NEURAL AND BEHAVIOURAL CORRELATES OF MOTOR PERFORMANCE IN CHILDREN WITH DEVELOPMENTAL COORDINATION DISORDER

by

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Abstract

Introduction: With a prevalence of 5-6%, developmental coordination disorder (DCD) is one of the most common disorders of childhood. Children with DCD struggle to learn new motor skills, but the neurological mechanisms underlying the disorder are essentially unknown.

Purpose: The purpose of this thesis was three-fold: (1) to present a synopsis of current literature examining the potential neural correlates of DCD; (2) to determine if patterns of brain activity differed between children with and without DCD while performing a fine-motor task; and (3) to investigate whether children with DCD are able to demonstrate improved motor learning as evidenced by increased accuracy on a fine-motor task and/or shifts in patterns of brain activation.

Methods: A comprehensive literature review of possible neural correlates of DCD was conducted, which provided the background for the two studies included in this thesis. Both of these studies employed a block design and used functional magnetic resonance imaging to map patterns of brain activation associated with motor performance (Chapter 3) and motor learning (Chapter 4) of a fine-motor task. Seven children who met the diagnostic criteria for DCD (ages 8-12 years) and seven typically-developing (TD), closely age-matched children participated in the studies.

Results: The literature review implicated the cerebellum as a likely source of dysfunction associated with DCD. Chapter 3 showed that, despite similar levels of behavioural motor performance, substantial differences in patterns of brain activity were noted between children with DCD and TD children. Differences in motor behaviour emerged in Chapter 4, with the DCD group showing little change in tracing accuracy compared to the improvements noted in the TD group. Neuroimaging results from Chapter 4 suggest that children with DCD may
have a deficit in updating internal models of movement through under-activation of the cerebellum and/or the cerebello-thalamo-cortical pathway.

**Conclusion:** Findings from this thesis have made several important and novel contributions to our understanding of children with DCD. This work has suggested support for several hypotheses related to the mechanisms underlying DCD and provided some of the first neuroimaging evidence to suggest possible explanations for findings of previous research in children with DCD.
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Co-Authorship Statement

Sections of this thesis have been or will be published as multi-authored manuscripts in peer-reviewed journals. Details of authors’ contributions are provided.

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Chapter One. Introduction and Literature Review

1.1. Description of Developmental Coordination Disorder

Matthew is a nine year old boy who has difficulty tying his shoes, a skill his peers learned how to do three years earlier. His mom helps him cut up his food and wash his hair, as he struggles to complete these tasks independently. He has not mastered how to ride his bicycle, so he is not able to ride to the park with his friends. Matthew has tried several team sports, but no one passes the ball or puck to him; as he feels excluded and inferior to his teammates, he does not want to participate in sports anymore. Matthew’s parents are worried that he is becoming socially isolated and withdrawn. At a recent parent interview, Matthew’s teacher commented that, while he is a bright and capable student, his printing is slow and often illegible. Matthew does not complete many of his school assignments and homework activities, and, as a result, his grades are suffering. Matthew’s parents are increasingly concerned, but do not know what is wrong with their son.

Matthew is like many children who have a neurodevelopmental disorder known as developmental coordination disorder (DCD). The disorder is heterogeneous, with some children having difficulty with only fine motor skills, only gross motor skills, or both. Regardless of which motor skills are affected, the motor performance of children with DCD is typically slower, less accurate, and more variable than that of their peers. Motor learning is also impacted, with children with DCD having difficulty acquiring typical childhood skills, such as tying shoes or riding a bicycle.

As per the Diagnostic and Statistical Manual, Fourth Edition – Text Revision (DSM-IV-TR), there are four diagnostic criteria for DCD:
A. Performance in daily activities that require motor coordination is substantially below that expected given the person’s chronological age and measured intelligence. This may be manifested by marked delays in achieving motor milestones (e.g., walking, crawling, sitting), dropping things, “clumsiness,” poor performance in sports, or poor handwriting.

B. The disturbance in Criterion A significantly interferes with academic achievement or activities of daily living.

C. The disturbance is not due to a general medical condition (e.g., cerebral palsy, hemiplegia, or muscular dystrophy) and does not meet the criteria for a Pervasive Developmental Disorder.

D. If mental retardation is present, the motor difficulties are in excess of those usually associated with it.

As Polatajko\(^\text{12}\) highlighted, DCD is more than just the lower end of normal variance in motor abilities. The motor impairment has a significant impact on daily life, and is not due to a neurological disorder or delayed cognitive development.

### 1.2. History of Developmental Coordination Disorder

First identified by Orton in 1937, the significance of “clumsiness” was not apparent in the literature until the early 1960s.\(^\text{13}\) Since that time, many terms have been used to describe children whose motor difficulties interfere with daily living.\(^\text{14-16}\) Some of these terms include clumsy child syndrome,\(^\text{17}\) sensory integrative dysfunction,\(^\text{18}\) developmental dyspraxia,\(^\text{19}\) physical awkwardness,\(^\text{20}\) and perceptual motor dysfunction.\(^\text{21}\) In Scandinavian countries, the acronym DAMP has been used to identify children with deficits in attention, motor control, and perception.\(^\text{22}\)
In an effort to improve communication and knowledge among clinicians and researchers working with “clumsy” children, an international consensus meeting was held in London, Ontario in 1994 to determine which terminology should be used to describe these children. At this “London Consensus”, the term DCD was accepted as the term to describe these children. The term “developmental coordination disorder” and the diagnostic criteria for DCD had been added to the revised third edition of the DSM, and remain in the most current edition. Ten years after the London Consensus meeting, over 50% of all published articles used the term DCD, showing that DCD is gaining acceptance as the preferred terminology to describe these children. The London Consensus was re-confirmed with the publication of the Leeds Consensus Statement in 2006. This document highlights the agreement of international researchers and clinicians to retain the term DCD and the recognition that DCD is a distinct and unique disorder.

1.3. Impact of Developmental Coordination Disorder on Daily Life

As outlined in Criterion B of the DSM-IV-TR diagnostic criteria, a child’s motor coordination difficulties must significantly interfere with activities of daily living or academic achievement in order to be diagnosed with DCD. The types of difficulties children with DCD experience have been well documented. Self-care challenges include difficulty with dressing, doing up buttons and zippers, tying shoelaces, using a knife and fork, and toileting. Difficulty with school-related tasks can negatively impact academic achievement: these include copying, drawing, painting, constructing, printing, handwriting, using scissors, organizing, and finishing work on time. School achievement can also be affected in physical education, as children with DCD have trouble with throwing, catching,
or kicking a ball, running, skipping, and playing sports. Despite average or above intelligence, children with DCD have poorer school outcomes compared to their peers.\textsuperscript{29-32}

Difficulty with motor skills also impacts on the leisure participation of children with DCD. Their motor impairment not only affects sport-related skills mentioned above, but also other skills that are important in childhood, such as riding a bicycle.\textsuperscript{26} Perhaps as a result of their poorer athletic and social competence,\textsuperscript{29,33} children with DCD engage in fewer physical and group activities than their peers.\textsuperscript{29,34-37} This reduced participation can lead to social isolation.\textsuperscript{38,39}

Beyond the motor domain, children with DCD can experience significant secondary emotional and mental health concerns. These include low self-worth and self-esteem,\textsuperscript{28,33,40,41} high rates of anxiety and depression,\textsuperscript{22,28,33,41,42} and emotional/behavioural disorders.\textsuperscript{43,44} Thus, DCD has far-reaching effects in multiple domains that significantly affect the daily life of children with this disorder.

1.4. Prevalence of Developmental Coordination Disorder

Depending upon the selection criteria used, prevalence estimates for DCD vary from 1.4 – 19.0\% of school-age children as having DCD.\textsuperscript{45-47} Using the most commonly reported prevalence of 5-6\%,\textsuperscript{11} approximately 190,000 Canadian children aged 5-11 years may meet the diagnostic criteria for DCD,\textsuperscript{48} along with well over a million children in the U.S.\textsuperscript{49} Data from other countries have ranged from a lower reported prevalence of severe DCD in the United Kingdom (1.8\%)\textsuperscript{45} to an unusually high prevalence estimate in Greece (19.0\%).\textsuperscript{47}

There are several reasons for the varying prevalence rates reported in the literature. One of the primary reasons is how cases of DCD are identified.\textsuperscript{45} Higher prevalence rates may be reported if not all of the diagnostic criteria for DCD are applied. Many studies
include children with motor coordination challenges without quantifying intelligence or impact on activities of daily living.\textsuperscript{50} In contrast, the prevalence of DCD may be under-reported due to lack of awareness of the disorder.\textsuperscript{51} For example, a survey of physicians in a large urban city in Canada showed that 174 of 191 (91\%) had never heard of DCD.\textsuperscript{52} Variations in reported prevalence may also be due to the selection of cut-off scores used to indicate motor impairment,\textsuperscript{25} differences in lifestyle in various cultures,\textsuperscript{47} or the terminology used to describe these children.\textsuperscript{14}

Clinical studies of children with DCD have reported a higher prevalence in boys as compared to girls. The gender ratio for boys to girls has been reported to vary from 3:1\textsuperscript{22,53} to as high as 7:1 males to females.\textsuperscript{54} However, recent population-based studies suggest a lower gender ratio (1.9:1.0 male to female)\textsuperscript{45} or almost equal gender distribution.\textsuperscript{42}

1.5. Common Co-morbidities Associated with Developmental Coordination Disorder

DCD often co-occurs with other developmental disorders, most commonly attention deficit hyperactivity disorder (ADHD).\textsuperscript{54-59} Up to 50\% of children with DCD have been shown to also meet the criteria for ADHD,\textsuperscript{54,59} with recent evidence suggesting a genetic link between these two disorders.\textsuperscript{60,61} Learning disabilities\textsuperscript{62,63} and speech/language impairment\textsuperscript{64-68} have also been associated with DCD. Children with DCD may have more than one of these co-morbid disorders\textsuperscript{62,69-71} and the high degree of overlap between these developmental disorders has led some researchers to speculate about a shared etiology.\textsuperscript{69}
1.6. Etiology of Developmental Coordination Disorder

The etiology of DCD is largely unknown, but the literature suggests that it may be related to central nervous system pathology. DCD was first conceptualized as a form of “minimal brain dysfunction” (MBD), a term used to describe a collection of symptoms reflecting learning, attention, and motor coordination deficits. This term was later replaced by complex “minimal neurological dysfunction” (MND), which reflects “a distinct form of perinatally acquired brain dysfunction, which is likely associated with a structural deficit of the brain.” MND has been proposed to occur as a result of stress associated with preterm birth, which supports the finding of higher prevalence of DCD in children born preterm; 12.5% to over 50% of children born preterm have motor impairments consistent with DCD. Debate still exists as to whether children born preterm should be diagnosed with DCD, as they may have another neurological condition that could explain their motor deficits (Criterion C).

