MOTOR SEQUENCE LEARNING IN ADULTS WITH ADHD

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MOTOR SEQUENCE LEARNING IN ADULTS WITH ADHD

A Thesis
Submitted to
The City College of New York

In Partial Fulfillment of
The Requirements for the Degree of
Masters of Arts in General Psychology

By
Karin Fisher
April, 2013

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ABSTRACT

A healthy motor system is able to switch and adapt to different environmental contexts and select the most suitable strategy, thus maximizing the efficiency of the movements and save time or energy. Motor hyperactivity in individuals with ADHD is clinically well recognized and can be understood as abnormal motor inhibition. Individuals with ADHD often have problems with responding effectively to a situation that requires a mobilization of complex motor programs. This deficient flexibility of the motor system in ADHD suggests hypofunctioning of the nigral-striatal dopaminergic system. This study used the motor sequence learning paradigm to examine the selection of movement kinematics and force production and modulation in adults with ADHD. A two-by-three mixed design ANOVA, post-hoc independent measure t-tests and Pearson’s correlations were performed. Our results found significantly greater reaction time variability in ADHD as compared to controls. Moreover, subjects with ADHD showed a decreased ability to optimize force production when reacting to different contexts despite intact learning. Thus, participants with ADHD seemed to not be able to integrate the new information and feedback from the environment to inform ongoing motor behavior. Our study provides additional support for the notion that individuals with ADHD have basal ganglia abnormalities and has clinical implications for the diagnosis of ADHD. The findings strongly suggest that motor indices should be further explored as possible biomarkers for ADHD and that the neurophysiological networks underlying motor dysfunctions in ADHD warrant further study.
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Conceived and designed the experiments: Hilary Gomes, Ph.D., ABPdN.
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Performed the experiments: Jared Goldman, Karin Fisher, Clara Moisello, Ph. D.
Analyzed and interpreted the data: Clara Moisello, Ph. D., Karin Fisher, Hilary Gomes, Ph.D., ABPdN.
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"The mind's first step to self-awareness must be through the body."

- George Sheehan

**Introduction**

Attention deficit hyperactivity disorder (ADHD) is a frequently diagnosed childhood disorder defined by three primary symptoms: inattention, impulsivity and hyperactivity that emerge primarily before the age of seven and persist into adulthood (Barkley, 1997). The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, APA, 1994) differentiates between three subtypes: Predominantly inattentive (ADHD-PI), predominantly hyperactive-impulsive (ADHD-PHI) and combined (ADHD-C). The inattention dimension includes difficulty in sustaining attention, distractibility, lack of persistence, and disorganization. Children with ADHD-PI are often non-hyperactive, rather dreamy, and inert children. Their attention problems are non-specific and associated with a family history of learning problems, sluggish cognitive processes, and school failure (Taylor et al., 1998; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). The hyperactivity/impulsiveness dimension comprises excessive motor activity, restlessness, fidgeting, and a general increase in gross body movements/impulsive responding, having difficulty waiting one’s turn when appropriate, and frequent interruption and intrusion on activities of other people (Teicher, Ito, Glod, & Barber, 1996, Lahey et al. 1998, Sagvolden, Johansen, Aase, & Russell, 2005). Children with ADHD-PHI often exhibit specific attention difficulties related to distractibility and reduced persistence. Moreover, these symptoms seem to exist even after controlling for intelligence (Taylor, Sandberg, Thorley, & Giles, 1991).

Approximately three to seven percent of children exhibit the symptoms of ADHD with a boy to girl ratio of 3:1 (Szatmari, 1992). Of children diagnosed with ADHD, 50%
to 70% have challenges in social adjustment and functioning and/or psychiatric problems as adolescents and young adults (Cantwell, 1996). Muglia, Jain, Macciardi, and Kennedy (2000) report that the majority of these individuals will continue to suffer from ADHD during late adolescence and adulthood. Thus, over development, ADHD is associated with greater risks for low academic achievement, poor school performance, retention in grade, school suspensions and expulsions, poor peer and family relations, anxiety and depression, aggression, conduct problems and delinquency, early substance experimentation and abuse, driving accidents and speeding violations, as well as difficulties in adult social relationships, marriage, and employment (Barkley, 1997).

Buchmann et al. (2003) have suggested that hyperactivity is the most outstanding symptom (Nigg, 2006). Halperin, Matier, Bedi, Sharma, and Newcorn (1992) found that only overactivity seems to be uniquely specific for ADHD when they tested children with and without ADHD on objective measures of inattention, impulsivity using a continuous performance test, and movement using solid state actigraphs. Gillberg (1995) argue that studies should not overlook ‘concomitant neuropsychological and motor coordination problems’ (p. 140) and that the potential for children with ADHD to have motor difficulties is clinically well recognized, with prevalence estimates varying from 8 to 52% (Piek et al., 2004; Barkley, 1990). Many of the impaired children have poor handwriting skills (Szatmari, Offord, & Boyle, 1989; Barkley, 1990), which suggests significant overlap of ADHD and movement problems. Piek et al. (2004) claim that the objective assessment of motor performance in children with ADHD should be a matter of routine clinical practice. Therefore, abnormal motor behavior in ADHD warrants further investigation.
Doyle, Wallen, and Whitmont (1995) found that impaired fine motor skills are associated with concentration difficulties and thus that the ADHD-PI group may be more at risk. However, Whitmont and Clark (1996) found a strong correlation between fine motor skill deficits and severity of ADHD pathology. Blind ratings of attention taken during the experiment revealed that the children with all ADHD subtype diagnoses paid attention while performing the kinaesthetic acuity task; therefore the authors discounted the influence of visual inattentiveness. Moreover, Piek et al. (2004) demonstrated that ADHD-PI and ADHD-C groups did not differ from control groups on tests of Kinaesthetic Sensitivity, on motor tasks that require a high level of attention and concentration. Therefore if the poor motor performance is attributed to concentration difficulties, the ADHD-PI group should have demonstrated more impaired performance. In their study nine of the 16 boys in the ADHD-C group and 11 of the 16 boys in the ADHD-PI group were identified as having motor difficulties pointing also to the insufficient recognition of motor difficulties within the DSM-IV (1994) ADHD section. Their results indicated that children with inattention, both predominantly inattentive-type and combined-type, were most at risk for motor coordination difficulties. However the type of problems differed by diagnosis: children with ADHD-PI were more likely to have manual-dexterity and fine motor skills challenges, while those with ADHD-C were more likely to have problems with balance and gross motor skills.

