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The effect of methylphenidate on postural stability under single and dual task conditions in children with attention deficit hyperactivity disorder — A double blind randomized control trial

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article info abstract

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Objectives: To investigate the effects of Methylphenidate (MPH) on postural stability in attention deficit hyperactivity disorder (ADHD) children in single and dual task conditions.

Methods: A randomized controlled double-blind study analyzing postural stability in 24 ADHD children before and after MPH vs. placebo treatments, in three task conditions: (1) Single task, standing still; (2) dual task, standing still performing a memory-attention demanding task; (3) standing still listening to music.

Results: MPH resulted in a significant improvement in postural stability during the dual task condition and while listening to music, with no equivalent improvement in placebo controls.

Conclusions: MPH improves postural stability in ADHD, especially when an additional task is performed. This is probably due to enhanced attention abilities, thus contributing to improved balance control during performance of tasks that require attention. MPH remains to be studied as a potential drug treatment to improve balance control and physical functioning in other clinical populations.

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1. Introduction

Attention deficit hyperactivity disorder (ADHD), is one of the most prevalent neuropsychiatric disorders in children. ADHD affects 3 to 5% of school age children [\[1\]](#page-5-0). The diagnosis of ADHD is currently made on the basis of inattention, impulsivity and motor restlessness [\[2\]](#page-5-0).

Comorbidity of ADHD and motor coordination problems, such as developmental coordination disorder (DCD), has been reported [\[3\].](#page-6-0) Jucaite et al. [\[4\]](#page-6-0) found that children with ADHD performed worse on the Movement Assessment Battery for Children than the age-matched control children. Children with ADHD showed significantly poorer performance in kinesthetic acuity tasks and fine motor tasks, compared to controls [\[5\]](#page-6-0). Piek et al. [\[3\]](#page-6-0) have demonstrated that the children with predominantly inattentive subtype ADHD had significantly poorer fine motor skill, while children with combined subtype ADHD were found to experience significantly greater difficulty with gross motor skill. Children with ADHD who perform different graphic tasks made slower, inaccurate strokes with relatively high axial pen force and less accurate strokes when accuracy demands increased, compared with the comparison group [\[6\]](#page-6-0). Recently, Leitner et al. [\[7\]](#page-6-0)

demonstrated alterations in the gait of children with ADHD. Teicher et al. [\[8\]](#page-6-0) found that compared to normal children, children with ADHD moved their head more times, moved a longer distance and covered a greater area during sitting.

Various anatomic brain abnormalities have been reported for ADHD in childhood, including smaller brain volumes in cerebellum, caudate nucleus, dorsolateral prefrontal cortex, pallidum, and corpus callosum [\[9\].](#page-6-0) Valera et al. [\[10\]](#page-6-0), who conducted a wide meta-analysis of brain imaging of ADHD, have concluded that brain regions showing differences include cerebellar regions, the splenium of the corpus callosum, total and right cerebral volume, several frontal regions, and right caudate. ADHD may be tied to functional abnormalities in the putamen, which is mainly involved in the regulation of motor behavior. Teicher et al. [\[11\]](#page-6-0) have used functional magnetic resonance imaging (fMRI) to indirectly assess blood volume in the brain, and found that the blood flow in the putamen is different in boys with ADHD compared to normal controls. They have also found that the blood flow is strongly correlated with the child's capacity to sit still and his accuracy in accomplishing a computerized attention task.

Children with ADHD are characterized by attention deficit and impulsive behavior [\[2\],](#page-5-0) and inhibition is hypothesized to be a core deficit. Since postural control requires attention it is logical to assume that children with ADHD will have difficulties in correctly changing the center of pressure (CoP) when trying to keep an upright posture. Upright posture and balance function is a continuous process of changing the CoP to one side and then returning the CoP back towards a relative

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equilibrium position. It was found that when trying to evaluate the stability of ADHD children in different conditions the sway velocity of these children was significantly greater than that of the controls [\[12\].](#page-6-0) Feng et al. [\[13\]](#page-6-0) have found that the equilibrium scores in a sensory organization test of ADHD boys were significantly lower than those of typical control boys.

Little has been studied about the effect of MPH on the balance and gait function of ADHD. Wade [\[14\]](#page-6-0) has shown that hyperactive children on MPH managed to balance on a board that rotated about a central steel shaft for a longer time than placebo controls. Feng et al. [\[13\]](#page-6-0) recently reported improvement in a sensory organization test after MPH treatment of ADHD children, compared to that test before treatment. Leitner et al. [\[7\]](#page-6-0) found that stride time variability was significantly reduced after MPH treatment, such that dual tasking no longer affected gait variability. Flapper et al. [\[1\]](#page-5-0) have found that the motor performance of children with a combined diagnosis of developmental coordination disorder and ADHD improved after taking MPH, as measured by the Movement Assessment Battery for children (MABC).

