ABSTRACT

Title of Document: BRAIN FUNCTION UNDERLYING ADAPTIVE SENSORIMOTOR CONTROL IN CHILDREN WITH AND WITHOUT DEVELOPMENTAL COORDINATION DISORDER

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One child in every classroom (6% of children) suffers from Developmental Coordination Disorder (DCD). Children with DCD exhibit marked impairments in movement planning and adaptive visuomotor behavior. However, few studies have investigated the brain functions that underlie behavioral difficulties exhibited by children with DCD. The overarching objective of this dissertation was to examine brain function using electroencephalography (EEG) both at rest and during the performance of visuomotor tasks of different levels of complexity (i.e. static vs. dynamic task environments) to determine if deficits in motor behavior are related to disrupted brain function in children with DCD. The first study revealed that the cortical activation patterns exhibited by children with DCD at rest were different than their typically developing (TD) peers, particularly for the left motor cortical region. Moreover, the activation patterns of children with DCD were similar to the patterns previously reported for young TD children, suggesting a "maturational lag" in brain activation specific to motor function.

For the remaining studies, children performed line drawing movements on a computer tablet towards visual targets presented on a computer screen. These studies examined whether or not children with DCD exhibit different cortical activation patterns during the execution of goal-directed drawing movements. In Study 2, children performed simple drawing movements to stationary targets. The performance of children with DCD followed the same age-related developmental trajectory as TD children. However, children with DCD engaged motor planning and control brain areas to a greater extent throughout the movement compared to TD children, suggesting greater cortical effort to complete the task. For the last two studies, children performed drawing movements in dynamic environments in which visual stimuli cued participants to either abruptly stop ongoing movements (Study 3.1) or to modify movements online to displaced target locations (Study 3.2). Results from Study 3.1 demonstrated that children with DCD do not have difficulties inhibiting movements, a finding that may be attributed to similar cortical activation patterns as the TD children in response to stop signals. Study 3.2 revealed that children with DCD exhibit difficulties modifying movements online, which may be due to a lack of preparatory cortical activation in this group. Taken together, this dissertation provides evidence that disrupted cortical function both at rest and during movement planning may underlie differences in motor performance in DCD.

BRAIN FUNCTION UNDERLYING ADAPTIVE SENSORIMOTOR CONTROL IN CHILDREN WITH AND WITHOUT DEVELOPMENTAL COORDINATION DISORDER

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Chapter 1: Introduction

Overview

Developmental Coordination Disorder (DCD) affects one child in every classroom in the US (~6% of all children) and significantly interferes with academic achievement and the ability to perform activities of daily living requiring motor coordination (APA, 2004). Children with DCD exhibit marked deficits in sensorimotor integration (Mon-Williams, Wann, & Pascal, 1999), movement planning (Smyth & Mason, 1997), and adaptive visuomotor behavior (Hyde & Wilson, 2011a; Hyde & Wilson, 2011b; King, Harring, Oliveira, & Clark, 2011). Kaplan et al. (1998), proposed that the behavioral impairments exhibited by children with DCD are related to "atypical brain development" – a hypothesis that is predominantly based on the comorbidity between DCD and other developmental disabilities, including attention-deficit hyperactivity disorder (ADHD) and developmental dyslexia (DD). However, there is little empirical evidence to support the hypothesis that the sensorimotor deficits in children with DCD are the result of atypical brain development; moreover, only a few studies to date have investigated brain function in DCD. This dissertation addressed this knowledge gap by examining potential differences in brain function both at rest and during adaptive sensorimotor behaviors in children with and without DCD.

Our previous research demonstrated that age-related differences in cortical dynamics, as measured with electroencephalography (EEG), reflect differences in the quality of movement kinematics in children and adults (Pangelinan et al., 2011). These measures are likely also sensitive to differences in motor planning and adaptive

sensorimotor control in children with and without DCD. The research in this dissertation extended our previous research examining age-related differences in cortical dynamics in typically developing (TD) children by employing similar methodology to investigate differences in children with and without DCD. Specifically, EEG and movement kinematics, when applicable, were recorded from children with and without DCD at rest and during the execution of goal-directed drawing movements of varying complexities in order to provide insights regarding differences in brain function between children with and without DCD. Taken together, this dissertation provides novel insights regarding the electrocortical correlates of functional deficits in adaptive sensorimotor control in children with DCD.

Specific Aims

SA 1 (Study 1): To determine if children with DCD, as compared to their TD peers, exhibit different patterns of brain activation at rest.

EEG spectral power quantifies the oscillatory characteristics of brain activation patterns. Developmental differences in the amount of slow and fast frequency components have been used to index brain maturation and cortical function in TD children (Benninger, Matthis, & Scheffner, 1984; Clarke, Barry, McCarthy, & Selikowitz, 2001a; Gasser, Jennensteinmetz, Sroka, Verleger, & Mocks, 1988; Gasser, Verleger, Bacher, & Sroka, 1988). Specifically, young children (4- to 6-year-olds) exhibit greater power in low frequency bands (theta and alpha) and a shift in peak alpha and theta power. Deviations from the patterns of the expected age-related changes in EEG spectral power at rest have been reported in children with learning disabilities including ADHD (Baving, Laucht, & Schmidt, 1999; Clarke, Barry, McCarthy, & Selikowitz, 2001b,

2002), autism spectrum disorder (ASD) (Sutton et al., 2005), and dyslexia (Colon, Notermans, de Weerd, & Kap, 1979). These children also exhibit greater power in low frequency bands and lower peak alpha frequencies. Given the high co-morbidity of motor coordination problems and these developmental learning disabilities, it is likely that children with DCD also exhibit different patterns of brain activity at rest, as compared to TD children.

Two minutes of EEG were recorded at rest from 65 electrode sites from three groups of children (age range: 7.5 – 12.5 years): children with DCD, children with moderate movement difficulties, and TD children. Differences in EEG spectral power by region (frontal, central, parietal, and occipital locations), hemisphere (left and right), and group were examined.

Hypothesis 1. It was hypothesized that children with DCD would exhibit greater spectral power in lower frequency bands (theta/alpha) at rest compared to TD children. In addition to a shift in power, it was hypothesized that the peak alpha frequency would be lower in children with DCD. In addition, children with DCD would exhibit regional differences in EEG spectral power consistent with their cognitive and motor deficits. Children with moderate movement coordination difficulties would represent an intermediate phenotype in terms of their brain activation patterns.

SA 2 (Study 2). To determine differences in electrocortical and kinematic indices of motor planning between children with and without DCD in a static movement environment.

Given that previous studies have found that children with DCD exhibit poor motor planning (Mon-Williams et al., 2005) and deficits in adaptive visuomotor behavior

(Hyde & Wilson, 2011a, 2011b; Kagerer, Bo, Contreras-Vidal, & Clark, 2004; Kagerer, Contreras-Vidal, Bo, & Clark, 2006; King et al., 2011), it was expected that these children will also exhibit different EEG activation patterns compared to TD children.

EEG and movement kinematics (movement time, movement length, jerk, spatial error, and directional error) were recorded during self-initiated, self-selected aiming-drawing movements to two peripheral targets presented on a computer screen to assess differences in cortical dynamics underlying motor planning and control. This study provided a replication and extension of a previous study that characterized EEG dynamics and kinematics for TD children and adults (Pangelinan, Kagerer, Momen, Hatfield, & Clark, 2011).

Movement-related cortical potentials (MRCPs), task-related spectral power (TRSpec), and movement kinematics were examined using regression analyses to determine if children with DCD follow the same developmental trajectory as TD children. In addition, mean comparison tests were examined to assess mean group differences for these measures.

Hypothesis 2. It was hypothesized that children with DCD would exhibit different movement-related activation patterns in comparison to their TD peers. Consistent with this hypothesis, children with DCD would exhibit decreased visuomotor performance, as compared to the TD children.

SA 3 (Study 3.1). To determine the relationship between frontally-mediated executive processes and the ability to inhibit pre-potent movement plans (stop signal).

SA 4 (Study 3.2). To determine the relationship between frontally-mediated executive processes and the ability to adapt pre-potent movement plans (target jump).

Adaptive motor behavior may be characterized as the ability to incorporate changes in the environment or task requirements in order to update or modify movements online. Inhibitory control mechanisms are also necessary to "overwrite" prepotent movement plans to move adaptively or modify plans when the environment or task requirements change. The Stop-Signal or Target Jump (Double-Step) paradigms have been employed to examine age-related differences in childhood (Johnstone et al., 2007; van den Wildenberg & van der Molen, 2004). In these tasks, the locations of target stimuli are presented prior to a 'Go' signal, which prompts participants to respond via a button press or aiming movement. For some trials, the target stimulus immediately turns red (Stop-Signal) or shifts to a new location (Target Jump) following the Go stimulus, indicating that the participant should immediately stop or modify their response, respectively. Compared to TD children, children with DCD exhibited impaired inhibitory control and difficulty adapting movement plans when targets changed (double-step) (Hyde & Wilson, 2011a, 2011b; Plumb et al., 2008). However, it is unclear if the poor behavioral performance exhibited by children with DCD is due to differences in frontal brain activation patterns.

Children with and without DCD participated in two studies in which EEG and movement kinematics were recorded. For Study 3.1, children completed a center-out drawing task during which participants either completed movements to a cued target

position or inhibited their movement in response to a stop cue (Stop-Signal). For Study 3.2, children completed a center-out drawing task during which participants completed movements to a cued target or adapted their movements online in response to a target displacement (Target Jump).

Hypothesis 3. Children with DCD will demonstrate movement kinematics that are more jerky, less spatially/directionally accurate, and slower than TD children when they have to inhibit movements (Stop-Signal). This difficulty will be reflected in the attenuated magnitude of activation in frontal motor planning regions (as measured by the amplitude of EEG movement-related cortical potentials).

Hypothesis 4. Similar to Hypothesis 3, difficulty adapting movement plans online (Target Jump) will be reflected in the decreased quality of movement kinematics in the children with DCD. In addition, the magnitude of movement-related EEG waveforms will be attenuated in children with DCD, compared to the TD children.

Significance

This research program is the first to examine if differences in brain function are related to behavioral deficits in visuomotor performance in children with and without DCD. Importantly, the results from this study may impact the way in which children with DCD are diagnosed and prescribed behavioral interventions aimed at improving visuomotor behaviors in the future. Given that differences in motor planning and control may be due to inefficient or attenuated activation of relevant brain areas, brain-based cortical facilitation protocols (e.g., stimulation protocols) or medications that increase cortical activation (e.g., stimulant medication) may aid in behavioral training protocols.

In addition to gaining a deeper understanding of children with DCD, this research provided new information regarding the relationship between cortical activation patterns and motor performance in TD children. It is likely that age-related improvements in adaptive sensorimotor behavior reported in previous developmental studies (Contreras-Vidal, 2006; Contreras-Vidal, Bo, Boudreau, & Clark, 2005; Ferrel-Chapus, Hay, Olivier, Bard, & Fleury, 2002; King, Kagerer, Contreras-Vidal, & Clark, 2009) may result from improved inhibition as well as online adjustments during motor performance. Results from the current research provide insights to the cortical mechanisms subserving these abilities and whether or not these mechanisms are disrupted in children with DCD.

Organization of the Dissertation Proposal

This first chapter presented an overview of the plan of research and outlined the specific aims, research methodology and significance. Chapter 2 is a review of the relevant literature including a conceptual framework for adaptive sensorimotor control, an examination of age-related changes in motor planning and a justification for the need to study impairments in visuomotor control and potential neural deficits in children with DCD. Chapter 3 contains the manuscript for the first study in this program of research, which addressed the question: Do children with DCD exhibit differences in brain activation patterns at rest, compared to TD children (SA1)? Chapter 4 details the second study, which addressed the question: Do children with DCD exhibit impairments in motor planning for goal-directed movements in comparison to TD children (SA2)? Chapter 5 contains the manuscript for the third and final study, which aimed at addressing the ability of children with DCD to adapt or inhibit movement plans online

(SA3 and SA4)? The final chapter is a general discussion of the three studies and avenues for future research.

Chapter 2: Review of Literature

Section 1: Overview

This chapter will provide a foundation for the program of research in this dissertation. Following this initial overview section, Section 2 provides an overview of the specific EEG methods employed and how these are relevant for understanding typical and atypical child development. Section 3 discusses the framework for motor planning and control and the proposed neural bases. The development of sensorimotor control in children and developmental changes in relevant brain structures are also discussed. Section 4 provides a characterization of DCD with respect to behavioral manifestations and potential neural underpinnings. Section 5 discusses the difficulties children with DCD exhibit in adaptive visuomotor control and outlines the potential neural bases that may underlie these behavioral deficits. Last, section 6 provides a summary of key findings that are directly relevant to the hypotheses and specific aims in the dissertation.

Section 2: EEG Methods for Understanding Typical and Atypical Development

Electroencephalography (EEG) is an ideal tool for studying cortical dynamics in children. It is non-invasive, relatively inexpensive to administer, allows the recording of brain activity in a variety of environmental contexts and task constraints, and does not require the participant to remain completely still. For these reasons, it is particularly useful in mapping brain dynamics both at rest and during movement conditions. Moreover, EEG allows us to probe how the brain is activated and how this activation may differ across typically developing (TD) children and those with motor coordination difficulties.

EEG at Rest – Differentiating Typical and Atypical Development.

EEG can be decomposed into frequency- and time-related changes with respect to different task conditions, mental states, age-related differences or differences among groups. EEG acquired at rest is typically decomposed using the Fourier transform to examine changes in the total or relative spectral power in different frequency bands (i.e., delta (< 3 Hz), theta (3 – 7 Hz), alpha (8 – 12 Hz), beta (13 – 30 Hz), gamma (30 – 70 Hz)). Developmental changes in the frequency components of EEG have been reported extensively for infants (Marshall, Bar-Haim, & Fox, 2002), children (Benninger et al., 1984; Clarke, Barry, McCarthy, & Selikowitz, 2001a; Gasser, Jennensteinmetz, et al., 1988; Gasser, Verleger, et al., 1988; Somsen, van't Klooster, van der Molen, van Leeuwen, & Licht, 1997) and adolescents (Cragg et al., 2011). Across each age group examined, a consistent trend has been reported: the power in lower frequency bands (i.e., delta and theta) decreases with age, while the power in higher frequency bands (i.e., alpha and beta) increases. Although the most robust decreases in delta and theta power occur over the first year of life (Marshall et al., 2002), continued changes in low to high frequency bands are evident in childhood and adolescence (Gasser, Verleger, et al., 1988). In addition to a developmental shift in the power across frequency bands, the peak power within each frequency band also shifts. Peak alpha shifts from 6-7 Hz in infancy to 8 Hz by 18^{th} months of age and then to 9 Hz by around 4 years of age (Marshall et al., 2002). Peak alpha power that is comparable with that of adults (10 Hz) is not established until late childhood (Somsen et al., 1997) or early adolescence (Cragg et al., 2011).

The developmental changes in EEG spectral power also differ by region, with the largest and earliest changes in theta and alpha band power found for posterior regions and

a more protracted developmental change for central and anterior regions. The central and parietal regions show the earliest changes in beta power whereas the posterior and anterior regions show a later developmental trajectory. This topological trend was found for both children and adolescents (Cragg et al., 2011; Gasser, Jennensteinmetz, et al., 1988). Interestingly, the topological changes in EEG spectral power are consistent with studies of structural brain development (Giedd et al., 1999; Gogtay et al., 2004), suggesting that the developmental changes in brain function, as indexed by EEG spectral power, correspond with regional changes in the structure of the cerebral cortex. Consistent with this hypothesis, a recent study of EEG spectral power and cortical thickness found that developmental changes in the low frequency bands parallel the developmental trajectory of cortical grey matter (Whitford et al., 2007). Based on these findings, it is likely that the developmental changes in EEG spectral power may be due to cortical refinement or pruning during childhood and adolescence.

The extensive characterization and the stability of developmental patterns in EEG spectral power in TD children facilitate comparisons with children with developmental disabilities and the interpretation of divergent EEG patterns. Differences in EEG spectral power at rest differentiate children with attention deficit hyperactivity disorder (ADHD) (Baving, Laucht, & Schmidt, 1999; Clarke, Barry, et al., 2001; Clarke et al., 2002), learning disabilities and reading problems (Clarke, Barry, McCarthy, & Selikowitz, 2002; Lubar et al., 1985) and those with intellectual disabilities (Gasser, Rousson, & Schreiter Gasser, 1974). Surprisingly, consistent findings were reported across these different developmental disabilities; specifically, children with developmental or learning

disabilities were found to exhibit greater power in low frequency bands compared to higher frequency bands.

These differences in spectral characteristics in atypical development have been suggested to reflect a "maturational" lag as the patterns exhibited by children with developmental and learning disabilities are similar to young TD children. The notion of a maturational lag has been supported by MRI studies of cortical thickness in ADHD. Children with ADHD reach peak cortical thickness much later than controls and this delay was most pronounced in prefrontal and supplementary motor areas (Shaw et al., 2007). There are very few longitudinal studies of sufficient size in other developmental disabilities to detect a maturational lag in the developmental trajectory of structural brain development.

Although these previous studies have provided insights regarding potential neurological factors that contribute to *general* behavioral symptoms in children with developmental and learning disabilities, a direct mapping of brain function to *specific* behavioral difficulties is necessary to establish the functional relevance of brain activation patterns derived from EEG. Further, multimodal approaches (EEG/MRI) will provide confirmation of potential structural developmental factors that contribute to changes in brain function as measured by EEG.

EEG During Movement Tasks – Neural Correlates of Motor Planning and Control.

The time-sensitive nature of EEG allows it to be mapped with respect to endogenous (i.e., self-generated) and exogenous (i.e., stimulus-related) factors during the performance of sensory, motor and/or cognitive tasks. In the context of the current study, the temporal sensitivity of EEG makes it an ideal tool to study preparatory and on-going

cortical processes during the performance of motor tasks. Movement-related cortical potentials (MRCPs) obtained from scalp locations overlying the supplementary motor area, premotor cortex and primary motor cortex have revealed age-related differences in TD children (Chiarenza, Papakostopoulos, Giordana, & Guareschi-Cazzullo, 1983; Pangelinan, Kagerer, Momen, Hatfield, & Clark, 2011; Warren & Karrer, 1984). Specifically, older children and adults exhibit larger negative-going waveforms in these relevant motor planning and control areas compared to young children.

Time-domain analysis of EEG during motor performance has also been examined in children with developmental and intellectual disabilities including Autism Spectrum Disorder (ASD) (Enticott, Bradshaw, Iansek, Tonge, & Rinehart, 2009; Rinehart et al., 2006), Down Syndrome (DS) (Chiarenza, 1993), and reading disabilities (Chiarenza, 1990). Across these different developmental disabilities, the amplitude of the MRCPs before and during movements was significantly attenuated in comparison to controls. This reduction in MRCP amplitude was consistent with poorer behavioral performance or motor skill for those with developmental or learning disabilities.

A complementary approach to time-domain analyses (i.e., MRCPs) is an examination of changes in the frequency content of the EEG between rest conditions and during the performance of movement tasks. Changes in coherence and spectral power specific to motor planning and execution (task-related coherence or task-related spectral power, respectively) have been well characterized for adults (Gerloff et al., 1998; Manganotti et al., 1998). Increased task-related coherence and decreased task-related spectral power (with respect to resting/baseline conditions) in the alpha and beta bands has been reported with increased movement complexity particularly among sensorimotor

areas prior to the onset of movement (Gerloff et al., 1998; Manganotti et al., 1998; Pfurtscheller & Berghold, 1989). Decreased task-related spectral power or desynchronization is most prominent over the contralateral sensorimotor cortex and is thought to reflect movement preparation (Neuper & Pfurtscheller, 2001; Pfurtscheller & Berghold, 1989). Bender and colleagues have investigated alpha desynchronization in children (6- to 11-year-olds) and adolescents (12- to 18-year-olds) during the performance of a forewarned reaction time task (Bender, Weisbrod, Bornfleth, Resch, & Oelkers-Ax, 2005). Although less pronounced in young children, alpha desynchronization was evident and corresponded with the developmental changes observed in the time-domain (i.e. age-related increases in the amplitude of movement-related waveforms), indicating that these children were engaged in task-specific movement preparatory processes in response to the warning stimulus. In addition, a recent study in our lab found that young children exhibit a relative increase in activation (alpha desynchrony) of frontal cortical areas compared to motor cortical areas during motor planning, which may reflect the greater effort or attention needed for young children to plan and control arm movements (Pangelinan et al., 2011). As the behavioral performance of children with DCD is often more similar to young TD children than their TD peers, it follows that these two cohorts would demonstrate similar cortical activation patterns; specifically, a lack of alpha desynchrony over motor cortical brain areas while exhibiting a relative increase in frontal desynchrony during motor planning.

Section 3: Sensorimotor Control and Potential Neural Bases

Optimal Feedback Control: A Framework for Motor Planning and Control.

The prominent computational motor control framework for conceptualizing motor planning and control is optimal feedback control (OFC) (Shadmehr & Krakauer, 2008; Todorov & Jordan, 2002). In this framework, movements are planned as an economical and sequential process of weighing gains and costs (error and energy costs) with minimal intervention. Several modules are proposed to decompose motor planning and control in the OFC framework and each of these modules will be discussed in greater detail in the subsequent section with respect to potential neural bases. First, movement goals are specified (e.g., move quickly, accurately, efficiently, etc.) and serve as optimization parameters. Second, the system predicts the sensory consequences of its actions (i.e., system identification) via forward models based on efferent motor commands. Third, the sensory predictions are combined/compared with delayed feedback signals from the sensory system to estimate ongoing performance (i.e., state estimation). Lastly, the system adjusts the feedback gains based on the estimated state to optimize performance online. Signal dependent noise inherent to the motor and sensory systems lead to random perturbations or movement errors in both task-relevant and task-irrelevant aspects of the performance. Deviations in the average movement trajectory are only corrected if they affect movement goals or act in task-relevant aspects of the performance; thus, OFC models reduce energy/effort associated with corrective processes (Shadmehr & Krakauer, 2008; Todorov & Jordan, 2002). Importantly, OFC models are able to account for a range of movements without the direct specification of explicit trajectories and intermediate states or representations.

Potential Neural Bases of OFC.

Each module in the OFC framework depends not only on particular brain regions, but also on a network of cortical and subcortical areas that transfer information via networks that are critical for the identification of targets and specification of movement goals, estimation of body state, prediction of sensory consequences of movement, and the detection/correction of online errors. The subsequent sections will discuss the role of the additional cortical and subcortical structures that are essential for planning and control of goal-directed movements. Specifically, the basal ganglia (BG), posterior parietal cortex (PPC), and cerebellum (CB) will be examined with respect to their function in the different OFC modules. Evidence from neuronal recording in non-human primates and various non-invasive neuroimaging techniques (e.g., EEG, functional magnetic resonance imaging (fMRI), or positron emission tomography (PET)) in healthy adults and clinical groups will be presented to shed light on the function of relevant brain areas in OFC processes.

The specification of movement goals depends on the intrinsic drive or motivation to achieve a goal as well as the relative weighting of associated cost and rewards. The BG are thought to be involved in sustaining motivation and drive via thalamo-cortical disinhibition (or activation of the "direct pathway") (Graybiel, Aosaki, Flaherty, & Kimura, 1994). Glutamatergic projections from the cortex innervate the striatum, which send GABAergic projections to the globus pallidus and substantia nigra. Inhibition of the globus pallidus and substantia nigra leads to a net disinhibition of the thalamus. The resulting thalamic activation stimulates the cortex facilitating movement and drive. In addition to facilitating cortical activation directly, the basal ganglia are also involved in

shaping behavior via reward processing (Brown, Bullock, & Grossberg, 1999). The dopaminergic pathways in the BG are central in the learning of reward and reward-prediction in both cognitive and motor contexts. The firing rates of dopaminergic neurons in the basal ganglia (specifically in the substantia nigra) are tuned to the anticipation of positive rewards, magnitude of the reward and the likelihood of a reward stimulus (Kawagoe, Takikawa, & Hikosaka, 1998; Schultz & Romo, 1992). In contrast to the substantia nigra, the activation of the striatal neurons is related to the anticipation of a behavioral outcome or event that was mapped to a previously learned reward and adjusts expectations with respect to new situations (e.g., during learning) (Schultz, Tremblay, & Hollerman, 1998). Differential activation of the dopaminergic neurons and the striatum may serve as a teaching signal for behavior by linking specific rewards to behavioral outcomes and modifying goals based on the reward-behavior relationship (Doyon et al., 2009).

Movement costs are determined based on energy and error costs, which are derived from the actual specification of motor plans and the execution of those plans. Specification of movement plans involves the identification of intended targets and the estimation of current body state. Although the primary and secondary sensory cortices (V1/V2, S1/S2) localize targets and estimate body position, the PPC (BA 7) integrates these redundant sources of sensory information to create a coherence and less uncertain estimate of state (Hikosaka, 2007; Kawagoe et al., 1998). Studies in non-human primates have shown that both the PPC and superior parietal region aid in the selection and planning of movements through the processing of visual, somatosensory, and motor signals (Sabes, 2000) and may even play a role in the development of a forward model

(Hikosaka, 2007; Kawagoe et al., 1998). Thus, a network between the PPC and premotor/primary motor cortices appears to underlie goal specification and state estimation.

Conduction delays between the sensory receptors and the cerebral cortex, as well as delays in information transfer between cortical regions, reduce the utility of sensory feedback for online control of movement. Therefore predictive mechanisms are needed for rapid updating of estimated state and for error correction. The CB is ideally situated for this task, as it is reciprocally connected with the cortex and receives inputs directly from the sensory receptors. The CB bases predictions of the sensory consequences of the intended movement on an efference copy of motor commands. These sensory predictions are tuned or updated based on afferent proprioceptive feedback during the movement and when necessary, adjustments to the motor commands are issued by the CB. Support for the CB's role in internal/forward models comes from evidence from computational modeling (Miall, Weir, Wolpert, & Stein, 1993), neuroimaging of healthy adults during predictive movement tasks (Blakemore, Frith, & Wolpert, 2001; Kawato et al., 2003) and in studies of adaptation in those with cerebellar degeneration or focal lesions (Diedrichsen, Hashambhoy, Rane, & Shadmehr, 2005; Donchin et al., 2011; Tseng, Diedrichsen, Krakauer, Shadmehr, & Bastian, 2007). The disruption of cerebellar function, either in the case of disease or in the case of "virtual lesions" induced using transcranial magnetic stimulation (TMS), results in inaccurate performance that reflects an inability to update motor plans with respect to a mismatch between predicted and actual sensory feedback during the movements. Conversely, the application of transcranial direct current stimulation (tDCS) to the CB, which enhances local neuronal

excitability, results in a faster rate of adaptation in novel visuomotor environments and a reduction in movement errors (Galea, Vazquez, Pasricha, Orban de Xivry, & Celnik, 2010). Thus, this integrated feedback system between the CB, PPC, and frontal motor areas (dorsal premotor and primary motor) enables adaptive control of the movement in any environment or task.

Age-Related Changes in Motor Planning and Control.

The development of adaptive sensorimotor control in childhood appears to proceed in different stages and these stages mirror the development of different aspects of the OFC framework. For example, studies of manual aiming have found that children younger than six year of age plan movements based on static visual information and do not adapt movements in response to feedback (Contreras-Vidal, Bo, Boudreau, & Clark, 2005; Hay, 1978). In contrast, visual feedback appears to be utilized in 7- to 8-year-old children and is evident in the prolonged deceleration phase of the movement (Contreras-Vidal et al., 2005; Hay et al., 2005). Proprioceptive feedback appears to be incorporated still later, by around 8- to 9-years of age, and is evident in tasks in which visual information is not available for online control of movements (Favilla, 2006). Adaptive, online control of movements is not yet evident until late childhood, around 9- to 10-years-of-age, at which time children are able to update movement plans in response to visuomotor (Contreras-Vidal, 2006; Contreras-Vidal, Bo, Boudreau, & Clark, 2005; King, Kagerer, Contreras-Vidal, & Clark, 2009) and force perturbations (Contreras-Vidal, 2006; Contreras-Vidal et al., 2005; King et al., 2009). These age-related performance differences are thought to result from an improved ability to use proprioceptive feedback and incorporate it with information from other sensory

modalities (multi-sensorimotor integration), which in turn, influence state estimation and resulting motor performance. Indeed, a recent study from our lab (Ferrel-Chapus et al., 2002; Konczak, Jansen-Osmann, & Kalveram, 2003) found that even after accounting for age-related differences, proprioceptive localization was found to be a significant predictor of sensorimotor performance in school-aged children. Moreover, the ability to use and integrate redundant sensory information not only affects static state estimation but also helps to refine predictions of sensory consequences of motor commands (i.e., forward model) to improve dynamic state estimation.

Brain Development Underlying Age-Related Improvements in Sensorimotor Control.

These behavioral improvements parallel the continued development of the cerebral cortex, with respect to changes in gray and white matter densities, over childhood. Specifically, Gogtay et al. (King, Pangelinan, Kagerer, & Clark, 2010) reported that the gray matter in the primary motor and somatosensory cortices mature during early childhood, while the frontal and parietal association areas develop later in childhood. The frontal and parietal association areas are critical for adaptive planning and sensorimotor integration and their later development likely underlies the emergence of adaptive motor skills in late childhood. In addition, there is evidence that the development of white matter tracts, such as the corticospinal tract, networks among the frontal and parietal areas, and the corpus callosum, also facilitate sensorimotor integration, motor planning, and motor control (Giedd et al., 1999). Thus, efficient integration of visual and somatosensory information within the cerebral hemispheres (i.e., between the frontal and parietal regions) and between the two hemispheres (across the

corpus callosum) may influence the ability to produce accurate motor plans and facilitate error correction for visuomotor tasks.

In addition to cortical changes, the development of the basal ganglia and cerebellum would also influence the emergence of adaptive sensorimotor control. These subcortical structures exhibit protracted structural development well into adolescence (Sowell, Trauner, Gamst, & Jernigan, 2002; Tiemeier, Lenroot, et al., 2010). The developmental of these structures is similar to, although further protracted than, volumetric changes in the cerebral cortex. It is likely that the developmental changes that occur in the cortex influence the development of the corresponding regions of these subcortical structures (and vice versa).

The changes in adaptive sensorimotor control that develop across childhood and the corresponding changes in the underlying brain structures provide support for the OFC framework and the proposed neural bases. Examinations of atypical development from both a brain and behavioral approach consistent with OFC may provide support for potential mechanisms that are linked to behavioral deficits in sensorimotor control. For example, children with developmental disorders such as ADHD and ASD, which are characterized predominantly as cognitive (attention) and socio-emotional (affective) disorders, respectively, also exhibit impaired motor functions. This includes: poor handwriting and fine motor skills (Racine, Majnemer, Shevell, & Snider, 2008; Tucha & Lange, 2004), difficulties planning movements (Nazarali, Glazebrook, & Elliott, 2009; van Swieten et al., 2010), and poor gross motor coordination (Fliers et al., 2009; Piek et al., 2004; Rinehart & McGinley, 2010; Whyatt & Craig, 2011). Consistent with these behavioral deficits, children with ADHD and ASD have been found to have structural

abnormalities in brain regions that mediate both cognitive and motor circuits, including: subdivisions within the frontal cortex (Courchesne & Pierce, 2005; Mostofsky, Cooper, Kates, Denckla, & Kaufmann, 2002), parietal cortex (Castellanos et al., 2002; McAlonan et al., 2007), striatum (Castellanos et al., 2002; Langen et al., 2009) and cerebellum (Cleavinger et al., 2008; Mostofsky et al., 2009).

Section 4. Characteristics of Developmental Coordination Disorder

Impaired Motor Planning in Children with DCD.

Developmental Coordination Disorder affects one child in every classroom in the US (~6% of all children) and significantly interferes with academic achievement and the ability to perform activities of daily living requiring motor coordination (APA, 2004). Difficulties with handwriting are prevalent in children with DCD. In addition, children with DCD exhibit marked deficits in sensorimotor integration (Mon-Williams, Wann, & Pascal, 1999), movement planning (Mon-Williams et al., 2005; van Swieten et al., 2010), and adaptive visuomotor behavior (Kagerer, Bo, Contreras-Vidal, & Clark, 2004; Kagerer, Contreras-Vidal, Bo, & Clark, 2006; King, Harring, Oliveira, & Clark, 2011).