Motor hyperactivity and decreased inhibition in the motor system of children (Moll et al., 2001) and adults with ADHD (Richter, Ehlis, Jacob, & Fallgatter, 2007) are considered to be influenced by dysfunction in the dopamine (Bender et al., 2012) and catecholamine systems (Kirley et al., 2002). Orally taken indirect dopamine-agonist
drugs, such as methylphenidate (MPH), have been effective in decreasing motor
excitability in ADHD children (Gilbert et. al, 2006; Elia, Ambrosini, Rapoport, 1999).
Methylphenidate (MPH) blocks the dopamine and norepinephrine transporters and
inhibits reuptake resulting in the increase of synaptic dopamine (Volkow, Fowler, Wang,
Ding, & Gatley, 2002). Moreover, neuroimaging studies have reported abnormalities in
nigrostriatal dopaminergic brain structures such as volume reduction in the basal ganglia
(Aylward et al., 1996; Castellanos, Giedd, Marsh & Hamburger, 1996) and reduced
striatal activation (Vaidya et al., 1998) in children with ADHD. Consistent with these
findings, some studies in ADHD adults have shown increased density of striatal
dopamine transporters (Dougherty et al., 1999; Krause et al., 2002).

Sagvolden et al. (2005) propose that motor problems are a result of deficient
extinction of previously reinforced behavior and according to Johansen, Aase, Meyer and
Sagvolden (2002) new learning fails to replace the prior overlearned behavior. Sagvolden
et al. (2005) claim that hypofunctioning of the nigral-striatal dopaminergic system causes
neurological “soft” signs such as clumsiness, poor motor control, longer and more
variable reaction times, poor nondeclarative habit learning, reduced response timing,
problems with handwriting and coordination of the activity of different body parts. These
may interact with the hypofunctioning mesolimbic dopamine pathway, thus resulting in
altered reinforcement of novel behavior and deficient extinction of previously reinforced
behavior (Johansen et al., 2002). Links between behavioral selection mechanisms and
dopamine neuron activity are considered to be responsible for strengthening connections
associated with reinforced (usually adaptive) behavior, while at the same time weakening
other neuronal connections linked to nonreinforced (usually maladaptive) behavior.
(Sagvolden et al., 2005). Thus, dysfunctions in the dopamine system seem to delay or stop the process of extinction, which can be observed as increased behavioral variability and incorrectly interpreted as failure to inhibit responses.

Children with ADHD also often exhibit steeper delay-reward gradients, which may have an effect on learning and failure of extinction because new learning fails to replace the prior overlearned behavior (Johansen et. Al., 2002, Sagvolden et al. 2005). Sonuga-Barke, Dalen, Daley and Remington (2002) suggest that ADHD children cannot tolerate waiting and prefer to complete tasks as soon as possible. They believe that abnormal judgment of delayed and immediate rewards leads to impulsivity and overreactivity; ADHD individuals consistently choose small instant rewards over delayed larger incentives because they want to finish their current activity.

Abnormal motor facilitation has been suggested by several studies (Buchman et al., 2003; Moll, Heinrich, Trott, Wirth, & Rothenberger, 2000). Mirsky and Duncan (2001) claim that children with ADHD often have a problem with responding effectively to a situation that requires a mobilization of complex motor programs. They suggest that the ability to shift or alternate response set appropriately for the particular situation is different from response inhibition because in a rapid change of context, children must strategically activate another response simultaneously. Such activation, after motor preparation for response output, is considered to involve left-lateralized dopaminergic circuits (Pribram & McGuinness, 1975) as well as the cerebellum (Monsell, 2003) and basal ganglia (Aron et al., 2003). Sagvolden et al. (2005) claim that increased reaction times and speed variability are not evidence of impaired executive functions or disinhibition, but reveal more fundamental, lower-level motor problems: impaired
modulation of motor functions in terms of poor timing of starting and stopping of responses; impaired acquisition, retrieval, and relearning of programs for sequential motor tasks; and deficient nondeclarative habit learning and memory. Brown and Vickers (2004) showed that adolescents with ADHD have timing difficulties only if the task also required motor responses.

Some studies found a deficient response modulation in ADHD and a failure to modify a dominant response set once initiated (Newman & Wallace, 1993; MacCoon, Wallace, & Newman, 2004). Newman and Wallace (1993) investigated response modulation as an automatic process by which new information is regularly sampled from the environment to inform ongoing behavior and conjectured that the dominant response is continually integrated with feedback from the environment to enable its modulation. Deficient response modulation in ADHD results in failure to modify a dominant response set once initiated. Other studies found that ADHD children had significantly different force modulation as well as planning of motor movement showing impaired adaptation to a changing context. For example, Pereira, Eliasson, and Forssberg (2000) demonstrated that children with ADHD have problems modulating grip force. Others reported difficulties in preparing and planning complete movements assessed by accuracy and velocity of arm and hand movement (Eliasson, Rosblad, & Forssberg, 2004; Yan & Thomas, 2002) indicating abnormality in the basal ganglia. Pereira et al. (2000) reported that ADHD participants exhibit higher, more variable grip-force output, and difficulties in adapting the motor output to targets suggesting impaired anticipation. Eliasson et al. (2004) found that ADHD children made more end-point errors, jerky actions, and
prolonged their movement time thus showing a reduced capacity to select the appropriate speed.

