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# The effect of a skipped dose (placebo) of methylphenidate on the learning and retention of a motor skill in adolescents with Attention Deficit Hyperactivity Disorder



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## KEYWORDS

Attention Deficit Hyperactivity Disorder (ADHD); Methylphenidate (MPH); Motor skill learning; Consolidation; Long-term procedural memory; Skipped dose

## Abstract

Individuals with Attention Deficit Hyperactivity Disorder (ADHD) have difficulties in achieving optimal performance in many everyday and academic tasks, deficits attributed to impaired skill acquisition and procedural memory consolidation. We tested the effect of a skipped dose of methylphenidate (MPH) on learning a movement sequence and its subsequent consolidation into procedural memory in adolescents with ADHD. A crossover double-blind design with placebo was used. Sixteen male adolescents, 16–18 years-old, with ADHD and taking MPH formulations on a daily basis, were trained on performing a 5-element sequence of finger-to-thumb opposition movements. Participants took part in two study conditions, 2 months apart. In each condition a different movement sequence was trained and tested. Participants trained on the task either with active medication or placebo on the day of training, crossed-over between study conditions. Learning effects, speed and accuracy, were assessed within-session, during a 24-h memory consolidation phase. Retention was tested by 2 weeks post-training. There were robust gains in performance both within-session and during the 24-h consolidation phase, in both conditions. However, the discontinuation of MPH on the day of training significantly reduced performance speed, with no loss of accuracy. By 2 weeks, post-training performance was comparable. Adolescents with ADHD who are treated daily but skip a dose of MPH show significant slowing of performance relative to their own performance on medication. However, on a background of daily treatment a skipped dose has no deleterious effect on memory consolidation and retention. © 2013 Elsevier B.V. and ECNP. All rights reserved.

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## 1. Introduction

Individuals with ADHD tend to be slower and less accurate than their peers without the disability in many motor tasks (Adi-Japha et al., 2011; Ben-Pazi et al., 2003; Rubia et al., 2003; Yan et al., 2002, but see Mostofsky et al., 2006). Concern has been raised that performance following a given learning experience, in individuals with ADHD, may be less effective than expected (Adi-Japha et al., 2011; Aman et al., 1998; Barnes et al., 2010; Silk et al., 2005). There is evidence in support of the notion of impaired skill acquisition in individuals with ADHD (Aman et al., 1998; Karatekin et al., 2003; Silk et al., 2005; but see Karatekin et al., 2009) and it was recently proposed that deficits in generating procedural memory may constitute a core deficit in ADHD (Nicolson and Fawcett, 2007, 2011). In a recent study (Adi-Japha et al., 2011), in which young adults with ADHD practiced a sequence of finger movements, learning and specifically, memory consolidation, as reflected in the expression of delayed “offline” performance gains (Korman et al., 2003), were found to be atypical in comparison to peers without ADHD. The acquisition of some motor skills in young adults with ADHD may thus significantly differ from skill acquisition in young adults, adolescents and even children without ADHD (Dorfberger et al., 2007).

The standard treatment for ADHD includes medication with methylphenidate (MPH) (Swanson et al., 2011; Wilens et al., 2006) but the results of studies of its effect on skill learning are not uniform (Advokat, 2010, Brossard-Racine et al., 2012). Evidence indicates that pharmacological treatment leads to an improvement in cognitive and motor performance, such as speed of information processing, reaction time and short-term memory span, which were found to be impaired among children and adolescents with ADHD (Aman et al., 1998; Bedard et al., 2004; Silk et al., 2005; Stray et al., 2009). We are not aware, however, of any study on the effects of skipped doses of MPH on the acquisition and retention of basic skills, although MPH dose skipping may be quite a common practice among individuals with ADHD (Pappadopulos et al., 2009). The aim of the current study was to examine the effect of a skipped dose (placebo) of MPH, on the day of training, on the learning (within-session gains), the expression of delayed gains by 24-h post-training and retention of a motor task in individuals with ADHD.

## 2. Experimental procedures

### 2.1. Subjects

Sixteen right-handed (Oldfield, 1970) adolescent boys with ADHD, aged 16-18 years old ( $16.69 \pm .81$ ), volunteered to participate in the study, with informed parental consent. The study protocol was approved by the ethics committee of the Shaare Zedek Medical Center. The participants were students in a special school for children with learning disabilities (specializing in children with ADHD). All were clinically diagnosed, either by a psychiatrist specializing in ADHD or by a pediatric neurologist before medication was prescribed, and met the DSM-IV criteria for the ADHD “combined type” (American Psychiatric Association (APA),

2000). On average, participants reported 14.5 ( $\pm 2.1$ ) of the 18 items of the DSM-IV criteria as positive (mid to high severity) (Table 1). All the participants were treated with MPH in a single daily (morning) dose (in different formulations, Table S1 in Supplement 1).

The participants underwent a semi-structured interview to assess learning disabilities and to rule out neurological, psychiatric and medical disorders, skeletal or muscle disease, serious sensory or motor impairments, or chronic medication (apart from MPH). None of the participants reported disorders other than ADHD or a learning disorder (Table 1, Table S2 in Supplement 2). None of the participants used medications other than MPH. Participants reported at least 6 h of sleep per night, and had no sleep-wake-cycle disruptions. Baseline assessment revealed that participants' performance in the Digit Span test was within the normal range.

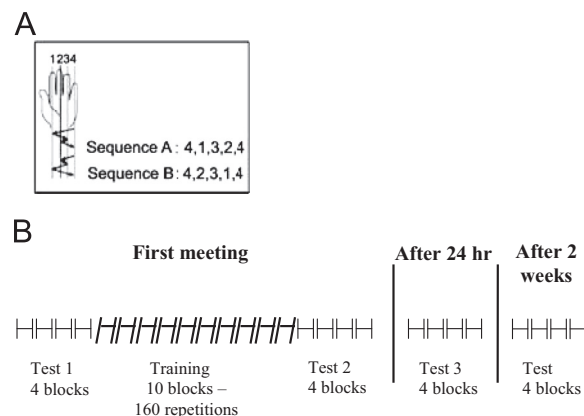
### 2.2. The task

Participants were instructed to oppose the fingers of the left (non-dominant) hand to the thumb in a given sequence (A or B) (Fig. 1A). The participants performed the instructed sequence of movements while sitting upright. Their left (task-performing) forearm was positioned on an arm rest and the elbow was flexed, in a direct view (palm-facing) of a video camera to allow recording of all digit movements. Visual feedback was not afforded; the participants were

**Table 1** Participants' characteristics.

	M	SD
Age	16.69	.81
Digit span, forward	7.14	1.95
Digit span, backward	5.06	1.34
% Items DSM-IV (ADHD)	.81	.12
# Participants with LD	6	

LD=learning Disabilities. All 16 participants met the DSM-IV criteria for the ADHD “combined type”. LD, four participants reported Dyslexia, one participant reported Dyscalculia, and one participant reported both Dyslexia and Dysgraphia.



**Fig. 1** (A) The trained movement sequences and (B) the three sessions in each of the study conditions.

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