Atypical Brain Development in Children with DCD

Kaplan et al. (1998) proposed that the behavioral impairments exhibited by children with DCD are related to "atypical brain development" – a hypothesis that is predominantly based on the comorbidity between DCD and other developmental disabilities, including attention-deficit hyperactivity disorder (ADHD) and developmental dyslexia (DD), and Autism Spectrum Disorder (ASD). The atypical brain development hypothesis has recently been examined using brain imaging methods. EEG and fMRI

have now been used to explore the neural (dys)functions that may underlie deficits in visuomotor coordination (Kashiwagi, Iwaki, Narumi, Tamai, & Suzuki, 2009; Zwicker, Missiuna, Harris, & Boyd, 2010; de Castelnau, Albaret, Chaix, & Zanone, 2008) and attention (Kashiwagi, Iwaki, Narumi, Tamai, & Suzuki, 2009; Zwicker, Missiuna, Harris, & Boyd, 2010; de Castelnau, Albaret, Chaix, & Zanone, 2008) in children with DCD.

EEG and fMRI have been employed to examine the connectivity patterns of children with DCD during motor task performance. Functional connectivity between brain areas, as measured by EEG coherence, was used during the performance of a finger-tapping synchronization task in children with and without DCD (de Castelnau et al., 2008). This study found increased coherence among fronto-central electrode pairs in children with DCD, compared to TD children, suggesting that frontal engagement may help compensate for perceptual-motor deficits exhibited by children with DCD. Similarly, (Querne et al., 2008) fMRI has been employed to study functional connectivity in children with DCD and found that during the performance of a motor inhibition and attention task (go-nogo) children with DCD exhibited greater functional connectivity between middle frontal cortex and both the anterior cingulate and the inferior parietal cortex. However, less connectivity was reported between the striatum and the parietal cortex for these children. This pattern of connectivity is similar to that found in children with ADHD suggesting impairment in cortical-striatal pathways. Collectively, these studies suggest greater involvement of frontal regions that may help compensate for atypical patterns of connectivity in task-related brain regions.

In addition to examining the connectivity between brain regions, the activation patterns of regions of interest have also been examined in children with DCD. Kashiwagi

and colleagues (2009) found that the poor behavioral performance of children with DCD during a tracking task may be due to attenuated activation of the left posterior parietal cortex and the postcentral gyrus in comparison to TD children. A more diffuse pattern of abnormal cortical and subcortical activation was found in a study employing fMRI during a tracing task (Zwicker et al., 2010). This study found greater activation in children with DCD compared to controls for a set of visuospatial brain regions, which the authors attributed to a dependence on vision to guide motor performance.

The differences in brain activation patterns and abnormal patterns of connectivity are consistent with the brain regions suggested as mediating different aspects of the OFC framework, including cortical-striatal networks and frontal-parietal brain regions. What is notably missing in these characterizations is the role of motor and premotor activation during planning and control of movement. It is very likely that differences in task-related activation of these brain regions may also contribute to performance deficits children with DCD, as they have been previously reported for young TD children.

Section 5: Adaptive Sensorimotor Behavior and Its Relevance to Understanding DCD

Adaptive motor behavior may be characterized as the ability to incorporate changes in the environment or task requirements to update or modify movements online. This ability depends on a prediction of the sensory consequence of motor commands (forward model) and the incorporation of sensory feedback in order to update motor plans efficiently, as well as the ability to inhibit inappropriate motor plans. The problems performing activities of daily living, including handwriting and eye-hand coordination skills, characteristic of children with Developmental Coordination Disorder (DCD) are

likely due to impairments in adaptive motor control. Indeed, children with DCD have deficits in predictive control (Wilmut & Wann, 2008), utilizing sensory feedback (Mon-Williams, Wann, & Pascal, 1999; Smyth & Mason, 1997), inhibiting inappropriate motor responses (Mandich, Buckolz, & Polatajko, 2002) and adapting motor plans online (Hyde & Wilson, 2011a, 2011b). Yet little is know about the neural mechanisms that underlie these difficulties in children with DCD.

The stop-signal or jump/double-step paradigms have been employed to examine adaptive motor behavior in typically developing (TD) children and children with DCD (Hyde & Wilson, 2011a, 2011b; Mandich, Buckolz, & Polatajko, 2002). In these tasks, the location of target stimuli is presented and following the presentation of a 'Go' signal the participants respond via a button press or aiming movement. For some trials, the target stimulus immediately turns red (stop signal) or shifts to a new location (jump) following the Go stimulus, indicating that the participant should immediately stop or modify their response, respectively. Compared to TD children, children with DCD exhibited impaired inhibitory control (stop-signal) and difficulty adapting movement plans when targets changed (jump) (Hyde & Wilson, 2011a, 2011b; Mandich, Buckolz, & Polatajko, 2002).

The deficit in rapid online correction in children with DCD has been attributed to a disruption in the function of the posterior parietal cortex (PPC), which has been implicated in processing representations of action and predictive control of movement (Della-Maggiore, Malfait, Ostry, & Paus, 2004; Desmurget et al., 1999; Mulliken et al., 2008). Consistent with this hypothesis, less activation of the PPC has been reported in children with DCD during the performance of a simple visuomotor task (Kashiwagi,

Iwaki, Narumi, Tamai, & Suzuki, 2009). However, the PPC networks with various regions in the frontal cortex as well as subcortical brain regions that mediate motor planning and adaptive motor control (Battaglia-Mayer, Archambault, & Caminiti, 2006; Houk & Wise, 1995; Middleton & Strick, 2002; Schultz & Romo, 1992; Shadmehr & Krakauer, 2008), and thus, the disruption of additional brain areas may underlie behavioral deficits in DCD. In fact, Zwicker and colleagues (2010) found atypical brain responses across several cortical and subcortical brain areas, providing support that a more complex visuomotor task would similarly implicate a network of cortical brain regions. However, no studies to date have directly recorded brain activation patterns during the performance of an adaptive motor task in which rapid online control is necessary.

Section 6: General Conclusions and Relevance to the Dissertation Studies

EEG is an ideal tool to characterize the patterns of brain activity both at rest and during motor task performance to determine potential neural mechanisms in DCD. The extensive use of EEG to characterize both TD children and those with developmental disabilities at rest provides a foundation for the findings from the first study (Chapter 3) both with respect to both typical and atypical development. Specifically, we hypothesized that children with DCD would exhibit greater power in lower frequency bands and a shift in the peak alpha frequency, similar to previous reports of young children and those with developmental disabilities. In addition, children with DCD were hypothesized to exhibit selective differences in brain regions relevant to motor planning and control, compared to TD children, which may contribute to generalized motor difficulties. With respect to the second study (Chapter 4), the direct mapping of brain activation and motor performance

during a visuomotor task allowed us to examine the relationship between cortical activation patterns and motor deficits in children with DCD. Based on previous studies examining brain activity in TD children and adults related to motor behavior, similar to young children, we hypothesized that children with DCD would exhibit less cortical activation during motor planning and control, which would be related to poorer performance on the visuomotor task. With respect to the last study (Study 3 – Chapter 5), given the difficulties of children with DCD exhibit during the performance of adaptive online control we hypothesized that these difficulties would be reflected in attenuated activation during motor planning and online control compared to TD children. Collectively, the specific aims of this dissertation were built upon the current developmental motor neuroscience literature and addressed knowledge gaps regarding the potential neural mechanisms underlying behavioral deficits in DCD.

Chapter 3: Specific Aim 1: Do Children with DCD Exhibit Differences in Cortical Dynamics At Rest?

Abstract

Electroencephalography (EEG) spectral power has been used to characterize developmental differences in brain activation patterns in typically developing (TD) children and those with developmental and learning disabilities. Given the considerable overlap in cognitive, social and motor developmental disabilities, it is likely that EEG spectral power is also sensitive to differences in brain activation patterns in children with Developmental Coordination Disorder (DCD). The purpose of the current study is to determine if children with DCD and those at risk for motor difficulties exhibit different patterns of cortical activation compared to TD children. Children with DCD (n = 9; mean age = 9.8yrs), as compared to TD children (n = 30; mean age = 10.5yrs) and those with moderate movement difficulties (n = 15; mean age = 10.0yrs), exhibited less relative alpha, greater theta/alpha ratio, and a shift in peak alpha power. In addition, a striking asymmetry is found for the central regions in children with DCD in which less relative theta and beta power are evident in the left motor region, compared to TD children and those with moderate motor difficulties. These results suggest that children with DCD exhibit a "maturational lag" in cortical function, particularly in brain regions relevant for motor control. Children with moderate movement difficulties exhibited cortical activation patterns intermediate to those exhibited by TD children and those with DCD, suggesting that the cortical activation patterns may be useful to better characterize and monitor this group of children. Collectively, these results identify potential biomarkers or neural

mechanisms that may contribute to behavioral deficits in children with motor coordination difficulties.

Introduction

There is growing evidence that different developmental disabilities are not discrete, but rather exhibit considerable overlap in terms of behavioral symptomology and potential neural mechanisms. Children with developmental disorders such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), which are predominantly characterized as cognitive (attention) and socio-emotional (affective) disorders, respectively, also exhibit impaired motor functions (Kopp, Beckung, & Gillberg, 2010; Piek & Dyck, 2004; Reiersen, Constantino, & Todd, 2008). Likewise, children that have been identified as having movement coordination difficulties (i.e., Developmental Coordination Disorder - DCD) also exhibit difficulties in executive function and attention (Dewey, 2002; Piek, Dyck, Francis, & Conwell, 2007; Piek et al., 2004) as well as social and emotional functioning (Dewey, 2002; Lingam et al., 2010). Although many studies have investigated brain structure and function in ASD and ADHD and have found disruptions in the development of brain areas that mediate cognitive, emotional and motor functions, the neural bases of DCD remain unclear. The current study examined brain function at rest in children with DCD, compared to typically developing (TD) children and those with moderate motor difficulties, to determine if DCD is characterized by atypical cortical dynamics.

Electroencephalography (EEG) is an ideal tool for studying cortical dynamics in children with and without developmental and learning disabilities. EEG is a direct measure of neuronal function, is non-invasive and does not require the participant to

remain completely still. EEG acquired at rest is typically decomposed into constituent frequency components using the Fourier transform to examine changes in the total or relative spectral power in different frequency bands (i.e., delta (< 3 Hz), theta (3 – 7 Hz), alpha (8 – 12 Hz), beta (13 – 30 Hz), gamma (30 – 70 Hz)). These oscillatory patterns index the level of activity of cortical neurons; slower rhythms such as delta and theta are linked to a lack of cortical engagement (i.e., sleep and cortical idling), while faster rhythms such as beta and gamma are linked to alert states and active engagement in sensory, motor and cognitive processes. The theta, alpha (i.e., sensorimotor mu) and beta bands have been found to be modulated by movement (Hari & Salmelin, 1997; Neuper & Pfurtscheller, 2001; Oishi et al., 2007; Pineda, 2005). Thus, differences in total contribution of these frequency bands to the total EEG signal may be relevant to motor function even when measured at rest.

Developmental changes in these frequency components have been reported extensively for infants (Marshall et al., 2002), children (Clarke, Barry, McCarthy, & Selikowitz, 2001; Gasser, Jennensteinmetz, Sroka, Verleger, & Mocks, 1988; Gasser, Verleger, Bacher, & Sroka, 1988; Somsen, van't Klooster, van der Molen, van Leeuwen, & Licht, 1997), and adolescents (Cragg et al., 2011; Segalowitz et al., 2010). These studies revealed that within each age group examined (e.g., infants or adolescents), the power in the lower frequency bands (i.e., delta and theta) decreases while the power in higher frequency bands (i.e., alpha and beta) increases with age. In addition to a developmental shift in the power *across* frequency bands, the peak power *within* each frequency band also shifts. Peak alpha power shifts from 6-7 Hz in infancy to 8 Hz by 18 months of age and then to 9 Hz by around 4 years of age (Marshall et al., 2002). An age-

related increase in peak alpha between 8 – 9.5 Hz has been demonstrated between 5- to 12- years of age (Somsen et al., 1997). However adult-like peak alpha power (~10Hz) is not evident until early adolescence (Cragg et al., 2011).

Developmental changes in EEG spectral power also differ by region; the largest and earliest changes are in theta and alpha power in the posterior regions whereas protracted developmental changes in these bands are evident for the central and anterior regions (Gasser, Jennensteinmetz, et al., 1988). Changes in the beta band also differ by region but with the greater power found early for central and parietal regions and much later for the anterior and posterior regions. This topological trend was found for both children and adolescents (Cragg et al., 2011; Gasser, Jennensteinmetz, et al., 1988; Kurth et al., 2010). Interestingly, the topological changes in EEG spectral power are consistent with studies of structural brain development (Giedd et al., 1999; Gogtay et al., 2004), suggesting that the developmental changes in brain function, as indexed by EEG spectral power, correspond with regional changes in the structure of the cerebral cortex. Specifically the motor and sensory cortices exhibit earlier development than anterior regions, corresponding to the development in the beta band. However, a general posterior-anterior gradient is also found and may correspond with the developmental trends found for theta and alpha.

The extensive characterization and the stability of developmental patterns in EEG spectral power in the TD children facilitate the comparisons to children with developmental disabilities and the interpretation of divergent EEG patterns. Differences in EEG spectral power at rest differentiate children with ADHD (Baving, Laucht, & Schmidt, 1999; Clarke, Barry, et al., 2001; Clarke et al., 2002), ASD (Cantor, Thatcher,

Hrybyk, & Kaye, 1986; Coben, Clarke, Hudspeth, & Barry, 2008), learning disabilities and reading problems (Cantor et al., 1986) and intellectual disabilities (Gasser, Rousson, & Schreiter Gasser, 1974). Surprisingly, consistent findings were reported across these different developmental disabilities. Children with developmental disabilities were found to exhibit greater power in low frequency bands compared to higher frequency bands, as well as disruptions in both frontal and central regions. These differences in spectral characteristics in atypical development have been suggested to reflect a "maturational lag" since the patterns exhibited by children with developmental and learning disabilities are similar to those observed in young TD children. The notion of a maturational lag in cortical function has been supported by MRI studies of cortical thickness in ADHD; children with ADHD reach peak cortical thickness much later than controls and this delay was most pronounced in prefrontal and supplementary motor areas (Shaw et al., 2007).

No study to date has examined EEG spectral power in children with DCD at rest. In the current study, we recorded EEG at rest from 7.5- to 12.5-year-old children in the following groups: children with DCD (n = 9), children with moderate movement difficulties (n = 15), and TD children (n = 30) in order to determine mean differences in EEG spectral power. Given that EEG spectral power changes are well characterized for both TD children and children with other developmental disabilities, results from the current study may be interpreted within the context of typical and atypical brain development. It was hypothesized that similar to young TD children and children with developmental disabilities, children with DCD would exhibit greater power in low frequency bands (relative theta) compared to higher frequencies (relative alpha and beta) and a downward shift in peak alpha power. In addition, children with DCD would exhibit

regional differences in EEG spectral power consistent with their cognitive and motor deficits.

Methods

Participants.

Children between the ages of 7.5 and 12.5 years were recruited from the local university area through school and community events. Potential children with DCD were referred to our study by local elementary school resource teachers, physical and occupational therapists and/or parent support groups for children with developmental disabilities. The Institutional Review Board at the University of Maryland College Park approved all procedures. Prior to participation, the parents and children provided informed consent and assent, respectively (Appendix A). For their participation, the children received a modest monetary compensation and a choice of an age-appropriate prize.

Inclusion Criteria.

Parents completed a pediatric health questionnaire (Appendix A) to provide details about their child's overall development. This questionnaire also inquired about the diagnosis of any general medical conditions and developmental learning disabilities (i.e., attention deficit hyperactivity disorder, autism spectrum disorder, speech/language difficulties, and academic problems). To quantify behavioral difficulties, particularly ADHD and ASD symptoms, parents completed the Disruptive Behavior Disorder (DBD – Appendix B) Questionnaire (Pelham, Gnagy, Greenslade, & Milich, 1992) and the Social Communication Questionnaire (SCQ – Appendix C) (Rutter, Bailey, & Lord,

2003), respectively. To ensure that all children were cognitively normal (i.e., IQ > 80), all children completed the Woodcock-Johnson III Tests of Cognitive Abilities (Woodcock, McGrew, & Mather, 2001). Last, the children completed a 10-item handedness test (Appendix D) (Fagard & Corroyer, 2003) to ensure right-hand dominance and the Movement Assessment Battery for Children, Second Edition (MABC-2) to characterize their motor skill ability in the areas of manual dexterity, ball skills and balance (Henderson, Sugden, & Barnett, 2007).

Children from all three groups met the following inclusion criteria: a) no history of neurological deficits; b) no head injuries/concussions; c) right-handed; and, d) normal intellectual ability (IQ > 80). The TD children did not meet criteria for learning or developmental disabilities, based on the pediatric health questions as well as the SCQ (for ASD) and the DBD (for ADHD inattentive, hyperactive, or combined types).

The total scores on the MABC-2 and the handwriting score on the WJ-III Test of Achievement (Woodcock et al., 2001) were used to separate children into three groups. TD children had MABC-2 scores $\geq 25^{th}$ percentile (for each component score as well as the total score) and handwriting performance at or above grade level. Children with DCD had MABC-2 total scores $\leq 5^{th}$ percentile *and* performed below grade level in handwriting. The children that were referred to our study by physical or occupational therapists or educational resource specialists, but whose performance on the MABC-2 did not meet the criteria for DCD (i.e., below the 5^{th} percentile) were put into an intermediate group (INT). The MABC scores and handwriting scores for the children in the intermediate group reflect moderate movement difficulties: total MABC-2 scores

between the 9th and 25th percentile[1] *and* a below grade level performance in handwriting An example of a handwriting sample from a 12-year-old child in this group in included in Appendix F.

In addition to the MABC-2 and handwriting scores, the criteria for inclusion in the DCD group were based on the parent questionnaire and included the following: a) marked impairments in activities requiring motor coordination; b) motor coordination difficulties interfere with academic achievement or activities of daily living; and, c) the disturbance is not due to a general medical condition[2].

Given the high co-morbidity between DCD and attention and/or social difficulties, the DBD and SCQ were used to assess ADHD and social communication difficulties, respectively. As mentioned, none of the children in the TD group met criteria for ADHD (inattentive, hyperactive, or combined). Two children in the INT group met criteria for ADHD-inattentive and two children met criteria for ADHD-combined. Three children in the DCD group met criteria for ADHD-inattentive and one child met criteria for ADHD-combined. All children in the TD and INT groups had scores on the SCQ that were considered low (score < 8) or moderately low (score between 8 -14). Two children in the DCD group had scores on the SCQ that were considered moderately high (score between 15 – 21) and two children's scores were considered high (score ≥ 22). Table 3.1 provides additional details for the three groups including the mean and standard deviations for age, number of ASD symptoms (from the SCQ), number of ADHD

[1] The MABC-2 considers children with performance between the 5th and 15th percentile to be "at risk" for movement difficulties. Three of the children in Study 1 and 3 children in Study 2 had total MABC-2 scores at the 9th percentile. However, we used a broader range of MABC-2 scores for this group since all of these children were referred to our study by clinical or educational specialists. These children exhibit movement difficulties in the classroom and/or at home and are receiving treatment.

[2] None of the children in the present study presented with intellectual disabilities, so Criterion D was not applicable to the diagnosis of DCD.

inattentive type symptoms (from the DBD), number of ADHD combined type (from the DBD), and the MABC-2 range and median scores for the manual dexterity component and total score.

Table 3.1. Specific Aim 1. Demographics of the children in each group.

Group	N	Age	General Intellectual Ability	SCQ Number of Symptoms	DBD – ADHD Inattentive Number of Symptoms	DBD – ADHD Hyperactive Number of Symptoms	DBD – ADHD Combined Number of Symptoms	MABC-2 Total Median
TD	30 (M: 16, F: 14)	10.5 years (1.2) 7.8 – 12.2	115.2 (11.0) 91 – 143	4.25 (2.4) 0 – 11	0.6 (1.4) 0 – 5	0.6 (1.0) 0 - 3	1.2 (2.2) 0 – 8	63rd percentile 25 – 91st
INT	15 (M: 8, F: 7)	10.0 years (1.3) 8.0 – 12.3	110.0 (16.2) 82 - 140	5.1 (3.4) 0 – 11	2.6 (3.4) 0 – 9	1.7 (2.6) 0 – 9	4.3 (5.7) 0 – 17	16th percentile 9 – 25th
DCD	9 (M: 6, F: 3)	9.8 years (1.5) 7.5 – 11.9	103.7 (15.4) 88 – 125	11.4 (10.9) 0 – 28	4.4 (3.6) 0 – 8	2.0 (1.8) 0 – 6	6.25 (5.2) 0 – 14	2nd percentile 0.1 – 5th

Experimental Apparatus and Procedures.

Brain Vision Recorder software and Brain Amp DC (Brain Vision LLC, Gilching, Germany) were used to collect continuous EEG (DC recording with a sampling rate of 500 Hz) from 64 active electrodes housed within a stretchable lycra cap (actiCAP, Brain Vision LLC, Gilching, Germany). These electrodes have integrated noise subtraction circuits that minimize external electrical noise. The electrode locations are consistent with the International 10/20 system. FCz served as the reference and AFz served as the ground. Eye movement artifacts were observable at Fp1 and Fp2. All channel impedances were maintained at or below 20 kΩ. A chin rest was used to stabilize and maintain the participant's head position and the height of the chair and chin rest were adjusted for each participant. Two minutes of eyes-closed resting EEG were recorded.

Data Analysis.

Brain Vision Analyzer 2 (Brain Vision LLC, Gilching, Germany) was used to re-reference the electrodes to an average of all electrodes. The purpose of the re-reference was to recover the activity at FCz (the original reference) and the neighboring electrodes. Data were filtered using an FIR low-pass filter (cut off frequency: 50 Hz, roll-off 24dB/octave). An ocular correction Independent Component Analysis (ICA – Infomax Restricted algorithm) was used to remove artifacts due to blinks and horizontal eye movements. A slope-based algorithm searched for blinks in Fp1 and components were selected with variance accounting for 30% in the respective channel. Similarly, Fp2 was used to search for horizontal activity. Components that met 30% of variance in the respective channel were selected. Each component was visually inspected with respect to the topography, activation, and the relative change to the signal if the component was

removed. On average, 4 out of 63 components were removed. Data were segmented/epoched in 1-second consecutive intervals. In addition to the ocular correction ICA, additional artifacts were removed during visual inspection of each segment/epoch based on the activation pattern (e.g., large change in amplitude, muscular artifacts, or electrocardiogram activity). Data were then exported into MATLAB^{TM} version 7.10 (Mathworks, Natick, MA USA). Fast Fourier transforms (FFT) were applied to these data. Power spectra were segmented into the following frequency bands: theta (4 – 7 Hz), alpha (8 – 12 Hz), beta (13 – 30 Hz), and broad band (1 – 50Hz). Spectral data were then log-transformed to meet the requirements for the statistical analysis (homogeneity of residuals). Relative spectral power was computed by summing the total power in a given frequency band and normalized sum of the broad band power. In addition to relative power, the ratio between theta and alpha power as well as the ratio between theta and beta power were computed to index differences across frequencies. Last, the maximum value and the location of the maximum power between 6 – 12 Hz were computed to determine a shift in alpha frequency. Data from a subset of electrodes (28 total) were used in the statistical analysis based on membership in the following functional groups: frontal left (F7, F5, F3 and F1), frontal right (F8, F6, F4, and F2), central left (C5, C3, and C1), central right (C6, C4, and C2), parietal left (P7, P5, P3, and P1), parietal right (P8, P6, P4, and P2), and parieto-occipital left (PO7, PO3, and O1), and parieto-occipital right (PO8, PO4, and O2).

Statistical Analysis.

Consistent with our previous work (Pangelinan et al., 2011), all dependent variables were analyzed using mixed-model analysis of variance (ANOVA) in SAS 9.2

(SAS Institute, Cary, NC). Separate mixed-model ANOVAs were used to examine the following dependent variables: relative theta, relative beta, relative alpha, theta-alpha ratio, theta-beta ratio, and the location of peak alpha power. Group (TD, INT, and DCD) was the between-subjects factor. Hemisphere (left. right) and region (frontal, central, parietal, and occipital) served as the within-subjects factors[3]. Significant main effects were decomposed using Scheffé's post-hoc multiple comparisons. Significant interactions were decomposed with respect to differential effects (difference of difference contrasts) (Levin & Marascuilo, 1972). For all analyses, a significance level of 0.05 was maintained.

Results

Relative Spectral Power.

Table 3.2 provides the details for the statistical results for relative spectral power (relative theta, relative alpha, relative beta).

Table 3.2. Specific Aim 1. Significant main effects and interactions for the relative spectral power measures.
$*p < 0.05$, $**p < 0.01$, $***p < 0.001$

Factor	Frequency	DOF	F Value	Post-Hoc Contrast T Value
Group	Alpha	$F_{(2,50)}$ $T_{(50)}$	6.5**	-TD > DCD = 3.5**
Region	Theta Alpha Beta	$F_{(3,150)}$ for all	15.2*** 141.2*** 13.4***	Theta & Beta: See Group x Region x Hemisphere Alpha: See Region x Hemisphere

[3] Age was included as a covariate in preliminary analyses. Age was not a significant predictor of the dependent measures and the inclusion of age as a covariate did not change the parameter estimates for the factors of interest. Moreover, the inclusion of age as a covariate did not improve the fit statistics for the models, so it was not included in the present results.

Hemisphere	Alpha	$F_{(1,50)}$	5.3*	See Region x Hemisphere
Region x Hemisphere	Theta Alpha Beta	$F_{(3,1210)}$ for all	3.1* 6.0*** 3.9**	Theta & Beta: See Group x Region x Hemisphere Alpha: -Left Frontal-Central < Right Frontal-Central = 2.2* -Left Frontal-Parietal < Right Frontal-Parietal = 4.0*** -Left Frontal-Occipital < Right Frontal-Occipital = 3.1*
Group x Region x Hemisphere	Theta Beta	$F_{(6,1210)}$ for all	2.9** for both	Theta & Beta (Same for both): -TD < INT: Left Central-Parietal & Right Central-Parietal = 2.8** -TD < INT: Left Central-Occipital & Right Central-Occipital = 2.6** -TD < DCD: Left Central-Parietal & Right Central-Parietal = 2.4** -TD < DCD: Left Central-Occipital & Right Central-Occipital = 2.3**

For all frequency bands, region main effects and region x hemisphere interactions were found ($p < 0.05$ for all). Figure 3.1 depicts the region x hemisphere interaction for the alpha band (similar results were found for the theta and beta bands – see the group x region x hemisphere analyses). Post-hoc contrasts for the alpha band revealed the difference between left and right hemispheres (direction and magnitude) for the frontal region was different than that observed for all other regions ($p < 0.05$ for all). These results provide support for a posterior to anterior gradient in alpha power with greater right-hemisphere activation in posterior regions, compared to anterior regions across all groups.

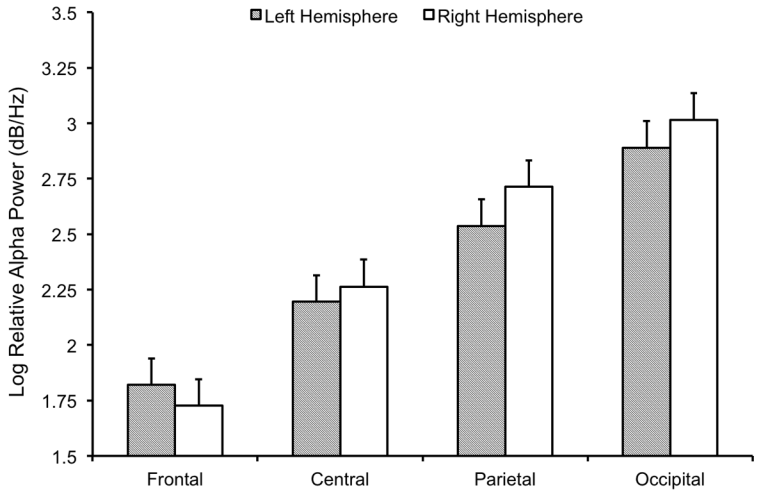

Figure 3.1. Specific Aim 1. Log relative alpha power by hemisphere and region. Left hemisphere = gray; right = white. Error bars = standard error.

A significant group main effect was found for alpha ($F_{(2,50)}$ =6.5, $p < 0.01$, see Figure 3.2). Scheffé's post-hoc analyses revealed that the DCD group exhibited significantly less alpha power than the TD group ($T_{(50)} = 3.49$, $p < 0.01$). There was no significant difference between the TD and INT group or between the INT and DCD group ($p > 0.05$ for both).

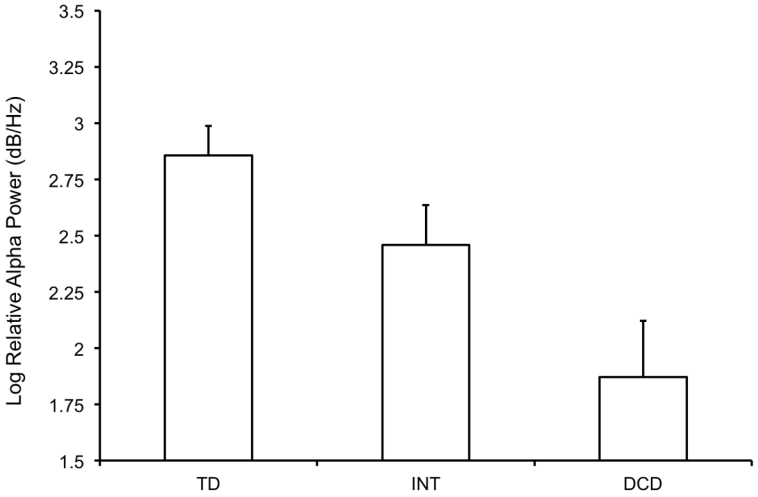

Figure 3.2. Specific Aim 1. Log relative alpha power by group. Error bars = standard error.

A significant group x hemisphere x region interaction was found for theta and beta ($p < 0.01$ for both). Figure 3.3 depicts the group x hemisphere x region for relative beta power (note: the figure for theta is nearly identical, See Appendix G). Post-hoc contrasts revealed that for relative beta and theta power, compared to the DCD and INT groups, the TD group exhibited a smaller difference in the left and right hemispheres (direction and magnitude) for the central and parietal regions ($p < 0.05$ for both). Similarly, compared to the DCD and INT groups, the TD group exhibited a smaller difference in the left and right hemispheres (direction and magnitude) for the central and occipital regions ($p < 0.05$ for both). The INT group and to a greater extent the DCD group both exhibited greater activity for the right-central region. In addition, the DCD group exhibits slightly greater right hemisphere activity compared to the left hemisphere for central, parietal, and occipital regions and compared to the other two groups.

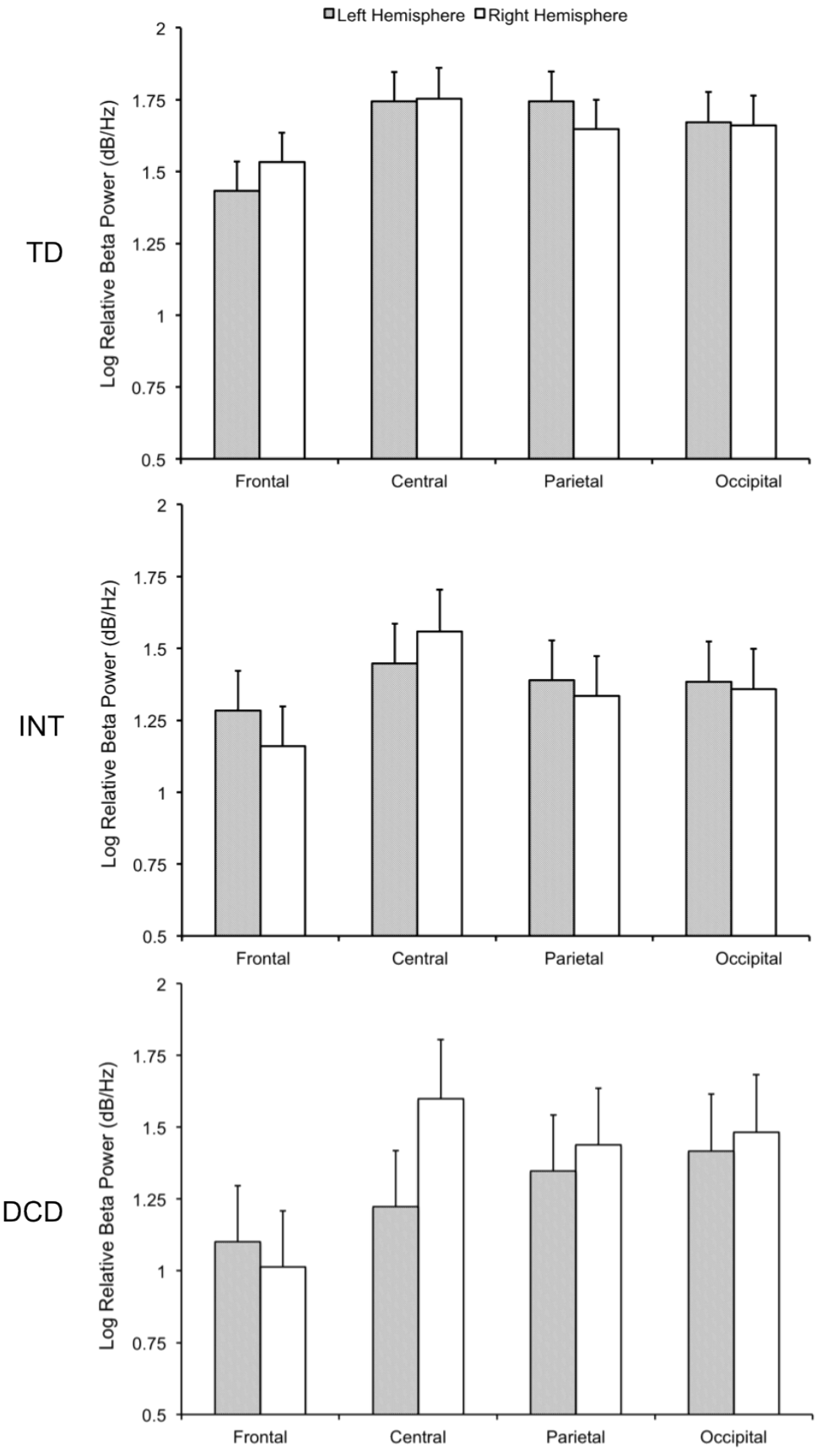
Left Hemisphere
Right Hemisphere
TD
INT
DCD
Log Relative Beta Power (dB/Hz)
2
1.75
1.5
1.25
1
0.75
0.5
Frontal
Central
Parietal
Occipital

Figure 3.3. Specific Aim 1. Log relative beta power by group, hemisphere and region. TD - top, INT - middle, and DCD – bottom; Left hemisphere = gray; right = white; Error bars = standard error.