According to Schmidt and Lee (1999) a healthy motor system is able to switch and adapt to a different environmental context and select the strategy more suitable for a specific situation thus maximizing the efficiency of the movements and save time or energy. Moisello et al. (2011) found that people with basal ganglia disorders have a reduced flexibility of the motor system and impaired ability to switch and select the strategy more suitable for the specific situation, to produce efficient movements and to save either time or energy even if motor symptoms are minimal. Their findings suggest that the basal ganglia plays role in appropriate selection and regulation of movement force. In their experimental design people executed faster movements if the targets were unpredictable than in a predictable context in which targets’ locations could be anticipated and thus advanced information about their spatial location was available. The differences in performances between reactive and anticipatory experimental contexts in Parkinson’s and Huntington’s diseases were used as a marker of kinematic flexibility. Moisello et al. (2011) also conjectured that kinematic variables of hand movements reflect the amount of muscle energy and effort. Their study thus investigated the flexible regulation of muscle force and the appropriate selection of movement force that depends on the proper functioning of the basal ganglia (Ghilardi et al., 2008; Grafton & Tunik, 2011).

Basal ganglia, which play a role in the execution of motor responses, may be impaired in ADHD and lead to inappropriate force of response (Nigg, 2006). Moreover, reduced functioning of the cerebellum as assessed by improper timing and temporal
integration of motor movements, may be involved in ADHD as well, and both brain systems are impacted by dopaminergic dysfunction (Nigg, 2006).

This study attempted to validate prior findings suggesting the involvement of the basal ganglia and cerebellum in ADHD by investigating the force modulation, timing variables and accuracy of movements as well as sequence learning. The same paradigm, used by Moisello (2010) in patients with basal ganglia disorders, was employed in this study to examine motor response systems, selection of movement kinematics and force production and modulation in adults with ADHD. We hoped that a comparison of the performance of adults with ADHD with that of adults who had known neurological damage, such as patients with Parkinson’s and Huntington’s Diseases (Ghilardi et al., 2008; Moisello et al., 2011), would improve localization of the neurophysiological networks underlying the cognitive and behavioral dysfunctions in ADHD (Sergeant, Geurts, Huijbregts, Scheres, & Oosterlaan, 2003).

If impaired motor skills in individuals with ADHD are due to inattention, it was hypothesized that ADHD participants would show significant differences in learning and reporting the sequence order verbally as well as executing the movements by arm (Doyle et al., 1995). In contrast, results more in line with Piek et al. (2004) would be that individuals would show only impaired movement production and adaptation to a context while keeping learning intact. We also could have found that individuals with ADHD exhibit an inability to shift or alternate responses due to a hypothesized lack of extinction process and inability to optimize movements, wait and relax, which would support the hypothesis that the basal ganglia are involved in appropriate selection and regulation of
movement force (Sagvolden et al., 2005; Johansen et. al., 2002; Ghilardi et al., 2008; Moisello et al., 2011).

Method

Participants

All participants were right-handed, between 18-29 years of age with normal or corrected to normal vision and hearing. Inclusion criteria for the ADHD group included previous diagnosis of ADHD or a score above 65 on the Conners Adult ADHD Rating Scale – Self Report: Long (CAARS) (Conners, Erhardt, & Sparrow, 1999). Pilot data were collected from 12 participants to test design parameters but are not included here. The final sample consisted of 15 individuals with ADHD (mean age = 24, sd = 2.8) and 18 controls (mean age = 23, sd = 2.4). Four out of 18 control subjects were disqualified because of inconsistent responding on the Conners self-report measure, one control participant was excluded because of taking medication that disrupts concentration and four control participants were eliminated due to such imprecise and unclear jerky movements on the task that the software could not mark properly the onset and ending of most of the movements. One participant from the control population was eliminated from the analysis for inability to report verbally the sequence of stationary targets displayed on the computer screen after finishing the task. Demographic characteristics are shown in Table 1. Medical and academic characteristics are shown in Table 2, 3 and 4.
Table 1. Demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (n=33)</th>
<th>Gender</th>
<th>Age Mean</th>
<th>Average Sleep Mean</th>
<th>Sleep night before Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Controls</td>
<td>18 (54.6%)</td>
<td>Male 2 (11.1%) Female 15 (83.3%) Missing 1 (5.6%)</td>
<td>23.29</td>
<td>6.94</td>
<td>6.31</td>
</tr>
<tr>
<td>ADHD</td>
<td>15 (45.4%)</td>
<td>Male 9 (60%) Female 6 (40%)</td>
<td>24.00</td>
<td>6.93</td>
<td>6.6</td>
</tr>
</tbody>
</table>

Table 2. Academic characteristics.

<table>
<thead>
<tr>
<th>School Difficulty</th>
<th>Gifted class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Controls</td>
<td></td>
</tr>
<tr>
<td>None 9 (50%)</td>
<td>Yes 8 (44.44%)</td>
</tr>
<tr>
<td>Academics 5 (27.78%)</td>
<td>No 8 (44.44%)</td>
</tr>
<tr>
<td>Academic + Social 2 (11.11%)</td>
<td>Missing 2 (11.11%)</td>
</tr>
<tr>
<td>ADHD</td>
<td></td>
</tr>
<tr>
<td>Academic 7 (46.67%)</td>
<td>Yes 6 (40%)</td>
</tr>
<tr>
<td>Academic + Social + Behavioral 4 (26.67%)</td>
<td>No 9 (60%)</td>
</tr>
<tr>
<td>Academic + Social 1 (6.67%)</td>
<td>Academic + Behavioral 3 (20%)</td>
</tr>
</tbody>
</table>

Table 3. Academic characteristics.