From a cognitive viewpoint, keeping upright posture, gait and the restoration of motor control require substantial central information processing [\[15,16\]](#page-6-0). In most cognitive theories, the available processing resources are assumed to be limited. As a result, resource competition may occur during the performance of more than one attentiondemanding task, leading to task interference and difficulty in motor tasks [\[16\].](#page-6-0) Studies using dual task paradigms have demonstrated the role of cognitive factors in the control of balance during standing and walking. Previous research shows that children without ADHD also have a trend toward greater length of Center of Pressure (CoP) when performing a concurrent cognitive task [\[17\]](#page-6-0). Using a dual-task methodology, Pellecchia [\[18\]](#page-6-0) found that postural sway increased with increasing attentional demands of concurrent cognitive tasks in children, with the most difficult cognitive task having the greatest influence on sway, suggesting that balance control requires cognitive processing. Studies have demonstrated that subjects with ADHD have quantifiable deficits in executive function and attention, distractibility, inattention and poor concentration [\[19\],](#page-6-0) making them an ideal cohort for studying the role of the cognitive domain in postural stability.

Given the known deficits in attention in ADHD, and the evidence suggesting that balance control during standing requires attention, we sought to investigate the effects of MPH on postural stability in ADHD children, in both single and dual task conditions. We tested the following hypotheses in order to gain insight into the effects of MPH on stability in ADHD: (1) After administering MPH, postural stability of ADHD children will improve; (2) the influence of MPH would be more prominent during a dual task condition. This hypothesis is based on recent results [\[7\]](#page-6-0) showing that MPH treatment significantly decreased stride time variability and enhanced the automaticity and consistency of gait in ADHD.

2. Methods

2.1. Study design and participants

The study group consisted of 24 children who were diagnosed as suffering from ADHD. The diagnoses were made after a complete neuro-developmental evaluation by an experienced pediatric neurologist using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) diagnostic criteria [\[2\]](#page-5-0). Diagnosis of ADHD was based on interviews with the parents and children, clinical examination, and Conners' parent and teacher questionnaires [\[20\].](#page-6-0) ADHD symptoms had to be severe for six or more items on the DSM-IV ADHD rating scale (ADHD RS-IV) parent version [\[21\]](#page-6-0), which was administered to the parents by an experienced pediatric neurologist. The parental ADHD RS-IV contains nine attentive and nine hyperactive/impulsive items. Teachers returned a personally completed version of this rating scale by mail. If at least six core DSM-IV ADHD symptoms were rated 'very often' among the nine attentive items, a child was classified as the inattentive ADHD type (3 children in the experimental group, and 4 children in the controls). If at least six core DSM-IV ADHD symptoms were rated 'very often' among the 18 inattentive and hyperactive/ impulsive items, a child was classified as combined type (9 children in the experimental group, and 8 children in the controls). The hyperactive/impulsive type was not represented in this study population. Eligibility criteria were: children who were 7–16 years old and treated by MPH on a daily basis for at least three months prior to the study. Only children with good clinical response with an improvement of ADHD symptoms after MPH treatment according to the parents' and teachers' reports on the ADHD RS-IV questionnaire and according to the pediatric neurologist follow-up were included in the study. Exclusion criteria were: ADHD children who were diagnosed with neurological, orthopedic, or psychiatric diagnoses according to DSM-IV criteria that can affect motor control and postural stability; cerebral palsy; neuropathic diseases; limb fracture; or head trauma during the previous year; use of any medication other than MPH during the study period; and ADHD children who had an IQ score below the normal range $(**70**)$, as assessed by the Wechsler Intelligence Scale for Children — Revised (Wisc-R) administered by a child psychologist. All the children were enrolled in age-appropriate grades in mainstream schools.

All ADHD children underwent a complete neuro-developmental evaluation as part of the initial assessment at the clinic and were found not to suffer from any major neurological or motor disability other than ADHD, such as ataxia, tremor, hemiparesis, gait disturbances, nystagmus, and pyramidal signs. The parents provided informed consent, in accordance with approved procedures by the Helsinki Ethics Committee in Soroka Medical Center (Clinical Trials Registration number #NCT00485797).