Low to High Spectral Power: Theta-Alpha and Theta-Beta Ratio.

Significant hemisphere and region main effects were found for the theta-alpha ($F_{(1,50 \text{ and } 3,150)}$ = 11.5 and 109.4, respectively, $p < 0.001$ for both) and theta-beta ratios ($F_{(1,50 \text{ and } 3,150)}$ = 5.7 and 4.0, respectively, $p < 0.001$ for both). Scheffé's post-hoc analyses revealed that the central region exhibited a smaller theta-beta ratio compared to the occipital region ($T_{(50)} = 3.2$, $p < 0.05$); all other regions were not significantly different ($p > 0.05$). In addition, a significant hemisphere x region interaction was found for the theta-alpha ratio ($F_{(3, 1210)} = 17.2$, $p < 0.001$, see Figure 3.4). Post-hoc differential contrasts revealed that the difference between the left and right hemispheres (magnitude and direction) for the parietal region was different than that of the frontal region ($T_{(1210)} = 3.2$, $p < 0.01$). Similarly the difference between the left and right hemispheres (magnitude and direction) for the parietal region was also different than that observed in the occipital region ($T_{(50)} = 2.1$, $p < 0.05$). These results suggest that all groups exhibit a shift in low to high frequency (theta to alpha) that is asymmetrical for posterior regions compared to anterior regions.

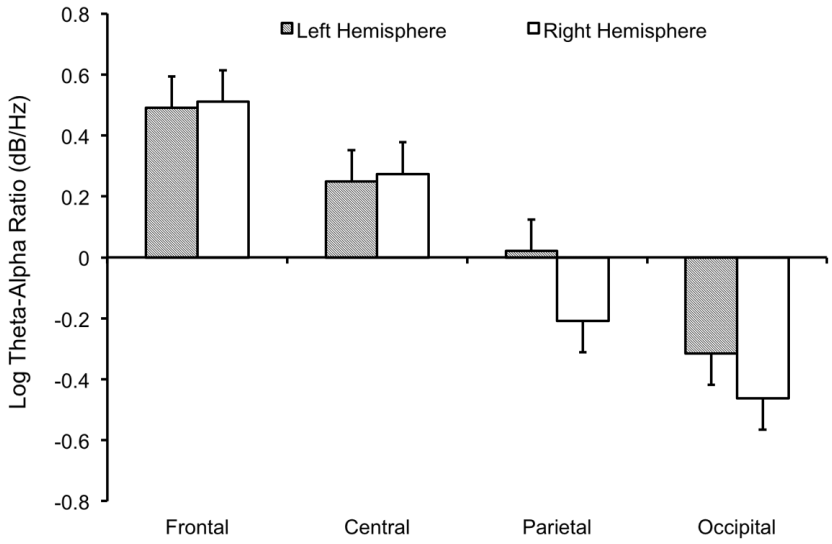

Figure 3.4. Specific Aim 1. Log theta-alpha power ratio by hemisphere and region. Left hemisphere = gray; right = white. Error bars = standard error.

A significant group main effect was found for the theta-alpha ratio ($F_{(2,50)} = 4.8$, $p < 0.05$). Scheffé's post-hoc analyses revealed that the theta-alpha ratio was significantly greater for the DCD group compared to the TD group ($T_{(50)} = 3.1$, $p < 0.01$), but no other group comparisons were significant ($p > 0.05$). These results suggest that children with DCD, as compared to the TD children, showed a greater low frequency activity compared to middle frequency activity (theta-alpha ratio). In addition, a significant group x hemisphere interaction was found for the theta-beta ratio ($F_{(2,50)} = 3.8$, $p < 0.05$; Figure 3.5). Differential contrast revealed that the difference between the left and right hemispheres (magnitude and direction) for DCD group was significantly different than that observed for both the TD ($T_{(50)} = 2.3$, $p < 0.05$) and INT groups ($T_{(50)} = 2.7$, $p < 0.01$). These results suggest that although the TD and INT groups appear to shift from low to high frequency (theta-beta ratio) symmetrically, the children with DCD appear to shift frequencies to a greater extent in the right compared to left hemisphere.

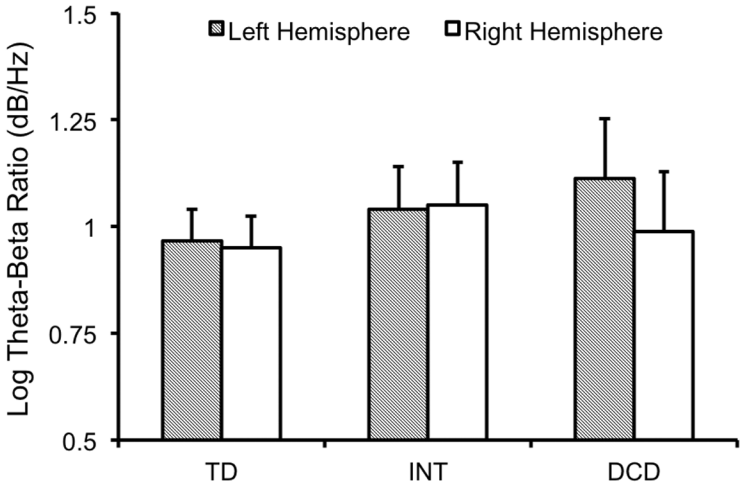

Figure 3.5. Specific Aim 1. Log theta-beta power ratio by group and hemisphere. Left hemisphere = gray; right = white. Error bars = standard error.

Peak Alpha Power.

A significant region main effect ($F_{(3,150)}$ = 13.4, $p < 0.001$) and region x hemisphere interaction ($F_{(3,1210)}$ = 3.5, $p < 0.05$) were found for peak alpha power (Figure 3.6). Post-hoc contrasts revealed that the difference between the right and left hemispheres (magnitude and direction) was different for the frontal and parietal regions ($T_{(50)}$ = 3.2 $p < 0.01$). The difference in peak alpha power between the right and left hemisphere was significantly different between the parietal and occipital regions ($T_{(50)}$ = 2.1 $p < 0.05$).

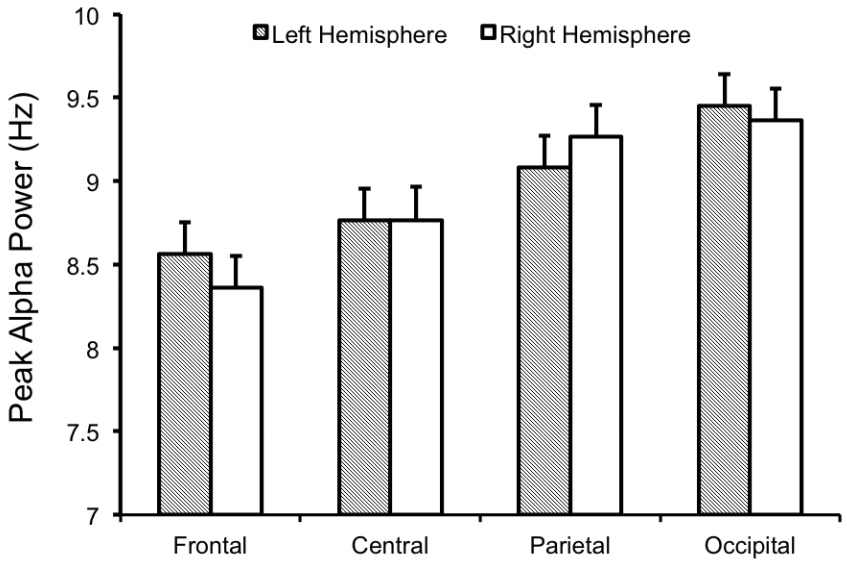

Figure 3.6. Specific Aim 1. Peak alpha power by hemisphere and region. Left hemisphere = gray; right = white. Error bars = standard error.

Significant group differences were found for peak alpha power ($F_{(2,50)} = 5.4$, $p < 0.01$, see Figure 3.7). Scheffé's post-hoc analyses revealed that the DCD group had a significantly lower peak alpha frequency compared to the TD and INT groups ($T_{(50)} = 2.9$ and 3.2, respectively, $p < 0.05$ for both).

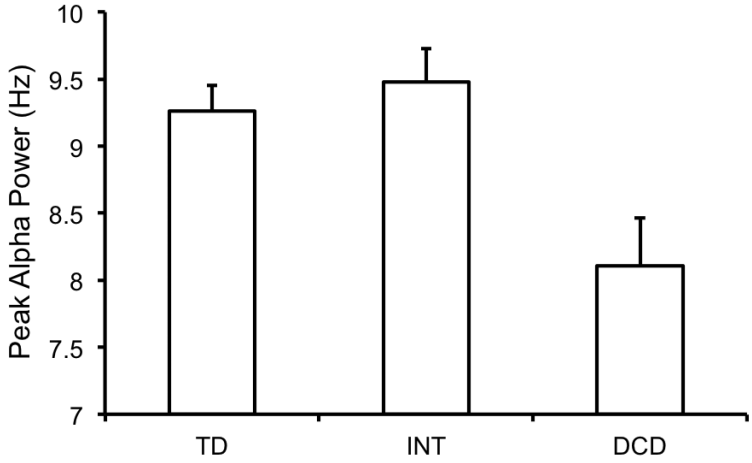

Figure 3.7. Specific Aim 1. Peak alpha power by group. Error bars = standard error.

Section 4: Discussion and Implications

This study is the first to examine differences in EEG cortical dynamics at rest in children with and without DCD. Children with DCD exhibited less relative alpha power, a greater theta/alpha ratio, and a shift in peak alpha power compared to TD children and to a lesser extent those with moderate motor difficulties (INT group). The similarity of activation patterns exhibited by the DCD group and those previously reported for young children and children with developmental disabilities, provides support that children with DCD exhibit a "maturational lag" in cortical function. Interestingly, children with DCD also exhibit an asymmetrical pattern of brain activation at rest (reduced relative theta, relative beta, and theta/beta ratio), whereas the TD children exhibit a more symmetrical pattern of activation. Importantly, the most striking of these cortical activation asymmetries occurs in the central region which overlays the primary motor cortex; this asymmetry may contribute to behavioral deficits in motor abilities in the children with DCD, and to a lesser extent the children with moderate motor difficulties.

Differences in Regional and Hemispheric Activation Patterns

The posterior regions (parietal and occipital) exhibited greater relative alpha power, ratio between theta and alpha power and peak alpha power compared to anterior regions (frontal and central). These findings are consistent with previous reports in which changes in theta and alpha spectral power proceed in a posterior to anterior direction (Cragg et al., 2011; Gasser, Jennensteinmetz, et al., 1988). A recent study of EEG spectral power and cortical thickness found that developmental changes in the low

frequency bands parallel the developmental trajectory of cortical grey matter (Whitford et al., 2007). Based on these findings, it is likely that the developmental changes in EEG spectral power may be due to cortical refinement or pruning during childhood and adolescence.

Although EEG spectral power asymmetry has been examined extensively for frontal regions, much less is known about the asymmetry in other regions. Gasser and colleagues (1988) did not find differences across the hemispheres, but did confirm posterior to anterior developmental differences in children and adolescents. The current study not only found posterior to anterior differences but also replicated the findings by Clarke et al (2001), in which greater relative alpha power was found for the left frontal region compared to the right. This asymmetry was reversed for posterior regions. Moreover, the current findings for the TD children were consistent with Clarke and colleagues (2001) in that the asymmetry in the frontal and posterior regions is reversed for relative beta (greater right frontal than left and greater left posterior than right). It can be hypothesized that these differences in asymmetry may be due to the relatively early development of abilities that rely on right lateralized posterior cortical areas (i.e., visual-spatial abilities).

Atypical EEG Spectral Power in Children with DCD

The present results suggest that for several indices of brain function the children with DCD are different than their TD peers, and to a lesser extent the children with moderate motor difficulties. The children with DCD exhibit values similar to previous reports on younger-aged cohorts and children with developmental and learning disabilities, suggesting a "maturational lag" in cortical function. For example, Marshall

and colleagues found that by the age of 4, TD children exhibit a peak alpha power at 9 Hz, whereas the children with DCD in the present study exhibit a peak alpha of 8 Hz. Similarly, children with ADHD have been shown to have decreased relative alpha and beta power compared to TD children (Barry, Clarke, & Johnstone, 2003; Clarke, Barry, et al., 2002), consistent with the present findings in children with DCD compared to TD children. In addition, children with DCD, consistent with reports from children with ADHD and ADHD comorbid with reading problems (Clarke, Barry, et al., 2002), exhibited significantly greater theta-alpha and theta-beta ratio suggesting elevated slow-wave activity that is not age-appropriate.

The specificity of regional and/or hemispheric differences between the three groups is interesting and suggests that the atypical patterns of brain activity may not be simply a generalized maturational lag. Rather, it is likely that the reduced relative theta and beta power and the elevated ratio of theta and beta power for the left hemisphere in the children with DCD may contribute to their deficits in manual dexterity (all children are right-handed). Indeed, a significant hemispheric asymmetry is evident in the central region for relative theta and relative beta for children with DCD, and to a lesser extent the children at risk for motor difficulties. The functional relevance of the theta, alpha and beta bands to sensorimotor processes, including motor planning and online control, has been well established in adults (Gerloff et al., 1998; Hari & Salmelin, 1997; Neuper & Pfurtscheller, 2001; Pfurtscheller & Berghold, 1989). However, the relationship between these frequency bands and sensorimotor processes is less established in children, with the notable exception of the recent studies exploring the mu rhythm (~8 – 10Hz overlaying the central region) (Berchicci et al., 2011; Marshall & Meltzoff, 2011). Based on the

adult literature, greater power in the beta band at rest may facilitate or prime the activation of the motor cortex for future motor tasks (Hari & Salmelin, 1997; Oishi et al., 2007), Therefore, the lack of beta power exhibited by children with DCD may have negative down-stream consequences on sensorimotor behavior. However, in order to establish a stronger link between EEG spectral power and behavioral deficits in DCD, an examination of cortical activation patterns during motor task performance would be necessary.

Moderate Movement Difficulties – Children in the Intermediate Group

The children in the INT group were clinically referred to the study for their movement difficulties, suggesting that these children do not simply represent the lower-end of the TD continuum. Yet, a subset of these children (10 out of the 15 children) do not meet the traditional classification for "At-Risk for DCD", which is defined as performance between the 5th and 15th percentiles on the MABC. Therefore, it is worthwhile to consider what this group represents. The children in this group exhibited cortical activation patterns that were intermediate to those exhibited by the TD and DCD groups. For example, children in the INT group were significantly different than the TD group for relative theta and relative beta power, but not significantly different than the DCD group. Notably, the children in the INT group did show the same asymmetrical activation pattern for the central region as the children with DCD, suggesting that this asymmetry may also contribute to their movement difficulties. At the same time, the INT group was found to be significantly different than the DCD group for theta-alpha ratio and peak alpha power, but not significantly different than the TD group. Therefore, INT group appears to represent a intermediate phenotype both in terms of their motor abilities

(handwriting and general coordination) and their brain activation patterns that are not quite typically developing and also not quite DCD. By including the INT group in the current study, we were able to extend our results beyond the traditional dichotomy between TD and DCD that is pervasive in the developmental literature. Given their intermediate characteristics, this group may be more dynamic than the children with DCD counterparts, who do not appear to resolve their movement difficulties. Thus, it would be worthwhile to follow the children in the INT group to determine if the movement difficulties and differences in cortical activation patterns exhibited in the current study are persistent, resolve, or become worse with age.

Conclusions and Future Directions

One limitation to the current study is that the DCD group included children with co-morbid attention and social communication difficulties. Therefore, it is not possible to quantitatively determine if differences in cortical dynamics exhibited by the DCD group are attributed to purely motor coordination problems. Qualitatively, an examination of the individual children within the DCD group suggests that those with comorbid attention or social difficulties were no different than those without co-occurring problems. However, a much larger sample of children with DCD is needed to stratify the group into those with only motor problems, motor and attention problems, motor and social problems, and the combination of these characteristics. Given the high comorbidity of motor, attention and social problems, and the qualitative observations of the individuals within the DCD group in the present study, it is likely that even with a group stratification of this nature, similarities in brain and behavior outcomes across the different groups will remain.

The results from the present study suggest that children with DCD exhibit a "maturational lag" in cortical function, similar to young children and those with developmental disabilities. However, in order to determine if the differences in cortical dynamics exhibited by the children with DCD in the present study remain delayed with respect to the children in the TD and INT groups, longitudinal follow-up examinations are necessary. By characterizing of the developmental trajectory of children with DCD, we may determine if this maturational lag is persistent or eventually is resolved either with age or with remediation.

Chapter 4: Specific Aim 2: Differences in Motor Planning Between Children with and without DCD

Abstract

Behavioral deficits in visuomotor planning and control exhibited by children with Developmental Coordination Disorder (DCD) have been well documented in the developmental literature. Although it has been proposed that these functional impairments are related to "atypical brain development," very few studies, to date, have identified potential neurological mechanisms. To address this knowledge gap, electroencephalography (EEG) was recorded from children with and without DCD (n = 13 and 20, respectively) during the performance of a visuomotor drawing task. Behavioral results suggest that although some children with DCD performed outside the typically developing (TD) landscape (i.e., age-related changes *within* the TD group), the developmental trajectory of the children with DCD is similar to that of the TD children. Despite the performance similarities, the engagement of cortical resources in the children with DCD is markedly different from their TD counterparts. Children with DCD engaged motor planning and control brain areas to a greater extent and for a longer period of time compared to TD children. These results suggest that the children with DCD increase engagement of relevant motor cortical resources in order to perform comparably to the TD children.

Introduction

Approximately 6% of school-aged children are diagnosed with Developmental Coordination Disorder (DCD). This motor learning disorder is characterized by marked

impairment in the performance of activities of daily living requiring movement coordination and interferes with the child's academic achievement (APA, 2004). In particular, children with DCD exhibit marked deficits in movement planning (Smyth et al., 1997) and adaptive visuomotor behavior (Kagerer et al., 2004; Kagerer et al., 2006; Ferrel-Chapus et al., 2002) in reaching and drawing tasks. Although the motor performance of children with DCD has been extensively studied, the neurophysiological mechanisms underlying these functional deficits are not well known. Kaplan and colleagues (1998) have suggested that DCD may be due to "atypical brain development". However, the relationship between the movement planning deficits exhibited by children with DCD and differences in cortical activation patterns in relevant brain structures is unclear. To address this knowledge gap, the current study not only characterized the cortical dynamics underlying motor planning and control in children with DCD using electroencephalography (EEG), but also investigated the relationship between cortical dynamics and movement kinematics in children with and without DCD.

The temporal sensitivity of electroencephalography (EEG) makes it an ideal tool to study preparatory and on-going cortical processes during the performance of motor tasks. In particular, movement-related cortical potentials (MRCPs) obtained from scalp locations overlying the supplementary motor area, premotor cortex, and primary motor cortex have revealed age-related differences in typically-developing children (Chiarenza et al., 1983; Warren & Karrer, 1984; Chiarenza et al., 1995; Pangelinan et al., 2011). Specifically, older children and adults exhibit larger negative-going waveforms in these relevant motor planning and control areas compared to young children.

A complementary approach to time-domain analyses (i.e., MRCPs) is an examination of changes in the frequency content of the EEG between rest conditions and during the performance of a movement task. Many studies have reported task-related spectral power changes (desynchrony) in the alpha and beta frequency bands in adults during the preparation of motor tasks (Pfurtscheller 1989; Gerloff et al., 1998; Manganotti et al., 1998; Pfurtscheller and Andrew, 1999; Neuper and Pfurtscheller, 2001). More recently, these analyses have been applied to developmental data and have lead to two important findings. First, young children lack the characteristic task-related changed (decreases) in alpha power reflecting a relative lack of movement preparation, in comparison to older children and adults (Bender et al., 2005). Second, young children exhibit a relative increase in frontal cortical areas compared to motor cortical areas during motor planning, which may reflect the greater effort or attention needed for young children to plan and control arm movements (Pangelinan et al., 2011). As the motor performance of children with DCD is often more similar to young TD children, it follows that these two cohorts will demonstrate similar cortical activation patterns; specifically, a lack of alpha desynchrony over motor cortical brain areas while exhibiting a relative increase in frontal desynchrony during motor planning.

The current study employed time and frequency domain analyses of EEG as well as an examination of movement kinematics during the performance of a center-out drawing task to determine if children with DCD follow a similar behavioral and cortical dynamic developmental trajectory as the TD children and if on average children with DCD differ from TD children. Given the visuomotor behavioral deficits exhibited by children with DCD, it was expected that these children would exhibit EEG activation

patterns that reflect inefficient engagement of relevant cortical motor resources and greater cortical activation from compensatory frontal brain regions. The results from this study provide insights into the neural mechanisms underlying visuomotor performance in children with DCD.

Methods

Participants.

Children were recruited from the local university area. Children with DCD were referred to our study by local elementary school resource teachers, physical and occupational therapists, and/or parent support groups for children with developmental disabilities. Thirteen children with DCD (7 female, age range: 6.1 – 12.3 years) and 20 typically developing (TD) children (10 female, age range: 6.0 – 12.6 years) were included in this study. Three additional 6- to 7-year old with DCD were recruited for the study but were unable to complete the task and not included in the analysis. The Institutional Review Board at the University of Maryland College Park approved all procedures. Prior to participation, the parents and children provided informed consent or assent, respectively (Appendix H). For their participation, the children received a modest monetary compensation and a choice of an age-appropriate prize.

Inclusion Criteria.

Parents completed a pediatric health questionnaire (Appendix B) to provide details about the child's overall developmental. This questionnaire also inquired about the diagnosis of any general medical conditions and developmental learning disabilities (i.e., attention deficit hyperactivity disorder, autism spectrum disorder, speech/language

difficulties, and academic problems). The children completed a 10-item handedness test (Appendix E) (Fagard & Corroyer, 2003) to ensure right-hand dominance and the Movement Assessment Battery for Children, Second Edition (MABC2 - Henderson & Sugden, 2007) to characterize their motor skill ability in the areas of manual dexterity, ball skills, and balance.

TD children were eligible for inclusion based on the following criteria: no history of neurological deficits, no head injuries/concussions, no learning or developmental disabilities, right-handed, and performance on the MABC2 $\geq 25^{th}$ percentile (MABC2 Total Score range: 25^{th} – 95^{th} percentile; MABC2 median: 63^{rd} percentile).

Inclusion criteria for the children with DCD were: no history of neurological deficits, no head injuries/concussions, no diagnosis of pervasive developmental disabilities (e.g., Autism Spectrum Disorder), no diagnosis of a medical condition that would impact movement (e.g., cerebral palsy), and right-handed. In addition, based on the parent questionnaire and the performance on the MABC, all children with DCD met the DSM-IV criteria for Developmental Coordination Disorder: a) Marked impairments in activities requiring motor coordination (MABC-2 Manual Dexterity $\leq 5^{th}$ percentile, median MABC 5^{th} percentile; MABC2 Total Score $\leq 9^{th}$ percentile[4], median MABC 5^{th} percentile); b) Motor coordination interferes with academic achievement or activities of daily living; and, c) The disturbance is not due to a general medical condition[5].

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[4] We acknowledge that the suggested research diagnostic criteria for DCD is a MABC2 Total Score $\leq 5^{th}$ percentile. MABC2 total scores between the 5^{th} and 15^{th} percentiles are considered "at risk" for movement difficulties. We accepted children with total scores up to the 9^{th} percentile if the child's manual dexterity scores at or below the 5^{th} percentile, providing support that the child exhibits marked impairments in visuomotor abilities relevant to the behavioral task assessed.

[5] None of the children in the present study presented with intellectual disabilities, so Criterion D was not applicable to the diagnosis of DCD.

Experimental Apparatus and Procedures.

The data collection procedures were similar to previous studies in our lab (Contreras-Vidal and Kerick, 2004; Pangelinan et al., 2011). The experimental set-up is depicted in Figure 4.1. Participants were seated at a table facing a computer monitor (21") with the center of the screen positioned at eye level. A chin rest was used to stabilize and maintain the participant's head position and the height of the chair and chin rest were adjusted for each participant.

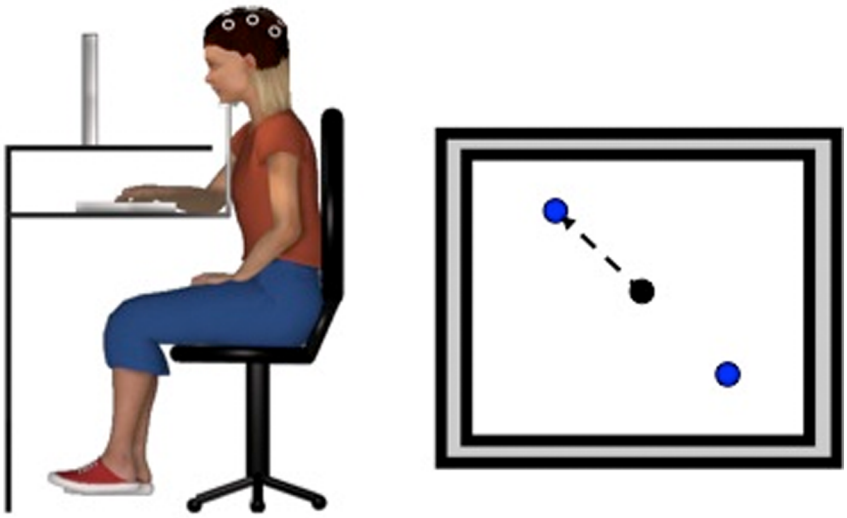

Figure 4.1. Specific Aim 2. Experiment set-up.
Top: The monitor displayed the center (black) circle and the two peripheral (blue) targets. Bottom: The participants were seated at a desk with their head stabilized with a chin rest. The participants made self-selected and self-initiated center-out drawing movements using a digitized pen on a digitizing tablet for each of 60 trials.

Vision of the hand/arm was occluded via a wooden platform upon which the computer screen was positioned; a digitizing tablet (12"×12" WACOM In-Tuos ™, Vancouver, Canada) was placed underneath. Custom programs using OASIS™ software (Kikosoft, Nijmegen) were used for the stimulus presentation and tablet data acquisition. The participants made line-drawing/aiming movements in the horizontal plane using a

computerized pen and digitizing tablet. The sampling rate of the digitizing tablet was 200 Hz. The monitor provided real-time visual feedback of pen movement. The OASIS program also generated event markers that were synchronized with the EEG data collection indicating the beginning of a trial, target appearance, movement onset, target acquisition, and the end of a trial.

Continuous EEG was acquired at a sampling rate of 512 Hz from 11 surface tin electrodes housed within a stretchable lycra cap (Electro Cap International™, Eaton, Ohio, USA) using Neuroscan Scan™ software (version 4.3, Herndon, Virginia, USA). These electrode sites are consistent with the International 10/20 system and included the following regions: frontal (F3, Fz, F4), central (C3, Cz, C4), parietal (P3, Pz, P4), and occipital (O1, O2). Eye movement artifacts were recorded from electrodes placed superior and inferior to the left eye and on the orbital fossi of the left and right eyes. Average mastoids served as the common reference and FPz served as the common ground was. All channel impedances were maintained at or below 10 kΩ. However, acceptable impedances (below 10 kΩ) for the occipital sites (O1 and O2) were difficult to obtain for some of the participants due to interference caused by hair displacement. These sites were not included in the final analysis. Continuous EEG signals were amplified (20,000x) and digitally filtered (0.01 Hz and 100 Hz) using Grass (12A5) Neurodata Acquisition Amplifiers (Grass Technology, Astro-Med, Inc., West Warwick, RI, USA). Prior to the drawing task, two minutes of eyes-open and eyes-closed resting EEG were recorded as baseline EEG measures.

The participants completed 12 practice trials to become familiar with the digital pen, tablet, and computer display. For some of the young children, an additional 12 trials

were provided if the participant did not demonstrate an understanding of the task after the first practice set. Figure 4.1 (top) depicts the behavioral task as presented on the computer monitor. The participants began a trial by moving the digital pen into a central home position indicated by a circle (0.5 cm diameter) presented on the computer monitor in the center of the workspace. Upon entering the home position, two target circles (0.5cm in diameter each) were presented 5 cm from the home position and located at 135º and 315º with respect to the home position. The participants were instructed to select one of the two targets and "plan or think how they will move quickly and accurately from the home position and stop in the target circle." The participants had to remain motionless in the start position for 2 seconds. The purpose of this hold period was to provide the participants with sufficient time for target selection and movement planning, and to allow ample time for electrophysiological data acquisition during this phase of the task. There was no external cue to move after the 2-second hold period, however, if the participants left the home position too soon (< 2 seconds), the targets would disappear and the trial would restart. After the hold period, the participants made one fast and straight movement with the digitizing pen from the home position to the target. The participants were able to see the pen trace displayed on the computer screen in real time. Once the pen reached the target position, the targets and pen trace disappeared and the participant returned the pen to the home position to begin the next trial. Between trials, the experimenter periodically reminded the participants to move "as quickly and as straight as possible". The participants were free to choose the location of the target for each trial, but were instructed to move to each of the targets equally across the 60 trials. On average

both groups of children met this requirement (mean DCD: 30.0/30.0, mean TD: 31.1/28.9).

Data Analysis.

Behavioral data analyses were consistent with previously reported studies conducted in our lab (King et al., 2009; King et al., 2010; Pangelinan et al., 2011) and conducted using programs written in MATLAB^{TM} version 7.10 (Mathworks, Natick, MA USA). The time series of x and y positions for each trial were filtered using an 8th order dual-pass Butterworth filter (cutoff frequency: 10 Hz). Automated algorithms were used to mark the x/y position and time of movement onset and offset (see Appendix I for an example of the marking for a TD child and a child with DCD). Each trial was visually inspected and manually re-marked if the onset/offset were incorrect. The following behavioral variables were computed from the movement trajectories: peak velocity (PV) (cm/s), movement time (MT) (seconds), movement length (ML) (centimeters), normalized jerk (NJ – unitless), root mean squared error (RMSE), and variability of initial direction error (VIDE – degrees). Peak velocity was the maximum velocity between the onset and offset. Movement time was the total time between movement onset and offset. Movement length was the total distance of the movement trajectory. NJ was calculated as the rate of change of the acceleration (j) normalized by the movement time (MT) and movement length (ML):

$$NJ = \sqrt{\frac{MT^5}{ML^2}\int j^2(t)dt} \qquad \text{(Eq. 3.1)}$$

RMSE was computed as the average deviation between an ideal vector between the movement onset to offset (x_a and y_a) and the actual movement trajectory:

$$RMSE = \sqrt{\sum_{i=1}^{N}[(x_a - x_i)^2 + (y_a - y_i)^2]\frac{1}{N}} \qquad \text{(Eq. 3.2)}$$

Initial directional error (IDE) was calculated as the angular deviation between actual movement trajectory 80 ms after movement onset (initial movement direction prior to visual feedback correction) and an ideal straight vector from the onset to target. The variability of IDE was assessed as the standard deviation of the IDE scores for each subject across all movements.