<table>
<thead>
<tr>
<th>Healthy Controls</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report card - Academics</td>
<td>Report card - Behavior</td>
</tr>
<tr>
<td>Excellent 12 (66.67%)</td>
<td>Excellent 11 (61.11%)</td>
</tr>
<tr>
<td>Satisfactory 4 (22.22%)</td>
<td>Satisfactory 5 (27.78%)</td>
</tr>
<tr>
<td>Missing 2 (11.11%)</td>
<td>Missing 2 (11.11%)</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD</td>
<td></td>
</tr>
<tr>
<td>Excellent 2 (13.33%)</td>
<td>Excellent 7 (46.67%)</td>
</tr>
<tr>
<td>Satisfactory 7 (46.67%)</td>
<td>Satisfactory 4 (26.67%)</td>
</tr>
<tr>
<td>Need improvement 6 (40%)</td>
<td>Need improvement 4 (26.67&amp;)</td>
</tr>
</tbody>
</table>

*Table 3. Three out of 6 control subjects who received services in school self-reported being in gifted classes. Two out of the remaining three control subjects self-reported having “excellent” evaluation on report cards.*
Table 4. Medical characteristics.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Conners T-score Mean (sd)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Healthy Controls</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None 17 (94.4 %)</td>
<td>41.41 (7.69)</td>
<td>None 15 (83.33%)</td>
</tr>
<tr>
<td>Missing 1 (5.6%)</td>
<td></td>
<td>Depression + Mania 1 (5.56%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Missing 2 (11.11%)</td>
</tr>
<tr>
<td><strong>ADHD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None 3 (20%)</td>
<td>60.8 (10.74)</td>
<td>None 1 (6.67%)</td>
</tr>
<tr>
<td>Some 12 (80%)</td>
<td></td>
<td>ADHD only 5 (33.33%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADHD + learning 2 (13.33%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADHD + depression + mania 6 (40%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADHD + conduct 1 (6.67%)</td>
</tr>
</tbody>
</table>

**Materials**

**Experimental setup:**

Participants sat on a comfortable chair of adjustable height in front of a computer monitor. The height was adjusted so that the subject kept the hand at a comfortable position on a table in front of him/her (see Figure 1). The table was equipped with a digitizing tablet (Calcomp Drawing Board III/IV) positioned horizontally. The surface of the tablet was 45 by 30 cm, with a resolution of 400 points per cm. The tablet was connected to a PC through a USB cable. The monitor of the PC (17”) was placed on top of the table in front of the subjects and was used for stimulus presentation. Subjects controlled a cursor on the computer screen by moving a hand-held “mouse” with their dominant arm on this digitizing tablet, which sampled the hand position at 200 Hz (Moisello, 2010).
Figure 1. Experimental setup.

Figure 1- The experimental setup for reaching movements recording (Moisello, 2010).

**MTM software:**

Customized software developed by a software company (ETT, www.ettsolutions.com) to design and run experimental protocols as well as to store data from a graphic digitizing tablet and compute some characteristic parameters concerning the hand trajectory was employed. The software platform is called MotorTaskManager (MTM) and is used to investigate motor performance in healthy subjects as well in patients with cognitive or motor disorders. MTM allows the user to define several experimental protocols, which basically consist of reaching exercises towards targets presented on the screen according to various criteria (Moisello, 2010).
**Motor Tasks:**

The experimental sequence learning task developed by Ghilardi, Eidelberg, Silvestri, and Ghez (2003) was employed with four conditions, to investigate the idea of a switch in kinematic strategy -from short to longer movement durations. In normal life, movement velocity and duration can be modulated and optimized depending upon the situations and the task requirements. Complex motor skills often consist of a fixed sequence of movements. The process of learning a motor sequence involves learning the single sequence elements and their order (“what”) and developing the ability to perform them as a well-articulated, single behavior (“how”).

In Moisello (2010), the tasks tried to reproduce different ecological contexts for movement execution, which have usually an impact on the selection of a motor strategy. Indeed, in normal life, movement duration can be modulated and optimized depending upon the situations and the task requirements. For instance, when subjects know “where and when” to go, they usually start moving in advance, using more time and less energy. On the other hand, when responses have to be made as fast as possible to unpredictable stimuli, subjects shorten movement duration, producing high velocities and accelerations.

**Four Designed Conditions:**

**RAN:** In the random condition (RAN) targets were presented in a non-repeating and unpredictable order. Instructions were to reach for each target after its appearance “as soon as possible”, minimizing reaction time but avoiding target anticipation in two blocks.
**CCW:** In the counterclockwise condition (CCW) targets appeared in a predictable counterclockwise order. Subjects had to reach the target in synchrony with the tone. Thus, they had to initiate each movement before target and tone presentation in two blocks.

**SEQ hard:** In the hard sequence learning condition (SEQ hard) eight targets were presented in a repeating order. Subjects were informed that there was a sequence, and instructed to learn its order while reaching for targets and to anticipate target appearance in three successive blocks of each. They were explicitly instructed to anticipate target appearance when they knew which one was going to be presented; otherwise, they had to wait for the target to appear and move to it afterwards.

**SEQ easy:** The easy sequence learning condition (SEQ easy) was similar to the SEQ hard, with the difference being that the sequence of targets appeared in order, which was easier to learn.

**History and Rating Scale:**

A history form (Appendix 1) was created for this study to determine potential learning or behavioral difficulties. Participants reported on sleep, medications, academic history and diagnosed disorders.

**The Conners Adult ADHD Rating Scale – Self Report: Long (CAARS):**

CAARS was completed by the participants (Conners et al., 1999). This 66-item self-report rating scale contains nine empirically derived scales assessing a broad range of problem behaviors. It includes four factor-derived subscales of inattention/memory problems, hyperactivity/restlessness, impulsivity/emotional liability and problems with

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self-concept. It also contains three DSM-IV ADHD symptom subscales (inattentive, hyperactive-impulsive and total ADHD symptoms), a 12-item ADHD index and a validity scale to capture careless response patterns.

