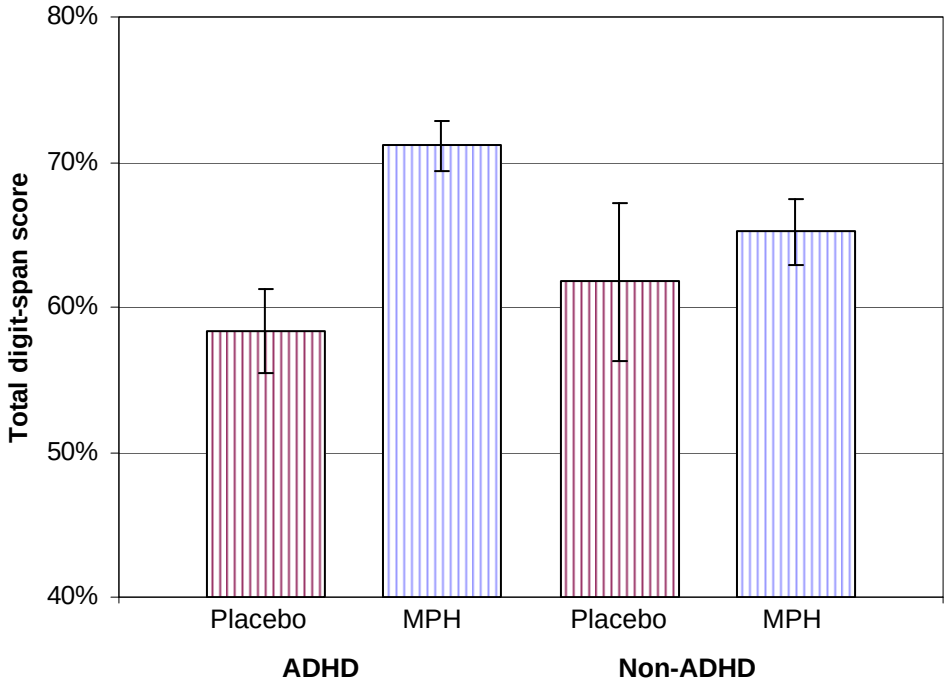

Figure 2. Results for the two decision making tasks by condition (MPH versus Placebo) and diagnosis (ADHD versus Non-ADHD). The bars indicate the average percent of disadvantageous choices in each condition. Error bars indicate standard errors. Top: Choices from the disadvantageous decks in the IGT. Bottom: Choices from the disadvantageous decks in the FPGT.