EEGLAB version 9.0.3 (Delorme & Makeig, 2004) was used to re-reference data to average mastoids and apply filters. The following filters were applied to the data. For the time-domain analyses a 10 Hz low-pass filter with a 24dB/octave roll-off was used. All subsequent analyses were conducted using customized programs written in MATLAB 7.10. Data were epoched/segmented into 1,000-ms windows beginning 500 ms prior to and 500 ms following movement onset. Data were baseline corrected using a 125-ms time window prior to the start of the epoch (725 ms prior to movement onset). These data were visually inspected for excessive movement and ocular artifacts. For the time-domain analyses or movement-related cortical potentials (MRCPs), the 60 trials were averaged in time for each electrode site. For the spectral analysis, fast Fourier transforms (FFT) were applied to data from the behavioral task as well as 1,000-ms epochs from the resting (eyes-open) baseline condition. Power spectra were segmented into the alpha (8-12 Hz) and beta (13-30 Hz) bands. These bands were selected for their relevance to motor tasks (Gerloff et al., 1998; Andres et al., 1999). Spectral data were then log-transformed to meet the requirements for the statistical analysis (homogeneity of residuals). Task-related spectral power (TRSpec) was computed for alpha and beta frequency bands as:

TRSpec = log (Spectral Power Task) - log (Spectral Power Rest) (Eq. 3.3)

Statistical Analysis.

A two-step statistical analysis was employed to examine mean group differences and the developmental trajectories of each group using SAS® 9.1 software (SAS Institute Inc., Cary, NC, USA). To examine mean group differences, each dependent measure (both behavioral and EEG) was analyzed using two sample t-tests. To examine the developmental trajectories of each group, each of the dependent measures were examined with respect to age-based regressions by group using. The following regression model was used:

$$Y = (\beta_o + \gamma_0 C) + ((\beta_1 + \gamma_1 C) * (age)) + e \qquad \text{(Eq. 3.3)}$$

where Y = dependent measure

β_0, β_1 = estimated fixed effects TD group (intercept and slope)

γ_0, γ_1 = adjustments to the β parameters for the DCD group

C = 0 for the TD group and 1 for the DCD group

e = residuals

The β_0 parameter represents the intercept term for the TD group. The γ_0 parameter is the adjustment to the TD intercept term; the sum of β_0 and γ_0 is equal to the intercept for the DCD group. Intercept terms were excluded from the discussion of the results because the value of these parameter estimates (i.e., when age = 0 years) does not provide any meaningful conclusions. The β_1 parameter represents the age-related changes (i.e., slope) for the TD children. The γ_1 parameter is an adjustment to the TD slope parameter for the DCD group; the sum of β_1 and γ_1 is equal to the age-related changes for the DCD group. Note that for the EEG dependent measures, regression models were created for each electrode of interest. For the MRCP analysis the following electrodes were examined

before and after movement onset: Fz, C3, Cz, and C4. These electrode locations were selected for their relevance to motor planning and have been found to be sensitive to age-related differences in children in our previous work (Pangelinan et al., 2011). For the TRSpec analysis separate regressions were examined corresponding to the frontal, central, and parietal regions for each of the two frequency bands of interest (alpha and beta).

Pearson's correlations between the all behavioral and EEG measures to determine the relationship across all children. For all statistical analyses, the level of significance was set to $p < 0.05$.

Results

Movement Kinematics.

No significant mean differences were found for any of the performance measures ($p > 0.05$). Table 4.1 provides the beta coefficients, standard error, and significance level for the slope parameters in the regression analyses.

Table 4.1. Specific Aim 2. Kinematic Results.
*Slope parameters and corresponding standard error for the behavioral analyses. *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.*

Behavioral DV	TD Slope (SE) (β_1)	DCD Slope (SE) ($\beta_1 + \gamma_1$)
MT	-0.12 (0.03)***	-0.02 (0.04)
ML	-0.14 (0.06)*	-0.04 (0.9)
VIDE	-1.60 (0.33) ***	-0.98 (0.44) *
NJ	-41.92 (20.15) *	-45.16 (24.80) *
PV	1.05 (0.71)	-1.22 (0.95)
RMSE	-0.02 (0.25)	-0.01 (0.02)

The regression analysis for each behavioral dependent measure revealed that the age-based regression slope for TD children was significant for MT, VIDE, ML, and NJ ($p < 0.05$ for all Figure 4.2). Similarly, the age-based regression slope for the DCD children was also significant for VIDE and NJ ($p < 0.05$ for both), but not for ML or MT. The slope coefficients for RMSE and PV were not significant for either group. Moreover, no differences between the coefficients for the two groups were found (either for the intercept or slope terms). Taken together, these behavioral results suggest that on average the two groups did not differ and that the developmental trajectories did not differ.

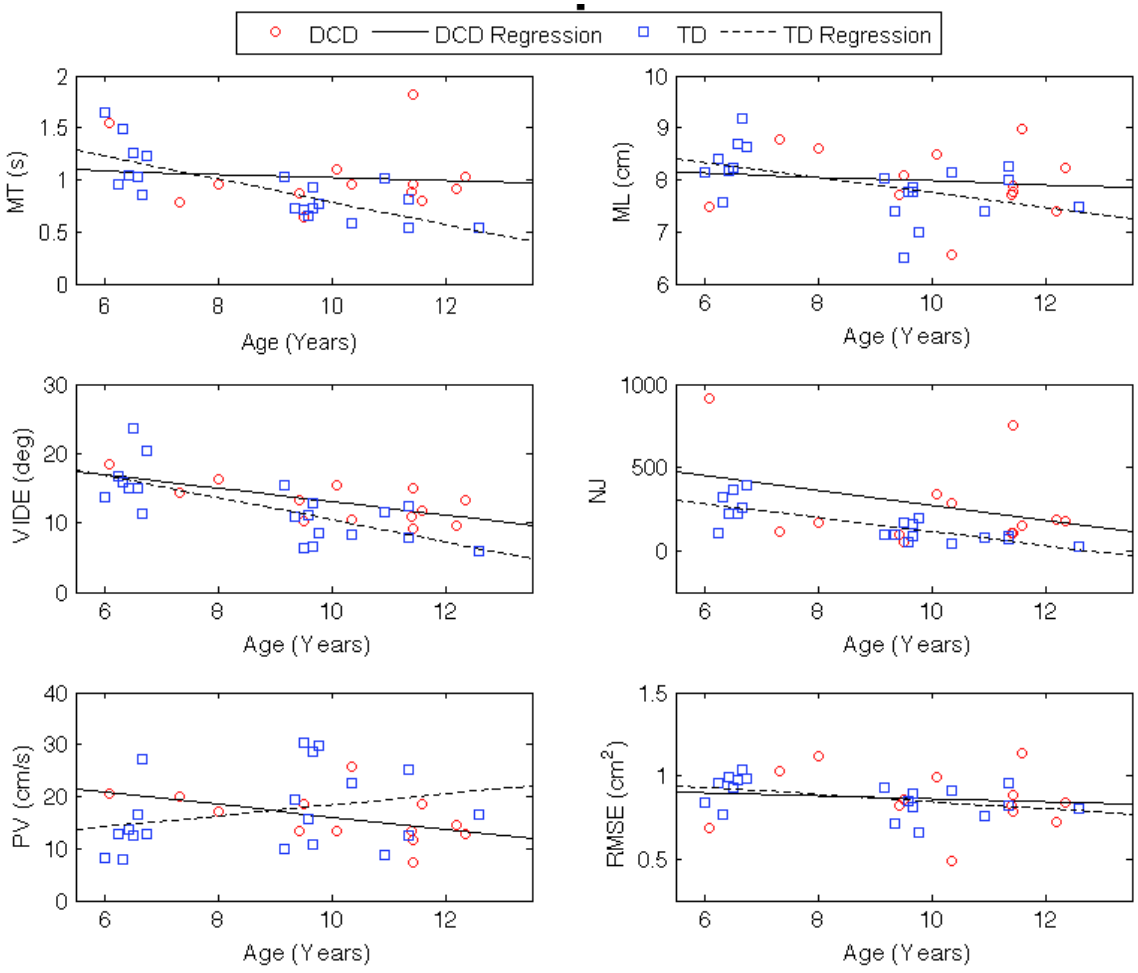

Figure 4.2. Specific Aim 2. Movement kinematics.
Movement time (1st row left), movement length (1st row right), variability of initial directional error (2nd row left), and normalized jerk (2nd row right), peak velocity (3rd row left), and root mean squared error (3rd row right). Children with DCD = red circles,

TD children = blue squares. Regression for children with DCD is indicated as the solid line. The regression for the TD children is indicated as the dotted line.

Movement-Related Cortical Potentials (MRCPs).

Figures 4.3 and 4.4 depict the time-averaged movement-related cortical potentials (MRCPs) for children with DCD and TD children, respectively. Each individual is depicted as a separate waveform by age to highlight the developmental differences within each group. The characteristic MRCP waveform consists of an increasingly negative amplitude leading to and immediately following movement onset. The young children, particularly the children with DCD exhibit very positive MRCP amplitudes, particularly after movement onset.

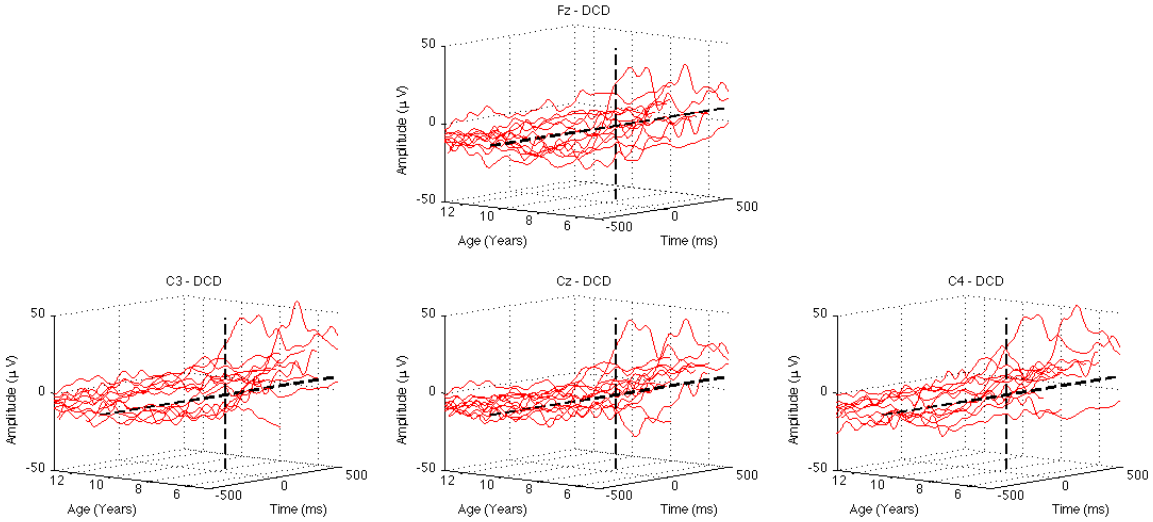

Figure 4.3. Specific Aim 2. Movement related cortical potentials - Children with DCD. Fz (top), C3 (bottom left), Cz (bottom middle), and C4 (bottom right). Horizontal and vertical dashed lines indicate 0 μV amplitude and 0 time (movement onset).

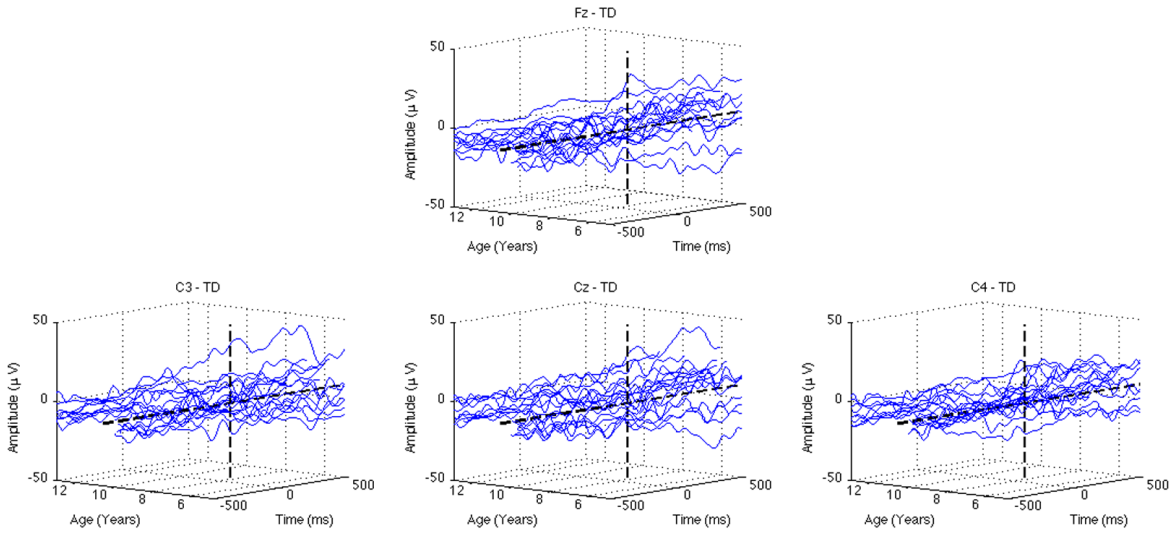

Figure 4.4. Specific Aim 2. Movement related cortical potentials – TD children. Fz (top), C3 (bottom left), Cz (bottom middle), and C4 (bottom right). Horizontal and vertical dashed lines indicate 0 μV amplitude and 0 time (movement onset).

To capture the age-related changes in MRCP amplitudes, regression analyses were conducted on mean MRCP amplitude before (-500 ms to movement onset) and after (onset to +500ms) movement onset for Fz, Cz, C3, and C4. Figure 4.5 depicts the significant age-related changes evident in the mean MRCP amplitude by group.

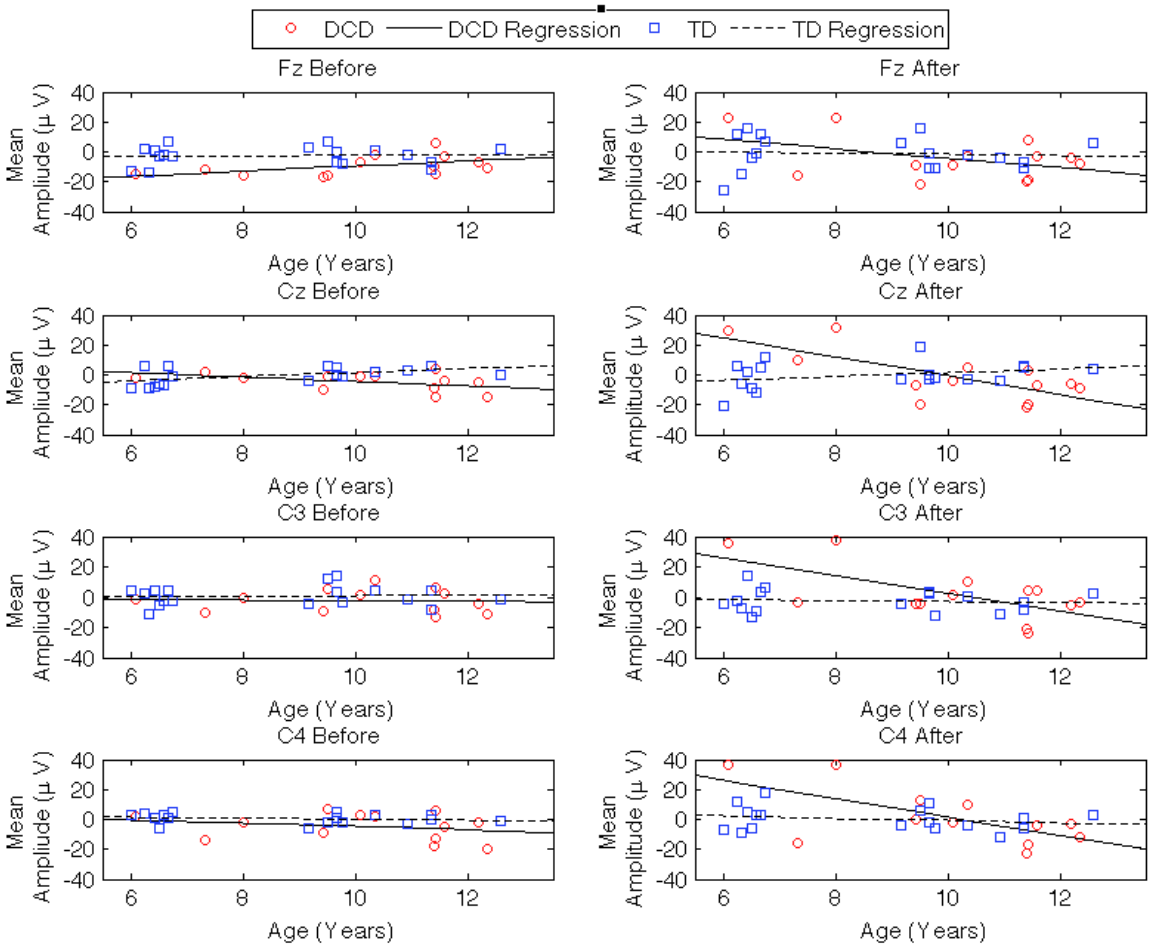

Figure 4.5. Specific Aim 2. Mean MRCP amplitudes.
Fz (1st row), Cz (2nd row), C3 (3rd row) and C4 (last row) averaged over the 500ms before movement onset (left column) and after movement onset (right column). Children with DCD = red circles, TD children = blue squares. Regression for children with DCD is indicated as the solid line. The regression for the TD children is indicated as the dotted line.

No significant group differences were found for the mean MRCP dependent measures ($p > 0.05$). The regression analysis revealed significant age-related changes (slope coefficients) for the children with DCD for the following measures: Cz after onset, C3 after onset, and C4 after onset ($p < 0.05$ for all). The slope coefficients, standard errors, and significance level are provided in Table 4.2. The regression slopes were not significant for the TD children ($p > 0.05$). Interestingly, there were significant group

differences in the slope coefficients for the following measures: Cz before onset, Cz after onset, C3 after onset, and C4 after onset ($p < 0.05$ for all). These results suggest a *different* developmental trajectory for the children with DCD, compared to TD children. Specifically, compared to their TD counterparts, the young children with DCD exhibit hypoactivation (greater positivity) for these motor cortical areas, where as the older children with DCD exhibit hyperactivation (greater negativity).

Table 4.2. Specific Aim 2. Regression coefficients and standard error for the MRCP analysis.
**** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.*

MRCP DV	TD Slope (SE) (β_1)	DCD Slope (SE) ($\beta_1 + \gamma_1$)	Difference in Slopes
Fz Before	0.12 (0.70)	1.70 (0.94)	1.58 (1.17)
Fz After	-0.40 (1.38)	-3.18 (1.85)	-2.78 (2.31)
Cz Before	1.38 (0.65)	-1.44 (0.77)	-2.82 (0.96) **
Cz After	1.25 (0.60)	-6.27 (1.54) ***	-7.52 (1.91) ***
C3 Before	0.23 (0.80)	-0.20 (1.08)	-0.43 (1.34)
C3 After	-0.32 (0.16)	-5.87 (1.63) **	-5.55 (2.04) *
C4 Before	-0.36 (0.75)	-1.10 (0.97)	-0.74 (1.22)
C4 After	-0.36 (0.23)	-6.19 (1.73) **	-5.46 (2.14) *

Task-Related Spectral Power (TRSpec) for Alpha and Beta.

No significant mean differences were found for any of the task-related spectral power measures (frontal, central, and parietal) for either frequency band (alpha and beta). Moreover, the regression analysis failed to reveal significant age-related changes for either group for the task-related spectral power measures ($p > 0.05$).

Correlations between EEG and Kinematic Measures.

The Pearson's correlation revealed significant relationships between NJ and the MRCP components following movement onset (Fz, Cz, C3, and C4). The magnitude of the correlations were: r = 0.41, 0.39, 0.46, and 0.48, respectively ($p < 0.05$ for all). Figure 4.6 depicts the relationship between NJ and the MRCP components. These results suggest that for both groups of children greater mean negativity in the MRCP waveforms following movement onset is related to greater smoothness (less jerk).

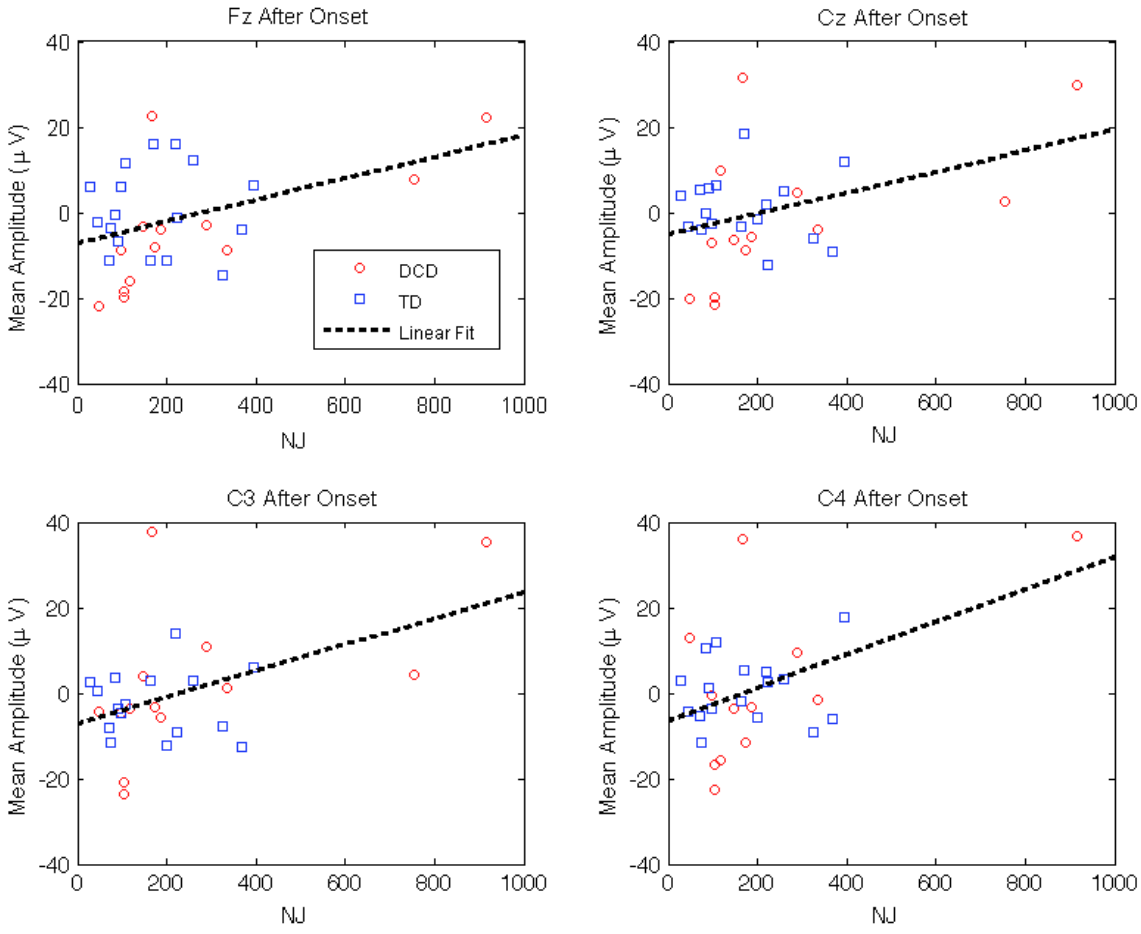

Figure 4.6. Specific Aim 2. Scatterplots of Mean MRCP amplitudes. Fz (top left), Cz (top right), C3 (bottom left), and C4 (bottom right) with respect to NJ scores. Children with DCD = red circles, TD children = blue squares. The linear fit is indicated as the dotted line.

Section 4: Discussion and Implications

This study is the first to examine differences in EEG cortical dynamics and movement kinematics in the context of a visuomotor task in children with and without DCD. Although the performance of some children with DCD fell outside the TD landscape (i.e., age-related changes *within* the TD group), the developmental trajectory of the children with DCD and the mean performance were similar to that of the TD children. Despite the similarities in the movement kinematics, the engagement of cortical resources in the children with DCD is markedly different from their TD counterparts. Children with DCD engaged motor planning and control brain areas to a greater extent and for a longer period of time compared to TD children. Global differences in brain activation (e.g., task-related spectral power) were not found. However, these results suggest that the children with DCD must increase engagement of relevant motor cortical resources in order to perform comparably to the TD children. In addition, this study found that across the two groups of children, greater engagement in movement-related brain areas (i.e., MRCP negativity) is related to greater movement smoothness. The results from this study provide insights into the differences in cortical dynamics in children with and without DCD and how the cortical dynamics relate to behavioral performance in these children.

The performance of the children with DCD on this goal-directed drawing task was not different than their TD counterparts both in the mean performance and in the developmental trajectory of behavioral improvements across age. These results confirm other studies that found that the performance of children with DCD does not differ from controls for simple discrete drawing or aiming movements (Smits-Engelsman et al., 2003; Wilmut & Wann, 2008; Hyde & Wilson, 2010). It is also possible that the age-

related improvements in the DCD group found for the planning and control measures may be due, in part, to the fact that the older children with DCD moved slower. This may reflect that the older children with DCD sacrificed speed for accuracy. In contrast, the TD children show age-related improvements in both speed (MT) and accuracy (ML), suggesting that older TD children are able to move both quickly and accurately for this task. However, it is likely that for more complex tasks, such as movements requiring greater involvement of additional joints or body segments or movements in which task conditions change (e.g., stop-signal or double-step tasks) the behavioral performance of children with DCD will degrade in comparison to TD children.

In order to accomplish behavioral equivalence with TD children, the children with DCD engage cortical motor resources to a greater extent and for a greater period of time than their TD counterparts. This seeming lack of efficient cortical activation confirms a previous report using fMRI, which also found greater activation in children with DCD compared to controls for a set of visuospatial brain regions (Zwicker et al., 2010). The authors of this previous study attributed this increase in visuospatial brain activation to a dependence on vision to guide motor performance. In the context of the present study, we did not find global differences in brain activation, but found that differences in activation were constrained to motor and motor planning brain areas. It is likely that this discrepancy between the current study and previous study is due to the methodology used to gauge cortical activation (EEG vs. MRI) and the nature of the two tasks (discrete drawing vs. maze tracing). The time sensitive nature of EEG allows us to track real-time changes in cortical activation linked directly to the task planning and performance. Thus, the results from the current study suggest that children with DCD continue to activate

motor cortical areas to aid in the *online control* of the movement (i.e., after the initiation of a ballistic movement), whereas TD children do not require enhanced activation of motor areas to perform the task effectively. If the current study employed a task that required continuous monitoring of performance online or if the task was dynamic (e.g., task constraints changed during performance), it is possible that additional brain regions may be implicated.

Our previous study (Pangelinan et al., 2011) found that the magnitude of movement-related cortical potentials was related to the quality of motor performance in typically developing children and adults. The current study confirms the relationship between task-related activation of midline frontal brain areas following movement onset and movement smoothness. It was also found that engagement in all motor-related cortical regions following movement onset was also related to movement smoothness. This finding substantiates the claim that an increased activation in motor planning and control brain regions would directly relate to online performance of the task.

The activation patterns and behavioral performance of the TD children supports a neural efficiency hypothesis in which those with greater motor (or cognitive) skill demonstrate a relative refinement in the activation across the cortex. This work has been supported by previous research in our lab investigating cortical processes of highly skilled versus novice athletes (Hatfield et al, 2004; Kerick et al., 2004). The attenuated brain activity demonstrated by the TD children, in comparison to the children with DCD, may reflect automatization and skill in performing the visuomotor task. With increased practice on this task or handwriting specific training the children with DCD may improve their behavioral performance and exhibit a similar reduction in motor cortical brain

activation. Indeed, practice and learning effects have been found in adults for a similar task in which the pen trace is rotated abruptly (visuomotor adaptation paradigm) and participants must adapt movements for this new visuomotor environment (Contreas-Vidal & Kerick, 2004; Gentili et al., 2011). Thus, evaluating the cortical dynamics of children with DCD before and after behavioral training may provide an additional metric for skill acquisition even after behavioral performance no longer reveals significant improvement.

Future studies are necessary to confirm the results presented here. In particular it would be worthwhile to determine if children with DCD are still able to maintain equivalent performance as TD children if the task complexity increases. We would hypothesize that increased activation of cortical resources may not be sufficient to maintain behavioral performance and that children with DCD may begin to recruit additional neural resources to complete the tasks.

As mentioned, it would also be worthwhile to compare the efficacy of different behavioral training programs using both the behavioral outcomes as well as brain dynamics. Currently, many different behavioral interventions are used to help children with DCD with fine motor and handwriting difficulties. Even with behavioral therapy, many children with DCD, particularly those with severe perceptual-motor difficulties, do not resolve their motor difficulties across childhood and adolescence (Cantell et al., 2003). Therefore, it is imperative that the behavioral interventions used are evaluated both at the level of brain and behavior to determine if that therapy should be continued or if alternative treatments are necessary. It is likely that the cortical dynamics will provide important insights to efficacy of behavioral treatments even once the behavioral outcomes have plateaued. Not only will this brain-based approach to therapy be useful for

the matching individual children with movement difficulties with interventions, but it will also provide valuable evidence regarding the persistence/resolution of DCD.

Chapter 5: Specific Aims 3 & 4: Do Children with DCD Exhibit Differences in Cortical Dynamics and Movement Kinematics during Adaptive Motor Planning?

Abstract

Children with Developmental Coordination Disorder (DCD) have demonstrated difficulties inhibiting and adapting movement plans online. Little is known about the relationship between these behavioral difficulties and the underlying brain functions. The purpose of the current study is to determine if children with DCD and those with moderate movement difficulties exhibit different cortical activation patterns, as measured with electroencephalography (EEG), and movement kinematics compared to typically developing (TD) children during the performance of two adaptive motor tasks. Children between 7.5 and 12.5 years of age participated in two studies in which EEG and movement kinematics were recorded. For Study 1, children with DCD (n = 10), children with moderate movement difficulties (n = 10), and TD children (n = 30) with no movement difficulties, completed a center-out drawing task during which participants either completed movements to a cued target position or inhibited their movement in response to a stop cue. For Study 2, children with DCD (n = 7), children with moderate movement difficulties (n = 9), and TD children (n = 30) completed a center-out drawing task during which participants completed movements to a cued target or adapted their movements online in response to a target displacement. Behaviorally, children with DCD, and to a lesser extent the children with moderate movement difficulties, exhibited an impaired ability to make adjustments to movement plans towards targets, compared to

TD children. In contrast, the children with DCD performed similarly to the other two groups when they had to abruptly stop their movements. Interestingly, the EEG patterns for both studies suggest that children with DCD do not engage relevant motor planning and control brain regions to the same extent as TD children in preparation for movement. Following movement onset, the children with DCD engage motor planning and control resources (i.e., left frontal, fronto-central and central regions) a similar extent as the TD children. However, despite this similar pattern of activation following movement onset, the behavioral performance of the children with DCD is still much poorer than the TD children for uninhibited movements and those requiring online adjustments. The children with moderate movement difficulties exhibit very different patterns of brain activation compared to the other two groups, with very little activation of task-relevant brain regions across all conditions. Taken together, this study provides support that a lack of engagement in frontal brain areas may underlie difficulties in adaptive motor behavior in children with DCD and those with moderate movement difficulties.

Introduction

Adaptive motor behavior may be characterized as the ability to incorporate changes in the environment or task requirements in order to update or modify movements online. This ability depends on the incorporation of sensory feedback and the ability to predict the sensory consequence of motor commands (forward model) in order to update or inhibit motor plans efficiently. The difficulties performing activities of daily living, including handwriting and eye-hand coordination skills, characteristic of children with Developmental Coordination Disorder (DCD) may be due to impairments in adaptive

motor control (Hyde & Wilson, 2011; Hyde & Wilson, 2011). Indeed, children with DCD have deficits in predictive control (Wilmut & Wann, 2008), utilizing sensory feedback (Mon-Williams et al., 1999; Smyth & Mason, 1997), and inhibiting inappropriate motor responses (Mandich et al., 2002). Yet little is known about the neural mechanisms that underlie these difficulties in children with DCD.

The stop-signal and target jump paradigms have been employed to examine adaptive motor behavior in typically developing (TD) children and children with DCD. In these tasks, the location of target stimuli is provided prior to a 'Go' signal that prompts participants to respond via a button press or aiming movement. For some trials, the target stimulus immediately turns red (stop signal) or shifts to a new location (jump) following the Go stimulus, indicating that the participant should immediately stop or modify their response, respectively. Compared to TD children, children with DCD exhibited impaired inhibitory control (stop-signal) and difficulty adapting movement plans when targets changed (jump) (Plumb et al., 2008; Hyde & Wilson, 2011).