Procedure

Adult participants with ADHD were recruited via the City College of NY AccessAbility Center (AAC) via letter/email (Appendix 2) sent to students registered as having ADHD and by recruitment poster (Appendix 3). ADHD subjects were also contacted via Mount Sinai hospital and the student disability offices at other university campuses in the New York City. Participants with typical development were recruited from the City College psychology subject pool as well as through the posters and word of mouth.

Testing was completed in one session of 1.5 hour or less. ADHD participants taking stimulant medication were asked not to take it on the day of testing. Participants taking other types of medication were excluded. All participants signed consent forms and were told that their participation was confidential and that they could discontinue testing at any time. They learned to perform the tasks in one or two training sessions before each condition. Training was complete when performance became stable (Ghilardi et al., 2008).

Participants moved a cursor on a digitizing tablet with their right hand out and back from a central starting point to one of eight radically arrayed targets at 4 cm distance (See Figure 2). Subjects were instructed to make smooth movements with a sharp reversal inside each target. Targets appeared on a screen in synchrony with a tone at a
constant interval of 1 s. Testing was done in separate trial blocks of 90 seconds each, for a total of 88 movements (11 complete movement cycles).

**Figure 2. Appearance of targets.**

![Figure 2 - Target array used in the experiments with sample trajectories (from Moisello et al. 2009).](image)

Participants performed two blocks of the RAN condition and two blocks of CCW condition. Then they filled out the history form and the CAARS. Then subjects completed three blocks of SEQ easy and three blocks of SEQ hard tasks. Additionally, they reported the order of the sequence verbally at the end of each 90-second trial block and declarative scores (from 0 to 8) were computed (Ghilardi, Moisello, Silvestri, Ghez, & Krakauer, 2009). The order in which the conditions were presented was the same for all participants; however to prevent order effects, usually two or three shorter target reaching tasks were inserted between the RAN, CCW and SEQ conditions. Lastly, subjects were debriefed about the purpose of the study; its hypotheses and some preliminary finding were elucidated. They were paid $20 for their participations or given course-credit for their time.
Data analysis

MTM data:

MTM records the hand path during all tasks and derives the velocity and acceleration profiles. Based on the characteristics of the velocity profiles, the following critical points are calculated (Moisello, 2010):

- **onset point**: the point where the movement to the target begins. It was identified as the moment in which the hand speed first exceeds the 10% of the peak outward velocity at the beginning of a trial.

- **reversal point**: the end of the outward movements, it was defined as the x-y location taken when the hand reached its maximal radial displacement from the center in the outward phase of the movement.

- **return point**: the point where the hand stabilizes again around the central position. It corresponds to the second relative minimum of the velocity profile.

Variables:

Based on the critical points, several variables are calculated for each movement:

- **onset time (OT)**: the time in seconds from target appearance to movement onset. In random blocks, OT always corresponds to reaction time (i.e. the values are positive). In
sequence blocks, negative values indicate movements starting before the presentation of the target;

- movement time (MT): the time in seconds from movement onset to movement reversal, see Figure 2B;

- index of force modulation (delta movement time): the difference of movement time in seconds between the RAN and CCW conditions (mathematically computed as MT in CCW – MT in RAN);

- index of force production in SEQ conditions ( % change in MT of anticipatory movements): the mean movement time in seconds of anticipatory movements expressed as percent change from individual RAN movement time (mathematically computed as [MT in SEQ – MT in RAN] * 100 / MT in RAN )

- number of “anticipatory movements” in the sequence conditions: the movements with onset time in seconds below the lowest value of the random (RAN) onset time (see Figure 2C). Anticipatory movements tend to have better spatial accuracy than reactionary movements; moreover, these movements are of longer duration and have decreased peak velocity and acceleration because they are better specified in advance.

- verbal declarative knowledge of the sequence: a score from 0 (unawareness of a repeating sequence) to 8 (or 100%, complete knowledge of the sequence);
Rationale behind the variables:

According to Moisello et al. (2011) movements to the targets are usually faster, with shorter movement times and higher peak velocities and accelerations and they are performed with greater force and lower duration in reaction RAN condition than in predictable CCW tasks in which advanced information about the spatial location of target occurrence are available (Figure 3). This difference in movement times between these two conditions is the index of force modulation and suggests a “flexibility” to appropriately adjust motor performance without awareness to respond appropriately to different contexts (Moisello et al., 2009).

Figure 3. Onset and movement times in RAN unpredictable and CCW predictable conditions.

The acquisition of motor sequences (SEQ) combines RAN and CCW tasks as well as learning of the target sequence with movement execution. Subjects acquire the
knowledge of the sequence order and the ability to execute the movements and thus “perform” the sequence (Moisello et al., 2009). Ghilardi et al. (2008) believe that the order of targets is learned explicitly and is quantified as a discrete variable by the progressive increase in the number of correct anticipatory movements. This variable has been highly correlated with the verbal scores collected at the end of each trial block. Such a high correlation has led to the decision to use correct anticipatory movements as a proxy measure for explicit learning and as an index of the declarative conscious knowledge of the sequence order (Ghilardi et al., 2008; Moisello, 2010).

According to Moisello et al. (2009) the observed changes in onset times might reflect an improvement of stimulus-response processing and movement planning (which can be considered automatic). However in their study onset time reductions were not similar in random and sequence learning conditions, and thus they reflect the awareness of the upcoming target and the acquisition of the sequence (a declarative component that influences decision making and results in the production of anticipatory movement). Moreover, during their intentional sequence learning experiment the decreases in onset times followed (not preceded) the development of the declarative knowledge of the target order providing the evidence that, first, awareness that a sequence is present expedites the development of the order learning. The voluntary execution of the movements can be seen in negative onset times (-300 ms) and the fact that the subjects started the movements ahead, reaching targets at the same time as they appeared on the screen. An alternative explanation would suggest that the number of correct anticipatory movements represents a variable that is as conscious as the Pavlovian reflex (Pavlov & Anrep, 1927);
less explicit and represents more of a priming effect in the motor acquisition of the sequence.