Other researchers have proposed a variant of atypical brain development (ABD) as the source of DCD. Due to the overlapping nature of developmental disorders, Kaplan et al. suggest that diffuse, rather than specific, areas of the brain may be involved. According to these authors, children may have one or more disorders (e.g., affecting motor, attention, and/or language), depending on the extent of disruption to brain development.

Although not a cause of DCD per se, two possible mechanisms underlying the disorder have been hypothesized. One such mechanism is the automatization deficit hypothesis, which suggests that children with DCD, similar to children with dyslexia, may have difficulty making motor skills automatic. This hypothesis leads naturally to a speculation that the cerebellum may be involved in the presentation of DCD. An alternative
explanation, but one that still suggests involvement of the cerebellum,\textsuperscript{81,82} is the internal modeling deficit hypothesis.\textsuperscript{83-87} Successful motor control is thought to result from an internal model that accurately predicts the sensory consequences of motor command.\textsuperscript{88} Theoretical models of motor learning posit that the cerebellum receives an efference copy of the motor command and compares the predicted movement with the actual movement; if there is a mismatch, the cerebellum sends an error signal as feedback to create a more accurate movement on subsequent occasions.\textsuperscript{89} Whether the mechanism underlying DCD is an issue with an automatization deficit or a deficit in forming an internal model, the cerebellum has been implicated in DCD.\textsuperscript{90}

1.7. Prognosis for Developmental Coordination Disorder

In the past, the common belief was that children with DCD would outgrow their motor difficulties.\textsuperscript{91,92} However, several longitudinal studies have shown that the motor problems of children with DCD can persist into adolescence\textsuperscript{29,32,93} and adulthood.\textsuperscript{94} Long-term outcomes often extend beyond the motor domain to include the development of secondary mental health, emotional, and behavioural issues.\textsuperscript{36,42,44} Based upon a qualitative exploration of experiences of parents of children with DCD, Missiuna et al.\textsuperscript{36} proposed that there may be a developmental trajectory of DCD, extending from motor and play concerns in the early years, to self-care, academic, and peer problems in middle childhood, and to issues with self-concept and emotional health in later childhood and adolescence. Children with DCD who have co-morbid conditions (e.g., ADHD) have poorer psychosocial outcomes\textsuperscript{95} and higher levels of depressive symptoms\textsuperscript{42,96} than those with a diagnosis of DCD alone.

Interestingly, children with DCD have also been shown to be at higher risk for obesity\textsuperscript{97} and coronary vascular disease.\textsuperscript{98} In comparison with typical peers, they have lower
cardiorespiratory and physical fitness\textsuperscript{99-102} with differences in fitness level increasing with age.\textsuperscript{101}

Despite the challenges facing children with DCD, functional outcomes can be improved with intervention.\textsuperscript{e.g.,103-106} In addition to child-focused interventions delivered by occupational therapists or physical therapists, parents and teachers can have a positive role in supporting the needs of children with DCD.\textsuperscript{107,108} As children grow, they may learn to use strategies to compensate for their difficulties and to adapt their occupations to ones with less demand on motor coordination; these factors have led to positive outcomes in the adult years.\textsuperscript{109}

1.8. Current Intervention Approaches for Developmental Coordination Disorder

A variety of different treatment approaches for DCD exist, many of which have been compared with one another\textsuperscript{110-112} and systematically reviewed.\textsuperscript{10,113-115} Interventions can be broadly categorized into two types: \textit{process} or \textit{deficit-oriented} and \textit{task-specific}.\textsuperscript{10,112} Deficit-oriented approaches include sensory integration therapy,\textsuperscript{116,117} sensorimotor-oriented treatment,\textsuperscript{118,119} and process-oriented treatment.\textsuperscript{21,120} The premise of these treatment approaches is that intervention is targeted at the underlying process deficit, and that remediation of the deficit will result in improved performance on tasks.\textsuperscript{112} Deficit-oriented approaches are based on outdated neuromaturational and hierarchical theories\textsuperscript{110,112} and evidence for their effectiveness is inconclusive.\textsuperscript{10,111,112}

Task-oriented approaches are grounded in current theories of motor control and motor learning\textsuperscript{121} and include task-specific intervention,\textsuperscript{122,123} neuromotor task training,\textsuperscript{105,106} Cognitive Orientation to daily Occupational Performance (CO-OP),\textsuperscript{103,104} and ecological
Evidence for task-specific interventions is promising,\textsuperscript{10,87,112} with general agreement that this approach is preferred over deficit-oriented approaches.\textsuperscript{10,112,125}

Despite the theory and evidence favouring task-specific interventions, no single approach has been fully substantiated by research.\textsuperscript{112} None of the treatment approaches have been grounded in neurobiological data or have been informed by neuroimaging studies. Wilson\textsuperscript{111} argues that examining brain-behaviour interactions using a \textit{cognitive neuroscientific approach} may help us better understand motor learning in children with DCD. Results from neuroimaging studies have the potential to increase our understanding of the neurobiology of DCD and inform our thinking about interventions for children with this disorder.

\textbf{1.9. Theoretical Framework: Neuroplasticity and Motor Learning}

The theoretical framework for this thesis is derived from two fields of study: neuroplasticity and motor learning. As there is a large amount of literature on each topic, only the concepts most relevant to the thesis will be highlighted.

Neuroplasticity is loosely defined as “the ability of the brain to change in response to external stimuli, experience, or damage.”\textsuperscript{126(p.685)} Much of what is known about neuroplasticity stems from animal studies\textsuperscript{127-132} and clinical studies of individuals post-stroke.\textsuperscript{133-136} While a myriad of factors may induce neuroplasticity, behavioural experience is one of the most powerful modulators of brain structure and function.\textsuperscript{137} Although the brain can be shaped in response to repetitive behavioural demands,\textsuperscript{138} not all behaviour induces plasticity. Research has shown that repetitive motor behaviour does not result in neuroplastic change; it is motor skill acquisition (motor learning) that drives plasticity.\textsuperscript{129,132,139,140}
Learning stimulates changes in the nervous system, including changes in neural connectivity and in patterns of brain activation.¹³⁹

Motor learning is defined as “a set of processes associated with practice or experience leading to relatively permanent changes in the capability for movement.”¹²¹(p.302) Thus, in order to create permanent change that is associated with motor learning, neuroplastic changes need to occur. Motor learning and neuroplasticity are inter-connected, with several principles common to both processes. These include repetition, task-specificity, and motivation.¹²¹,¹³⁹ Each of these will be discussed in turn.

Repetition and practice are key to motor learning. Practice schedules, such as massed versus distributed practice and blocked versus random practice, have been studied extensively in motor learning literature.¹²¹,¹⁴¹-¹⁴⁶ While the frequency and intensity of training (repetition) vary across studies, information from neuroscience states that the amount of repetition and intensity of training is critical in order to induce neuroplasticity.¹³⁹ For example, animal studies have shown that several days of training are required to promote neuroplasticity¹⁴⁷,¹⁴⁸ and that higher intensity training promotes neuroplastic change¹³⁰ whereas lower intensity training does not.¹⁴⁹

Task-specificity is another key component of motor learning and neuroplasticity. The current task-oriented treatment approaches for DCD are based on motor learning principles and involve some component of task-specificity. e.g.,¹⁰³,¹⁰⁵,¹²³,¹²⁴ Most approaches involve selection of a functional activity that the child wishes to learn or improve, and intervention is targeted at mastering that particular task. These approaches are consistent with the principle of specificity that is required for neuroplasticity. According to Kleim et al.,¹³⁹ the specific
acquisition of a motor skill, rather than mere use, is required to produce changes in neural connectivity.

Motivation is vital for motor learning to occur, and consideration of its importance is evident in current interventions for children with DCD that are grounded in motor learning theory.\textsuperscript{106,112,150} Child-chosen goals are the focus of therapy and, thus, the tasks are meaningful and relevant to the child. The concept of relevance is closely related to the principle of neuroplasticity known as salience.\textsuperscript{139} Information that is salient, or important, is more likely to be encoded; motivation and voluntary drive are factors that increase salience and promote neuroplasticity.\textsuperscript{139,151}

Another principle of motor learning that is related to neuroplasticity is “use it and improve it,”\textsuperscript{139} which is based on the observation that plasticity can be induced within specific brain regions with extended training. This principle may or may not be as relevant for children with DCD. Children with DCD struggle to learn new motor skills and tend to make the same errors repeatedly;\textsuperscript{152} thus, repetitive practice alone does not necessarily translate into improved motor performance or motor learning. One possible explanation for this finding is that children with DCD may have a deficit in forming or updating internal models of movement (as discussed in Section 1.6). Theoretical models of motor learning suggest that one of the crucial steps in motor learning is the ability to form internal models.\textsuperscript{153}

Based on principles of motor learning and neuroplasticity, it is conceivable that children with DCD can demonstrate improved motor skill and relatively permanent change in association with motor learning training.\textsuperscript{121,139} At this point in time, it is not known what type and how much training is required to induce neuroplastic change, or what training, if any, can
facilitate updating of the internal model of movement in children with DCD. Functional magnetic resonance imaging (fMRI) is a tool that can help elucidate some answers to these questions.