The deficit in rapid online correction in children with DCD has been attributed to a disruption in the function of the posterior parietal cortex (PPC), which has been implicated in processing representations of action and predictive control of movement (Della-Maggiore et al., 2004; Desmurget et al., 1999; Mulliken et al., 2008). Consistent with this hypothesis, less activation of the PPC has been reported in children with DCD during the performance of a simple visuomotor task (Kashiwagi et al., 2009). However, the PPC networks with various regions in the frontal cortex as well as subcortical brain regions that mediate motor planning and adaptive motor control (Battaglia-Mayer et al., 2006; Houk & Wise, 1995; Middleton & Strick, 2002; Schultz & Romo, 1992; Shadmehr

& Krakauer, 2008); thus, the disruption of these frontal brain areas may underlie performance differences in DCD. Zwicker and colleagues (2010) found atypical brain responses across several frontal cortical regions, providing support that a more complex visuomotor task would similarly implicate these areas. However, the precise role of these frontal motor planning and control brain regions during the execution of adaptive online control is not well known in children with DCD.

To determine differences in brain activation patterns underlying adaptive motor control, electroencephalography (EEG) and movement kinematics were recorded during the performance of two experimental tasks (stop-signal or target jump) from children with DCD, children with moderate movement difficulties, and TD children. It was hypothesized that children with DCD, and to a lesser extent children with moderate movement difficulties, will demonstrate movement kinematics that are more jerky, less spatially/directionally accurate, and slower than TD children for both the stop and jump tasks. These difficulties would be reflected in the cortical activation patterns. Specifically, children with DCD and those with moderate movement difficulties would exhibit reduced amplitude of movement-related EEG waveforms in frontal brain regions, compared to TD children.

Methods

Participants.

Typically developing (TD) children (age range: 7.5 to 12.5 years) were recruited from the local university area through school and community events (see Table 5.1 for participants' characteristics). Children identified with handwriting and/or movement difficulties were referred to our study by local elementary school resource teachers,

physical and occupational therapists, and/or parent support groups for children with developmental disabilities. All procedures were approved by the Institutional Review Board at the University of Maryland, College Park. Prior to participation, the parents and children provided informed consent and assent (Appendix A), respectively. For their participation in each study, the children received a modest monetary compensation and a choice of an age-appropriate prize.

Inclusion Criteria.

To assess the children's overall heath and development, including academic performance, parents completed a pediatric health questionnaire (Appendix B). This questionnaire inquired about the diagnosis of any general medical conditions or developmental learning disabilities (i.e., attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), speech/language difficulties, and academic problems). To quantify symptoms of ADHD and ASD, parents completed the Disruptive Behavior Disorder (DBD - Appendix C) Questionnaire (Pelham et al., 1992) and the Social Communication Questionnaire (SCQ - Appendix D) (Rutter, Bailey, & Lord, 2003), respectively. To ensure normal intelligence (IQ > 80), all children completed the Woodcock-Johnson III Tests of Cognitive Abilities (Woodcock, McGrew, & Mather, 2001). The children also completed a 10-item handedness test (Appendix E) (Fagard & Corroyer, 2003) to ensure right-hand dominance and the Movement Assessment Battery for Children, Second Edition (MABC-2) to characterize their motor skill ability in the areas of manual dexterity, ball skills, and balance (Henderson & Sugden, 2007). To be included in this research, children had to have no history of neurological deficits, no head injuries/concussions, normal intellectual ability (IQ > 80), and be right-handed.

The total scores on the MABC-2 and the handwriting score on the WJ-III Test of Achievement (Woodcock et al., 2001) were used to separate children into three groups. TD children had MABC-2 scores ≥ 25th percentile (for each component score as well as the total score) and handwriting performance at or above grade level. Children with DCD had MABC-2 total scores ≤ 5th percentile *and* performed below grade level in handwriting. The children that were referred to our study by physical or occupational therapists or educational resource specialists, but whose performance on the MABC-2 did not meet the criteria for DCD (i.e., below the 5th percentile) were put into an intermediate group (INT). The MABC scores and handwriting scores for the children in the intermediate group reflect moderate movement difficulties: total MABC-2 scores between the 9th and 25th percentile[6] *and* a below grade level performance in handwriting (see Appendix F for a handwriting sample from a 12-year-old in this group).

In addition to the MABC-2 and handwriting scores, the criteria for inclusion in the DCD group were based on the parent questionnaire and included the following: a) marked impairments in activities requiring motor coordination; b) motor coordination difficulties interfere with academic achievement or activities of daily living; and, c) the disturbance is not due to a general medical condition[7].

A total of 40 children were able to complete both studies over the course of two testing sessions (counter-balanced for study condition). However, due to scheduling constraints, not all children were able to complete two testing sessions. Therefore, an

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[6] The MABC-2 considers children with performance between the 5th and 15th percentile to be "at risk" for movement difficulties. Three of the children in Study 1 and 3 children in Study 2 had total MABC-2 scores at the 9th percentile. However, we used a broader range of MABC-2 scores for this group since all of these children were referred to our study by clinical or educational specialists. These children exhibit movement difficulties in the classroom and/or at home and are receiving treatment.

[7] None of the children in the present study presented with intellectual disabilities, so Criterion D was not applicable to the diagnosis of DCD.

additional 10 and 6 children participated in study 1 (stop) and study 2 (jump), respectively. Table 5.1 provides the details for the three groups for each of the two studies.

Table 5.1. Specific Aims 3 and 4. Demographics of the children in each group by study. The mean and standard deviation are presented for all variables except for the MABC-2 percentile (the median is provided). Ranges for all variables are presented on the second row of each cell.

Group	N	Age	General Intellectual Ability	SCQ Number of Symptoms	DBD – ADHD Inattentive Number of Symptoms	DBD – ADHD Hyperactive Number of Symptoms	DBD – ADHD Combined Number of Symptoms	MABC-2 Total Median
Study 1 (Stop)								
TD	30 (M: 16, F: 14)	10.2 years (1.3) 7.8 – 12.1	115.2 (10.9) 91 – 143	3.7 (2.6) 0 – 12	0.6 (1.4) 0 – 5	0.5 (1.0) 0 - 3	1.1 (2.2) 0 – 8	63rd percentile 25 – 99th
INT	10 (M: 8, F: 2)	9.9 years (1.3) 8.0 – 12.3	106.0 (15.5) 82 - 140	5.1 (3.4) 0 – 11	3.6 (34.3 0 – 9	2.2 (2.6) 0 – 7	5.8 (5.3) 0 – 14	16th percentile 9 – 25th
DCD	10 (M: 6, F: 4)	9.9 years (1.5) 7.5 – 11.9	105.0 (15.9) 88 – 129	9.4 (10.5) 0 – 28	2.7 (3.4) 0 – 8	1.1 (1.0) 0 – 2	3.8 (4.2) 0 – 10	2nd percentile 0.1 – 5th
Study 2 (Jump)								
	30 (M: 14; F: 16)	10.3 years (1.3) 7.8 – 12.1	115.1 (13.8) 90 - 151	3.6 (2.3) 0 – 9	0.5 (1.3) 0 – 5	0.5 (1.0) 0 - 3	1.0 (2.1) 0 – 8	63rd percentile 25 – 91st
	9 (M: 8, F: 2)	9.9 years (1.4) 9.0 – 12.3	106.0 (15.5) 82 - 140	6.2 (2.2) 4 – 11	4.0 (3.2) 0 – 9	2.4 (2.6) 0 – 7	6.4 (5.2) 0 – 14	16th percentile 9 – 25th
	7 (M: 3; F: 4)	9.4 years (1.5) 7.5 – 11.9	108.6 (17.1) 88 - 129	11.3 (11.3) 0 – 28	2.9 (3.5) 0 – 8	1.3 (1.0) 0 – 2	4.1 (4.1) 0 – 10	1.25th percentile 0.1 – 5th

Given the high co-morbidity between DCD and attention and/or social difficulties, the DBD and SCQ were used assess ADHD or social communication difficulties, respectively. For both studies, none of the children in the TD group met criteria for ADHD (inattentive, hyperactive, or combined) and had scores on the SCQ in the low (score < 8) or moderately low (score between 8 - 14) categories. For Study 1 (stop-signal task), the INT group included: one child with ADHD combined type, two children with ADHD inattentive type, and one child with ADHD hyperactive type. All children had SCQ scores in the low or moderately low categories. The DCD group included three children that met criteria for ADHD inattentive, 2 children had SCQ scores in the moderately high (score between 15 – 21) and 2 children had SCQ scores considered high (score ≥ 22). For Study 2 (jump task), one child in the INT group met criteria for ADHD combined type, two children met criteria for ADHD inattentive type, and one child was considered ADHD hyperactive type. All children in this group had SCQ scores in the low or moderately low categories. The DCD group included two children that met criteria for ADHD inattentive type. One of the children that met criteria for ADHD inattentive type also had SCQ scores considered high. In addition, one child had SCQ scores considered high and another child with scores considered high.

Experimental Apparatus and Procedures.

The experimental apparatus and procedures were nearly identical for Study 1 and Study 2; accordingly, the methodological details for the two studies are presented concurrently. Vision Recorder software and Brain Amp DC (Brain Vision LLC, Gilching, Germany) were used to collect continuous EEG (DC recording, sampling rate: 500 Hz) from 64 active electrodes with integrated noise subtraction circuits housed within a

stretchable lycra cap (actiCAP, Brain Vision LLC, Gilching, Germany). The electrode locations are consistent with the International 10/20 system. FCz served as the reference and AFz served as the ground. Fp1 and Fp2 were used to monitor vertical and horizontal eye movements, respectively. All channel impedances were ≤ 20 kΩ. A chin rest was used to stabilize and maintain the participant's head position and the height of the chair and chin rest were adjusted for each participant. Two minutes of eyes-open resting EEG was recorded as a baseline condition prior to starting the behavioral task.

Behavioral Task.

The data collection procedures were similar to previous studies in our lab (Contreras-Vidal & Kerick, 2004; Pangelinan et al., 2011) and Study 2. Participants were seated at a table facing a wooden platform that held a computer monitor positioned at eye-level. The platform occluded vision of the arm during the task. Participants used a computerized pen on a digitizing tablet (12"×12" WACOM In-Tuos ™, Vancouver, Canada) positioned below the platform. The monitor provided real-time visual feedback of the pen position on the tablet. OASIS™ software (Kikosoft, Nijmegen) was used to present stimuli, acquire the tablet data (sampling rate: 200 Hz), and generate event markers that were synchronized with the EEG data collection. Event markers indicated the start of a trial, false starts, movement onset, and target acquisition.

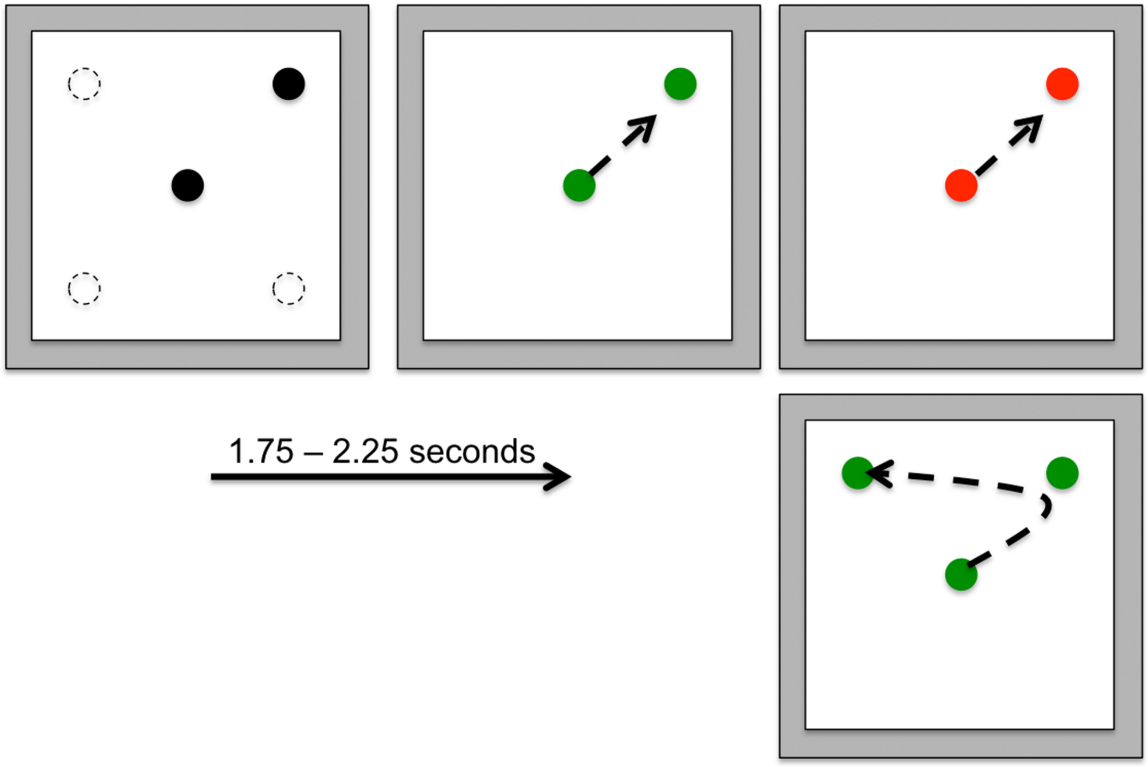

Figure 5.1. Specific Aims 3 and 4. Task presentation.
Once participants remain stationary in the center home circle, a target appeared in one of 4 positions (top left panel). The three other potential target positions are indicated by the dotted circles. After a variable hold of 1.75 – 2.25 seconds, the target and home position turned green signaling the participant to move to the target (top middle). In Study 1 (stop signal), participants would either reach the target circle (not shown) or the start and target circles would turn red immediately following movement onset, providing a 'stop' signal (top right). In Study 2 (jump), participants would either reach the target circle (not shown) or the target jumped to an adjacent target position (bottom right). Participants were instructed to modify their trajectory accordingly.

Figure 5.1 depicts the event sequence for one trial. To begin a trial, the participant placed the pen in the central "home" circle. A visual target (black open circle) appeared 8cm from the home position in one of four locations (45°, 135°, 225°, 315° with respect to the start circle). After a variable hold of 1.75 – 2.25 seconds, the target and home position turned green signaling the participant to initiate movement. This hold time was selected to allow for sufficient time for the participants to plan their movements and to characterize the underlying brain processes leading up to movement initiation. The

participants were instructed to move "as quickly and accurately as possible as soon as the circles turned green". For Study 1 (stop signal), the target and home positions turned red immediately following movement onset on randomly inserted trials, providing a signal for the participants to stop their movements as soon as possible. For Study 2 (jump), the target and home remained green but the target jumped to an adjacent target position on randomly inserted trials. Participants were instructed to move towards the displaced target position as fast and as accurately as possible. For both studies, once the participants remained stationary for 500ms, the trial was terminated and the participants moved the pen back to the home position to begin the next trial. For each of the two studies, 80 unperturbed trials and 60 perturbed trials (stop / jump) were completed. This ratio of perturbed to unperturbed trials afforded the computation of the appropriate EEG measures and was an appropriate number for the children to complete without becoming fatigued.

Behavioral Data Analysis.

The same behavioral data analysis methods were used for both studies (stop and jump). These analyses were consistent with previously reported studies conducted in our lab (Contreras-Vidal & Kerick, 2004; Pangelinan et al., 2011) and conducted using programs written in MATLAB^{TM} version 7.10 (Mathworks, Natick, MA USA). For each trial, the time series of x/y positions were filtered using an 8th order dual-pass Butterworth filter (cutoff frequency: 10 Hz). The onset was determined as the first point

at which the velocity profile reached 5% of peak velocity[8]. The offset was determined as first point at which the velocity profile returned to 5% of peak velocity and maintained a velocity below that value for 500ms. Each trial was visually inspected and manually re-marked if necessary. The following behavioral variables were computed from the movement trajectories: peak velocity (PV; units of cm/s), movement time (MT; seconds), movement length (ML; centimeters), normalized jerk (NJ – unitless), root mean squared error (RMSE), and variability of initial direction error (VIDE – degrees). PV and MT were the maximum velocity and the total time, respectively, between the onset and offset.. ML was the total distance of the movement trajectory. NJ was calculated as the rate of change of the acceleration normalized by MT and ML (Contreras-Vidal, 2005). RMSE was computed as the average deviation between an ideal vector between the movement onset to offset and the actual movement trajectory and is a measure of spatial error. Initial directional error (IDE) was calculated as the angular difference between actual movement trajectory 80 ms after movement onset (initial movement direction prior to visual feedback correction) and an ideal straight vector from movement onset to target. VIDE was assessed as the standard deviation of the IDE scores for each subject across all movements within each condition.

EEG Data Analysis.

The same EEG data analysis procedures were used for both studies (stop and jump). Brain Vision Analyzer 2 (Brain Vision LLC, Gilching, Germany) was used to re-reference the electrodes to an average of all electrodes. The re-referencing allowed the

[8] For an example of the markings for one child with DCD and an age-matched control for one unperturbed and one perturbed (stop or jump) trial for each study please see Appendices K - M.

recovery of activity at FCz (the original reference) and the neighboring electrodes. An FIR low-pass filter (cut off frequency: 50 Hz, roll-off 24dB/octave) was applied to these data. An ocular correction Independent Component Analysis (ICA – Infomax Restricted algorithm) was used to remove artifacts due to blinks and horizontal eye movements. A slope-based algorithm searched for blinks in Fp1 and components were selected with variance accounting for 30% in the respective channel. Similarly, Fp2 was used to search for horizontal activity. Components that met 30% of variance in the respective channel were selected. Each component was visually inspected with respect to the topography, activation, and the relative change to the signal if the component was removed. On average, 4 out of 63 components were removed. Data were then exported into MATLAB^{TM} version 7.10 (Mathworks, Natick, MA USA).

Consistent with our previous studies, for the movement-related cortical potential (MRCP) analysis, data were low-pass filtered at 10 Hz. Data were then epoched into 2-second segments with respect to movement onset (1 second before and after onset) and separated by trial type (unperturbed or perturbed). Data were baseline corrected using the period 250ms before the epoch (-1.25 to -1 second before onset). Data were again visually inspected and trials removed for excessive artifact (i.e., noise or amplitudes exceeding +/-100 μV). For each participant, time averages were computed for the perturbed and unperturbed trials. Data from a subset of electrodes (9 total) were selected for their relevance in motor planning and control tasks: F3, Fz, F4, FC3, FCz, FC4, C3, Cz, and C4. The mean amplitude from the 1-second period prior to and 1-second period following movement onset was computed.

Statistical Analysis.

Consistent with our previous work (Contreras-Vidal et al., 2005; King et al., 2011; King, Kagerer, Contreras-Vidal, & Clark, 2009; Pangelinan et al., 2011), the behavioral dependent variables from each study (stop or jump) were analyzed using analysis of covariance (ANCOVA) with age as the covariate, group as the between-subjects factor, and condition (perturbed/unperturbed) as the within-subjects factor in SAS 9.2 (SAS Institute, Cary, NC). For the MRCP analysis, the mean amplitude for the time before and after movement onset were analyzed with separate mixed-model ANOVAs with group (TD, INT, and DCD), condition (perturbed and unperturbed), hemisphere (left, midline, and right), and region (frontal, fronto-central, and central) as factors. Significant main effects were decomposed using Scheffé's post-hoc multiple comparisons. Significant interactions were decomposed with respect to differential effects (i.e., difference of difference contrasts) (Contreras-Vidal et al., 2005; King et al., 2011, 2009; Pangelinan et al., 2011). For all analyses, a significance level of 0.05 was maintained.

Results

Study 1 – Stop Task

Movement Kinematics.

Figure 5.2 depicts the mean movement trajectories (and standard deviation) for the unperturbed (go) and perturbed (stop) trials by group. The trajectories for the unperturbed trials appear similar across all groups. In addition, the TD and INT groups

also appear similar for the perturbed (stop) trials. The DCD trajectories for the perturbed trials are considerably shorter than the trajectories for the other groups.

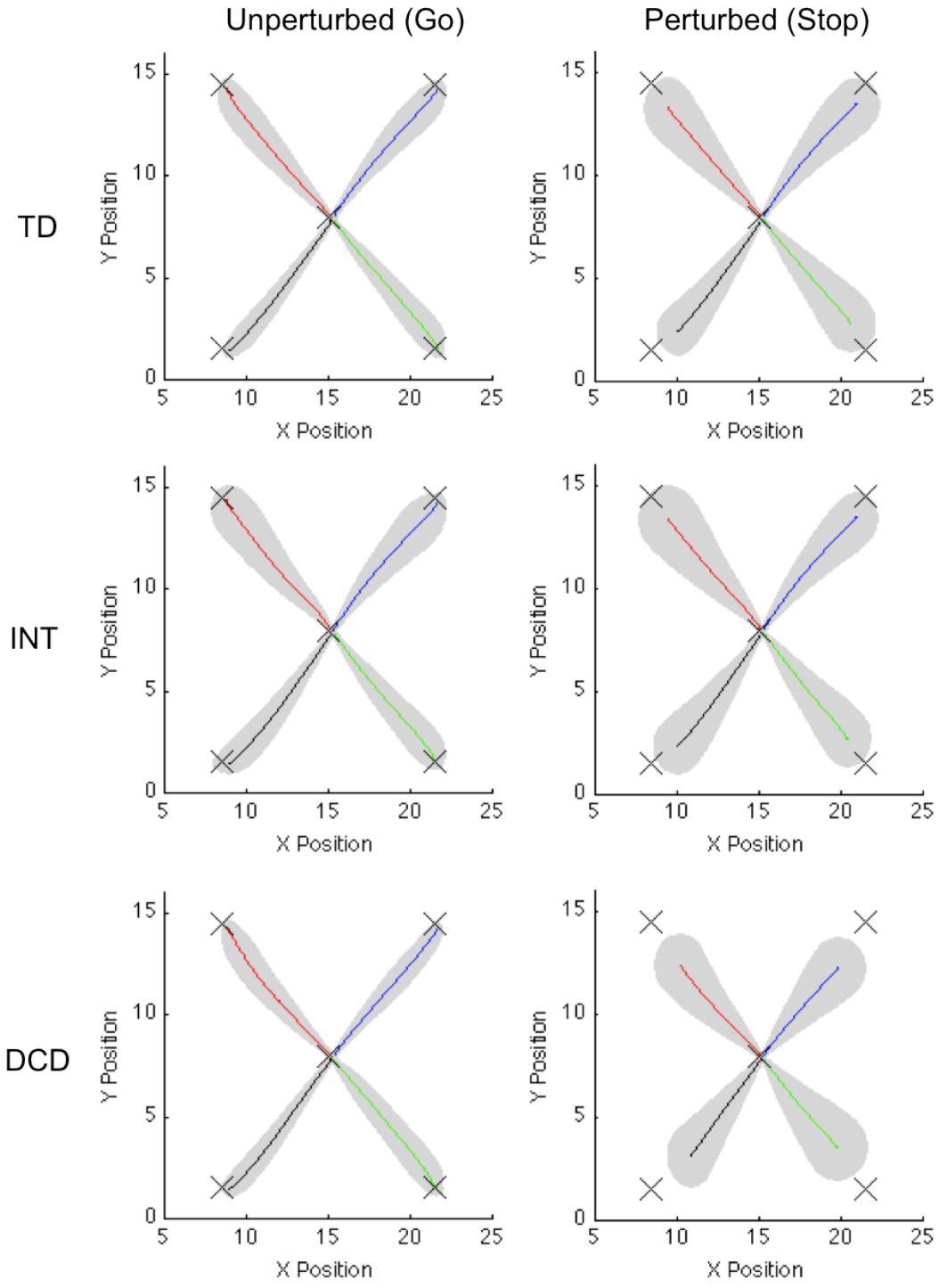

Figure 5.2. Specific Aim 3. Movement paths.

Mean movement trajectories and standard deviation (gray shaded region) for the unperturbed and perturbed (stop) by group. An "X" marks the home and target positions. The blue, red, black, and green lines indicate the mean trajectory for each target.

Table 5.2 presents the significant main effects and interactions for the performance measures. A significant main effect was found for PV ($p < 0.01$), indicating that the children with DCD were generally slower than their TD peers (Figure 5.3. There was no difference between the INT group and the other two groups for this measure ($p > 0.05$, for both contrasts), although the difference between the INT and DCD groups was marginally significant ($T(47) = 2.39$, $p = 0.07$).

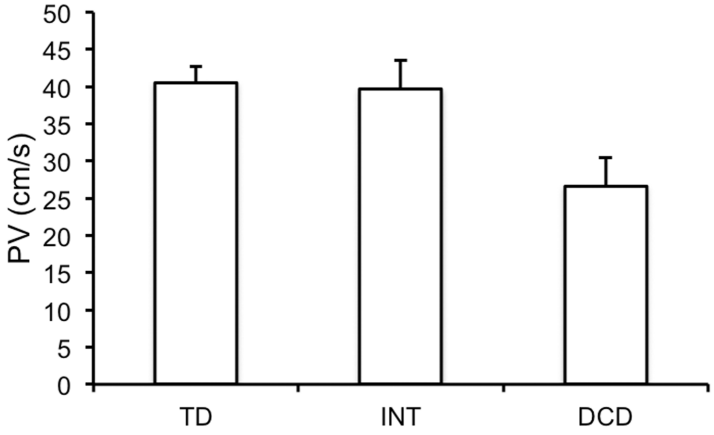

Figure 5.3. Specific Aim 3. Peak Velocity (PV).
Group mean estimates (adjusted for age) for PV by group (TD, INT, and DCD). Error bars indicate standard error.

Group x Condition interactions were found for the following variables: MT, VIDE, ML, NJ, and RMSE ($p < 0.05$ for all, Figure 5.4). The difference between the unperturbed and perturbed (stop) conditions is greater for the DCD group compared to the other two groups for MT, ML, NJ, and RMSE. For VIDE, the difference between the two conditions is greater for the INT group than the other two groups. The children in the INT group were more directionally variable during the stop condition than unperturbed

condition, while there was no difference between the two conditions for the other two groups.

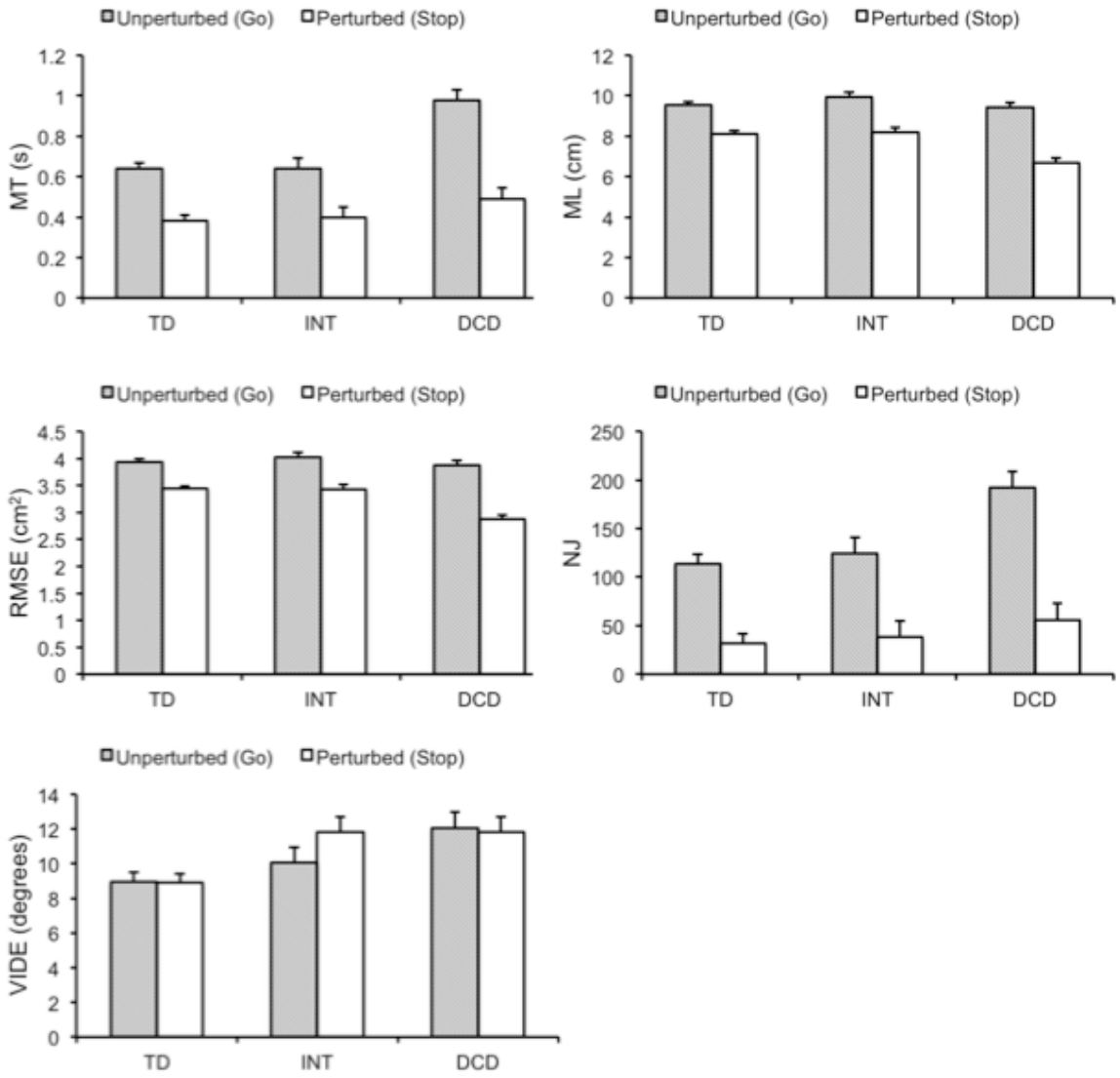

Figure 5.4. Specific Aim 3. Movement Kinematics.
Group mean estimates (adjusted for age) for MT (top left), ML (top right), RMSE (middle left), and NJ (middle right), and VIDE (bottom left) by group (TD, INT, and DCD) and condition (unperturbed and perturbed). Error bars indicate standard error.

Interestingly, the different performance of the children with DCD can likely be attributed to decreased movement velocity (Figure 5.3). Since the children with DCD moved more slowly than their TD peers, their movements in the stop condition were significantly shorter (ML) and as a result had less spatial error (RMSE) compared to the

other two groups. Interestingly, the performance of the children with DCD during the stop condition was relatively better than their performance during the unperturbed condition. This was likely due to the fact that the unperturbed movements were both longer and required corrective movements at the end of the trajectory to acquire the target. Collectively, the three groups performed similarly on the stop task.

Table 5.2. Specific Aim 3. Significant main effects and interactions.
**p < 0.05, **p < 0.01, ***p < 0.001*

Behavioral DV	Effects	F Statistic	Post-Hoc Comparisons (T Statistic)
PV	Group	F(2,46) = 5.1*	TD vs. DCD: T(46) = 3.1*
MT	Group Condition Group*Cond	F(2,46) = 9.6*** F(1,47) = 158.2*** F(2,47) = 8.2***	TD vs. DCD: Cond1 – Cond2: T(47) = 3.8** INT vs. DCD: Cond1 – Cond2: T(47) = 3.4**
ML	Group Condition Group*Cond	F(2,46) = 6.6*** F(1,47) = 208.4*** F(2,47) = 8.7***	TD vs. DCD: Cond1 – Cond2: T(47) = 4.2** INT vs. DCD: Cond1 – Cond2: T(47) = 2.6*
RMSE	Group Condition Group*Cond	F(2,46) = 8.6*** F(1,47) = 222.7*** F(2,47) = 11.4***	TD vs. DCD: Cond1 – Cond2: T(47) = 4.8*** INT vs. DCD: Cond1 – Cond2: T(47) = 3.1**
NJ	Group Condition Group*Cond	F(2,46) = 4.4* F(1,47) = 145.2*** F(2,47) = 4.1*	TD vs. DCD: Cond1 – Cond2: T(47) = 2.8** INT vs. DCD: Cond1 – Cond2: T(47) = 2.2*
VIDE	Group Group*Cond	F(2,46) = 5.6** F(2,46) = 3.4*	TD vs. INT: Cond1 – Cond 2: T(46) = 2.4 * INT vs. DCD: Cond1 – Cond2: T(46) = 2.2*

Movement Related Cortical Potentials - MRCPs.