The *automatic/procedural* ability to perform the sequence, to modulate and optimize movements and to change motor strategy was measured by movement time changes and by comparing the kinematic and spatial characteristics of anticipatory and non-anticipatory movements – *the index of force production*. Learning the sequence is reflected as a decrease of onset times as well as prolonged movement time and improved spatial accuracy, which happens outside of subject awareness. Participants make an unconscious shift from a time-saving reactive (as in RAN condition) to an energy-saving anticipatory (as in CCW condition) strategy with less muscle force execution (Figure 4).

**Figure 4. The development of anticipatory movements during sequence learning.**

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*Figure 4 - Schematic illustration of the development of anticipatory movements during sequence learning. At the beginning (a.), movements must be initiated by responding in time to the target appearance. In the course of learning (b.), movements start before the target (boxed hand paths). Finally, when the sequence is entirely known (c.), all target appearances are anticipated (Moisello et al., 2009).*
As movements become anticipatory because the subject learns the sequence order, the MT of anticipatory movements increases and the percent change of MT of anticipatory movements (index of force production) increases as well (Ghilardi, et al., 2008), thus showing a significant savings in energy and changes from values in the range of the RAN to values in the range of CCW (Figure 5 and Figure 6). The force production index represents a progressive transition from the unknown, or unpredictable, to the known, or predictable; the participant’s unconscious gradual tendency to relax, wait, conserve energy and react with less force and haste, as the sequence and the appearance of the targets become known.

**Figure 5.** The % increase in MT of anticipatory movements – index of force production in SEQ condition.

![Graph showing the % increase in MT of AM per cycle in SEQ condition](image)

*Figure 5 - % increase in the anticipatory movements increase per cycle in SEQ condition (Moisello et al. 2009)*
Figure 6 - The MT of anticipatory movements in SEQ increases in the course of learning, going from values in the range of the RAN task to values in the range of CCW (orange – RAN, yellow – CCW, red – SEQ) (Moisello et al., 2009).

**Statistical analyses:**

In the RAN and CCW conditions, the means and standard deviations of movement times and index of force modulation (delta MT) were calculated. An independent measures t-test was performed to detect significant differences between ADHD and control participants in variability of movement times and the force modulation.

In the SEQ condition, a two-by-three mixed design ANOVA (ADHD/control group x SEQ block) was run to test for main effects and interaction. Post-hoc
independent measure t-tests were performed to investigate significant differences in the force production index between ADHD and control participants.

A Pearson’s correlation between the number of anticipatory movements and verbal scores of newly learned sequences was calculated for each SEQ block; Moisello (2009) found these to be highly correlated. Pearson’s correlations were performed to look for a relationship between each motor performance variable and the CAARS T-scores and DSM-IV T-scores.

Results

**Increased onset time variability in ADHD group in RAN condition**

Mean onset reaction time in the RAN condition was not significantly different between ADHD and controls with p=0.227 (Figure 7). However, variability in onset times in RAN condition (Figure 8) was significantly higher in ADHD (p=0.005*), consistent with prior research findings of greater response time variability in individuals with ADHD (Sagvolden et al., 2005; Nigg, 2006).
Figure 7. Onset time in RAN condition.

Figure 8. Onset time variability.
**Decreased force modulation in ADHD group**

Mean movement time was similar in both groups for both RAN (p=0.302) and CCW conditions (p=0.087) as seen in Figure 9. However, when using the index of force modulation (delta MT), a measure of the ability to optimize motor performance without awareness to respond appropriately to different contexts computed as the difference of movement time in seconds between the RAN and CCW condition, the independent measure t-test found a significantly decreased range for ADHD compared to controls with p=0.017* (Figure 10). This suggests that ADHD subjects have a reduced flexibility in changing their strategy when responding to two different environmental contexts.

When comparing the means of movement times of ADHD and controls, it can be seen that ADHD subjects are much faster in the CCW condition (M=418.3 ms) than control participants (M=444.3 ms), in the task in which it is possible to wait and relax because the target appearance is known in advance. The ADHD group is also slightly slower in the RAN condition (M=308.2 ms) than control participants (M=292.3 ms). This means that CCW movement times in the ADHD group are predominantly responsible for the reduced index of force production 110 ms (delta movement time) as opposed to the value of 152.1 ms in the control group. Since the difference in the movement times in the RAN conditions between the groups is smaller (15.9 ms) than the difference in the CCW condition (26 ms), motor speed is controlled in the force production index variable. ADHD participants are more similar to controls in the RAN task and more different from controls in the CCW task with regard to movement times. The results suggest that ADHD subjects do not alter the movements and do not align them to the task, which would require changing from RAN reaction to CCW anticipation.
Figure 9: Mean movement times in Ran and CCW conditions.

Figure 10. Index of force modulation expressed as the difference in movements times between RAN and CCW conditions.

Figure 10 - the bigger difference in delta movement time reflects the greater ability to modulate the motor response
Decreased ability to optimize force production during sequence learning in ADHD

There was no significant difference in the number of correct anticipatory movements per block between ADHD and healthy controls in SEQ (p always >0.05; Figure 11, Figure 12). Interestingly, differently from control, Pearson’s correlation between the number of anticipatory movements per block and verbal scores was not significant for ADHD participants in the first block (r=0.420, p>0.05). Since in the controls the number of anticipatory movements is significantly correlated with the verbal scores collected at the end of each trial block (Ghilardi et al, 2003; Moisello, 2010), this might indicate a delay for ADHD individuals in aligning the movement execution with the verbal sequence knowledge during the initial acquisition of the target order.