1.10. Functional Magnetic Resonance Imaging (fMRI) of the Brain

fMRI is a neuroimaging technique that allows analysis of changes in patterns of blood flow and, hence, investigation of changes in brain function over time. Magnetic resonance imaging (MRI) uses strong magnetic fields to create images of the brain by using a series of changing magnetic gradients and oscillating electromagnetic fields (known as the pulse sequence). Based on the properties of hydrogen atoms attached to water (H₂O) in brain tissue, pulse sequences can differentiate types of tissue, such as gray or white matter in the brain. One of the simplest forms of MRI contrasts used to create images is proton-density imaging, which is sensitive to the number of protons from the hydrogen atoms present within each voxel (a three-dimensional volume element, usually 1-2 mm in each dimension for anatomical MRI and 3-5mm for fMRI). When an individual enters the magnetic field of the MRI scanner, all the protons in the body align with the external magnetic field. During the MRI scan, a second external magnetic field is applied via a radio-frequency pulse, which causes the protons to wobble around their axis like a spinning top. When the scan is over, the protons gradually align back to their original orientation, which is known as relaxation time. Different images are created based on differences in relaxation times (T₁, T₂ and T⁺₂); T₁ images provide good gray matter/white matter contrast for anatomical images, whereas T₂ images increase contrast for fluid-filled regions. T⁺₂ images are sensitive to the amount of deoxygenated hemoglobin in the blood, thus form the basis of fMRI. Deoxygenated hemoglobin has magnetic properties, whereas oxygenated blood does not.
An increase in brain activity alters the ratio between the types of hemoglobin, which is known as the blood oxygen-level dependent (BOLD) contrast. Increased neural activity results in increased blood flow to activated brain regions; nearby blood vessels show a relative decrease in levels of deoxygenated hemoglobin in response to the increased supply of oxygenated blood. Thus, the BOLD signal represents the hemodynamic response to neural activity, providing an indirect measure of this activity.

The BOLD signal can be used to reveal where and with what intensity brain activity occurs during a behavioural task. Because fMRI allows for the measurement of patterns of brain activation associated with motor performance, it has the potential to measure if and how therapeutic interventions stimulate neuroplastic change. Thus, fMRI, along with other neuroimaging techniques, can advance clinical practice by informing clinician scientists how interventions shape patterns of brain activity and lead to improved function.

1.11. Objectives and Hypotheses of the Thesis

The overall purpose of this thesis is to describe the neural and behavioural correlates of motor performance in children with DCD. The body of this thesis is comprised of three manuscripts that have been published or submitted for publication in peer-reviewed journals. The manuscripts are reproduced in Chapters 2 - 4. Outlined below are the objectives and hypotheses for each study, as well as a statement of how each study contributes to the literature.
1.11.1. Chapter Two

Objective

Central nervous system pathology is thought to be the cause of DCD,\textsuperscript{11} but the precise mechanisms underlying the disorder are essentially unknown. Several authors have proposed various hypotheses as to the neuropathology in children with DCD.\textsuperscript{90,157-159} The purpose of this paper was to present a synopsis of current literature examining the potential neural correlates of DCD.

Hypothesis

Given the cerebellum’s known role in motor coordination and postural control,\textsuperscript{160} we expected that the cerebellum would be implicated in DCD.

Contribution

This comprehensive review of behavioural studies and related research on co-morbid conditions strongly suggests that the cerebellum is a logical source of dysfunction in DCD; this review also informed our hypotheses for the two studies outlined in Chapters 3 and 4.

1.11.2. Chapter Three

Objective

In an attempt to explain why children with DCD struggle with motor performance, the purpose of this study was to determine if patterns of brain activity differed between children with and without DCD while performing a fine-motor task.

Hypotheses

We expected that children with DCD would be less accurate on the task and would show a different pattern of activation in the cerebellum relative to typically-developing (TD) children.
**Contribution**

This study demonstrated that, despite similar levels of behavioural motor performance, children with DCD activated different brain regions from typical children when performing the same motor task. Our results contribute to a growing body of recent literature\textsuperscript{161,162} that suggests that children with DCD exhibit differences in neural networks and patterns of brain activation relative to same-age peers.

**1.11.3. Chapter Four**

**Objective**

While the study outlined in Chapter 3 showed differences in patterns of brain activation between children with DCD and TD children while performing a motor task, no previous neuroimaging studies have been conducted to examine shifts in brain activation as a result of motor learning. Thus, we designed a behavioural and neuroimaging study to investigate whether children with DCD are able to demonstrate improved motor learning as evidenced by increased accuracy on a trail-tracing task and/or shifts in patterns of brain activation.

**Hypothesis**

We expected that children with DCD would demonstrate greater accuracy in the trail-tracing task with practice, but that they would be significantly less accurate on the tracing task as compared to TD children. We hypothesized that children with DCD would underactivate the cerebellum during our experimental tracing task, and that they would show a compensatory pattern of brain activity in the prefrontal and posterior parietal cortices when compared with typical peers.\textsuperscript{163}
Contribution

To our knowledge, this is the first neuroimaging study to examine patterns of brain activation associated with motor learning in children with DCD. Children with DCD did not improve their tracing accuracy with practice. This finding, together with under-activation in the cerebellum, suggests that children with DCD may have a deficit in updating internal models of movement.
1.12. References


107. Missiuna C, Rivard L, Pollock N. They’re bright but can’t write: developmental coordination disorder in school aged children. *Teach Except Child* [serial online].
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Chapter Two: Neural Correlates of Developmental Coordination Disorder: A Review of Hypotheses

2.1. Introduction

Developmental coordination disorder (DCD) is characterized by marked impairment of motor coordination that significantly interferes with activities of daily living and academic achievement.\(^1\) DCD is one of the most common disorders in childhood,\(^2\) as it affects 5-6% of school-age children.\(^1\) In recent years, there has been a dramatic increase in experimental, applied and health services research about this disorder.\(^3\) Despite the prevalence and increased attention to this condition,\(^4\) little is known about the etiology of DCD.\(^5\) Evidence suggests that it may be related to central nervous system pathology,\(^1\) but the precise mechanism(s) underlying the condition are essentially unknown. Several authors have proposed various hypotheses as to the neuropathology in children with DCD.\(^6\)-\(^9\) The purpose of this paper is to present a synopsis of current literature examining the potential neural correlates of DCD, offer an opinion on the most likely hypothesis, and suggest a direction for future research. Given the limited literature pertaining to the neurobiology of DCD, a systematic review was not conducted; instead, major databases including PubMed, CINAHL, and EMBASE were searched, key articles selected and related literature sought to augment our understanding of the state of the evidence.

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\(^1\) A version of this chapter has been published. Zwicker JG, Missiuna C, Boyd LA. Neural correlates of developmental coordination disorder: a review of hypotheses. *J Child Neurol.* 2009;24:1273-1281.
2.2. Characteristic Presentation of Children with Developmental Coordination Disorder

Children with DCD experience numerous functional difficulties related to their motor skills. These can include difficulty with dressing, tying shoes, using utensils, riding a bike, catching a ball, handwriting, physical education, play skills, and engagement in leisure activities. While it was once believed that children with DCD would outgrow their motor dysfunction, evidence suggests that these difficulties persist into adolescence and adulthood.

Children with DCD tend to avoid social and physical activities and are at higher risk for obesity and coronary vascular disease. In addition to physical concerns, children with DCD experience a host of secondary psychosocial issues, including difficulty with social and peer relationships, lower self-worth and self-esteem, anxiety and depression, and emotional/behavioural disorders.

The functional difficulties experienced by children with DCD stem from motor impairments, primarily in three areas: posture, motor learning and sensorimotor coordination. As summarized by Geuze, “the main characteristics of DCD in the motor domain are poor postural control (moderate hypotonia or hypertonia, poor distal control, static and dynamic balance), difficulty in motor learning (learning new skills, planning of movement, adaptation to change, automatization), and poor sensorimotor coordination (coordination within/between limbs, sequencing of movement, use of feedback, timing, anticipation, strategic planning).” Children with DCD also have difficulty in processing visual spatial information and in recognizing facial emotion.
While the characteristics described above provide initial direction regarding potential neural correlates of DCD, the exploration is complicated by the heterogeneous presentation of the children who are studied. All children with DCD experience difficulty with motor learning and motor skill acquisition; however, they may experience difficulty with gross motor skills, fine motor skills, or both. In a similar vein, while DCD is recognized as a diagnosis in-and-of itself, the disorder often co-exists with language impairment and learning disabilities. A large proportion of children with DCD meet diagnostic criteria for attention deficit hyperactivity disorder (ADHD). Evidence suggests that subtypes of DCD and ADHD may be genetically linked, which again provides support for the idea of a shared etiology of DCD with other developmental disorders. While these issues create challenges in interpreting the results of studies about children with DCD, it is still important to begin to examine the neural correlates that may be associated with DCD, while also considering the neurobiological evidence related to these commonly comorbid conditions.

2.3. Potential Neural Correlates of Developmental Coordination Disorder

2.3.1. Cerebellum

Given the cerebellum’s role in motor coordination and postural control, it comes as no surprise that it may be involved in the neuropathology of DCD. Animal experiments and human studies have demonstrated the role of the cerebellum in clumsiness and poor coordination, the hallmarks of DCD. Soft neurological signs also suggest cerebellar involvement, as children with DCD tend to perform poorly on traditional tests of cerebellar function, such as finger-to-nose touching and rapid alternating hand movements. Poor postural control, specifically related to the timing of muscle recruitment and poor anticipatory postural activity, has been found in children with DCD. In addition to
postural muscles, several researchers have also noted impaired timing of more distal musculature in the DCD population, resulting in slower, less accurate, and more variable performance in motor tasks compared to controls.\textsuperscript{34-39}

Poor motor adaptation, which is also thought to reflect cerebellar dysfunction,\textsuperscript{39} has been demonstrated in DCD.\textsuperscript{8,40,41} Motor adaptation involves the modification of learned motor actions in response to contextual changes. Motor actions are modified by updating internal models (neural representations) of movement located within the cerebellum based on the error signal created during motor learning.\textsuperscript{42,43} Studies of motor adaptation in children with DCD that have used visuomotor distortion paradigms show that children with DCD are less affected by visual distortions than typical peers on a drawing task, as their performance does not change significantly across trials.\textsuperscript{40,41} The authors of these studies have hypothesized that children with DCD may have difficulty in modifying internal models of movement. However, when presented with an abrupt visuomotor distortion, children with DCD seem able to recognize errors and adjust their internal map.\textsuperscript{40} Presumably, the error signal to the cerebellum is more obvious with an abrupt distortion, thereby promoting motor adaptation in children with DCD under these conditions. Similar findings have been noted by Cantin et al.\textsuperscript{8} who found that children with DCD did not have difficulty in motor adjustment on a prism adaptation test, which evoked an abrupt visual distortion. Evidence from these motor adaptation studies suggests cerebellar dysfunction in DCD.