Figure 5.5 depicts the grand mean (ensemble) averages for the three groups for the unperturbed (go) and perturbed (stop) conditions. The waveforms for the two conditions appear similar before onset but diverge after onset. Across the two conditions,

the left hemisphere activation (F3, FC3, and C3) for the TD group, and to a lesser extent the DCD group, exhibits a double-humped pattern in which increasing negativity leading to a peak in negativity occurs around movement onset and then a more sustained activation (negative amplitude) emerges later in the movement. The left hemisphere activation for the INT group does not show the same pattern of activation, at least for F3 and FC3, as evidenced by the mostly positive amplitude of the waveform for these regions. For the midline sites, the amplitude of the waveforms for all groups is mostly positive for Fz and Cz. The TD and DCD groups show some activation in FCz, as evidenced by their negative-going waveforms, particularly after movement onset. The magnitude of activation exhibited by the INT group was greater than the other two groups following movement onset for the midline sites. The right hemisphere sites do not appear to systematically change across the time windows, although the DCD group exhibits the same double-hump waveform for FC4 and the left hemisphere activation pattern.

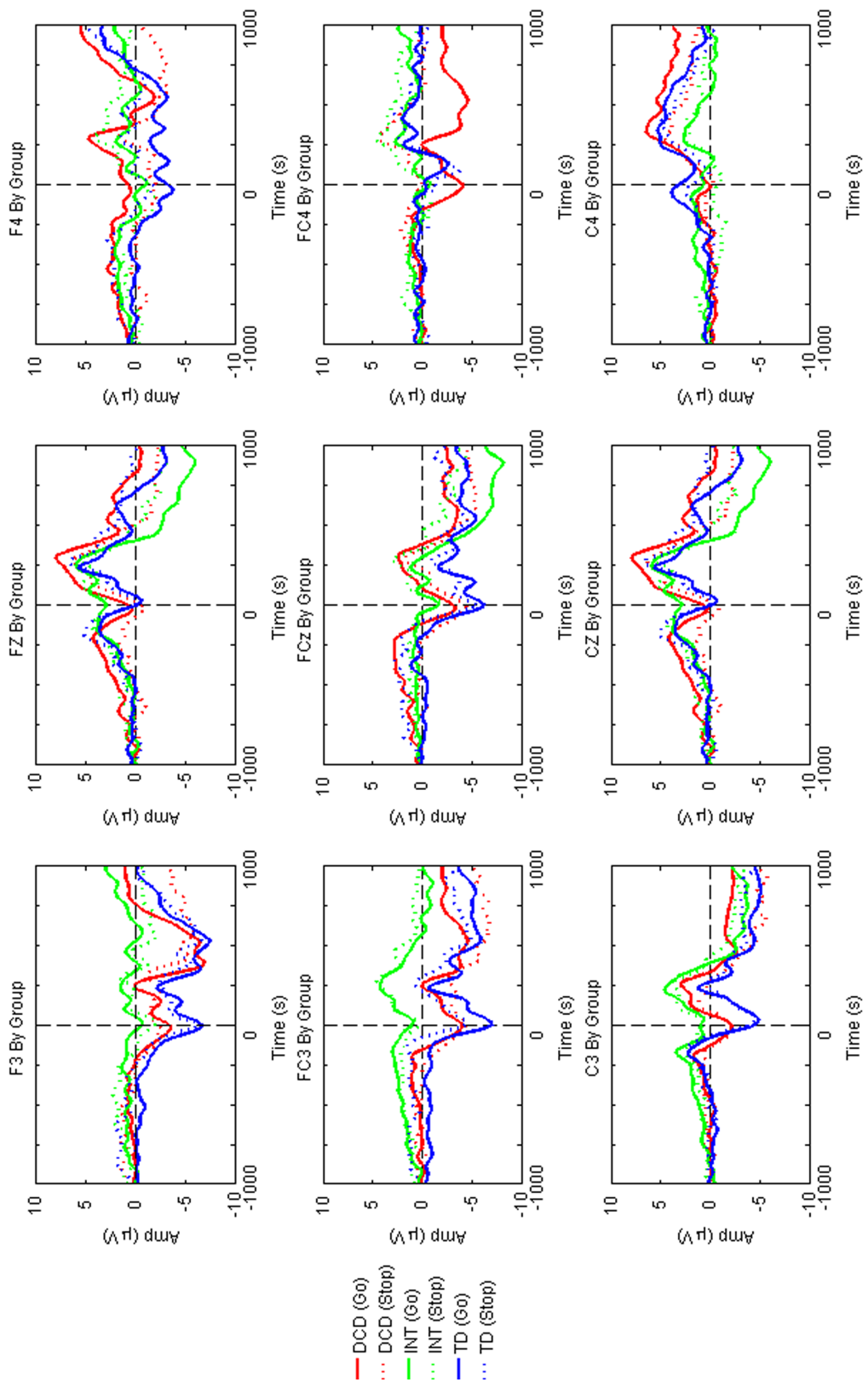

Figure 5.5 Specific Aim 3. Movement-related cortical potentials (MRCP).

Group mean MRCP waveforms (μV) by group and condition. The solid lines indicate the MRCPs during the unperturbed (go) condition and the dotted lines indicate the MRCPs during the perturbed condition (stop). The dashed line at time = 0 represents movement onset.

Inspection of the mean MRCP amplitudes before onset, revealed a significant hemisphere main effect ($F_{(2, 340)} = 5.0$, $p < 0.01$), as well as significant group x condition interaction ($F_{(2, 340)} = 7.0$, $p < 0.01$). No other main effects or interactions were significant ($p > 0.05$ for all). Figure 5.6 depicts the group x condition interaction. Post-hoc differential contrasts revealed that the difference between the two conditions for the TD group was different than the DCD group ($T_{(340)} = 3.8$, $p < 0.001$) and INT group ($T_{(340)} = 2.0$, $p < 0.05$). The DCD group showed a reduction in amplitude for the perturbed compared to the unperturbed condition, while the TD group demonstrated the opposite trend and the INT group showed no significant change between the two conditions.

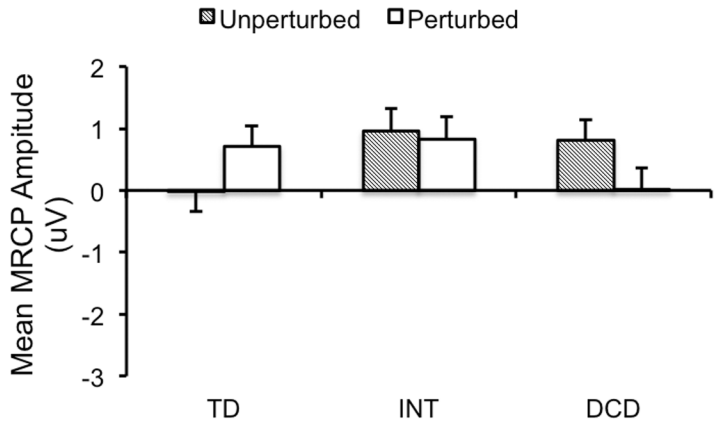

Figure 5.6. Specific Aim 3. Mean MRCP amplitude prior to movement onset. Error bars indicate standard error.

The analysis of the mean MRCP amplitudes after movement onset, revealed a significant hemisphere main effect ($F_{(2, 340)} = 25.5$, $p < 0.01$) and region main effect ($F_{(2,}$

$_{340)}$ = 5.6, p < 0.01). Significant group x condition ($F_{(2, 340)}$ = 6.8, p < 0.01), group x hemisphere ($F_{(4\ 340)}$ = 5.7, p < 0.001) and region x hemisphere ($F_{(4\ 340)}$ = 6.0, p < 0.001) interactions were revealed. Figure 5.7 depicts the group x condition interaction.

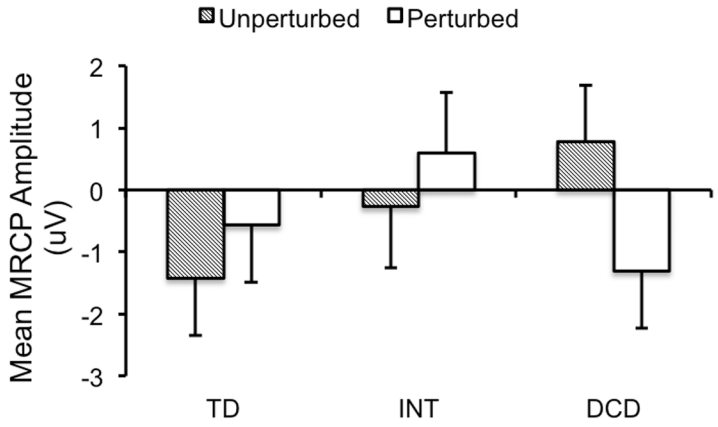

Figure 5.7. Specific Aim 3. Mean MRCP amplitude following movement onset. Error bars indicate standard error.

Post-hoc differential contrasts revealed that the difference between the two conditions for the DCD group was different than the TD group ($T_{(340)}$ = 3.2, p < 0.001) and INT group ($T_{(340)}$ = 3.0, p < 0.001). The DCD group showed greater activation (greater negative amplitude) during the perturbed (stop) trials compared to the unperturbed (go), whereas the TD group and INT groups showed less activation (less negative amplitude) during the perturbed (stop) trials compared to the unperturbed (go).

Figure 5.8 depicts the group x hemisphere interaction. The INT group showed a very different pattern of activation across the three areas (left hemisphere, midline, and right hemisphere) than the TD and DCD groups. Specifically, the differences between the left hemisphere and midline sites were different for the INT group compared to the TD group ($T_{(340)}$ = 3.9, p < 0.001) and the DCD group ($T_{(340)}$ = 4.0, p < 0.001). In addition,

the difference between the left and right hemispheres was different for the INT group compared to the TD ($T_{(340)} = 3.1$, $p < 0.01$) and DCD groups ($T_{(340)} = 3.3$, $p < 0.01$). The TD and DCD groups were not significantly different in their activation patterns across the three areas ($p > 0.05$).

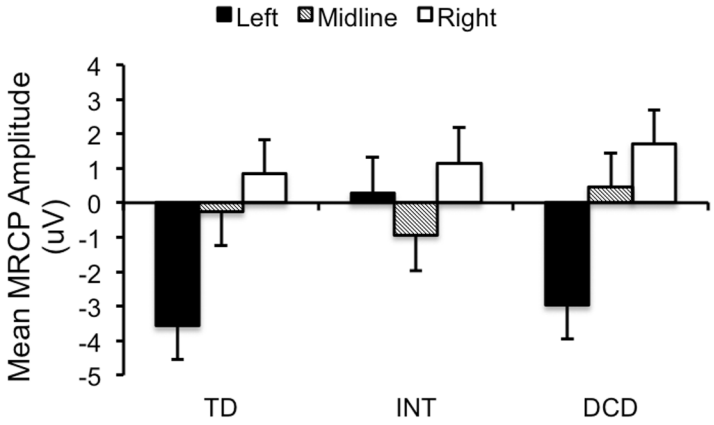

Figure 5.8. Specific Aim 3. Mean MRCP amplitude after movement onset for the left hemisphere, midline, and right hemisphere.
Error bars indicate standard error.

With respect to the region x hemisphere interaction (Figure 5.9), the difference between the left hemisphere and midline sites for the frontal region was different than that for the fronto-central ($T_{(340)} = 3.7$, $p < 0.001$) and central region ($T_{(340)} = 3.7$, $p < 0.001$). The difference between the left hemisphere and midline was also different between the fronto-central and central regions ($T_{(340)} = 3.3$, $p < 0.001$). The difference between the midline and right hemisphere for the frontal-central region was different than that frontal ($T_{(340)} = 4.3$, $p < 0.01$) and central ($T_{(340)} = 2.7$, $p < 0.01$) regions. There are no differences between the three regions for the left and right hemisphere comparison ($p > 0.05$). These results confirm the expected patterns of activation for right hand movements, in which activation (negative amplitude) is expected for the left hemisphere (for all regions) and midline fronto-central areas compared to the other brain areas.

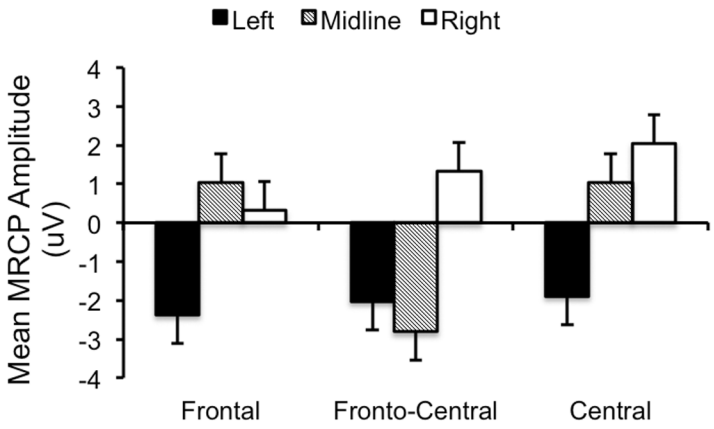

Figure 5.9. Specific Aim 3. Mean MRCP amplitude for the left hemisphere, midline, and right hemisphere for the three regions (frontal, fronto-central, and central). Error bars indicate standard error.

In sum, although the children with DCD moved more slowly that the other groups, their movement kinematics suggest that these children do not have difficulties inhibiting goal-directed movements. Similarly, the brain activation patterns revealed that children with DCD generally activate similar brain regions as the TD children (activation of the left hemisphere and midline fronto-central brain areas). However, the children with DCD exhibited less activation prior to movement onset than the TD children, suggesting that these children do not engage brain areas in preparation for movement. During the movement, the children with DCD exhibited greater activation (negative amplitudes) for the perturbed (stop) condition compared to the unperturbed (go) condition, while the opposite is the case for the TD children. Therefore, it appears that children with DCD compensate for the lack of engagement prior to onset with relatively greater amplitudes during the movement for the stop condition.

The kinematics of the children with moderate movement difficulties (INT group) were similar to the TD children for most performance measures, with the exception of the variability of initial directional error. However, the patterns of activation were very different in the INT group compared to the other two groups. There was an overall lack of activation (negative amplitude waveforms) across both conditions. In addition, the children in this group showed a relative increase in the activation of the midline brain regions in comparison to the other brain regions, whereas the TD and DCD group showed a relative increase in the left hemisphere brain regions. Collectively, these results suggest that different cortical mechanisms result in similar behavioral performance between this group and the TD group.

Study 2 – Jump Task

Movement Kinematics.

Figure 5.10 depicts the mean movement trajectories (and standard deviation) for the unperturbed and perturbed (jump) trials by group.

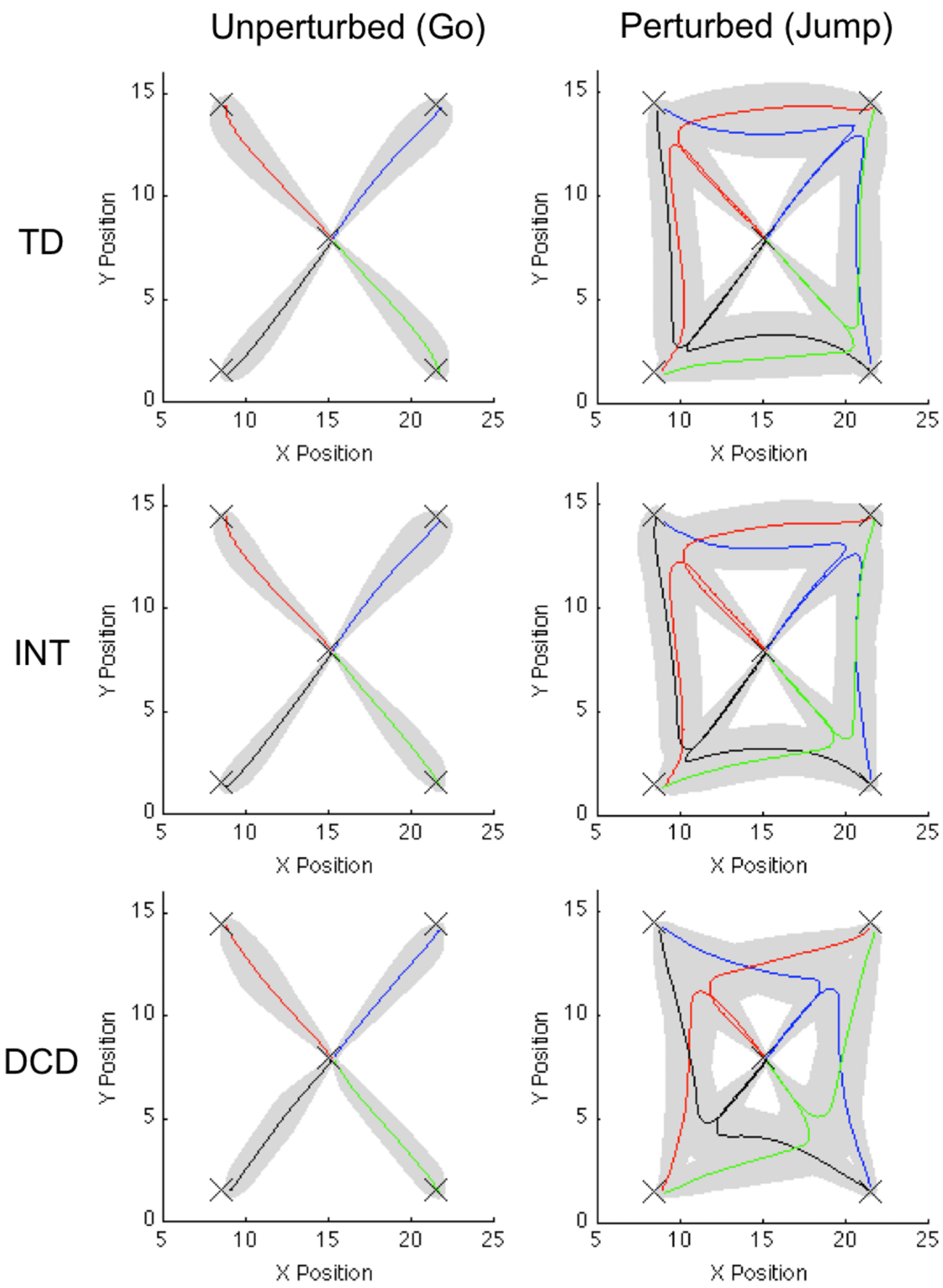

Figure 5.10. Specific Aim 4. Movement Paths.
Mean movement trajectories and standard deviation (gray shaded region) for the unperturbed and perturbed (jump) by group. An "X" marks the home and target

positions. The blue, red, black, and green lines indicate the mean trajectory for each target.

Similar to Study 1, the trajectories for the unperturbed trials appear similar across all groups. In addition, the TD and INT groups also appear similar for the perturbed (jump) trials, in that both groups nearly reach the original target before adjusting movements to the updated target location. For the perturbed trials, the children with DCD appear to initiate their corrective movements earlier in the trajectory and demonstrated substantially more movement variability.

Table 5.3 presents all of the significant main effects and interactions. Group main effects were found for PV and VIDE ($p < 0.05$, Figure 5.11). Children with DCD were significantly slower and more directionally variable than TD children. In addition, the children with moderate movement difficulties were significantly more directionally variable than the TD children.

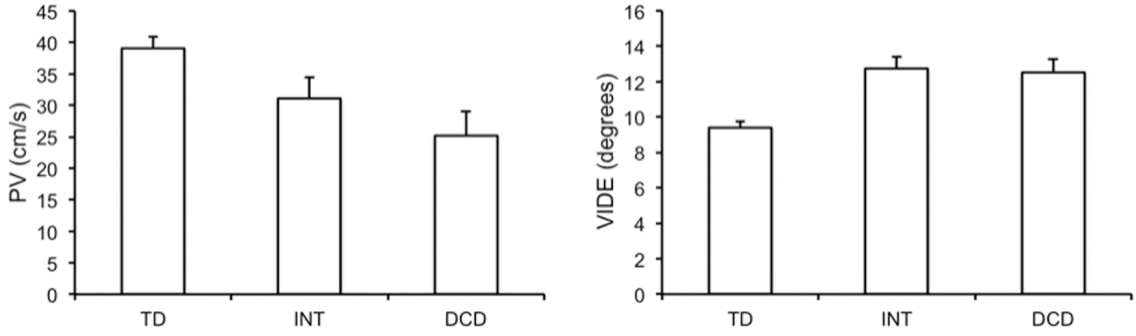

Figure 5.11. Specific Aim 4. Peak velocity (PV) and variable initial directional error (VIDE).
Group mean estimates (adjusted for age) for PV (left), VIDE (left) by group (TD, INT, and DCD) and condition (unperturbed and perturbed). Error bars indicate standard error.

Group x Condition interactions were found for the following variables: MT, ML, NJ, and RMSE ($p < 0.05$ for all, Figure 5.12). The difference between the unperturbed

and perturbed (jump) conditions is greater for the DCD group compared the TD group for MT and NJ. The difference between the two conditions is also greater for the INT group compared to the TD group for NJ. These results suggest that the performance of the children with DCD and to a lesser extent the children INT for movement difficulties were differentially affected by the perturbation and were much less smooth in their corrective movements to the jumped targets.

For ML and RMSE, the difference between the two conditions is greater for the TD group, compared to the DCD group and to a lesser extent the INT group. In addition, the difference between the two conditions is also greater for the INT group compared to the DCD group for ML and RMSE. These results suggest that the movements of the TD children, and to a lesser extent the children in the INT group, were much longer and resulted in greater spatial error for the jump compared to unperturbed trials.

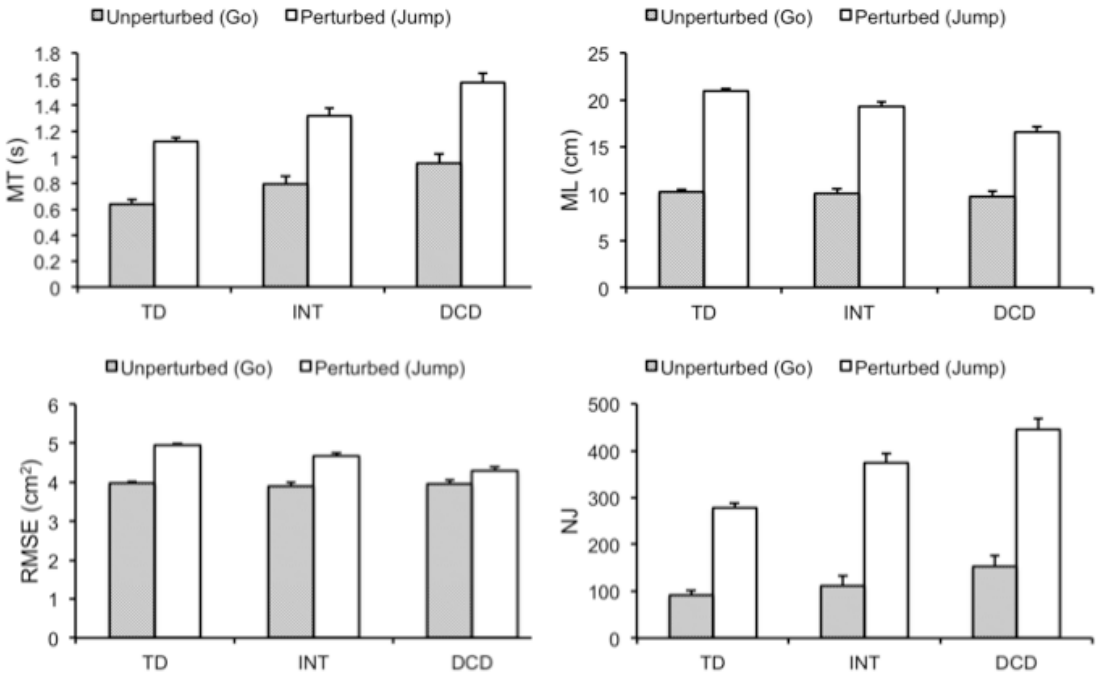

Figure 5.12. Specific Aim 4. Movement time (MT), movement length (ML), normalized jerk (NJ) and root mean squared error (RMSE).

Group mean estimates (adjusted for age) for MT (top left), ML (top right), RMSE (bottom left), and NJ (bottom right) by group (TD, INT, and DCD) and condition (unperturbed and perturbed). Error bars indicate standard error.

The reduction in ML and RMSE exhibited by the DCD group during the jump trials is likely due to their reduced velocity allowing them to initiate corrective movements earlier in the movement trajectory, where as the other two groups moved much more quickly and were nearly at the original target location before making corrective responses. However, based on the increased movement time and jerk for the jump trials compared to unperturbed trials, the DCD group appeared to be more impacted by the perturbation than the TD and INT groups. These results provide additional support that children with DCD have difficulties making online corrective movements in comparison to TD children and those with moderate movement difficulties.

Table 5.3. Specific Aim 4. Significant main effects and interactions.
**p < 0.05, **p < 0.01, ***p < 0.001*

Behavioral DV	Effects	F Statistic	Post-Hoc Comparisons (T Statistic)
PV	Group Condition	F(2,42) = 6.0* F(1,42) = 16.8*	TD vs. DCD: T(42) = 3.2* Cond1 vs. Cond2: T(42) = 4.1***
VIDE	Group	F(2,46) = 13.1***	TD vs. INT: T(42) = 4.4*** TD vs. DCD: T(42)=3.6*
MT	Group Condition Group*Cond	F(2,42) = 14.5*** F(1,42) = 737.0*** F(2,42) = 4.47*	TD vs. DCD: Cond1 – Cond2: T(42) = 2.9**
ML	Group Condition Group*Cond	F(2,42) = 10.5*** F(1,42) = 769.5*** F(2,42) = 13.4***	TD vs. INT: Cond1 – Cond2: T(42) = 2.1* TD vs. DCD: Cond1 – Cond2: T(42) = 5.7*** INT vs. DCD: Cond1 – Cond2: T(42) = 2.6*
RMSE	Group Condition Group*Cond	F(2,42) = 6.9** F(1,42) = 236.4*** F(2,42) = 17.7***	TD vs. INT: Cond1 – Cond2: T(42) = 2.1* TD vs. DCD: Cond1 – Cond2: T(42) = 5.8*** INT vs. DCD: Cond1 – Cond2: T(42) = 3.3**

NJ	Group Condition Group*Cond	F(2,42) = 15.9*** F(1,42) = 362.5*** F(2,42) = 8.1***	TD vs. INT: Cond1 – Cond2: T(42) = 2.6** TD vs. DCD: Cond1 – Cond2: T(42) = 3.5**

Movement Related Cortical Potentials - MRCPs.

Figure 5.13 depicts the grand mean (ensemble) averages for the three groups for the unperturbed (go) and perturbed (jump) conditions. Although the waveforms for the two conditions depict similar activation patterns, the conditions are distinguishable within each site (i.e., there is a separation between the waves). Similar to the waveforms from Study 1, there is a double-humped pattern in which increasing negativity leading to a peak in negativity occurs around movement onset and then a more sustained activation emerges later in the movement. Again, this pattern is more obvious for the frontal and fronto-central left hemisphere sites as well as the fronto-central midline site. Again, similar to the results from Study 1, the DCD group exhibits the same double-hump waveform for FC4 as that exhibited by the left hemisphere.

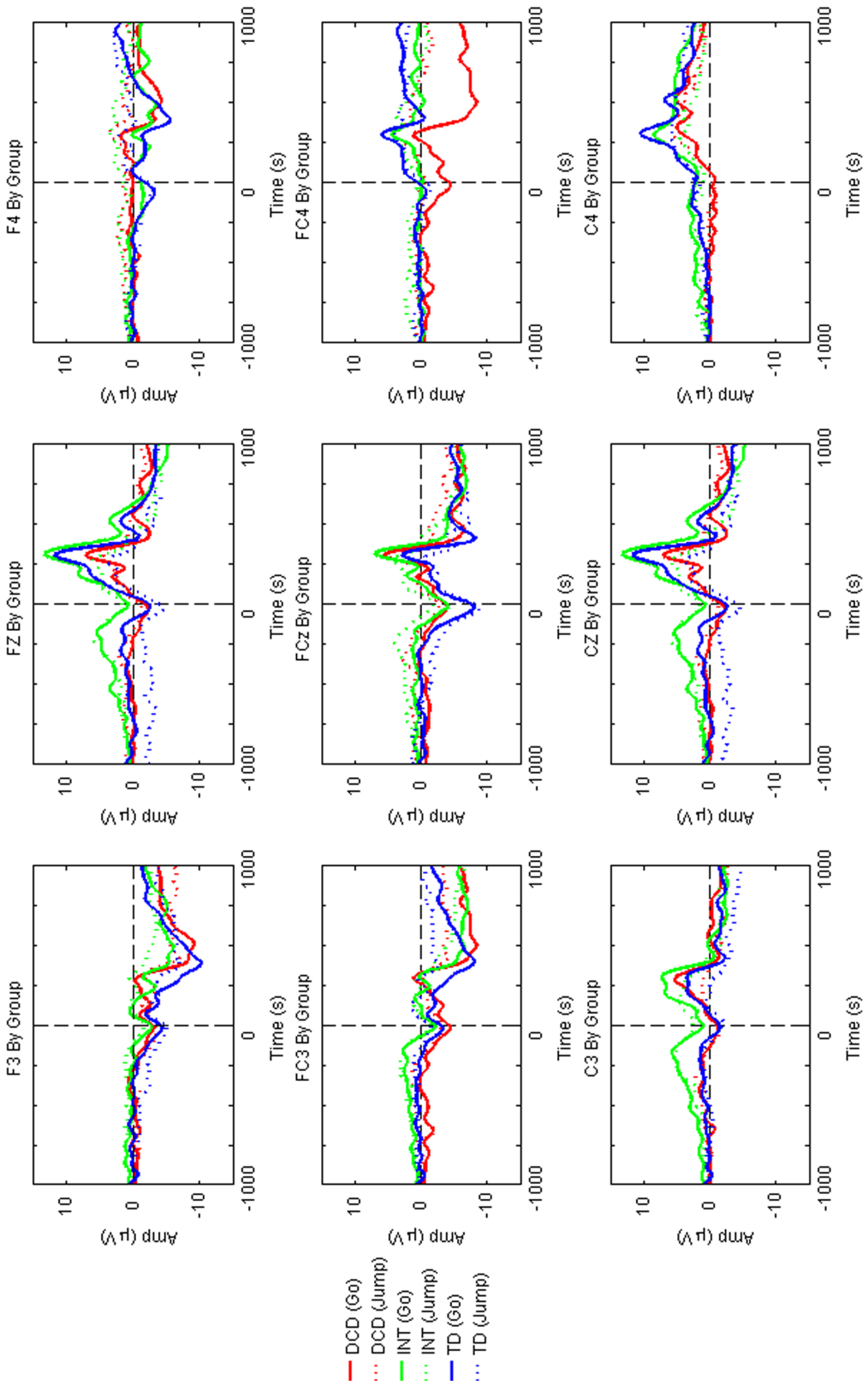
F4 By Group
FZ By Group
FC4 By Group
FCz By Group
C4 By Group
CZ By Group
F3 By Group
FC3 By Group
C3 By Group
Amp (μV)
Time (s)
10
0
-10
1000
-1000
DCD (Go)
DCD (Jump)
INT (Go)
INT (Jump)
TD (Go)
TD (Jump)

Figure 5.13. Specific Aim 4. Movement-related cortical potentials (MRCP).
Group mean MRCP waveforms (μV2) by group and condition. The solid lines indicate the MRCPs during the unperturbed (go) condition and the dotted lines indicate the MRCPs during the perturbed condition (jump). The dashed line at time = 0 represents movement onset.

Analysis of the MRCP amplitude for the period before movement onset revealed significant group ($F_{(2, 47)} = 3.8$, $p < 0.05$) and region main effects ($F_{(2, 440)} = 5.7$, $p < 0.01$). In addition, significant group x condition ($F_{(2, 447)} = 3.0$, $p < 0.05$, Figure 5.14) and group x hemisphere ($F_{(4, 440)} = 2.7$, $p < 0.05$, Figure 5.15) interactions were found. Post-hoc contrasts decomposing the group x condition interaction revealed that the difference between the unperturbed (go) and perturbed (jump) conditions for the TD group was different than that of the DCD group ($T_{(440)} = 2.3$, $p < 0.05$). The difference between the TD and INT group was marginally significant ($T_{(440)} = 1.8$, $p = 0.07$). Whereas the TD group increased the level of activation (negative amplitude) for the perturbed trials, the opposite was the case for the DCD group and to a lesser extent the INT group.