Figure 11. The number of correct anticipatory movements per block in SEQ condition.
The two-by-three mixed design ANOVA (ADHD/control group x SEQ block) found significant main effects for the block (F (2,60) = 31.89 at p<0.001*) and group (F (1,30) = 4.0 at p< 0.05*) and no significant interaction between the group and blocks (F (2,60)<1).

Post-hoc independent measure t-tests were performed to investigate significant differences in the force productions index between ADHD and control participants. The percent change in movement time for anticipatory movements was significantly lower in ADHD compared to controls in each block (block 1: p=0.034*; block 2: p=0.027*; block 3: p=0.050*), as well as all blocks combined (p<0.031*) thus confirming a reduced force production (Figure 13). The sequence learning showed a different pattern for each group: in contrast to the controls, ADHD participants did not seem to change the initial “reactive” strategy to “anticipation” but continued to do what seemed to work from the
start despite the acquired verbal knowledge of the target appearance. This inability to adjust the performance as they learn the sequence is completely outside of their awareness and conscious control. ADHD participants showed shorter movement times of anticipatory movements than healthy controls in SEQ condition in each block which can be seen in Figure 14 and Figure 15.

Figure 13. Percent increase of movement time of anticipatory movements in SEQ hard.
Figure 14. The mean movement time of anticipatory movements in SEQ condition.

Figure 15. The development of movement time of anticipatory movements in SEQ condition across the cycles.
Discussion

To our knowledge this research study is the first attempt to investigate motor response systems in an ADHD population by using the motor sequence learning paradigm designed by Ghilardi et al. (2008). Our investigation of particular deficits in movement optimization and learning attempted to uncover evidence of an inefficient or deficient processing in specific neurophysiological networks.

A consistent finding in the ADHD literature is that individuals with ADHD show greater reaction time variability than typical controls (Rommelse et al., 2007, Sagvolden et al., 2005; Nigg, 2006). Our findings are consistent with the prior findings of increased reaction time variability in ADHD as compared to controls and confirmed that increased symptom severity is related to increased response variability.

Across two independent measures, the results indicate that individuals with ADHD show a decreased ability to optimize force production when reacting to different contexts. Further, increased symptom severity was related to decreased capacity for force modulation. The fact that ADHD participants were much faster and more different from controls in the CCW condition suggests impaired anticipation, as they have difficulties in adapting the motor output to predictable targets (Pereira et al., 2000). In the RAN condition, given that the motor responses were completely stimulus-dependent and were presented both at a moderate rate and in short runs, the motor performance of participants with ADHD was comparable to that exhibited by controls except for the variability in reaction times. More typical performance in the RAN condition than in the CCW supports the notion of deficits in motor timing (Rommelse et al., 2007).
Motor hyperactivity can be understood as abnormal motor inhibition (Buchman et al., 2003; Moll et al., 2000) and is considered to be influenced by dysfunction in the dopamine system (Bender et al., 2012). Links between behavioral selection mechanisms and dopamine neuron activity are responsible for strengthening connections associated with reinforced (usually adaptive) behavior, while at the same time weakening other neuronal connections linked to nonreinforced (usually maladaptive) behavior (Sagvolden et al., 2005). According to Schmidt and Lee (1999), a healthy motor system can switch and adapt to a different environmental context and select the strategy more suitable for a specific situation, thus maximizing the efficiency of the movements and save time or energy. Our findings belie a healthy motor system in ADHD.

The significantly lower index of force modulation and inability to conserve energy for ADHD found in this experiment is in line with the study of Johansen et. al. (2002), who proposed that ADHD subjects fail to replace prior overlearned behavior with new learning. Moreover, according to Sagvolden et al. (2005), hypofunctioning of the nigral-striatal dopaminergic system causes neurological “soft” signs such as longer and more variable reaction times, poor nondeclarative habit learning and reduced response timing, all of which are reflected in our data. Participants with ADHD showed less evidence of automatic motor learning despite adequate declarative behavior. This is in line with the research of Wanabe, Ikeda and Miyao (2010) who found that explicit learning of visuomotor sequences in ADHD is largely unimpaired. Also, the study of Barnes, Howard, Howard, Kenealy and Vaidya (2010) likewise found atypical procedural sequence learning in ADHD population. Statistical analyses confirmed a different pattern in performing the learned sequence despite the similarities in knowledge of the target
order as evidenced by the number of correct anticipatory movements. Thus learning was not impaired, but the unconscious motor performance was not optimal and efficient.

The reduced force production index in sequence learning tasks confirms the conclusions of Mirsky and Duncan (2001) that children with ADHD often have a problem with responding effectively to a situation and shifting motor responses appropriately for the particular situation. According to Sagvolden et al. (2005) this indeed reveals more fundamental, lower-level motor problems: impaired modulation of motor functions in terms of poor timing of starting and stopping of responses and impaired acquisition, retrieval, and relearning of programs for sequential motor tasks.

Our results also validated a deficient response modulation in ADHD and a failure to modify a dominant response set once initiated (Newman & Wallace, 1993; MacCoon et al., 2004; Pereira, et al., 2000). ADHD subjects seem not be able to integrate the new information and feedback from the environment to inform ongoing motor behavior and enable modulation of motor responses.

Basal ganglia, which play a role in the execution of motor responses, may be impaired in ADHD and lead to inappropriate force of response (Nigg, 2006). The imaging studies of Croxson, Walton, O'Reilly, Behrens, & Rushworth (2009) and Vaillancourt, Mayka and Corcos (2007) showed that basal ganglia play a role in “selecting” the appropriate effort and force levels. Moisello et al. (2011) tested a group of patients in the early stage of Parkinson’s disease (PD) and a group of pre-symptomatic carriers of Huntington’s disease (pHD), populations with basal ganglia involvement, dopaminergic deficits in substantia nigra (PD) and atrophy of the caudate (pHD) but minimal or no motor impairment. They found a significantly smaller index of force
modulation (delta MT) in both populations compared to controls. The decreased abilities of our ADHD sample to wait and conserve energy in CCW condition are in line with pHD patients who do not exploit the option of reducing muscle effort in predictable tasks to the same degree as normal controls (Moisello et al., 2011). Thus, it can be hypothesized that our study provides additional support for the notion that individuals with ADHD have basal ganglia abnormalities, since their motor characteristics and reduced range of movement time (delta MT) between predictable and unpredictable conditions resemble those shown by patients with abnormalities in this brain region despite the existence of minimal motor symptoms. Moreover, as is the case for patients with pHD, particular deficits in movement optimization are consistent with Sergeant et al.’s (2003) suggestion of deficits in motor organization.