\subsection*{2.3.2. Parietal Lobe}

Results of a meta-analysis of the information processing deficits associated with DCD showed that children with DCD have significantly poorer visual spatial processing than healthy controls.\textsuperscript{24} This visual spatial deficit was present even when a motor response was
not required and did not appear to be related to ophthalmic factors, such as visual acuity or accommodation. This evidence suggests that the parietal lobe may be implicated in DCD given its primary role in processing visual spatial information. Children with DCD may also have difficulty with facial emotion recognition,\(^{25}\) which has been linked to parietal lobe involvement.\(^{44}\)

Further support for the involvement of the parietal lobe in DCD stems from studies that have examined the differences in motor imagery in children with and without DCD.\(^{45,46}\) Compared to controls, children with DCD were significantly slower in the execution of imagined movements and were not able to reliably predict the duration of real movements from imagined motor sequences on a visually-guided pointing task. Given that children with DCD had difficulty with imagined movements that did not require a motor response, the authors concluded that the children had an impairment in the processing of an efference copy, a process which is thought to occur in the parietal lobe.\(^{47}\) Katschmarsky et al.\(^{48}\) also concluded that children with DCD may have difficulty processing efference copy signals. This hypothesis, together with the observation that the performance of children with DCD on the visually-guided pointing task was reportedly similar to that of patients with parietal lobe damage,\(^{49}\) suggest that a network of regions that includes the parietal lobe may be involved in DCD.

Wilson et al.\(^{50}\) assessed the hypothesis of deficient motor imagery in children with DCD using a mental rotation task. Although response accuracy on a limb rotation task did not show a difference between DCD and control groups, the authors inferred that children with DCD did not automatically use motor imagery when mentally rotating the limbs. Findings from another study using a similar limb rotation paradigm in combination with
electroencephalogram found no significant differences between DCD and control groups, suggesting that children with DCD did not have a reduced ability to use motor imagery. Recent work in mental imagery by Deconinck et al. also contradicted Wilson et al.'s findings. The discrepancy in findings between these studies may be related to a continuum of severity of DCD; Williams et al. found that children with more severe DCD (based on a measure of motor impairment) had more difficulty with motor imagery compared to children with less severe DCD.

Despite the apparent evidence for parietal lobe involvement in DCD based on difficulties with visual spatial processing and motor imagery, the same evidence could support a cerebellar hypothesis. Neuroimaging studies have demonstrated that the cerebellum is activated during mental imagery and visual perceptual processing. Deconinck et al. suggest that motor imagery in children with DCD may be based on a poor forward internal model, which relies more on the cerebellum than the parietal lobe.

It is possible that a broad network of regions associated with visuospatial processing is impacted by DCD, including regions in the parietal lobe that have known roles in motor representation and mental transformations. Disruptions across networks of brain regions in children with DCD was supported by data from Querne et al. who showed decreased connectivity (using path coefficients from structural equation modeling) between striatum and inferior parietal lobe in children with DCD during a go/ no-go task. This task requires response inhibition, a function that typically requires coordinated frontal cortical, anterior cingulate, and parietal lobe activations. Interestingly, children with DCD demonstrated equivalent behavioural ability with typically developing children on the task; however, they accomplished this feat by activating differentially their network of brain regions. When
compared with typically-developing children, significantly stronger anterior cingulate activation and weaker prefrontal activity were apparent in children with DCD. The anterior cingulate is well known for its role in error-detection\textsuperscript{60,61} and, presumably, the increased activity in this region was a direct compensation for the poor prefrontal cortical and parietal lobe activity. However, the anterior cingulate has been shown to become more active as response inhibitions become more difficult;\textsuperscript{62} for example, during simultaneous execution of two tasks. This leads to speculation that children with DCD may show a higher failure rate under dual-task conditions due to their use of an already over-taxed network of brain activation during simpler, single-task operations. Future work will be needed to verify this hypothesis.

2.3.3. Corpus Callosum

Only a few studies have postulated that the corpus callosum may be involved in DCD. In a study designed to examine inter- and intra-sensory modality matching in children with and without eye-hand coordination problems, Sigmundsson et al.\textsuperscript{63} concluded that the corpus callosum may be involved in DCD. Subjects were required to point (without seeing their hand) at target pins under four different conditions: seeing target (vision only), seeing and feeling target (vision and hand), feeling target (hands only), and closing eyes (visual memory). Contrary to performance of control subjects, children with poor eye-hand coordination were significantly worse in both the inter-modal (vision and hand) and intra-modal (hands only) conditions when pointing with their non-dominant hand. This laterality effect suggests a problem with hemispheric transfer of information across the corpus callosum. Studies have found that the corpus callosum was smaller in children with ADHD,\textsuperscript{64-66} which may also be the case in DCD. However, Sigmundsson et al.\textsuperscript{63} did not
control for the potential coexistence of ADHD in the sample of children with DCD, so it is possible that the results may be due in part to this confounding variable.

2.3.4. Basal Ganglia (Striatum)

Although basal ganglia are involved in motor control and motor learning, their role in the presentation of DCD is essentially unknown. Weak evidence suggests that there is a subgroup of children whose clumsiness may be attributable to basal ganglia; Lundy-Ekman et al. reported that children who scored below the 40th percentile on the Bruininks-Oseretsky and who had “soft” neurological signs of basal ganglia dysfunction (e.g., choreiform or athetoid movements) had difficulty in modulating force of movement. To the contrary, Wilson et al. did not find evidence supporting the hypothesis that basal ganglia are implicated in DCD. Children with DCD performed similarly to controls on the sequencing of simple movements, which presumably would have involved cortico-striatal circuitry.

2.3.5. Other Areas

Children with DCD have been shown to have difficulty in visual-proprioceptive mapping, which may be related to activation of the right insula/claustrum alone or in conjunction with anterior cingulate cortex, inferior parietal lobules, and dorsal lateral prefrontal cortex. Mandich et al. propose that children with DCD may have an inhibition deficit, which would suggest frontal lobe involvement; however, other researchers have found that the performance of children at risk for DCD on response inhibition tasks was related to poor timing of movement, implicating the cerebellum.
2.4. Neurobiology of Developmental Conditions that Co-occur with Developmental Coordination Disorder

Given the review of literature, the bulk of evidence points to the cerebellum as the dominant source of neuropathology in children with DCD. Converging evidence for a cerebellar role in DCD also comes from evidence of cerebellar involvement in commonly co-occurring disorders, such as ADHD, dyslexia, and language impairment.\(^{75,76}\)

### 2.4.1. Developmental Coordination Disorder and Attention Deficit Hyperactivity Disorder

DCD and ADHD frequently co-occur, with up to 50% of children diagnosed with ADHD having significant motor difficulties consistent with DCD.\(^{77-79}\) The reverse relationship has also been found, with approximately 50% of children with DCD meeting the criteria for ADHD.\(^{29,30}\) This overlap of attention and motor problems has long been recognized, particularly by Scandinavian researchers who describe the co-existence as DAMP: deficits in attention, motor control, and perception.\(^{80}\)

The common presentation of ADHD with DCD suggests a shared etiology, with the cerebellum posing a logical common source of neuropathology. Yet, not all children with ADHD have DCD (or the reverse), which also demonstrates that, while these disorders may be linked, they are also distinct. Neurobiological and behavioural features of ADHD and DCD suggest that different parts of the cerebellum and cerebrum are involved in each condition.

Abnormalities in the cerebellum have consistently been implicated in ADHD,\(^{81-83}\) most notably in studies showing significantly smaller cerebellar volume in children with
ADHD as compared to controls. Specifically, the inferior posterior cerebellar vermis (lobules VIII–X); and superior vermis (lobules I–V); are reduced in volume.

Neuroimaging confirms the cerebellar source of ADHD with resting state functional magnetic resonance imaging showing decreased regional homogeneity in the bilateral cerebellum (indicating less metabolism or hypofunction). Further evidence of cerebellar involvement in ADHD stems from diffusion tensor imaging technology, which measures the integrity of white matter tracts using fractional anisotropy (FA). Ashtari et al. found decreased FA in the left middle-cerebellar peduncle and left cerebellum in children with ADHD compared to age- and gender-matched control subjects.

Behaviourally, many children with ADHD have difficulty with manual dexterity and fine motor skills, which cannot be attributed to the functions of the vermis. Initially, fine motor difficulties in children with ADHD were believed to be attributable to inattention, but Pitcher et al. showed that motor performance is not related to ADHD symptomatology. Motor impairment in ADHD increases as a function of co-occurring disorders, which implies that some other underlying neurobiology must account for the presentation of motor deficits in ADHD.

In summary, neuroimaging data demonstrate that individuals with ADHD differ from typically developing children in anatomy and neural activity of the cerebellum. Taken together with behavioural deficits, it appears that disrupted function of the vermis is a logical explanation for at least a portion of the dysfunction associated with the diagnosis of ADHD. As will be illustrated in the remainder of this review, the behavioural portrait of children with DCD suggests that other regions of the cerebellum, in association with the parietal lobe and
basal ganglia, may be responsible for DCD. It follows, then, that more encompassing areas of the cerebellum may be affected when there is a dual diagnosis of ADHD and DCD.