2.2. Blinded outcome assessments

After eligibility was determined, subjects were randomly assigned, using a table of random numbers, to either the intervention group, who received MPH drug treatment, (Experimental) or the placebo group (Control), who received placebo drug treatment. The placebo pill was identical in appearance to the MPH pill. Each group had 12 participants. After completion of the baseline examination the subjects of both groups were given medication in a double-blinded, randomized fashion (5 mg of short-acting MPH to the experimental group and 5 mg of placebo medication to the controls). The participants (parents and children) and the tester administering the examinations were blinded to group assignment. After completion of baseline examination the subjects had an hour and a half break, following with an identical testing procedure. The duration of the break after taking the drug was based on the time to maximum effect of MPH which is within 1.5 to 2 h [\[22\].](#page-6-0)

2.3. Postural stability protocol

The subjects were instructed to stand upright on the force platform with the feet positioned as close as possible (heels and toes touching). They were also instructed to stand upright as still as possible, with their hands folded on their back. A total of five 30-second trials were conducted for three task conditions, always in the same order. The three task conditions were: (1) single task — standing upright viewing an "X" displayed on a screen 3 m in front of them; (2) dual task — standing upright while performing a memory-attention demanding task. During this task condition the children were instructed to stand as still as possible while listening to a collection of different sets of 6 fragments of familiar children's songs, each lasting for 5 s. The children were instructed to try and memorize the songs while standing still. After the completion of each of the 5 trials, a list of 15 children's songs was

shown to the children and their task was to recall from the list which songs they had heard during the last trial. The number of mistakes was counted in each of the 5 trials and presented as an average number of mistakes in all trials; (3) standing still viewing an "X" displayed on a screen 3 m in front of them while listening to quiet relaxing music with no additional instruction.

On the day of the experiment the children did not take MPH before the experiment, which means that they had at least 24 h without drug administration. The half-life of MPH is about 1.5 to 2 h [\[22\]](#page-6-0); therefore the drug's influence is negligible after 24 h.

Balance measurements were collected with a Kistler 9287 single force platform (Kistler Instrument Corp., Winterthur, Switzerland) which measures the time-varying displacement of the Center of Pressure (CoP) under the subject's feet. The force platform data were sampled at a frequency of 100 Hz and stored on a hard disk for later processing. Force platform data were analyzed using automatic code written in Matlab (Math Works Inc., Cambridge, MA, USA) to extract four well-established parameters of postural stability: 1) Mediolateral CoP range (mm) (ML-sway range); 2) Anterioposterior CoP range

(mm) (AP-sway range); 3) Mean velocity of CoP sway (mm/s) (Mean sway velocity); 4) Sway area $\text{(mm}^2\text{)}$ – the elliptical area of the CoP points. Lower postural stability scores indicate higher levels of postural control. These parameters were computed for each subject's trials, and then averaged for each set of 5 trials to obtain an average value for each parameter and for each subject, in each experimental condition.

2.4. Sample size

Sample size estimation was based on data presented by Schmid et al. [\[17\]](#page-6-0) who have shown that the mean velocity of postural sway in children was 17 ± 10 mm/s with no cognitive task, whereas the mean velocity of postural sway of the same children during a concurrent cognitive task was 26 ± 10 mm/s. For a conservative estimation we have used a standard deviation of 10, based on their work. Using the above numbers for a two-sided estimation at a significance level of 0.05 and 80% power, it was calculated that a minimum of 12 children would be required to find significant differences.

Fig. 1. Flow of study participants.

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Table 1

Baseline characteristics of patients randomized to methylphenidate drug treatment (experimental) and placebo (controls)

Characteristic, mean ± SD	Experimental	Control	p-value
Age (years)	10.06 ± 2.50	10.88 ± 3.25	0.494
Gender (female/female+male)	8.33%	8.33%	$\mathbf{1}$
Weight (kg)	34.28 ± 10.16	40.99 ± 19.54	0.306
Height (m)	1.40 ± 0.17	1.42 ± 0.19	0.721
BMI	17.09 ± 1.27	18.99 ± 4.08	0.149
Single-task			
ML-sway range (mm)	41.2 ± 2.7	41 ± 3.4	0.96
AP-sway range (mm)	38.1 ± 4.3	35.6 ± 3.3	0.66
Mean sway velocity (mm^2/s)	16.9 ± 0.9	17.0 ± 1.4	0.94
Sway area (mm^2)	151.6 ± 19	151.3 ± 26.6	0.99
Memory attention-demanding task			
ML-sway range (mm)	37.0 ± 2.4	36.3 ± 3.2	0.86
AP-sway range (mm)	38.5 ± 3.6	37.2 ± 5.2	0.85
Mean sway velocity (mm^2 /s)	16.8 ± 1.1	16.3 ± 1.5	0.78
Sway area $\rm (mm^2)$	133.3 ± 18.5	133.1 ± 27.3	0.99
Music only			
ML-sway range (mm)	36.5 ± 2.5	39.3 ± 2.9	0.56
AP-sway range (mm)	36.7 ± 3.8	33.6 ± 2.8	0.50
Mean sway velocity (mm^2/s)	17.0 ± 1.2	16.5 ± 1.4	0.76
Sway area $\rm (mm^2)$	134.5 ± 18.7	129.8 ± 20.6	0.87

Values are means +1 SEM.