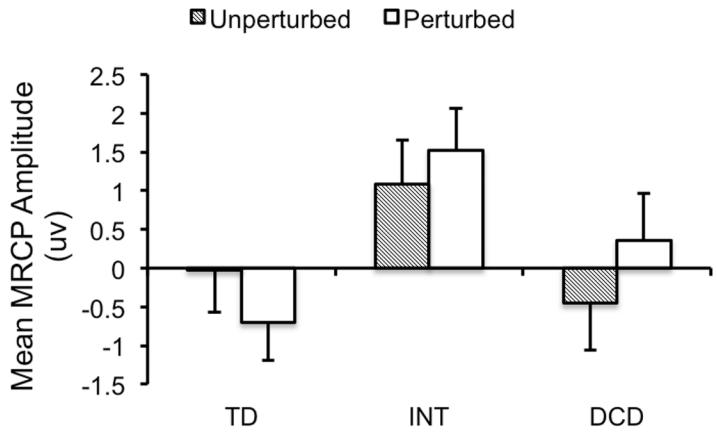

Figure 5.14. Specific Aim 4. Mean MRCP amplitude prior to movement onset.
Error bars indicate standard error.

With respect to the group x hemisphere interaction, post-hoc contrasts revealed that the difference between the left and right hemisphere for the TD group was

significantly different than the INT group ($T_{(440)}$ = 2.5, $p < 0.05$). In addition, the difference between the midline and right sites for the TD group was also different than that of the INT group ($T_{(440)}$ = 3.0, $p < 0.01$). There were no differences between the TD and DCD group or the DCD and INT group for any differential contrast ($p > 0.05$).

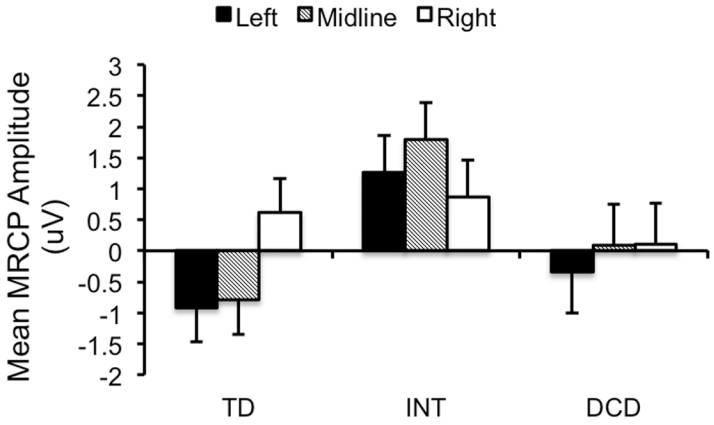

Figure 5.15. Specific Aim 4. Mean MRCP amplitude prior to movement onset by hemisphere.
Error bars indicate standard error.

With respect to the mean MRCP amplitudes after movement onset, there were no group main effects or interactions with group and other factors ($p > 0.05$ for all), suggesting that all groups activated brain regions similarly following movement onset. However, significant region and hemisphere main effects ($F_{(2,300)}$ = 32.9 and 16.4, $p < 0.001$ for both) and a significant region x hemisphere interaction were found ($F_{(4,300)}$ = 4.3, $p < 0.01$, Figure 5.16). The post-hoc analysis revealed that difference between the midline and right hemisphere sites for the frontal region was different than that for the fronto-central and central sites ($T_{(300)}$ = 3.3 and 2.5, $p < 0.001$ and < 0.05, respectively). Again, similar to the results from Study 1, it was expected that greater activation (negative amplitude) would be evident for the left hemisphere and fronto-central midline sites, which is different than that for the right hemisphere for all regions.

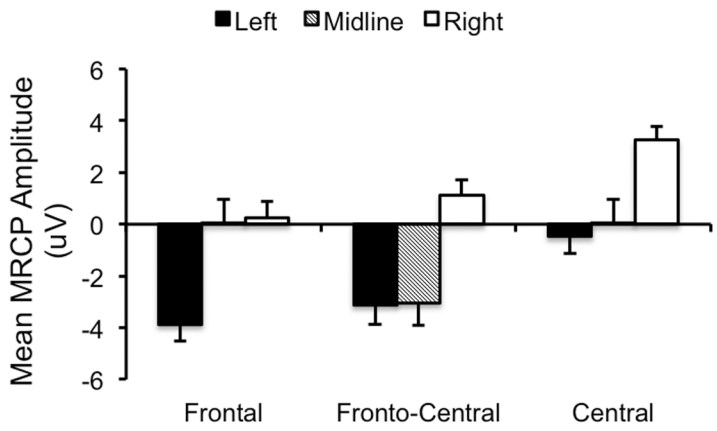

Figure 5.16. Specific Aim 4. Mean MRCP amplitude following movement onset by hemisphere and region.
Error bars indicate standard error.

In sum, children with DCD were differentially affected during the adaptive control (jump) paradigm. The difference between the unperturbed and perturbed values for jerk and movement time exhibited by the children with DCD was much greater than that exhibited by the other two groups. The DCD group, and to a lesser extent the children in the INT group, were less accurate (greater ML) and were more directionally variable (VIDE), despite moving more slowly than the TD group. The cortical activation patterns during the jump task suggest that, similar to the stop task, that the children with DCD generally activate the appropriate movement-related brain regions as TD children but not to the same magnitude. Moreover, the children with DCD do not engage movement-related brain regions to the same extent in anticipation of movement (prior to onset) as the TD children. The lack of group differences in cortical dynamics following movement onset suggests that all groups engaged relevant motor cortical resources to the same extent. However, this degree of cortical activation during the movement does not

appear sufficient for the DCD and INT groups to maintain similar levels of behavioral performance as the TD children.

Discussion and Implications

The current study took advantage of the time-sensitive nature of EEG to examine differences in brain activation patterns during the execution of two adaptive motor tasks in children with DCD, those with intermediate/moderate movement difficulties, and those without any movement difficulties (TD children). Across both studies, children with DCD moved more slowly and were directionally more variable than TD children. Even though the children moved more slowly, their performance reflected a general difficulty correcting movements online and adapting movement. In contrast the children with DCD exhibited less difficulty inhibiting movements (stop). Considering the results from the two studies together, it appears that children with DCD exhibit a selective impairment in online adaptive control that does not appear to be due to difficulties inhibiting motor plans. The problems in modifying movement trajectories online (i.e., the jump paradigm) may be due to a relative lack of engagement in motor planning and control cortical brain region in anticipation of movement, which cannot be compensated for by cortical activity during the movement.

Disrupted Cortical Functions in Children with DCD

Based primarily on the behavioral characterization of children with DCD and a limited number of neuroimaging studies, potential underlying neural bases for this disorder have been proposed, with a particular focus on dysfunction in subcortical

structures such as the basal ganglia and cerebellum (Zwicker, Missiuna, & Boyd, 2009). Although subcortical structures likely also play a role in the behavioral deficits exhibited by children with DCD, the results from the current study suggest that that difference in frontal cortical function also underlie difficulties in adaptive motor behavior. Consistent with the present findings, Zwicker and colleagues (2010) found a that children with DCD exhibit reduced activation of the left superior and inferior frontal cortices, which have been found to support planning and inhibitory motor control functions. In addition to the activation of motor planning and control brain regions, given the extensive networking between these areas with the posterior parietal cortex (PPC), disruptions in PPC function would have downstream effects on adaptive motor control. Indeed, Kashiwagi and colleagues (2009) found that the poor behavioral performance of children with DCD during a tracking task was attributed to attenuated activation of the left posterior parietal cortex and the postcentral gyrus in comparison to TD children. These studies, along with the results from the current study, suggest that differences in motor performance in children with DCD involve a lack of activation of sensorimotor cortical brain areas.

Children with Moderate Movement Difficulties (INT Group).

Based strictly on the performance on the MABC-2, many of the children in this intermediate group did not meet criteria for the "at risk" (5^{th} – 15^{th} percentile) or DCD (below the 5^{th} percentile) categories; however, the children in this group were referred to our study by occupational therapists or educational specialists for their movement difficulties. It is possible the strict classifications for the levels of movement impairment based on the MABC-2 may not capture all movement difficulties that are clinically or educationally relevant. Therefore, the MABC-2 in combination with other measures,

such as handwriting and performance on other functional tasks were used to stratify the groups in this research. In the current study, the movement difficulties of the children in this group were evident in their relatively poor performance on the MABC-2 (below the 25th percentile) and below-grade level handwriting problems. Moreover, support for this stratification is provided by the different movement kinematics in the jump task, as compared to the TD children.

It is likely that the moderate movement difficulties exhibited by this group are due to the lack of engagement of relevant motor planning and control brain regions. However, whereas the children with DCD exhibited similar patterns of activation as the TD children (i.e., engagement of left hemisphere frontal brain regions) but with a reduced magnitude of response, the patterns of activation exhibited by the children in the intermediate group are markedly different than the other two groups. These results suggest that this group may actually represent a different brain-behavior phenotype.

One possible explanation for this phenomenon is that the intermediate group has a greater number of ADHD symptoms (as measured by the DBD). The overall lack of frontal cortical engagement is consistent with brain imaging studies of children with ADHD during movement inhibition and task-switching (Rubia et al., 1999; Smith, Taylor, Brammer, Toone, & Rubia, 2006). The moderate movement impairments in this group, specifically the handwriting difficulties, are also consistent with studies of children with ADHD (Piek & Dyck, 2004; Racine et al., 2008). However, a follow-up investigation with a focus on the performance of children with ADHD on this task and their underlying brain activation patterns would be necessary to confirm this hypothesis.

It would be very interesting if children with ADHD do indeed exhibit EEG waveforms during adaptive and inhibitory motor tasks compared to children with DCD and TD children, similar to the INT group in the present study.

Conclusions and Future Directions.

This study provides new evidence that the magnitude of engagement of motor planning and control brain regions underlies behavioral performance on adaptive motor tasks in those with and without movement coordination difficulties. In the future, it would be would be worthwhile to investigate the relationship between these frontal brain regions and posterior brain regions in children with DCD. It is possible that a disruption in the early activation of the PPC or differences in the connectivity pattern between these two brain areas contributes to the downstream lack of frontal activation found in the present study. In addition to examining underlying brain functions, examining the structure of relevant brain areas may also lead to insights into the neuronal mechanisms in DCD. Given that the trajectory for structural development of the cortex and associated fiber tracts mirror the development of higher-order motor and cognitive functions in typically developing children, it is very likely that the movement difficulties and patterns of brain activity exhibited by children with DCD may be due to disrupted or abnormal patterns of structural brain development (i.e., differences in cortical thickness and white matter architecture). By combining different neuroimaging modalities, we may gain a deeper and multilevel understanding of how underlying neural structures contribute to the emergence of adaptive motor behavior in both children with and without movement difficulties.

Finally, it would be interesting to determine if the patterns of brain activation and the performance on adaptive motor tasks change in response to therapeutic interventions. A brain-based approach to the selection and assessment of therapies for children with DCD is much needed. Based on the current findings, the children with DCD do engage relevant motor cortical resources but do not do so in anticipation of movement. Cognitive based therapies that stress motor planning for different tasks may help children with DCD engage and strengthen the underlying brain functions as well as improve their motor skills. Indeed, one such therapeutic approach (CO-OP) appears to have positive outcomes for children with DCD (Miller, Polatajko, Missiuna, Mandich, & Macnab, 2001), but the neural outcomes have yet to be investigated.

Chapter 6: General Discussion & Future Directions

Summary and Implication of Current Findings

This research program was the first to examine if differences in cortical activation, as assessed with EEG, underlie the movement difficulties in children with DCD. Specifically, we examined cortical activation at rest (Specific Aim 1 - Chapter 3) and during the performance of visuomotor tasks in a static environment (e.g., targets remain valid/stationary – Specific Aim 2 - Chapter 4) and a dynamic environment (e.g., targets indicate stop signals or jump to a different location – Specific Aims 3 and 4 - Chapter 5). Collectively, the results from these studies demonstrated that the activation patterns differed between children with and without DCD; and, these differences may contribute to the differences in sensorimotor performance. This discussion highlights the key results from each study and how each study provided new insights into different aspects of brain function and its relevance to motor behavior in children with DCD, typically developing children, and those with moderate movement difficulties. In addition, directions for future research are discussed.

Implications of the Current Findings for Understanding DCD.

The activation patterns of children with DCD at rest (Study 1 – Chapter 3) were characterized with greater low-frequency activity, which is indicative of cortical idling. In contrast, the patterns of brain activity exhibited by TD children were characterized by greater high-frequency activity, indicative of a restful but alert state. The cortical activation patterns of children with DCD in the present study are similar to the patterns previously reported for younger TD children (i.e., 4 – 6 year olds) and children with

developmental disabilities, suggesting that children with DCD exhibit a "maturational lag" in cortical function. Children with DCD also exhibited asymmetrical cortical activation in the central region which overlays the primary motor cortex for the beta and theta band. Given the functional relevance of these bands for sensorimotor function, a lack of activity in the left central region in children with DCD may contribute to behavioral deficits in motor abilities in the right-handed children with DCD. This first study established that inherent differences existed between the cortical activation of children with and without DCD. However, the precise relationship between resting brain activation and motor abilities is not clear. An examination of the brain activation patterns during a motor task may provide confirmation for the hypothesized relationship observed at rest.

To address this knowledge gap, the relationship between atypical activation patterns and motor performance in children with DCD was examined in Studies 2 and 3 (Chapters 4 and 5). The second study (Chapter 4) investigated the cortical activation patterns of children with and without DCD during the performance of a goal-directed visuomotor task in a static environment (i.e., the targets remained stationary). The results from this second study suggest that the age-related trajectory of behavioral performance on this task was similar between children with and without DCD. Despite similar behavioral performance, differences in the trajectory for brain activation were found between the two groups of children, particularly following movement onset. Children with DCD engaged motor planning and control brain areas to a greater extent and throughout the movement compared to TD children, suggesting greater cortical effort to complete the task. The results from this study were contrary to our initial hypothesis that

children with DCD would exhibit differences in both the motor performance *and* movement-related cortical activation patterns. It is likely that the simplified and static nature of this task (i.e., movements were short and self-initiated, and the target were self-selected and remained stationary) allowed children with DCD to perform equivalently to TD children by activating motor cortical areas to a greater extent than their TD peers.

The third study (Chapter 5) employed more complex and dynamic visuomotor tasks in order to further differentiate the patterns of activation and motor performance in children with and without DCD. Study 3.1 examined the ability to inhibit movements while Study 3.2 examined the ability to modify movement trajectories online. Given that children with DCD appear to have difficulties in adaptive motor behavior, it was expected that this difficulty would also be reflected in different patterns of cortical activation compared to TD children. The performance of the children with DCD was similar to TD children for the stop task (Study 3.1); however, the children with DCD exhibited greater activation of motor cortical areas. This increased activation may have contributed to the lack of differences in behavioral performance. When movement trajectories had to be modified online (i.e., the jump task, Study 3.2), the children with DCD demonstrated decreased behavioral performance. Although children with DCD and TD children exhibited similar patterns of activation *during* the movement, the children with DCD showed less activation *prior to movement*. These results suggest that the difficulty in adaptive motor control appears to be due to a lack of preparatory cortical activation for this group.

Taken together, the findings from this program of research suggest that inherent differences in brain activity at rest may contribute to movement difficulties in children

with DCD. Based on the studies examining brain activation during the performance of visuomotor tasks, it appears that children with DCD were able to achieve similar levels of motor performance as TD children for simple visuomotor tasks and tasks requiring movement inhibition. The activation of motor planning and control brain regions during the movement may be sufficient for children with DCD to achieve similar levels of behavioral performance as the TD children in these cases. However, for tasks requiring online trajectory modifications, a lack of preparatory activation may underlie behavioral difficulties in adaptive motor control for children with DCD.

Implications of the Current Findings for Understanding Typical Development.

In addition to gaining a deeper understanding of children with DCD, this study also sheds light on cortical function in TD children and its relevance to key aspects of goal-directed movement planning. The results from the first study (Chapter 3) demonstrate that the cortical activation patterns of TD children at rest consist of less low-frequency components and greater high-frequency components (as evidence by the greater relative beta and lower theta/beta ratio), confirming previous reports (Benninger, Matthis, & Scheffner, 1984; Clarke, Barry, McCarthy, & Selikowitz, 2001a; Gasser, Verleger, et al., 1988). Moreover, the differences in theta-alpha components of the EEG follow a posterior-to-anterior gradient, with greater power in the posterior regions and less power in frontal regions. This result is consistent with previous EEG studies (Gasser, Jennensteinmetz, et al., 1988) as well as studies of structural brain development in which cortical maturation follows a similar directional pattern (Giedd et al., 1999; Gogtay et al., 2004). In addition, consistent with previous studies in this age range, the children in the present studies show a peak alpha power around 9 Hz, suggesting that they have not yet

reached adult-like values previously reported for this measure. Taken together, it appears that the TD children are following the expected developmental pattern of cortical function, in contrast to the other groups of children.

In addition to confirming the previous findings at rest, more importantly, the mapping of brain function with motor behavior in TD children is a valuable contribution to the developmental motor neuroscience literature. The results from the second study (Chapter 4) replicate the findings from our previous work (Pangelinan et al., 2011) in that age-related improvements in sensorimotor performance on a static visuomotor task are reflected in greater activation of motor cortical planning and control regions. Moreover, the final study contributed new insights into relationship between brain activation pattens and adaptive sensorimotor control. Specifically, TD children exhibit greater cortical activation prior to movement for the jump task and exhibit better kinematic performance compared to the other groups studied. It is possible that similar preparatory cortical activation may similarly underlie ability of older children to engage in adaptive sensorimotor behavior reported in previous developmental studies (Ferrel-Chapus, Hay, Olivier, Bard, & Fleury, 2002; Contreras-Vidal, Bo, Boudreau, & Clark, 2005; King, Kagerer, Contreras-Vidal, & Clark, 2009).

Implications of the Current Findings for Understanding Children with Moderate Movement Difficulties.

In addition to investigating differences between TD children and children with DCD, Study 1 (Chapter 3) and Study 3 (Chapter 5) also investigated a group of children with moderate movement difficulties. Based strictly on the performance on the MABC-2, many of the children in this intermediate group did not meet criteria for the "at risk for

DCD" (6^{th} – 15^{th} percentile) or DCD (below the 5^{th} percentile) categories; however, the children in this group were referred to our study by occupational therapists or educational specialists for their movement difficulties. It is possible the strict classifications for the levels of movement impairment based on the MABC-2 may not capture all movement difficulties that are clinically or educationally relevant. Therefore, the MABC-2 in combination with other measures, such as handwriting and performance on other functional tasks were used to stratify the groups in this research. In the current studies, the movement difficulties of the children in this group were evident in their relatively poor performance on the MABC-2 (below the 25^{th} percentile) and below-grade level handwriting problems. Moreover, support for this stratification is provided by the different movement kinematics in the jump task, as compared to the TD children.

It is likely that the moderate movement difficulties exhibited by this group are due to the lack of engagement of relevant motor planning and control brain regions. However, whereas the children with DCD exhibited similar patterns of activation as the TD children (i.e., engagement of left hemisphere frontal brain regions) but with a reduced magnitude of response, the patterns of activation exhibited by the children in the intermediate group are markedly different than the other two groups. These results suggest that this group may actually represent a brain-behavior phenotype that is in between that exhibited by children with DCD and TD children.

One possible explanation for this phenomenon is that the intermediate group has a greater number of ADHD symptoms (as measured by the DBD). The overall lack of frontal cortical engagement is consistent with brain imaging studies of children with

ADHD during movement inhibition and task-switching (Rubia et al., 1999; Smith, Taylor, Brammer, Toone, & Rubia, 2006). The moderate movement impairments in this group, specifically the handwriting difficulties, are also consistent with studies of children with ADHD (Piek & Dyck, 2004; Racine et al., 2008). However, a follow-up investigation with a focus on the performance of children with ADHD on this task and their underlying brain activation patterns would be necessary to confirm this hypothesis. It would be very interesting if children with ADHD do indeed exhibit EEG waveforms during adaptive and inhibitory motor tasks similar to the INT group in the present study.

A Clarification Regarding the Term "Maturational Lag"

The terms "brain maturation" and "maturational lag" are common in the developmental cognitive neuroscience literature, and indeed, are also used here. The use of the terms brain maturation and maturational lag as discussed in Study 1, is meant only to highlight the developmental trajectory of characteristic brain activation patterns in TD children established in the previous literature. Deviations from this trajectory are thought to reflect maturational lag. However, it is not the belief of this author that the process of the brain maturing is simply a result of genetic or biological factors. Rather, brain development is the product of biological, individual experiential and environmental factors that together support the growth and changes in brain structure and function. Indeed, providing children with enrichment opportunities in a variety of domains (social, cognitive, and motor) has been found to change the developmental trajectory of brain development and brain function. This is also of relevance to understanding DCD, in that therapeutic interventions may serve to improve both the behavioral and brain functional outcomes.

Future Directions

Given that the trajectory for structural development of the cortex and associated fiber tracts mirror the development of higher-order motor and cognitive functions in typically developing children, it is very likely that the movement difficulties and patterns of brain activity exhibited by children with DCD may be due to disrupted or abnormal patterns of structural brain development (i.e., differences in cortical thickness and white matter architecture). By combining different neuroimaging modalities that assess brain structure and brain function, we may gain a deeper and multilevel understanding of how underlying neural structures contribute to the emergence of adaptive motor behavior in both children with and without movement difficulties.

The current program of research and the future studies in this vein may impact the diagnosis and prescription of behavioral interventions aimed at improving visuomotor behaviors. Since differences in motor planning and control are due to inefficient or attenuated activation of relevant brain areas, particularly prior to movement onset, then brain-based cortical facilitation protocols (e.g., stimulation protocols) or medications that increase cortical activation (e.g., stimulant medication) may aid in behavioral training protocols. Since the children with DCD in the current study did not engage relevant motor planning and cortical brain region in anticipation of movement, cognitive-based therapies that stress motor planning and breaking down different tasks into subcomponents may help children with DCD engage and strengthen the underlying brain functions as well as improve their motor skills. Indeed, one such therapeutic approach (Cognitive Orientation to Occupational Performance) appears to have positive outcomes

for children with DCD (Miller et al., 2001), but the neural outcomes have yet to be investigated.

The incorporation of neuroimaging techniques to track behavioral and brain plasticity in response to different interventions would also be worthwhile. It is likely that these brain-based approaches will shed light on an individual's progress even once the behavior plateaus. Within the larger developmental context, these therapeutic strategies may also benefit other clinical populations of children such as those with ADHD, DD, or Autism Spectrum Disorder, which also exhibit impairments in visuomotor behaviors.

Appendices

Appendix A. Consent Form for Child Participants – Studies 1 and 3

Appendix 2a: Consent Form 2a – for **child** participant (EEG)

CONSENT FORM

University of Maryland, Cognitive-Motor Neuroscience Laboratory

Project Title Brain Structure and Function in Adaptive Planning –Children with and without Developmental Coordination Disorder.

Statement of Age of Participant This research project being conducted by Drs. Jane Clark and Brad Hatfield in the Department of Kinesiology at the University of Maryland, College Park. You are over 18 years of age and are the parent or legal guardian of 6.5- to 12.5-year-old child. We are inviting your child to participate in our study.

Purpose The purpose of the research is to investigate how children and adults plan movements, inhibit movements, or have to replan movements when the task constrains change. In particular we are interest in the relationship between the motor behavior, brain function, and brain structures in those with and without coordination difficulties.

Procedures This study will take place at the Cognitive Motor Neuroscience Lab (CMNL) at the University of Maryland. Prior to coming to the lab, you will complete a phone interview to discuss your child's neurological health, puberty status and to provide you with the details of the study. The purpose of these questionnaires is to ensure typical neurological development of your child and to ensure that your child is pre- or early-pubescent.

This study requires 2-3 visits each lasting 2-2.5 hours. Your child will complete a handedness inventory to determine his or her preferred hand for completing different activities of daily living. In addition, your child will complete the Woodcock-Johnson Psychoeducational Test of Achievement and the Movement Assessment Battery for Children. These 3 assessments will take about 2.5 hours to complete. . You may request a formal report with the results of these assessments following the testing. During this time, you will be asked to complete the following questionnaires: the Disruptive Behavior Disorders Rating Scale, the Children's Behavioral Checklist, and the Social Communication Questionnaire. These parent questionnaires will take about 30 minutes to complete For completing the cognitive testing, your child will be able to pick out 2 toy prizes.

Electroencephalography (EEG) will be recorded for two rest periods and during two different line drawing games. This will require 1-2 sessions each lasting 1-1.5 hours. For the EEG, your child will be fitted for a special electrode cap. The cap is similar to a swim cap and placed on your child's head. The purpose of the cap is to record electrical brain activity (EEG) from up to 128 locations along the scalp. Using an applicator tube a small amount of conducting gel will be applied to each sensor to enable continuous connection between each sensor and the scalp. The gel is water-soluble and FDA approved. These set-up procedures will take approximately 20 minutes. These procedures are completely non-invasive and each step will be explained so that you and your child feel comfortable with the process.

After the initial EEG set-up your child will be asked to sit quietly with his/her eyes open and then closed for about 2 minutes each. The purpose of these recordings is to

record your child's brain activity at rest. Next, your child will be asked to make line drawing movements with his/her right and left hands using a computer and digitizing pen. For your child's participation in the EEG recordings he/she will receive $15 for each day of testing (up to $30 total).

Confidentiality

All information collected in the study is strictly confidential except as you specify on the signed permission form for video and image illustrations, and your child's name will not be identified at any time. All participants will be assigned a study identification number and this number will be used on all data and video images. The data your child provides will be grouped with data others provide for reporting and presentation. Data will be stored in a locked file cabinet and/or on password protected computers in a secured university laboratory facility. Only the investigators and their collaborators will have access to this locked file. All those with access to the data are NIH certified in the procedures for protecting participants in scientific experiments. Your child's information may be shared with representatives of the University of Maryland, College Park and government authorities if we are required to do so by law.

Risk

There are a few potential risks that may result from your child's participation in this study. The EEG caps may feel tight on your child's head and may cause a headache if the cap is on for too long. However, there are no other known risks or known long-term effects of the EEG sensor nets.

Your child may feel fatigued from the concentration necessary for completing the cognitive and motor testing. However, there are not other known risks or known long-term effects of the cognitive and motor testing.

Benefits, Freedom to Withdraw and to ask questions

Your child's participation is completely voluntary. The experiment is not designed to help your child specifically, but it may have substantial impact on understanding how the brain controls movement. You and your child are free to ask questions or to withdraw from participation at any time without penalty. A signed copy of this consent form will be given to you and that the investigators will provide you with the results of this study.

The University of Maryland does not provide any medical or hospitalization insurance coverage for participants in the research study nor will the University of Maryland provide any compensation for any injury sustained as a result of participation in this study except as required by law.

Investigators

Dr. Jane Clark (Co-PI),
Dr. Brad Hatfield (Co-PI),
Department of Kinesiology,
2351 School of Public Health Bldg
University of Maryland,
College Park, MD 20742
(301) 405-2450

Informed Consent Requirements

"I am voluntarily making a decision whether or not to allow my child to participate in the research study described above. My signature indicates that the information above has been explained to me, have had all of my questions answered, and have decided to allow my child to participate in this study. I will be given a copy of this

consent form to keep."

Name of Participant: _____

Participant's Date of Birth: _____

Signature of Participant's Parent/Guardian: _____

Today's Date: _____

If you have questions about your child's rights as a research subject or wish to report a research-related injury, please contact: Institutional Review Board Office, University of Maryland, College Park, Maryland, 20742; (email) irb@deans.umd.edu; (telephone) 301-405-0678

Appendix B. Pediatric Health Questionnaire

Child's Name _____

Sex_____ Age_____ Date of Birth_____ Handedness: _____

Birth History

1) Any problems with the pregnancy? Yes No
   if yes, what? _____
2) Was your child born full term? Yes No
   if no, how early? _____
3) Medical problems at birth? Yes No
   if yes, what_____

Hospitalization/Surgery/Injury

4) Except at birth, has your child been hospitalized? Yes No
   if yes, list age(s) and reason_____
5) Has your child ever had surgery? Yes No
   if yes, list age(s), and reason_____
6) Has your child ever had to see a neurologist for any reason? Yes No
   if yes, list age(s), and reason_____
7) Has your child ever had a head injury involving unconsciousness? Yes No
   if yes, how long? _____
8) Has your child had any illness that caused a permanent decrease in memory or cognition (ability to think)? Yes No
   if yes, please explain_____
9) Had any illness that caused a permanent decrease in motor ability (including speech)? Yes No
   if yes, please explain_____

Review of Developmental and Learning Disabilities

10) Seizure disorder? Yes No
_____
11) Developmental delay (including ASD)? Yes No
_____
12) Speech Delay? Yes No
_____
13) Motor Delay? Yes No
_____
14) Learning Disabilities (including ADHD)? Yes No
_____
15) Academic Difficulties (any performance below grade level)? Yes No
_____

16) Taking any medications (allergy, stimulants, etc.)? Yes No

_____

17) Any other concerns about your child's development? Yes No

_____

The above information is accurate to the best of my knowledge.

Signature of Parent or Guardian_____
Printed Name of Parent or Guardian_____
Date_____

Appendix C. Disruptive Behavior Disorder Questionnaire

Parent / Teacher DBD Rating Scale

Child's Name: _____ Form Completed by: _____

Grade: _____ Date of Birth: _____ Sex: _____ Date Completed: _____

Check the column that best describes your/this child. **Please write DK next to any items for which you don't know the answer.**

		Not at All	Just a Little	Pretty Much	Very Much
1.	often interrupts or intrudes on others (e.g., butts into conversations or games)				
2.	has run away from home overnight at least twice while living in parental or parental surrogate home (or once without returning for a lengthy period)				
3.	often argues with adults				
4.	often lies to obtain goods or favors or to avoid obligations (i.e., "cons" others)				
5.	often initiates physical fights with other members of his or her household				
6.	has been physically cruel to people				
7.	often talks excessively				
8.	has stolen items of nontrivial value without confronting a victim (e.g., shoplifting, but without breaking and entering; forgery)				
9.	is often easily distracted by extraneous stimuli				
10.	often engages in physically dangerous activities without considering possible consequences (not for the purpose of thrill-seeking), e.g., runs into street without looking				
11.	often truant from school, beginning before age 13 years				
12.	often fidgets with hands or feet or squirms in seat				
13.	is often spiteful or vindictive				
14.	often swears or uses obscene language				
15.	often blames others for his or her mistakes or misbehavior				
16.	has deliberately destroyed others' property (other than by fire setting)				
17.	often actively defies or refuses to comply with adults' requests or rules				
18.	often does not seem to listen when spoken to directly				
19.	often blurts out answers before questions have been completed				
20.	often initiates physical fights with others who do not live in his or her household (e.g., peers at school or in the neighborhood)				
21.	often shifts from one uncompleted activity to another				
22.	often has difficulty playing or engaging in leisure activities quietly				
23.	often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities				
24.	is often angry and resentful				
25.	often leaves seat in classroom or in other situations in which remaining seated is expected				
26.	is often touchy or easily annoyed by others				
27.	often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)				
28.	often loses temper				
29.	often has difficulty sustaining attention in tasks or play activities				
30.	often has difficulty awaiting turn				
31.	has forced someone into sexual activity				
32.	often bullies, threatens, or intimidates others				
33.	is often "on the go" or often acts as if "driven by a motor"				
34.	often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)				
35.	often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)				
36.	has been physically cruel to animals				
37.	often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)				
38.	often stays out at night despite parental prohibitions, beginning before age 13 years				
39.	often deliberately annoys people				
40.	has stolen while confronting a victim (e.g., mugging, purse snatching, extortion, armed robbery)				
41.	has deliberately engaged in fire setting with the intention of causing serious damage				
42.	often has difficulty organizing tasks and activities				
43.	has broken into someone else's house, building, or car				
44.	is often forgetful in daily activities				
45.	has used a weapon that can cause serious physical harm to others (e.g., a bat, brick, broken bottle, knife, gun)				

parent/teacher dbd.v1 © CTADD

Appendix D. Social Communication Questionnaire (Front Page)

1. Is she/he now able to talk using short phrases or sentences? If *no*, skip to question 8.	yes	no
2. Can you have a to and fro "conversation" with her/him that involves taking turns or building on what you have said?	yes	no
3. Has she/he ever used odd phrases or said the same thing over and over in almost exactly the same way (either phrases that she/he has heard other people use or ones that she/he has made up)?	yes	no
4. Has she/he ever used socially inappropriate questions or statements? For example, has she/he ever regularly asked personal questions or made personal comments at awkward times?	yes	no
5. Has she/he ever got her/his pronouns mixed up (e.g., saying *you* or *she/he* for *I*)?	yes	no
6. Has she/he ever used words that she/he seemed to have invented or made up her/himself; put things in odd, indirect ways; or used metaphorical ways of saying things (e.g., saying *hot rain* for *steam*)?	yes	no
7. Has she/he ever said the same thing over and over in exactly the same way or insisted that you say the same thing over and over again?	yes	no
8. Has she/he ever had things that she/he seemed to have to do in a very particular way or order or rituals that she/he insisted that you go through?	yes	no
9. Has her/his facial expression usually seemed appropriate to the particular situation, as far as you could tell?	yes	no
10. Has she/he ever used your hand like a tool or as if it were part of her/his own body (e.g., pointing with your finger, putting your hand on a doorknob to get you to open the door)?	yes	no
11. Has she/he ever had any interests that preoccupy her/him and might seem odd to other people (e.g., traffic lights, drainpipes, or timetables)?	yes	no
12. Has she/he ever seemed to be more interested in parts of a toy or an object (e.g., spinning the wheels of a car), rather than using the object as it was intended?	yes	no
13. Has she/he ever had any special interests that were *unusual* in their intensity but otherwise appropriate for her/his age and peer group (e.g., trains, dinosaurs)?	yes	no
14. Has she/he ever seemed to be *unusually* interested in the sight, feel, sound, taste, or smell of things or people?	yes	no
15. Has she/he ever had any mannerisms or odd ways of moving her/his hands or fingers, such as flapping or moving her/his fingers in front of her/his eyes?	yes	no
16. Has she/he ever had any complicated movements of her/his whole body, such as spinning or repeatedly bouncing up and down?	yes	no
17. Has she/he ever injured her/himself deliberately, such as by biting her/his arm or banging her/his head?	yes	no
18. Has she/he ever had any objects (*other* than a soft toy or comfort blanket) that she/he *had* to carry around?	yes	no
19. Does she/he have any particular friends or a best friend?	yes	no

LIFETIME

Social Communication Questionnaire (SCQ)

AutoScore™ Form

Michael Rutter, M.D., F.R.S., Anthony Bailey, M.D., Sibel Kazak Berument, Ph.D., Catherine Lord, Ph.D., and Andrew Pickles, Ph.D.