2.4.2. Developmental Coordination Disorder and Learning Disabilities

DCD also frequently co-occurs with language-based learning disabilities, including dyslexia. Cerebellar lesion studies and functional magnetic resonance imaging studies have demonstrated cerebellar involvement in reading (see Vlachos, Papathanasiou, & Andreau\textsuperscript{94} for a review), suggesting that it may be implicated in reading disabilities. Using positron emission tomography, Nicolson et al.\textsuperscript{95} demonstrated that adults with dyslexia and motor learning difficulties have lower brain activation in the right cerebellar cortex when performing pre-learned and novel sequences of finger movements. Dyslexic children appear to have difficulty in performing skills automatically, the putative ability of the cerebellum.\textsuperscript{96} This automatization deficit may also be the case with children with DCD.\textsuperscript{3}

While not a learning disability per se, children with DCD may also have deficits in visual-spatial and visual working memory;\textsuperscript{97} both of these types of memory processing have been linked to cerebellar function.\textsuperscript{98} Executive functions may also be deficient in children with DCD,\textsuperscript{38} one of many cognitive functions that have been shown to involve the cerebellum.\textsuperscript{98-101}

2.4.3. Developmental Coordination Disorder and Language Impairment

Children with DCD have also been noted to have co-occurring specific language impairment,\textsuperscript{3,26,102} a developmental language disorder that may also be related to cerebellar involvement. The cerebellum has been shown to have a role in language and linguistic functions, although the precise nature of cerebellar involvement is not well understood.\textsuperscript{103}
Only a small number of neuroimaging studies have focused on the contribution to language. A systematic review of this literature showed that cerebellar activation occurred during auditory input, visual input, semantic processing, speech output, and written output. The cerebellum is also thought to be involved in verbal fluency, word retrieval, syntax, and metalinguistic abilities.

2.5. Discussion

Although the parietal lobe, basal ganglia, and other brain regions may be involved in DCD, the strongest evidence suggests that the cerebellum and/or its network of connections are implicated in DCD. Kaplan et al. have suggested that the high co-occurrence of DCD with other developmental disorders provides evidence for a shared etiology of atypical brain development. While they do not suggest the cerebellum as the source of atypical development, evidence from premature infants also suggests this may be the case. There is a high incidence of DCD in children born prematurely at extremely low birth weight. Cerebellar development may be disrupted as a consequence of prematurity, as infants with very low birth weight have reduced cerebellar volume. Currently, it is not known if the neuropathology of DCD is in the cerebellum itself, within the cerebrocerebellar circuitry, or both. Despite the growing evidence implicating the cerebellum in DCD, it is highly likely that it is not the only neural correlate, given the heterogeneity of the disorder.

To date, neural correlates of DCD have only been hypothesized from behavioural data. With the exception of one study that showed normal computerized tomography on two boys with DCD, and the recent go/no-go study of Querne et al., no other neuroimaging studies have been conducted with children with DCD to determine which areas of the brain may be affected. Neuroimaging studies are essential to confirm the neural correlates of, and
associated neurobiological reorganization with, DCD. High-resolution anatomical magnetic resonance images could determine whether or not there are morphological differences in the brains of children with and without DCD. Functional magnetic resonance imaging (while performing a motor task) could be used to characterize differences in patterns of brain activation in children with DCD as compared to controls and to determine if these patterns can change in response to rehabilitative interventions. Finally, diffusion tensor imaging could be used to examine the integrity of white matter tracts to determine if neural connections within the brain are implicated in DCD. Data from neuroimaging studies are the next critical step in enhancing our understanding of DCD.

2.6. Conclusion

DCD is a highly prevalent childhood disorder, the impact of which has profound implications for behaviour, quality of life, and overall health extending well into adulthood. A comprehensive review of the existing literature regarding the neurobiology and behavioural deficits associated with DCD strongly suggests the cerebellum as a logical source of the dysfunction. The paucity of research regarding the neural correlates of DCD means that there are currently no scientifically-grounded explanations of the mechanisms that may be affected. Careful characterization of the neuropathology associated with DCD is essential to enhance our understanding of the neurobiology and neuroplastic potential of the brains of children with DCD.
2.7. References


Chapter Three: Children with Developmental Coordination Disorder

Activate Different Brain Regions than Peers to Support Motor Performance

3.1. Introduction

Affecting 5-6% of school-age children, developmental coordination disorder (DCD) is a motor impairment that significantly interferes with activities of daily living and school performance.\(^1\) The etiology of DCD is largely unknown, but the observed motor difficulties do not result from major neurological impairment or low intelligence.\(^1\) Children with DCD have difficulty learning new motor skills\(^2\) and their motor performance is generally more variable and less accurate than their typically-developing (TD) peers.\(^2\)-\(^6\) In an attempt to explain why children with DCD struggle with motor performance, we sought to determine if patterns of brain activity differed between children with and without DCD as they completed a fine-motor, trail-tracing task. We expected that children with DCD would be less accurate on the task as compared to TD peers. Given the known role of the cerebellum in motor coordination,\(^7\) we expected that children with DCD would show a different pattern of cerebellar activation relative to control children.\(^8\)

\(^2\) A version of this chapter has been submitted for publication. Zwicker JG, Missiuna C, Harris, SR, Boyd LA. Children with developmental coordination disorder activate different brain regions than peers to support motor performance.
3.2. Methods

3.2.1. Study Design and Procedure

Using functional magnetic resonance imaging (fMRI), we employed a blocked design to measure differences in motor performance and brain activation in children with and without DCD. To index motor behaviour, we used a trail-tracing task that allowed for collection of accuracy data (e.g., out of bounds of the trace). Brain activity was represented as percent signal change between rest (no tracing) and respond (tracing) conditions.

3.2.2. Measures

The Movement Assessment Battery for Children-2 (MABC-2)\(^9\) was used to assess the degree of motor impairment; the MABC-2 is a frequently used test to identify children with DCD\(^10\) and has good reliability and validity.\(^9\) The test provides an overall score compiled from eight subtests across three domains: manual dexterity (3), aiming and catching (2), and balance (3). A commonly used parent questionnaire, the Developmental Coordination Disorder Questionnaire (DCDQ),\(^11\) was used also to identify children with DCD. It has high internal consistency (alpha = 0.94) and sensitivity (85%).\(^12\)

The Kaufman Brief Intelligence Test-2 (KBIT-2)\(^13\) provided an estimate of intelligence. It is a quick and reliable measure that yields three scores: verbal, nonverbal and an overall intelligence quotient composite. The Conners ADHD DSM-IV Scale (CADS)\(^14\) is a 26-item parent questionnaire with excellent reliability and validity. It was used as a screening tool for attention deficit hyperactivity disorder (ADHD), as DCD frequently co-occurs with this disorder.\(^15,16\)
3.2.3. Participants

Sixteen right-handed children with parent- or teacher-reported motor difficulties (15 boys, 1 girl) were recruited through advertisement in local schools. Parents who were interested in having their child participate in the study contacted the Brain Behaviour Lab at the University of British Columbia for more information. After telephone or email screening, potentially eligible families attended an in-person appointment for further assessment to determine if the child met the inclusion criteria for the study. As the diagnosis of DCD is rarely given, children were assessed by an occupational therapist (JGZ) to determine if they met the four diagnostic criteria for DCD as per the Diagnostic and Statistical Manual, Fourth Edition – Text Revision (DSM-IV-TR). Criterion A (performance in daily activities that require motor coordination is substantially below that expected, given the person’s chronological age and measured intelligence) was determined by a score of \( \leq 15 \)th percentile on the MABC-2 and a score > 80 on KBIT-2. A structured clinical interview with the parent and child, as well as a score in the DCD range on the DCDQ, confirmed that coordination difficulties significantly interfered with academic achievement or activities of daily living (Criterion B). Parental report of the child’s medical history and therapist observation (JGZ) of the child’s physical status were used to determine if other medical conditions were present (Criterion C). Criterion D was not of concern, as no child who had an estimated IQ < 80 was included in the study. Children were also screened for ADHD using a cut-off score of >70 on the CADS, with children exceeding this score excluded.

Five of the children did not meet criterion C, as they were suspected of having other medical conditions (i.e., Asperger’s syndrome, cerebral palsy, perinatal brain injury, history of seizures, essential tremor). Four children did not complete the brain scan (i.e., illness, too
afraid, too loud, ferrous metal appliance in mouth). The remaining seven participants formed our sample of children with DCD (6 boys, 1 girl), with a mean age of 10.8 (SD 1.5) years. Table 1 shows demographic information and results of clinical assessments. Two children who scored at the 16th percentile on the MABC-29 were included in the study, as they experienced significant functional difficulties at home and school that were attributed to their motor impairment. Because Brown and Lalor18 caution against basing clinical decisions solely on the MABC-2, these children were included in the study because their clinical presentation and supplemental information were entirely consistent with DCD. Two other children in the sample had been diagnosed with DCD by a pediatrician.

Nine right-handed, typically-developing (TD) children were also recruited (6 boys, 3 girls). The same assessments were administered to this group as to the DCD group (Table 1), and the same cut-off scores on the KBIT-213 and CADS14 were applied. A score of ≥ 25th percentile on the MABC-29 and a score in the “probably not DCD” range on the DCDQ11 were the inclusion criteria on these measures for the peer (control) group. We selected seven of these children to form a comparison group that was most closely matched in age to the DCD group (mean age 10.9 [SD 1.5] years).

All participants were screened for safety to undergo MRI (i.e., no metallic objects in their body or history of major psychiatric diagnosis, claustrophobia, epilepsy, or seizures). Parent consent and child assent were obtained prior to and during all aspects of the study. Ethical approval was granted by the University of British Columbia Clinical Research Ethics Board (Appendix A) and approval for recruitment was obtained from the Vancouver Coastal Health Research Institute and the Vancouver School Board. At the time of consent, all children had the opportunity to try the experimental trail-tracing task.
3.2.4. Behavioural Task Acquisition and Data Analysis

During fMRI scanning, brain function was mapped while performing a fine-motor task adapted from the original Movement Assessment Battery for Children: the flower-shaped trail-tracing task\(^\text{19}\) (Figure 1). For fMRI scanning, participants lay supine with foam padding placed around their head to limit head motion and under their knees for comfort. A non-ferrous joystick was placed on the participant’s stomach and fastened securely with Velcro straps. The joystick had a finger-only attachment that each child held like a pen in the right hand. The trail-tracing task was displayed using a computer back-projection system linked to fMRI image acquisition. When children were at rest, the flower was red (1 minute before and after tracing). When instructed to “Go”, the flower was outlined in green; participants used the joystick to trace between two lines for 2 minutes for each of four runs (Appendix B). Children were instructed to trace as accurately as possible in a clockwise direction (arrows indicated tracing direction).