This experiment has several limitations. The sample sizes were small, as the recruitment of ADHD subjects proved to be more challenging than expected. Moreover, our ADHD sample consisted of predominantly college ADHD students who are high functioning and thus are not representative of the general ADHD populations. However that we found a significant abnormality even in these high functioning ADHD suggests a likely problem in more impaired individuals. An extension of this study should recruit adult ADHD participants who are not attending college so the results could be validated and generalized to the larger low functioning ADHD group. It can be hypothesized that such research would found more significant differences in the flexibility to modulate motor responses to the environmental changing context.

According to Gillberg (1995), ADHD research should focus on ‘concomitant neuropsychological and motor coordination problems’ (p. 140). Future studies may
combine the motor learning sequence paradigm with neuroimaging to detect the neural clusters involved while learning and performing the sequence. Our results have clinical implications in the possibility of enhancing the validity of teacher and parental self-reports and increasing the accuracy of ADHD diagnosis. The findings strongly suggest that motor indices should be further explored as possible biomarkers for ADHD and that the neurophysiological networks underlying motor dysfunctions in ADHD warrant further study.
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Appendices

Appendix 1. Demographic and academic history form

DEMOGRAPHIC AND ACADEMIC HISTORY FORM

Date: ______/_____/_____
Participant Number: ______/_____/_____

BACKGROUND INFORMATION

What is your date of birth? ______/_____/_____
What is your gender? Female Male
What hand do you write with? Left Right
What is your ethnicity?
On average, how many hours of sleep do you get? ___________________
How many hours of sleep did you get last night? __________________
Have you ever taken medicine for a problem with your behavior, for example Ritalin to help with attention?
If yes, please list:
  a. Are you currently taking this medicine? Yes No
  b. Did you take it today? Yes No
Do you take any other medications on a regular basis?
If yes, please list:

SCHOOL HISTORY

What is the last grade of school you completed?
Did you or do you have any difficulties in school?
If yes, was/is it:
  a. Academics / School work Yes No
  b. Behavioral Yes No
  c. Social Yes No
Did you ever repeat a grade in school?
If yes, what grade?
Did you ever skip a grade in school?
If yes, what grade?
Did you ever have trouble
with math?
If yes, can you describe the problem?

Did you ever have trouble with reading?
If yes, can you describe the problem?
Were you ever in a class for children with special needs?
Yes  No
If yes, what kind of program was this?

Were you ever in a class for gifted children?
Yes  No
If yes, what kind of program was this?

In general, what kinds of comments or grades did you receive on report cards for school work?
Excellent  Satisfactory  Needs Improvement

In general, what kind of comments or grades did you receive on report cards for behavior?
Excellent  Satisfactory  Needs Improvement

Did you ever receive any of the following services in school:

a. Counseling (help with behavior) Yes  No
b. Help with arithmetic Yes  No
c. Help with reading Yes  No
d. Language therapy (help with using words) Yes  No
e. Occupational therapy (help with movement) Yes  No
f. Social skills (help with getting along with others) Yes  No
g. Speech therapy (help with talking clearly) Yes  No
h. Other Yes  No

Please describe:

Did you ever receive any of the following services outside of school:

a. Counseling (help with behavior) Yes  No
b. Help with arithmetic Yes  No
c. Help with reading Yes  No
d. Language therapy Yes  No

55
Has any doctor or other professional ever told you that you have any of the following?

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<td>f.</td>
<td>Social skills (help with getting along with others)</td>
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<td>Speech therapy (help with talking clearly)</td>
<td>Yes</td>
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Please describe:

Thank you.
Appendix 2. Recruitment letter

The City College of
The City University of New York

February 22, 2011

Dear Student,

We are writing to invite you to participate in a new study at City College. This study will look at how people learn simple motor tasks to help us to better understand the causes of ADHD. These tasks ask you move a cursor on a digitized tablet sitting on top of the table in patterns and when you see circles light up. The study will require one, 1 hour visit to our lab here at City College and we will pay participants $20 for their time.

You are receiving this letter because you are registered with the AccessAbility Center. The office kindly agreed to mail out these letters for us. They did not tell us your name and we will not tell them who participated. We provided them with blank, stuffed envelopes and they addressed and mailed them for us and we never saw the names. Participation in this study is completely voluntary and independent of your relationship with the AccessAbility Center. If you are not interested in participating, that is fine; it will not affect the services you receive from the AccessAbility Center and in fact, they will never know whether or not you participated.

If you think that you might be interested in participating in this study or have further questions, please call Jared at (917-597-9862) or email him at (jedgoldman@hotmail.com). Please note, email transmissions are not secure, so please do not send any private information by email. Alternatively, you can cut-off and complete the form on the bottom of this letter and send it back to us in the enclosed postage-free envelope. We will then get in touch with you.

Thank you considering our study.

Sincerely,

The City College Motor Learning Team

Please call me so that I can find-out more about the new study that looks at how people learn simple motor tasks being conducted by the City College Motor Learning Team.

Name:

Email Address:

Phone number:
RESEARCH OPPORTUNITY

A research group at City College is looking for participants …

• Who have ADHD
• Are between 18 and 29
• Are right-handed

Study Pays $20

If interested, contact the City College Motor Learning team at karin_fisher@yahoo.com