Published by
WESTERN PSYCHOLOGICAL SERVICES
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Publishers and Distributors

Name of Subject

Date of Birth

Date of Interview

Chronological Age _____ F _____ M Gender

Name of Respondent

Relation to Subject

Clinician Name

School/Clinic

Directions

Thank you for taking the time to complete this questionnaire. Please answer each question by circling *yes* or *no*. A few questions ask about several related types of behavior; please circle *yes* if *any* of these behaviors have ever been present. Although you may be uncertain about whether some behaviors were ever present or not, please answer *yes* or *no* to every question on the basis of what you think.

Appendix E. Children's Handedness Assessment

Item	Left	Right	Comments
throwing a ball			
raising one hand			
using an eraser			
combing hair			
brushing teeth			
using a toy hammer			
cutting with scissors			
retrieving marbles from a cup			
unscrewing a lid			
rewinding a tape or turning the hour hand on a play clock			

Appendix F. Handwriting Sample of a 12-Year-Old Child in the INT Group

13. 

theboy is about to trip

14.

(1) Place one cup of flour in a small bowl.

(2) craack the eggs

(3) Beat eggs and flour slightly.

15. 

they give light

16.

Play at the arcade

Go to the borde walk

and Swim

17.

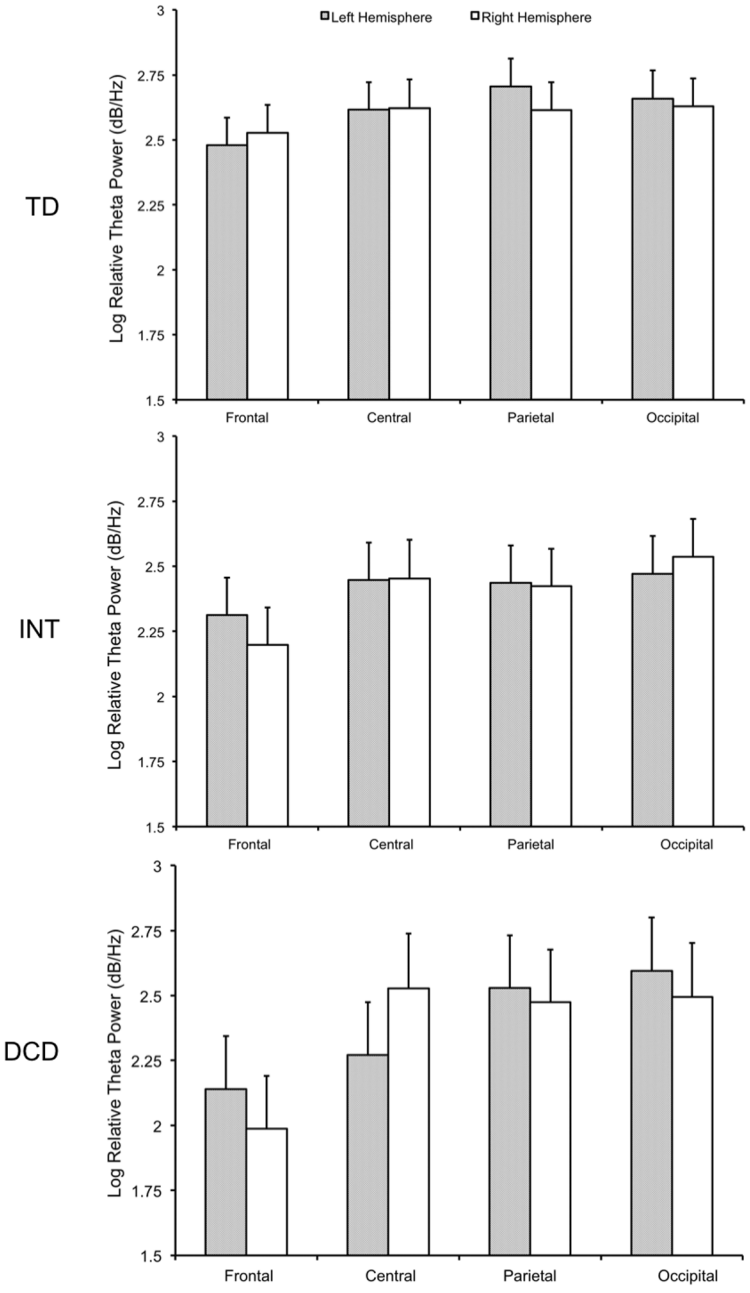
you could hit yoar head bleedoat and Die

18.

(1) When my father agrees to build a house, he follows several steps. (2) looks at the blue prints

(3) Next, he determines the exact plan his customer has in mind.

Appendix G. Relative Theta Power By Group, Hemisphere and Region



Appendix H. Consent Forms for Child Participants – Study 2

Appendix 2: Permission Form A2 – for **child** participant (EEG)

PERMISSION FORM

University of Maryland, Cognitive-Motor Neuroscience Laboratory

Identification of Project	Project Title: Brain dynamics in children and adults related to motor behavior.
Statement of Age of Participant	This research project is being conducted by Dr. Brad Hatfield, Dr. Jane Clark, & Dr. Marcio Oliveira at the Department of Kinesiology, University of Maryland, College Park. You are over 18 years of age and are the parent or legal guardian of 5- to 17-year-old child. We are inviting your child to participate in our study.
Purpose	The purpose of the research is to investigate brain wave patterns related to motor behavior in children who are typically-developing, children with developmental coordination disorder, and adults.
Procedures	Prior to performance, you will complete a neurological health questionnaire for your child to ensure typical neurological development. Next, your child will perform a series of tasks to determine if your child is right-handed or left-handed. These tasks include throwing a ball, using an eraser, pretending to brush his or her teeth, and drawing, among other items. Next, your child will be fitted for a special electrode cap similar to a swim cap placed on his or her head. The purpose of the cap is to record electrical brain activity from up to 64 locations along the scalp. In addition skin sensors will be placed above and below your child's left eye in order to record eye blinks, and placed behind his or her ears to serve as a references for the recordings. These areas will be lightly rubbed with a 3M plastic abrasive pad and then rubbed with alcohol in order to remove any extra oil or skin cells on the surface. Your child's skin will be lightly rubbed at each skin sensor on the electrode cap with the blunt end of a wooden q-tip but the skin will not be broken. The purpose of this step is to gently move the hair away from the sensors and allow contact between the skin and the electrodes. Using a blunt end needle and tube, Using a blunt end needle and tube, Food & Drug Administration (FDA) approved non-toxic conducting gel will be applied to each sensor to that enable continuous connection between each sensor and the skin of the scalp. Again, the skin will not be broken. These set-up procedures will take approximately 10 minutes and each step will be explained to you and your child so that he/she feels comfortable with the process. After the initial set-up your child will be asked to participate in a task that is outlined in a second consent form. The procedures of this task will be explained in full. These types of activities may include computer drawing, memory tasks, standing and sitting with your eyes open and closed, or measuring how strong your fingers are when you press up or down. These tasks are completed during this one visit and range in time from 30-minutes to 1.5-hours.
Confidentiality	All information collected in the study is strictly confidential except as you specify on the signed permission form for video and image illustrations, and your child's name will not be identified at any time. The data your child provides will be grouped with data others provide for reporting and presentation. Data will be stored in a locked file cabinet and/or on password protected computers in a secured university laboratory facility. Only the investigators and their collaborators will have access to this locked file. All those with access to the data are NIH certified in the procedures for protecting participants in

scientific experiments. Your child's information may be shared with representatives of the University of Maryland, College Park and government authorities if we are required to do so by law.

Risk

As a result of your child's participation in this study, and specifically wearing the electrode cap to measure brain activity, your child may experience some slight sensation and irritation of the skin as the scalp is lightly rubbed at the electrode sites. Additionally, he/she may experience a modest degree of fatigue from the concentration required during the performance of the test but there are no other known risks and no known long-term effects associated with participation in this study.

Benefits, Freedom to Withdraw and to ask questions

Your child's participation is completely voluntary. The experiment is not designed to help your child specifically, but it may have substantial impact on understanding how the brain controls movement. You are free to ask questions or to withdraw permission for your child's participation at any time without penalty. You will be given a signed copy of this permission form and the investigators will provide you with the results of this study.

The University of Maryland does not provide any medical or hospitalization insurance coverage for participants in the research study nor will the University of Maryland provide any compensation for any injury sustained as a result of participation in this study except as required by law.

Investigators

Dr. Brad Hatfield (PI),
Dr. Jane Clark (Co-PI),
Dr. Marcio Oliveira (Co-PI)
Department of Kinesiology, 2305 HHP Bldg
University of Maryland, College Park, MD 20742
(301)-405-2495

Informed Consent Requirements

"I am voluntarily making a decision whether or not to permit the participation of my child in the research study described above. My signature indicates that I have read the information provided above, have had all of my questions answered, and have permitted my child to participate in this study. I further understand that my child has agreed to participate in this study. I will be given a copy of this consent form to keep."

Name of Participant: _____

Participant's Birth date: _____

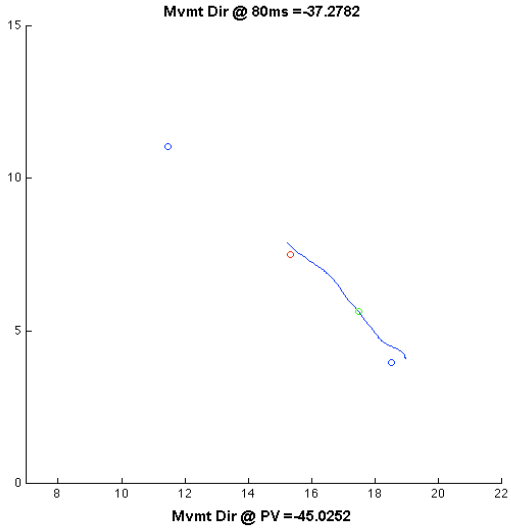
Signature of Participant's Parent/Guardian (if minor): _____

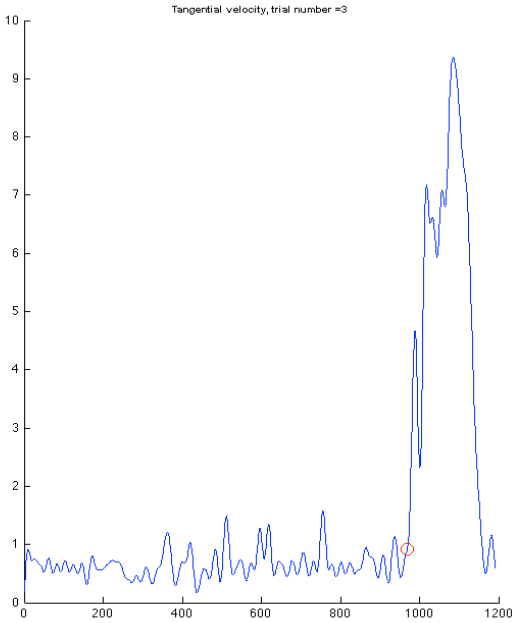
Today's Date: _____

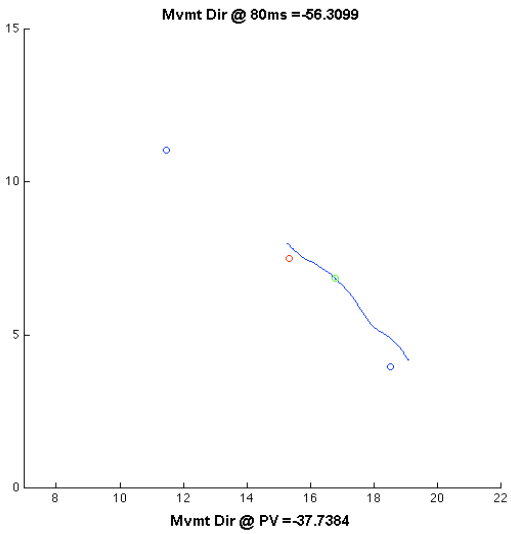
If you have questions about your rights as a research subject or wish to report a research-related injury, please contact: Institutional Review Board Office, University of Maryland, College Park, Maryland, 20742; (email) irb@deans.umd.edu; (telephone) 301-405-0678

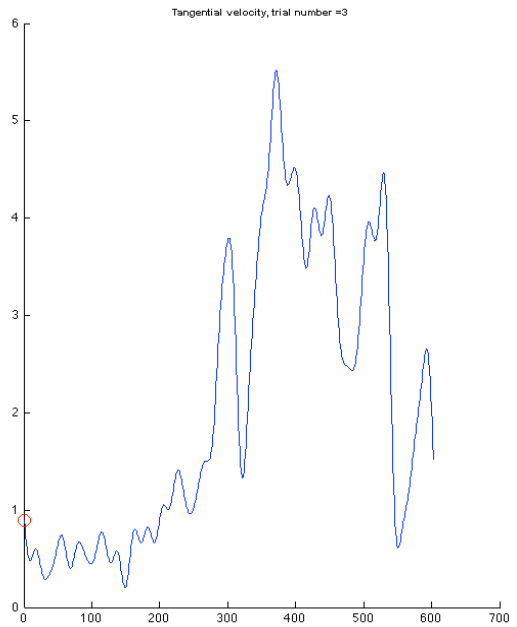
Appendix I. Trial Marking for a TD Child (Top) and Child with DCD (Bottom)

The left panel shows movement trajectory from the time marked at onset to the end of the trial. The point at which the peak velocity is reached is marked as green circle on the movement trajectory. The right panel shows the corresponding velocity profile. Although the movement trajectories are similar between the child with DCD and the TD child, the velocity profiles are much different. The velocity profile for the child with DCD is much wider (i.e., they took longer), has many more changes in velocity (i.e., is more jerky), and the peak velocity is smaller than the TD child.



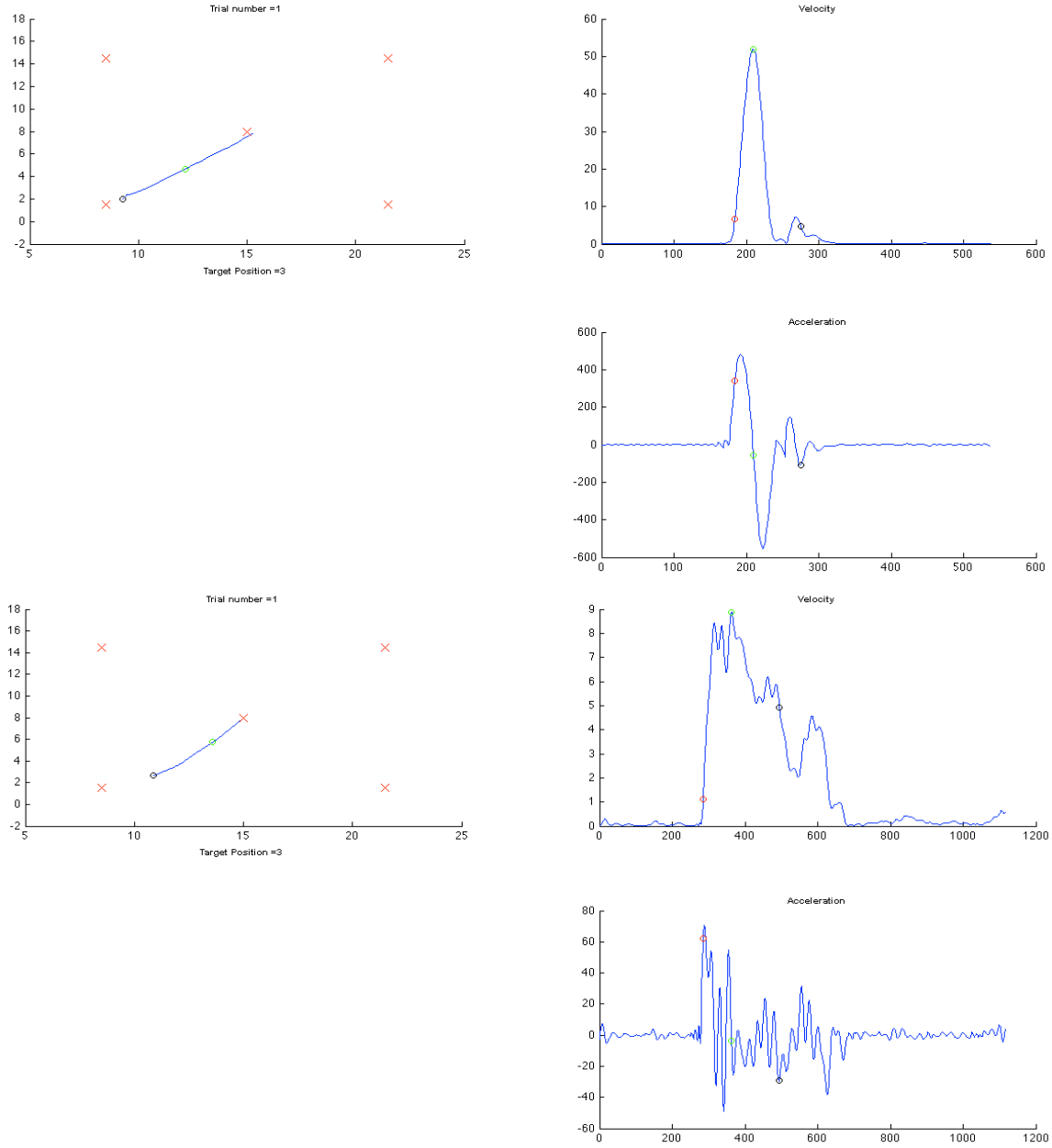






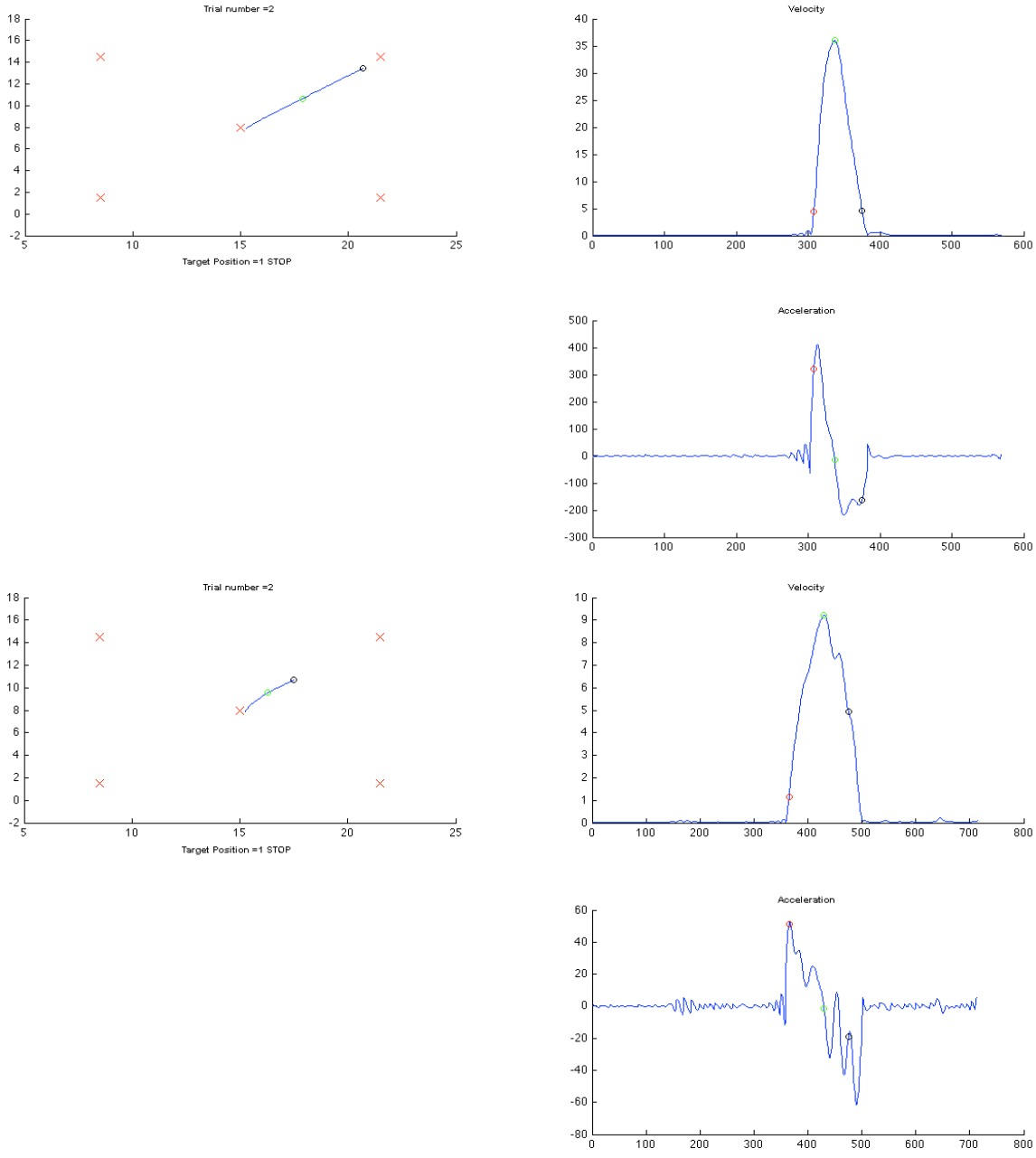
Appendix J. Marking for a TD Child (Top) and Child with DCD (Bottom) for an Unperturbed Trial for Study 3.1 - Stop

The left panel shows movement trajectory from the time marked at onset to the end of the trial. The point at which the peak velocity is reached is marked as green circle on the movement trajectory. The right panel shows the corresponding velocity and acceleration profiles. Although the movement trajectories are similar between the child with DCD and the TD child, the velocity profiles are much different. The velocity profile for the child with DCD is much wider (i.e., they took longer), has many more changes in velocity (i.e., is more jerky), and the peak velocity is smaller than the TD child.



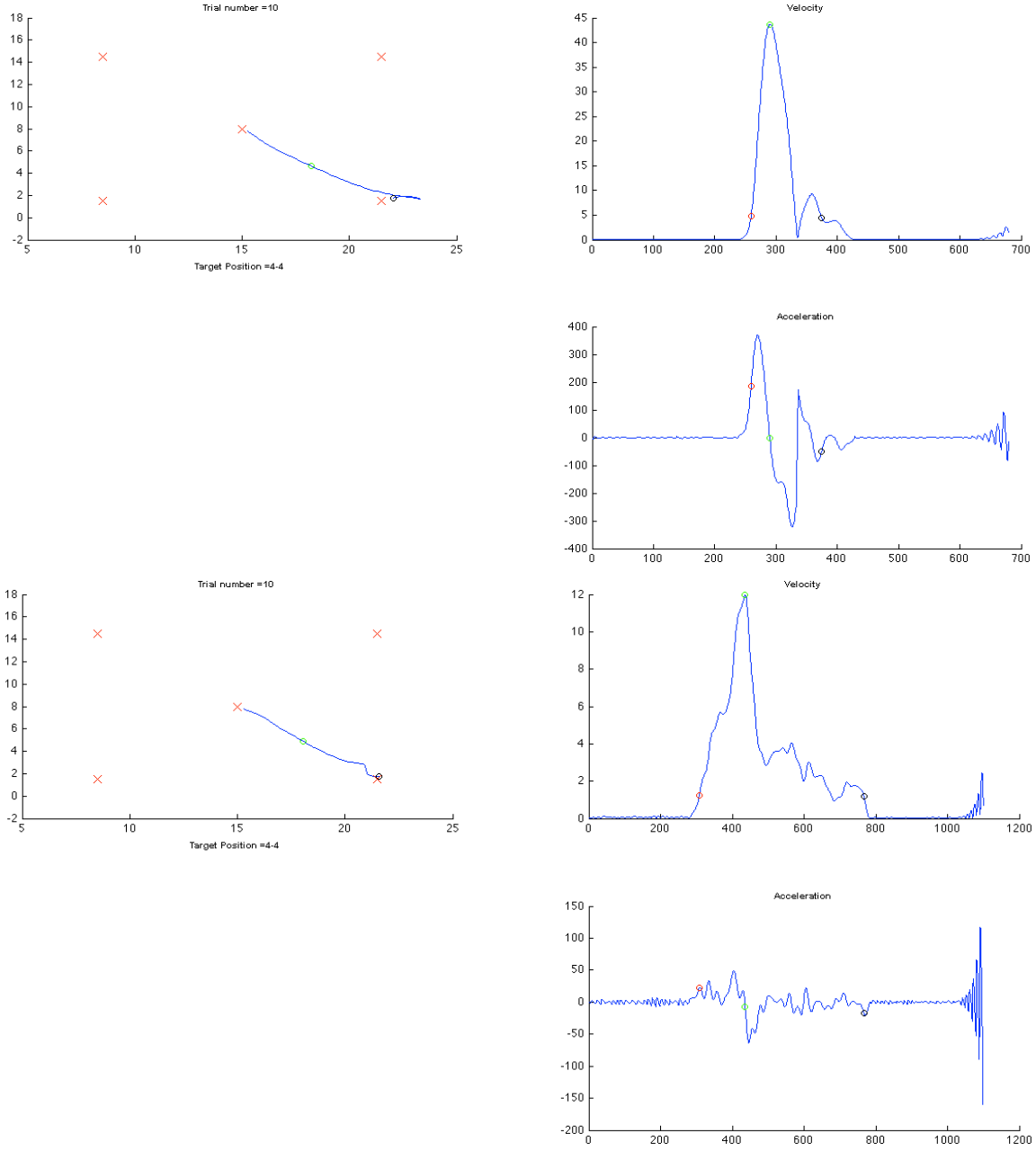
Appendix K. Marking for a TD Child (Top) and Child with DCD (Bottom) for a Perturbed Trial for Study 3.1 - Stop

The left panel shows movement trajectory from the time marked at onset to the end of the trial. The point at which the peak velocity is reached is marked as green circle on the movement trajectory. The right panel shows the corresponding velocity and acceleration profiles. The movement trajectories are different between the child with DCD and the TD child; the child with DCD moves much less distance. The velocity profile for the child with DCD is similar to the TD child but the peak velocity is smaller. The acceleration profile shows more changes for the child with DCD.



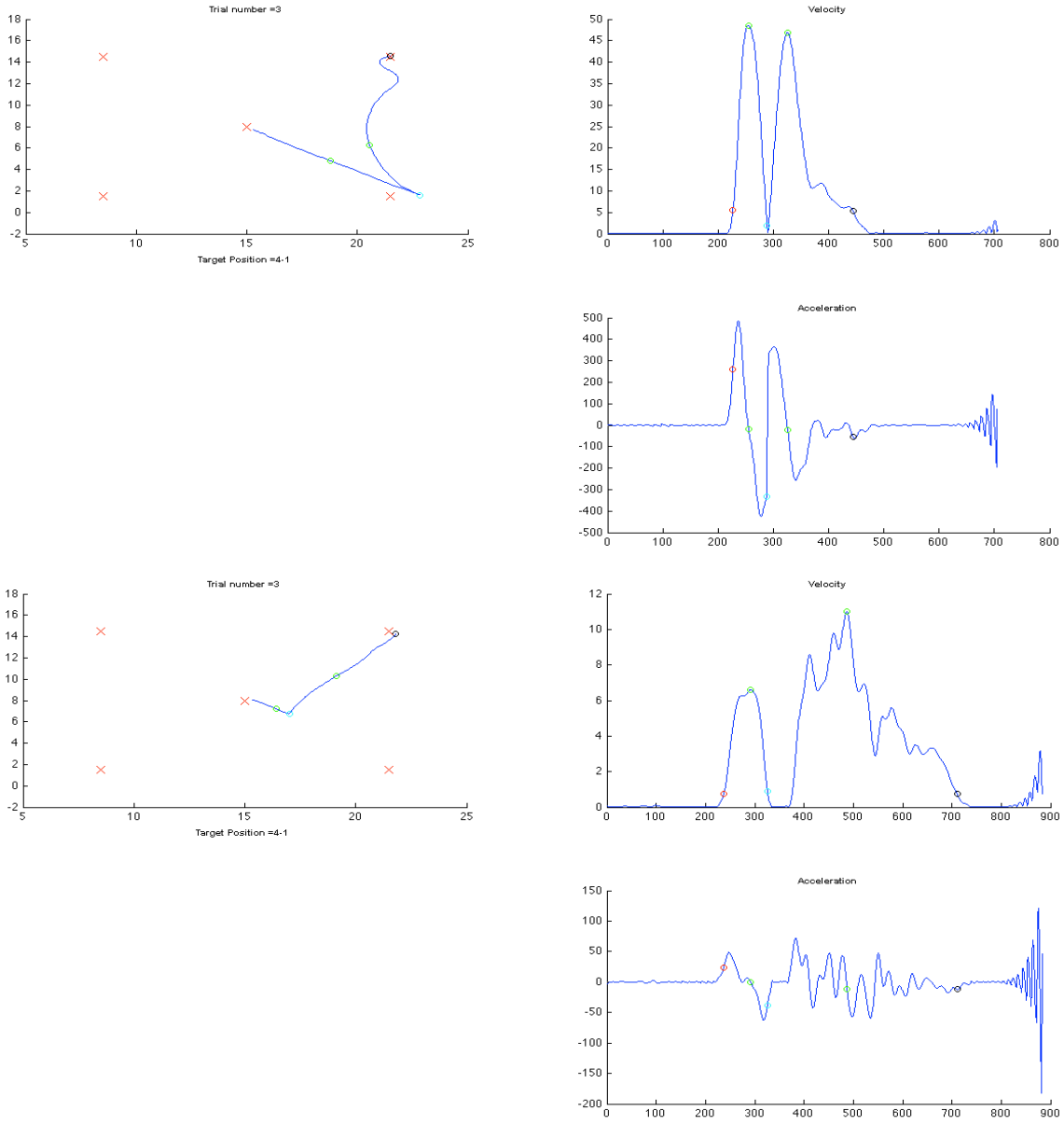
Appendix L. Marking for a TD Child (Top) and Child with DCD (Bottom) for an Unperturbed Trial for Study 3.2 - Jump

The left panel shows movement trajectory from the time marked at onset to the end of the trial. The point at which the peak velocity is reached is marked as green circle on the movement trajectory. The right panel shows the corresponding velocity and acceleration profiles. The movement trajectories are similar between the child with DCD and the TD child. However, the velocity profile for the child with DCD different than the TD child: lower peak velocity, longer time interval, and more changes in the velocity. The acceleration profile shows more changes for the child with DCD.



Appendix M. Marking for a TD Child (Top) and Child with DCD (Bottom) for an Perturbed Trial for Study 3.2 - Jump

The left panel shows movement trajectory from the time marked at onset to the end of the trial. The point at which the peak velocity is reached is marked as green circle on the movement trajectory. The right panel shows the corresponding velocity and acceleration profiles. The movement trajectories are very different for the child with DCD and the TD child. The TD child essentially reaches the original target before making a corrective movement. The velocity profile for the TD child shows two humps with a slightly extended deceleration for the second hump, whereas the DCD child's velocity profile is shows many changes in velocity. The acceleration profile for the TD child is very smooth, whereas the child with DCD is very jerky.



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