Using custom Matlab software (Mathworks, Natick, Massachusetts), trail-tracing data were analyzed for the average number of traces from four runs, the average time per trace, and the average number of times out of bounds (tracing error). A MANOVA with significance set at \(p < 0.05\) was used to assess differences in these three variables between the two groups of children.

3.2.5. fMRI Acquisition and Data Analysis

Brain activity was mapped with a 3.0 Tesla (3T) MRI scanner during tracing task performance. To time-lock motor responses, presentation of stimuli was controlled by using computer software linking stimuli presentation with fMRI image acquisition. The visual stimulus was presented by a back-projection system. A Philips 3T Achieva with Dual Quasar
gradients MRI scanner equipped with a three-axis, local-gradient radio frequency coil was used to collect whole brain fMRI (36 axial, 3 mm with 1-mm skip slices). Functional imaging data were collected as echo-planar images, by using a single-shot, blipped, gradient-echo, echo-planar pulse sequence (TE = 30 ms, TR = 2.0 s, 90° flip angle, FOV = 240 mm, 64 X 64). Four, 4-minute runs of functional data were collected (120 volumes each). Each run contained two periods of rest (30 volumes each) that bracketed one period of trail-tracing (60 volumes each). After the functional imaging, high-resolution 3D T1 anatomical images were collected for anatomic localization and co-registration (TE = 5 ms, TR = 24 ms, 40° flip angle, NEX = 1, thickness = 1.2 mm, FOV = 256 mm, 256 X 256).

Analysis of Functional NeuroImages (AFNI) software (NIMH, Bethesda, Maryland) was used for fMRI data processing. Functional images were generated by condition (rest, trace). All functional images were spatially registered to correct for head motion. Runs with excessive head motion (4/56) were removed from analysis; average head motion across groups for remaining analyses was 5.3 mm. Anatomic images were registered in Talairach space and then co-registered with functional images. An 8-mm, full-width-half-maximum Gaussian kernel was used to spatially smooth functional data. Hemodynamic responses were modeled as a box-car function, producing estimates of the blood oxygen level dependent (BOLD) response relative to baseline. The dependent variable, percent signal change, was calculated from rest to respond (trace) conditions. Whole-brain patterns of activity were analyzed using a one-way ANOVA corrected for multiple comparisons (minimum voxel volume threshold of 200 microlitres and 1.8 mm connectivity radius) at a p value < 0.01. We extracted percent signal change values from regions that were significantly different between the two groups.
3.2.6. Data Analysis to Explore Brain-behaviour Relationships

To determine the relationship between brain activation and motor behaviour, we conducted an exploratory Pearson product-moment correlation analysis. As we had no *a priori* hypotheses regarding brain-behaviour relationships, significance was set at $p < 0.05$ without correcting for multiple comparisons.

3.3. Results

3.3.1. Demographic and Clinical Results

Demographic and clinical data are summarized in Table 3.1. Boys were over-represented in the DCD group, which is consistent with the literature.\(^{15,22,23}\) Independent *t*-tests revealed no significant between-group differences in terms of age or estimates of intelligence. As expected, there were statistically significant differences between the two groups on the MABC-2, ($t (12) = 5.58, p = 0.000$), and DCDQ, ($t (12) = 6.26, p = 0.000$). Despite the fact that none of the children had been diagnosed with ADHD, or fell within the clinical range for ADHD on the CADS, the DCD group still had significantly more attentional symptoms endorsed by their parents than the TD group, ($t (12) = 2.66, p = 0.02$). This finding is consistent the literature indicating that children with DCD may have more attentional problems than their peers.\(^{24}\)

3.3.2. Behavioural Results

As per the MANOVA, there were no significant differences between children with DCD and TD children on the number of traces completed [$F (1, 12) = 0.673, p = .428$], time per trace [$F (1, 12) = 0.638, p = .440$], or tracing error, [$F (1, 12) = 0.071, p = 0.794$]. However, calculation of effect sizes revealed a small to moderate effect between groups for
the number of traces \((d = -0.44)\) and time per trace \((d = 0.43)\), with the DCD group performing slower and completing fewer traces than TD children (Table 3.2). The children with DCD also demonstrated more variable and less controlled movement compared to typical children (Figure 3.1). For example, Figure 3.1A at the top of the flower-trail shows that, although still within bounds, this child with DCD did not provide the fine movement necessary to follow the zig-zag portion of the trail. The tracing is also more out-of-bounds compared to that of a TD child of the same age (Figure 3.1B).

### 3.3.3. fMRI Results

A one-way ANOVA revealed significant differences in patterns of brain activation between the two groups (Table 3.3). The DCD group showed significantly more activation as compared to the TD group in eight brain regions, including the left inferior parietal lobule [Brodmann Area (BA) 40], right supramarginal gyrus (BA 40), right parahippocampal gyrus (BA 30), right middle and inferior frontal gyrus (BA 9, 46), right posterior cingulate gyrus (BA 30), right lingual gyrus (BA 19), and two different activations in the right superior parietal lobule (BA 7) (Figure 2). The TD group demonstrated significantly more activation as compared to children with DCD in four brain regions: left precuneus (BA 39) and three separate activations in bilateral insula (BA 13, 21), including the right superior temporal gyrus and left claustrum (Figure 3.3).

### 3.3.4. Brain-behaviour Correlations

Table 3.3 and Figure 3.4 outline significant correlations of brain activations with motor behaviour. For the DCD group, activation in the right middle and superior frontal gyri was negatively correlated with the number of traces completed \((r = -0.97, p < 0.01)\) and
positively correlated with the time per trace \((r = 0.86, p < 0.05)\). TD children showed a negative correlation of activation in the posterior cingulate gyrus with the number of traces completed \((r = -0.78, p < 0.05)\).

### 3.4. Discussion

Interestingly, we noted substantial differences in patterns of brain activity despite similar levels of behavioural motor performance between the two groups. Although our small sample size may have prevented us from detecting significant differences in motor behaviour between the two groups, our results revealed that, compared to TD peers, children with DCD employed a very different network of brain regions during the trail-tracing task. The DCD group showed an increased BOLD response in frontal, parietal, and temporal regions (Figure 3.2), whereas the TD group relied more on the insular area and precuneus to support their motor performance (Figure 3.3). The statistically significant patterns of brain activation and brain-behaviour correlations for the DCD group will be discussed first, followed by the findings for the TD group.

The DCD group showed the greatest BOLD signal in BA 40 bilaterally: the left inferior parietal lobule and right supramarginal gyrus. These areas have been associated with the interpretation of sensory information\(^{25,26}\) and visual-motor/visual-spatial processing\(^{27,28}\) respectively. These findings, along with other significant activations in other brain regions, suggest that the DCD group relied heavily on visual and spatial processing to complete the trail-tracing task. These regions include the superior parietal lobule, which has been associated with visual-spatial\(^{29}\) and spatial-motor\(^{26}\) processing, the posterior cingulate gyrus for spatial attention,\(^{30}\) the lingual gyrus for visual-spatial processing,\(^{31}\) and the parahippocampal gyrus for spatial memory.\(^{32,33}\) Greater reliance on visual-spatial processing
is an interesting finding, as children with DCD have been shown to have a deficit in processing this type of information. However, other researchers have found that children with DCD rely more on visual information, suggesting that this may be a strategy to compensate for poor proprioceptive feedback or a poorly developed internal model of movement.

Greater activation in the parietal regions for the DCD group is contrary to the findings of Kashiwagi et al. During a continuous, visual-motor tracking task, children with DCD showed significantly less activation than control children in the left superior and inferior parietal lobules. The discrepant findings may be related to task differences, with our task having greater demand for visual-spatial processing, as the children were required to precisely manipulate the joystick cursor between two lines.

Kashiwagi et al. suggest that the poorer performance of the DCD group as compared to controls was related to lower activation in the posterior parietal cortex. In contrast, we did not find any significant correlations of performance with BOLD responses in parietal regions. Rather, we found that activation in the right middle and superior frontal gyri [dorsolateral prefrontal cortex (DLPFC)] in the DCD group was negatively correlated with the number of traces completed ($r = -0.97$, $p < 0.01$) and positively correlated with the time per trace ($r = 0.86$, $p < 0.05$) (Figure 3.4A). Activation of the DLPFC has been linked to attentional control and the initial stages of explicit motor learning. Greater activation in the DLPFC suggests that the DCD group used greater cognitive effort to complete the task, resulting in fewer traces and more time per trace. This finding supports the common observations that children with DCD are slower in performing everyday tasks and need to concentrate more than other children during activities that require eye-hand coordination.
Interestingly, greater activation in the DLPFC was not significantly correlated with greater tracing accuracy.

Relative to the DCD group, the TD group showed greater BOLD responses in four brain regions, three of which were in the insula and neighboring regions (claustrum and superior temporal lobe). The insula has been associated with motor control\textsuperscript{41,42} and motor learning,\textsuperscript{43} as well as with error processing.\textsuperscript{44-46} The other region that was significantly different for the TD group was the precuneus, which has been linked to visual-spatial processing\textsuperscript{47} and initiation of movement programming.\textsuperscript{48} While these regions may have supported performance of TD children on the task, only activation in the right posterior cingulate gyrus was significantly correlated with motor performance (Figure 3.4B). Lower activation of this region was associated with a greater number of traces ($r = -0.78$, $p < 0.05$).

The posterior cingulate gyrus is thought to be part of the resting default network of the brain, which shows deactivation with attention-demanding tasks.\textsuperscript{49,50} While the TD group did not show a negative BOLD signal in the posterior cingulate gyrus, lower activation of this region was associated with improved task performance; this same relationship was not apparent for the DCD group.