 $mm²$ = millimeter squared. $mm²/s = millimeters square/seconds.$

2.5. Data and statistical analyses

The postural stability parameters were checked for normality distribution with Shapiro–Wilk statistics. The parameters were found to be normally distributed. Descriptive statistics are reported as mean \pm SEM. We used the independent t-test to compare the experimental and control subjects with respect to different background characteristics (age, gender, weight, height, BMI, postural stability measures) and with respect to number of mistakes made during the memory-attention demanding task. In case the variable was not normally distributed, Wilcoxon signed rank test was performed to compare the different baseline characteristics.

In order to estimate the effect of MPH and dual tasking on postural stability measures (ML-sway range, AP-sway range, mean sway velocity and sway area) we applied mixed effect models for repeated measures to evaluate within group and between group differences. For each of the four postural stability measures, we applied a separate model where the dependent variable was the postural stability measures (a continuous one) and the independent variables were categorical: the group (experimental vs. controls) and time (pre-test vs. post-test). An additional two separate repeated measure ANOVAs that included group (Experimental vs. Controls) by time (pre- vs. posttests) were used including age as a covariate in the first ANOVA model and cognitive function (the performance of the memory-attention demanding task) as a covariate in the second ANOVA model. The ANOVAs were performed to explore if differences in stability remain statistically significant in dual task condition even after including age and cognitive function as a covariates. p-values reported are based on two-sided comparisons. A p-value of 0.05 was considered statistically significant. All data were analyzed using SPSS software (SPSS Inc., Chicago, IL).

For each outcome, the effect size (ES) of Hedge's g and the 95% confidence interval (CI) were calculated. The ES of g was calculated by taking the difference between the means of both groups divided by the average population standard deviation (SD). To estimate the SD for

Fig. 2. The effect of methylphenidate on postural sway parameters for experimental group and controls. Filled squares represent experimental group, open circles represent controls. Placement of symbols indicates mean values; the whiskers of each plot indicate ±1 SEM. *Indicates significant differences between groups based on repeated measures ANOVA (Time $*$ Group) (p < 0.05).

mm = millimeters.

 $s =$ seconds

g, baseline estimated SDs of both groups were pooled. The following guidelines were used when interpreting correlation magnitudes: 0.0– 0.2 is considered small, 0.2–0.5 is considered moderate and 0.5–0.8 is considered large [\[23\].](#page-6-0)

3. Results

3.1. Flow of patients

As shown in [Fig. 1,](#page-2-0) 24 of 80 patients (30%) enrolled in the present study, met the entry criteria, agreed to participate, and were randomized. At baseline, the experimental $(n=12)$ and control $(n = 12)$ groups had similar characteristics, postural sway parameters, and number of mistakes made during the memory attentiondemanding task ([Table 1](#page-3-0)). There were no drop-outs in either group and no adverse events of drug treatment were experienced.

3.2. The effect of methylphenidate on postural stability

The effects of MPH on postural stability of the experimental and controls are summarized in [Fig. 2](#page-3-0). MPH did not have a significant effect on postural sway parameters during single task condition. However, during the memory attention-demanding task, a significant group-by-time interaction was found for ML-sway range and AP-sway range ($p = 0.03$, effect size [ES] = 0.52 and $p = 0.016$, effect size [ES] = 0.42, respectively). ADHD children from the experimental group significantly reduced ML-sway range from 37.0 ± 2.4 to 33.2 ± 3.7 mm and AP-sway range from 38.5 ± 3.6 to 31.4 ± 3.5 mm (10.3% and 18.4%, respectively). A significant group-by-time interaction effect was found for mean-sway velocity and sway-area after taking MPH medication ($p = 0.008$, effect size [ES] = 0.47 and $p = 0.019$, effect size $[ES] = 0.49$, respectively); the analysis revealed reduced mean-sway velocity from 16.8 ± 3.7 mm/s to 14.7 ± 2.9 mm/s and reduced swayarea from 133.3 ± 64.0 mm² to 102.3 ± 45.6 mm² in the experimental group (12.5% and 23.3%, respectively), with no equivalent improvement in placebo controls (see [Fig. 2](#page-3-0)). Additional ANOVA was used to explore whether differences in stability remain statistically significant in dual task condition even after including age as a covariate and it showed that ML-sway range, AP-sway range, mean sway velocity and sway-area remained statistically significant even after including age as a covariate ($p = 0.040$, $p = 0.002$, $p = 0.005$ and $p = 0.011$, respectively). Including cognitive function (the memory-attention demanding task condition) as a covariate in the ANOVA model showed that ML-sway

Fig. 3. The effect of MPH on number of mistakes during the memory attentiondemanding task in the experimental and control groups. Filled squares represent experimental group, open circles represent controls. p-value compares baseline means in the two groups, and post-intervention means ± SEM between the two groups based on repeated measures ANOVA (Time^{*}Group).

range, AP-sway range, mean sway velocity and sway-area remained statistically significant ($p= 0.042$, $p= 0.023$, $p= 0.012$ and $p= 0.028$, respectively).

During the relaxing music task, a significant group-by-time interaction effect of MPH treatment on postural stability (except MLsway range) was seen, but with a lower effect size. The AP-sway range decreased in the experimental group from 36.7 ± 3.8 to 33.1 ± 3.5 mm $(p= 0.029;$ effect size [ES] = 0.11), mean sway velocity decreased from 17.0 ± 1.2 to 15.2 ± 0.6 mm ($p = 0.04$; effect size [ES] = 0.48) and swayarea decreased from 134.5 ± 18.7 to 107.9 ± 11.4 mm² ($p = 0.003$; effect size $[ES]=0.24$ (8.8%, 10.6% and 19.8%, respectively). Postural sway measures in the placebo controls were not significantly different from the baseline (see [Fig. 2\)](#page-3-0).

A non-significant group-by-time interaction effect of MPH treatment ($p=0.5$) was found for a number of mistakes made during the memory-attention demanding task (Fig. 3). The following observations were also made on the data file. Under dual task conditions 3 of 12 (25%) of the ADHD children did not improve their stability following MPH treatment, while 2 ADHD children in the control group (17%) improved their stability in response to treatment with placebo MPH.

4. Discussion

In this study we sought to investigate the effects of MPH on postural stability in ADHD children, in both single and dual task conditions. Previous studies reported mean sway velocity of ∼17 mm/s in healthy children, whereas the mean sway velocity during a mentally counting backwards task was ∼26 mm/s [\[17\].](#page-6-0) ADHD children in the present study showed ∼17 mm/s mean velocities during both single task condition and during memory attention-demanding task condition, suggesting less attentional demands during the memory-attention demanding task used in the present study. In a different study, Blanchard et al. [\[24\]](#page-6-0) found that ML-sway range and AP-sway range in healthy children were 28 mm and 25 mm, respectively; this is somewhat lower compared with the results of ADHD children in the present study during single task condition (41 mm and 38 mm, respectively), which might suggest that ADHD children in the present study reached normal postural sway limits during the single task condition. Blanchard et al. [\[24\]](#page-6-0) revealed lower values of ML-sway range and AP sway range for the counting backward task than for the standing still task, similar to results of the present study. This might show that due to ceiling, ADHD children in the present study switched to a more secure strategy to control their body sway during dual task conditions.

To our knowledge, the present study is the first to quantitatively investigate effects of MPH on postural stability of ADHD children under both single and dual task conditions. ML-sway range, AP-sway range, mean sway velocity and sway-area were not different compared to controls at baseline [\(Table 1\)](#page-3-0), but were reduced after MPH treatment compared with placebo treatment ([Fig. 2](#page-3-0)). The results support the first, to a degree, and the second hypotheses. Key findings of the present study include: (1) Postural stability did not improve significantly during single task condition after MPH treatment, and the average sway parameters were similar in experimental and control subjects at baseline and during the post-test. (2) As expected in our second hypothesis, MPH significantly improved postural stability during the memory attention-demanding task and also during listening to relaxing music only. When interpreting our findings, we argue that ADHD children were already operating closer to their stability boundaries under single-task conditions and therefore could not "afford" to sway even more in the dual task conditions, and (unconsciously) focused on keeping their balance and not on the performance of cognitive task. Thus they might choose a different strategy to control stability (a more secure strategy). In addition, the effect of MPH during dual task condition might be stronger than in single task, because MPH might specifically improve the ADHD