Contrary to our hypothesis, there was no significant difference in cerebellar activation between the two groups. This finding suggests that children with DCD and TD peers are showing similar activation in the cerebellum for motor performance, which is consistent with both groups having similar results for tracing behaviour. Because the cerebellum has been shown to be active during early stages of motor learning,\textsuperscript{51} it is possible that differences in activation would become more apparent between the two groups if more task practice was provided. A second fMRI would be necessary to assess motor learning effects.
Because pediatricians are frequently involved in assessing children with motor disorders, and in prescribing appropriate therapy services, awareness of the differences in patterns of brain activation in children with DCD as compared to typically-developing peers is important to their understanding of DCD, particularly as to how these differences may affect school performance and activities of daily living for these children.

3.5. Conclusion

While our results should be interpreted with caution given the small sample size, our findings indicate that children with DCD activate different brain regions than typical children when performing the same tracing task. Our results contribute to a growing body of recent literature suggesting that children with DCD exhibit differences in neural networks and patterns of brain activation relative to same-age peers. These lines of evidence highlighting the neurobiological differences between children with DCD and TD children may serve to dispel the perspective that DCD is not a bona fide disorder. Further neuroimaging studies will help elucidate the functional significance of these differences, and may help to inform our thinking about rehabilitation interventions for children with DCD.
Table 3.1. Demographic and clinical characteristics of children with developmental coordination disorder and typically-developing comparison children

<table>
<thead>
<tr>
<th></th>
<th>DCD</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>TD</th>
<th></th>
<th></th>
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<td>Sex</td>
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<td>KBIT-2</td>
<td>CADS</td>
<td>Sex</td>
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<td>KBIT-2</td>
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<td>114</td>
<td>49</td>
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<th>112.6</th>
<th>57.6&lt;sup&gt;c&lt;/sup&gt;</th>
<th></th>
<th>10.9</th>
<th>48.3&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>18.4</td>
<td>7.7</td>
<td>15.4</td>
<td>6.8</td>
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<sup>a</sup> Scores are represented as percentiles

<sup>b</sup> Means for MABC-2 and DCDQ are statistically significant between groups, \( p < 0.001 \)

<sup>c</sup> Means for CADS are statistically significant between groups, \( p < 0.05 \)
Table 3.1. Demographic and clinical characteristics of children with developmental coordination disorder and typically-developing comparison children, continued

<table>
<thead>
<tr>
<th>CADS, Conners ADHD DSM-IV Scale</th>
<th>DCD, developmental coordination disorder</th>
<th>DCDQ, Developmental Coordination Disorder Questionnaire</th>
<th>KBIT-2, Kaufman Brief Intelligence Test-2</th>
<th>MABC-2, Movement Assessment Battery for Children -2</th>
<th>NS, not statistically significant</th>
<th>TD, typically-developing children</th>
<th>y, years</th>
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...
Table 3.2. Means, standard deviations, and effect sizes for motor performance between groups

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<tr>
<th></th>
<th>Mean (SD)</th>
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<tr>
<td></td>
<td>DCD</td>
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<tr>
<td>Number of Traces</td>
<td>5.54 (2.07)</td>
<td>6.44 (2.06)</td>
</tr>
<tr>
<td>Time Per Trace [sec]</td>
<td>22.84 (10.58)</td>
<td>19.14 (6.23)</td>
</tr>
<tr>
<td>Tracing Error [points out of bounds]</td>
<td>196.92 (138.35)</td>
<td>178.67 (116.65)</td>
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</table>

DCD, developmental coordination disorder; NS, not significant; TD, typically-developing children.
Table 3.3. Coordinates for significant activation One Way ANOVA (corrected, $p < 0.01$) and significant correlations with behavioural measures

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>BA</th>
<th>Volume</th>
<th>Talairach Coordinates (peak activation)</th>
<th>Brain-Behaviour Correlations</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(µl) x y z Traces Time Error</td>
<td></td>
</tr>
<tr>
<td>Developmental Coordination Disorder (&gt; TD)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>L inferior parietal lobule</td>
<td>40</td>
<td>4847</td>
<td>41 37 44</td>
<td></td>
</tr>
<tr>
<td>R supramarginal gyrus</td>
<td>40</td>
<td>2164</td>
<td>-37 46 36</td>
<td></td>
</tr>
<tr>
<td>R parahippocampal gyrus</td>
<td>30</td>
<td>888</td>
<td>-22 42 4</td>
<td></td>
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<tr>
<td>R middle and superior frontal gyrus</td>
<td>9, 46</td>
<td>880</td>
<td>-47 38 29</td>
<td>-0.97a 0.86b</td>
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<tr>
<td>R posterior cingulate gyrus</td>
<td>30</td>
<td>608</td>
<td>-15 68 14</td>
<td>-0.78b</td>
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<td>R lingual gyrus</td>
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<td>-14 66 -6</td>
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<tr>
<td>R superior parietal lobule</td>
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<td>280</td>
<td>-23 47 58</td>
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<tr>
<td>R superior parietal lobule</td>
<td>7</td>
<td>233</td>
<td>-32 59 61</td>
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</table>
Table 3.3. Coordinates for significant activation One Way ANOVA (corrected, \( p < 0.01 \)) and significant correlations with behavioural measures, continued

<table>
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</thead>
<tbody>
<tr>
<td>L precuneus</td>
<td>39</td>
<td>1903</td>
<td>39</td>
<td>64</td>
</tr>
<tr>
<td>R superior temporal gyrus</td>
<td>13</td>
<td>1667</td>
<td>-47</td>
<td>43</td>
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<tr>
<td>L claustrum, insula</td>
<td>13</td>
<td>460</td>
<td>29</td>
<td>-12</td>
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<tr>
<td>L insula</td>
<td>13, 21</td>
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<td>41</td>
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\( a \ p < 0.01 \quad b \ p < 0.05 \)

**bold** correlations, developmental coordination disorder; *italicized* correlations, typically-developing children

BA, Brodmann Area; DCD, developmental coordination disorder; TD, typically-developing
Figure 3.1. Sample of trail-tracing task

A. Tracing from child with developmental coordination disorder.

B. Tracing from typically-developing child
Figure 3.2. Patterns of significantly greater brain activation for children with developmental coordination disorder relative to typically-developing children (corrected, $p < 0.01$)
Figure 3.3. Patterns of significantly greater brain activation for typically-developing children relative to children with developmental coordination disorder (corrected, $p < 0.01$)
Figure 3.4. Significant brain-behaviour correlations

A. Developmental coordination disorder

B. Typically-developing children

\(^a p < 0.01\)

\(^b p < 0.05\)
3.6. References


Chapter Four: Formation of an Internal Model for Motor Learning may be Affected in Children with Developmental Coordination Disorder

4.1. Introduction

Developmental coordination disorder (DCD) is a condition characterized by marked impairment of motor coordination that significantly interferes with an individual’s academic achievement and/or activities of daily living. Children with DCD experience numerous functional challenges secondary to their motor impairment, including difficulty with dressing, tying shoelaces, handwriting, and playing sports. The motor impairments associated with DCD can be broadly described in three areas: poor postural control, difficulty in motor learning, and poor sensorimotor coordination. Given the cerebellum’s known role in motor control and coordination, researchers have hypothesized that the cerebellum is a possible source of the motor dysfunction associated with DCD.

Several behavioural studies have been conducted that lend support to a cerebellar hypothesis for DCD. These include studies of motor adaptation, postural control, and timing of movements. Findings consistently report that children with DCD are less accurate and more variable in their motor performance compared to control children. Similar to patients with cerebellar degeneration, children with DCD tend to repeat the same movements over and over again, without making corrections to their performance. It is unknown if children with DCD do not correct movements because they are not aware of their poor performance, or if they lack the ability to correct their mistakes.

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3 A version of this chapter has been submitted for publication. Zwicker JG, Missiuna C, Harris, SR, Boyd LA. Formation of an internal model for motor learning may be affected in children with developmental coordination disorder.
Other researchers have hypothesized that parietal dysfunction may be the source of motor impairment in children with DCD. This speculation has largely been based on behavioural studies on motor imagery and mental rotation,\textsuperscript{18-20} but one neuroimaging study has provided evidence for parietal involvement in DCD.\textsuperscript{21} Children with DCD showed under-activation of the posterior parietal cortex compared to controls during the performance of a continuous tracking task. In this work, the DCD group was significantly less accurate in a single session of experimental task practice; however, it remains unclear whether additional practice would have shifted patterns of brain activity. Knowing how a child with DCD learns a motor task, and how this differs from typically-developing (TD) children, is the next critical step in increasing our understanding of this motor learning disorder.

Currently, no neuroimaging studies have been conducted to examine the mechanisms underlying motor learning deficits in children with DCD. Thus, we designed a behavioural and neuroimaging study to investigate whether children with DCD are able to demonstrate improved motor skill as evidenced by increased accuracy on a trail-tracing task and/or shifts in patterns of brain activation. With practice, we expected that children with DCD would demonstrate more accurate tracing of our trail-tracing task, as evidenced by change from early practice to retention. Despite this anticipated improvement, we hypothesized that children with DCD would be significantly less accurate on the tracing task as compared to age-matched, TD children. As cerebellar activation has been related to visual motor tracking performance,\textsuperscript{22-24} we predicted that children with DCD would under-activate the cerebellum during our experimental tracing task. Finally, we hypothesized that children with DCD would show a compensatory pattern of brain activity in the prefrontal and posterior parietal cortices as compared to typical peers. Individuals with cerebellar infarcts have been shown to
recruit these regions to support task performance;\textsuperscript{25} given the cumulative speculation centered on cerebellar involvement in DCD,\textsuperscript{6,7,9,26} we expected that children with DCD would also employ regions in the prefrontal cortex and parietal lobe of brain activity to compensate for decreased activation in the cerebellum.