children's abilities to perform concurrent activities along with "standing still" task. It is well-documented that attention is impaired in ADHD [\[19\]](#page-6-0) and that MPH improves attention in ADHD [\[25\]](#page-6-0); substantial improvement of different types of motor control was found after MPH treatment [1,14]. It was suggested this was in part due to its action on dopamine networks, especially in the frontal and prefrontal cortex, an area of the brain that is largely responsible for dual tasking and attention [\[7\].](#page-6-0) Dopamine deficits in the basal ganglia play a central role in motor dysfunction [\[26\]](#page-6-0). Perhaps MPH enhances the function of dopamine networks in ADHD, improving postural stability, similar to the way that dopaminergic medications modify postural control in Parkinson disease. The mechanism of action of MPH is dopamine reuptake inhibition, thereby increasing extracellular dopamine levels in the striatum (part of the basal ganglia) [\[27\].](#page-6-0) Previous work has also shown that MPH augments frontal activation [\[28\]](#page-6-0). This may also impact other systems that directly or indirectly influence motor control, such as balance and locomotion, including catecholamine regulation in locomotor control networks in the brainstem and spinal cord. According to this explanation, the enhanced attention that comes about as a result of MPH may lead to an improved balance control found in ADHD children in the present study. In fact, sway remained statistically significant even after including cognitive performance (the memory attention-demanding task test performance) as a covariate; this might suggest a direct effect of MPH on the postural control system. Our findings that MPH improves postural stability can be explained not just by its effect of attentional improvements and improvement of other symptoms of ADHD (e.g., hyperactivity and impulsivity), but can also indicate that MPH has a direct influence on areas of the brain that deal with motor and balance control. Teicher et al. [\[11\]](#page-6-0) found that in children with ADHD MPH significantly changed the blood flow in the putamen which is mainly involved in the regulation of motor behavior. Buchmann et al. [\[29\]](#page-6-0) have shown that in ADHD children, MPH modulates intracortical disturbed facilitatory and inhibitory motor circuits, which for the latter is associated with clinical improvement.

Similar to the present study results, Leitner et al. [\[7\]](#page-6-0) found that MPH significantly enhanced the automaticity and consistency of gait in ADHD by decreasing stride time variability. They have also found that both MPH and dual tasking had similar effects on the variability of gait [\[7\].](#page-6-0) Taken together, we note that MPH improved postural stability of ADHD children in more complicated tasks that require additional attention (dual tasking), while it did not affect a simpler task, i.e., single task condition. These findings indicate that MPH enhances postural stability in ADHD children especially when dual tasking is required, a situation commonly encountered in real-life. This shows that the impairments in balance function in ADHD children may be improved by MPH and enhances a fundamental ability that forms the basis for executing daily activities. Previous investigations using other dual task paradigms have also reported that MPH reduces the decrement associated with tasks that require executive function and the splitting of attention in children with ADHD [\[25\]](#page-6-0). Cepeda et al. [\[30\]](#page-6-0) suggested that the MPH effect on executive function is what produces the improvement in task-switching performance. It may be argued that after MPH treatment, ADHD children might focus their attention more strongly on the postural stability test in the dual-task situation,whereas the controls had the tendency to invest their resources into the cognitive task (e.g., tried to perform as well as possible in the memory attention-demanding task). This potential differentialemphasis behavior might explain the finding of group differences in the postural stability test post-MPH intervention under dual-task conditions. This explanation is supported by age-comparative laboratory research on cognitive-sensorimotor dual-task situations showing that weaker and less stable old adults have larger dual-task related performance decrements than healthy young adults, and tend to focus their attention more strongly on the sensorimotor task when both tasks are very resource demanding [\[31\].](#page-6-0) However, this is not a likely explanation; in our study the number of mistakes made during the memory attentiondemanding task in the experimental group during the post-testing procedure was not increased [\(Fig. 3\)](#page-4-0), suggesting that they invest their resources into the cognitive task (e.g., tried to perform as well as possible in the memory test) as well as into the postural task, thus attention was shared between both tasks. Another explanation might be that the impact of MPH on function such as hyperactivity and impulsivity, common symptoms of ADHD, has changed these symptoms and this change contributed to the increase in ability to invest in motor tasks in situations when attention has to be divided between more than one task, with no impact on the additional cognitive task. Thus, it seems likely that MPH, and not placebo effect, was responsible for the improvement in balance observed in the dual task condition.

Beilock et al. [\[32\]](#page-6-0) and Swan et al. [\[33\]](#page-6-0) argued that focusing one's attention exclusively on balancing (during the single-task) is actually harmful to task performance, maybe because people overcompensate for minor balance disturbances. Thus it is possible that the additional cognitive load required under dual task conditions creates an "automatic pilot" control of posture. This is consistent with the constrained action hypothesis, according to which an external focus promotes the use of more automatic postural control processes [\[34\]](#page-6-0). It was suggested that an external focus of attention enhances movement economy, and presumably reduces noise in the motor system that hampers fine movement control and reduces movement outcome [\[35\].](#page-6-0) MPH treatment may improve external focus of attention of ADHD children and thus improve the performance of motor tasks such as postural control. MPH's therapeutic effects are made apparent when the subject performs a targeted activity (e.g., classroom work) [\[27\].](#page-6-0) Volkow et al. [\[27\]](#page-6-0) hypothesized that MPH-induced dopamine increases are contextdependent on dopamine cell activity. Since dopamine cell activity is responsive to environmental stimulation [\[36\]](#page-6-0), this predicts that MPH's effects should be context-dependent [\[27\].](#page-6-0) If this hypothesis is correct, then MPH-induced dopamine increases would be greater while performing a task that is salient to the individual as compared to a non-salient task [\[27\]](#page-6-0), since salient stimuli activate dopamine cells [\[37\].](#page-6-0) This theory could explain the significant reduction in postural sway especially during dual tasking (e.g., memory task and music only) in the experimental group with no similar tendency in the control ADHD subjects. This suggests that dual tasking is more salient to the participants than single tasking, therefore MPH improved the postural stability in the dual tasking and not in the single tasking.

In conclusion, regardless of the precise explanation, the effect of MPH on dual tasking can be viewed as improving balance performance in dual tasking, with no significant effects seen in the controls. This supports the idea that enhanced attention abilities contributed to the improved balance control in dual task condition seen when ADHD children were tested on MPH. As noted above, this could also largely account for the effects of MPH in the present study on a sustained attention, but other mechanisms may have also played a role (e.g., effects of dopamine on the motor system, directly). MPH, a drug whose main effect is the enhancement of attention, apparently reinforces balance automaticity in ADHD children. It remains to be studied how the present findings extend to other clinical populations and whether MPH therapeutics can be used to enhance postural control.

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References

- [1] Flapper BC, Houwen S, Schoemaker MM. Fine motor skills and effects of methylphenidate in children with attention-deficit-hyperactivity disorder and developmental coordination disorder. Dev Med Child Neurol 2006;48:165–9.
- [2] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994 (DSM-IV).

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- [3] Piek JP, Pitcher TM, Hay DA. Motor coordination and kinaesthesis in boys with attention deficit-hyperactivity disorder. Dev Med Child Neurol 1999;41:159–65.
- [4] Jucaite A, Fernell E, Forssberg H, Hadders-Algra M. Deficient coordination of associated postural adjustments during a lifting task in children with neurodevelopmental disorders. Dev Med Child Neurol 2003;45:731–42.
- [5] Whitmont S, Clark C. Kinaesthetic acuity and fine motor skills in children with attention deficit hyperactivity disorder: a preliminary report. Dev Med Child Neurol 1996;38:1091–8.
- [6] Schoemaker MM, Ketelaars CE, van Zonneveld M, Minderaa RB, Mulder T. Deficits in motor control processes involved in production of graphic movements of children with attention-deficit-hyperactivity disorder. Dev Med Child Neurol 2005;47:390–5.
- [7] Leitner Y, Barak R, Giladi N, Peretz C, Eshel R, Gruendlinger L, et al. Gait in attention deficit hyperactivity disorder: effects of methylphenidate and dual tasking. J Neurol 2007;254:1330–8.
- [8] Teicher MH, Ito Y, Glod CA, Barber NI. Objective measurement of hyperactivity and attentional problems in ADHD. J Am Acad Child Adolesc Psychiatry 1996;35:334–42.
- [9] Seidman LJ, Valera EM, Makris N. Structural brain imaging of attention-deficit/ hyperactivity disorder. Biol Psychiatry 2005;57:1263–72.
- [10] Valera EM, Faraone SV, Murray KE, Seidman LJ. Meta-analysis of structural imaging findings in attention-deficit/hyperactivity disorder. Biol Psychiatry 2007;61:1361–9.
- [11] Teicher MH, Anderson CM, Polcari A, Glod CA, Maas LC, Renshaw PF. Functional deficits in basal ganglia of children with attention-deficit/hyperactivity disorder shown with functional magnetic resonance imaging relaxometry. Nat Med 2000;6:470–3.
- [12] Cheng J, Wang YF. [Comparison of postural control between normal and attention deficit hyperactivity disorder boys.]. Beijing Da Xue Xue Bao 2007;39:531–4 [abstract in Chinese].
- [13] Feng L, Wang YF, Cao QJ. [A pilot study on effect of methylphenidate on balance function of children with attention deficit hyperactivity disorder.]. Beijing Da Xue Xue Bao 2007;39:304–9 [abstract in Chinese].
- [14] Wade MG. Effects of methylphenidate on motor skill acquisition of hyperactive children. J Learn Disabil 1976;7:443–7.
- [15] Schmidt RA. Motor control and learning: a behavioral emphasis. Ed 2. Champaign, Human kinetics Publishers; 1988. p. 457–91.
- [16] Neumann O. Automatic processing: a review of recent findings and a plea for an old theory. In: Prinz, W, Sanders, AF, editors. Cognition and motor processes. Berlin: Springer-Verlag; 1984. p. 255–93.
- [17] Schmid M, Conforto S, Lopez L, D'Alessio T. Cognitive load affects postural control in children. Exp Brain Res 2007;179:375–85.
- [18] Pellecchia GL. Postural sway increases with attentional demands of concurrent cognitive task. Gait Posture 2003;18:29–34.
- [19] Willcutt EG, Doyle AE, Nigg JT, Faraone SV, Pennington BF. Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. Biol Psychiatry 2005;57:1336–46.
- [20] Du Paul GJ. Parent and teacher rating of ADHD symptoms: psychometric properties. J Clin Child Psychol 1991;20:245–53.
- [21] Conners CK, Sitarenios G, Parker JD, Epstein JN. The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. J Abnorm Child Psychol 1998;26:257–68.
- [22] Taketomo CK. Pediatric dosage handbook with international index. 12th ed. Hudson, OH: Lexi-Comp, Inc.; 2005.
- [23] Hedges L, Olkin I. Statistical methods for meta-analysis. Orlando, FL: Academic Press; 1985.
- [24] Blanchard Y, Carey S, Coffey J, Cohen A, Harris T, Michlik S, et al. The influence of concurrent cognitive tasks on postural sway in children. Pediatr Phys Ther 2005;17:189–93.
- [25] Jensen PS, Arnold LE, Severe JB, Vitiello B, Hoagwood K. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. Pediatrics 2004;113:754–61.
- [26] Beuter A, Hernández R, Rigal R, Modolo J, Blanchet PJ. Postural sway and effect of levodopa in early Parkinson's disease. Can J Neurol Sci 2008;35:65–8.
- [27] Volkow ND, Wang GJ, Fowler JS, Logan J, Franceschi D, Maynard L, et al. Relationship between blockade of dopamine transporters by oral methylphenidate and the increases in extracellular dopamine: therapeutic implications. Synapse 2002;43:181–7.
- [28] Vaidya CJ, Austin G, Kirkorian G, Ridlehuber HW, Desmond JE, Glover GH, et al. Selective effects of methylphenidate in attention deficit hyperactivity disorder: a functional magnetic resonance study. Proc Natl Acad Sci U S A 1998;95:14494–9.
- [29] Buchmann J, Gierow W, Weber S, Hoeppner J, Klauer T, Benecke R, et al. Restoration of disturbed intracortical motor inhibition and facilitation in attention deficit hyperactivity disorder children by methylphenidate. Biol Psychiatry 2007;62(9):963–9.
- [30] Cepeda NJ, Cepeda ML, Kramer AF. Task switching and attention deficit hyperactivity disorder. J Abnorm Child Psychol 2000;28:213–26.
- [31] Huxhold O, Li SC, Schmiedek F, Lindenberger U. Dual-tasking postural control: aging and the effects of cognitive demand in conjunction with focus of attention. Brain Res Bull 2006;69:294–305.
- [32] Beilock SL, Carr TH, MacMahon C, Starkes JL. When paying attention becomes counterproductive: impact of divided versus skill-focused attention on novice and experienced performance of sensorimotor skills. J Exp Psychol Appl 2002;8 $(1):6-16$
- [33] Swan L, Otani H, Loubert PV, Sheffert SM, Dunbar GL. Improving balance by performing a secondary cognitive task. Br J Psychol 2004;95(Pt 1):31-40
- [34] Wulf G, McNevin N, Shea CH. The automaticity of complex motor skill learning as a function of attentional focus. Q J Exp Psychol A 2001;54:1143–54.
- [35] Zachry T, Wulf G, Mercer J, Bezodis N. Increased movement accuracy and reduced EMG activity as the result of adopting an external focus of attention. Brain Res Bull 2005;67:304–9.
- [36] Overton PG, Clark D. Burst firing in midbrain dopaminergic neurons. Brain Res Brain Res Rev 1997;25:312–34.
- [37] Schultz W. Predictive reward signal of dopamine neurons. J Neurophysiol 1998;80:1–27.