4.2. Methods and Materials

4.2.1. Participants

Recruiting from local schools, 7 right-handed children with reported motor difficulties (6 boys, 1 girl) met the Diagnostic and Statistical Manual, Fourth Edition – Text Revision (DSM-IV-TR)\textsuperscript{1} criteria for DCD and were included in the study; these were the same children who participated in the study outlined in Chapter Three. To be included, children had to have: scored \( \leq 15^{th} \) percentile on the Movement Assessment Battery for Children – 2\textsuperscript{nd} edition (MABC-2)\textsuperscript{27} and/or within the DCD range on the Developmental Coordination Disorder Questionnaire (DCDQ),\textsuperscript{28} had an estimated intelligence score within the average to above average range on the Kaufman Brief Intelligence Test – 2\textsuperscript{nd} edition (KBIT-2),\textsuperscript{29} and had no diagnosis of attention deficit hyperactivity disorder (ADHD) as per parent report and a score of \( \leq 70 \) on the Conners ADHD DSM-IV Scale (CADS)\textsuperscript{30} (Table 4.1). Children were excluded if the assessing occupational therapist suspected that the child’s motor difficulties were a result of another diagnosis (e.g., cerebral palsy, autism spectrum disorder). Children with DCD ranged in age from 8-12 years (mean 10.8 years, SD 1.5). Seven right-handed, age-matched, TD children (4 boys, 3 girls) formed the comparison group (mean age 10.9 years, SD 1.5).
All participants were screened for safety to undergo MRI (i.e., no metallic objects in their body or history of major psychiatric diagnosis, claustrophobia, epilepsy, or seizures). Parent consent and child assent were obtained prior to and during all aspects of the study. Ethical approval was obtained from the University of British Columbia Clinical Research Ethics Board (Appendix A) and approval for recruitment was obtained from the Vancouver Coastal Health Research Institute and the Vancouver School Board. At the time of consent, children had the opportunity to try the experimental trail-tracing task.

4.2.2. Study Design and Procedure

As an important first step towards understanding whether or not children with DCD are capable of demonstrating motor learning and neuroplastic change, we designed a behavioural and neuroimaging study (blocked design) to measure change in motor performance and functional brain activation in children with and without this disorder. We selected a practice paradigm as an initial step to explore potential motor learning differences with equivalent practice between the two groups of children. To index motor behaviour, we used a trail-tracing task that allowed for collection of accuracy data (e.g., out of bounds of the trace). Motor learning was operationally defined as a reduction in tracing errors associated with practice of the experimental task. We assessed changes in brain activation across two functional magnetic resonance imaging (fMRI) sessions. Early task practice (Day 1) and a retention test (Day 5) took place inside a 3-Tesla Phillips MRI scanner. Three days (Days 2-4) of behavioural practice (tracing outside the scanner) occurred in between the scanning sessions, which were scheduled within two weeks of one another (Appendix C). Brain activity was represented by using fMRI as a summed-weighted threshold of percent signal change. Consideration of alterations in patterns of brain activation in conjunction with
change in the accuracy of tracing behaviour allowed us to assess changes in the brain network associated with practice of a novel motor task.

4.2.3. Behavioural Task Acquisition

During experimental task practice (both inside and outside the scanner), we mapped brain function associated with a fine-motor task adapted from the original Movement Assessment Battery for Children: the flower-shaped trail-tracing task\(^{31}\) (Figure 4.1). For fMRI scanning, participants lay supine with foam padding placed around their head to limit motion and under their knees for comfort. A non-ferrous joystick was placed on the participant’s stomach and fastened securely with Velcro straps. The joystick had a finger-only attachment that was held like a pen in the right hand of each child. The tracing task was displayed using a computer back-projection system linked to fMRI image acquisition. When children were at rest, the flower was red (1 minute before and after tracing). When instructed to “Go”, the flower was outlined in green; participants used the joystick to trace between two lines for 2 minutes for each of four runs (Appendix B). Children were instructed to trace as accurately as possible in a clockwise direction (arrows indicated tracing direction).

For the practice sessions between the fMRI scans, children completed four runs of 2 minutes each of continuous tracing on each of the three days (8 minutes each day, for a total of 24 minutes). Children sat at a table in front of a computer and used the same finger-only joystick attachment to complete the practice sessions.

4.2.4. Behavioural Data Analysis

To assess motor learning, we compared tracing behaviour from the first to the second fMRI session using a repeated measures ANOVA. Using custom Matlab software
(Mathworks, Natick, Massachusetts), tracing data were analyzed for the average number of traces across four runs for each day, the average time per trace, and the average number of times out of bounds (tracing error). To determine the effect of practice on tracing behaviour, we assessed: 1) between group differences at early practice and retention for numbers of traces completed, time per trace, and tracing error; and 2) within group changes from early practice to retention for the same three dependent variables. Our primary outcome of interest was tracing error, with a reduction in error reflecting motor learning. Owing to our small sample size, we also calculated effect sizes (ES) to assess the impact of practice of our tracing task.\textsuperscript{32} We interpreted an effect size of 0.2 - 0.5 as a small effect and 0.5 - 0.8 as a moderate effect.\textsuperscript{33}

4.2.5. fMRI Data Acquisition

Brain activity was mapped with a 3.0 Tesla (3T) MRI scanner during fine motor-task performance. To time-lock motor responses, presentation of stimuli was controlled with computer software that linked stimuli presentation with image acquisition. The visual stimulus was presented by a back-projection system. A Philips 3T Achieva with Dual Quasar gradients MRI scanner equipped with a three-axis, local-gradient radio frequency coil was used to collect whole brain fMRI (36 axial, 3 mm with 1-mm skip slices). Functional imaging data were collected as echo-planar images, using a single-shot, blipped, gradient-echo, echo-planar pulse sequence (TE = 30 ms, TR = 2.0 s, 90° flip angle, FOV = 240 mm, 64 X 64). Four, 4-minute runs of functional data were collected (120 volumes each). Each run contained two periods of rest (30 volumes each) that bracketed one period of trail-tracing (60 volumes) (Appendix B). After the functional imaging, high-resolution 3D T1 anatomical
images were collected for anatomic localization and co-registration (TE = 5 ms, TR = 24 ms, 40° flip angle, NEX = 1, thickness = 1.2 mm, FOV = 256 mm, 256 X 256).

4.2.6. fMRI Data Analysis

Analysis of Functional NeuroImages (AFNI) software (NIMH, Bethesda, Maryland)\textsuperscript{34} was used for fMRI data processing. Functional images were generated by condition (rest, trace). All functional images were spatially registered to correct for head motion. Runs with excessive head motion (8/111) were removed from analysis; average head motion across groups for remaining analyses was 5.8 mm. Anatomic images were registered in Talairach space\textsuperscript{35} and then co-registered with functional images. An 8-mm, full-width-half-maximum Gaussian kernel was used to spatially smooth functional data. Hemodynamic responses were modeled as a box-car function, producing estimates of the BOLD response relative to baseline. The dependent variable, percent signal change, was calculated from rest to respond (trace) conditions. Whole-brain patterns of activity were analyzed using a 2 x 2 (Group [DCD, TD] x Time [early practice, retention test]) ANOVA corrected for multiple comparisons (minimum voxel volume threshold of 200 microlitres and 1.8 mm connectivity radius) at a \textit{p} value < 0.01. Activation foci were delineated using the Talairach atlas for the cerebral cortex\textsuperscript{35} and the Schmahmann atlas for the cerebellum.\textsuperscript{36} We extracted percent signal change values from regions that were significantly different between the two groups.

4.3. Results

4.3.1. Behavioural Results

Behavioural results are summarized in Table 4.2 and Figure 4.2 (Day 1 data are the same as reported in Chapter Three). Repeated measures ANOVA indicated that there were no
significant differences between groups in the number of traces completed [time x group, \( F(1, 12) = 1.185, p = 0.298 \)], time per trace [time x group, \( F(1, 12) = 1.591, p = 0.231 \)], or tracing error [time x group, \( F(1, 12) = 0.019, p = 0.894 \)]. However, ES testing revealed small to moderate effects within and between groups. Contrary to our hypothesis, children with DCD showed essentially no change in tracing error from early practice to retention test (weak ES, \( d = 0.09 \)); in contrast, TD children demonstrated less tracing error with practice (small ES, \( d = -0.31 \)). We predicted that children with DCD would be less accurate than TD children, which was more apparent at retention (approaching moderate ES, \( d = 0.48 \)) than at early practice (weak ES, \( d = 0.14 \)). With practice, children with DCD took less time per trace (moderate ES, \( d = -0.54 \)), allowing them to complete more traces (approaching moderate ES, \( d = 0.48 \)).

4.3.2. fMRI Results

A 2 x 2 ANOVA revealed a significant interaction between Group [DCD, TD] and Time [early practice, retention test], \( F = 13.58, p < 0.01 \), corrected. Table 4.3 summarizes the Talairach coordinates for the nine brain regions that showed significant activation, which are represented in Figure 4.3. Figure 4.4 illustrates the percent signal change between rest and respond conditions for each brain region. Compared to children with DCD, TD children showed higher change in percent signal change from early practice to retention in the right inferior parietal lobule (Brodmann Area (BA) 40), right middle occipital and right temporal gyrus (BA 37), left thalamus, left cerebellar lobule VI, right middle frontal gyrus (BA 46), left middle and inferior frontal gyrus (BA 46), and left and right posterior cingulate gyrus (BA 31). From early practice to retention, children with DCD demonstrated higher percent
signal change as compared to TD children in the claustrum/putamen. Activation in the left middle and inferior temporal gyri (BA 20) was also significant, but difficult to interpret.

Our results partially support our hypothesis. Relative to TD peers, the DCD group showed under-activation of the cerebellum at retention; however, children with DCD did not demonstrate a compensatory pattern of over-activity in the prefrontal or posterior parietal cortices as was predicted.

4.4. Discussion

Our results reveal that children with DCD showed essentially no change in tracing accuracy with the amount of practice delivered in the current study. Though not statistically significant, TD children demonstrated improvement in tracing accuracy, resulting in a difference between the two groups in tracing error that approached a medium effect size. The DCD group increased their tracing speed with practice, which may have contributed to their decreased accuracy on the trail-tracing task.37

Differences in task performance between children with DCD and TD children may also be explained by significant differences in brain activation patterns between the two groups. Overall, children with DCD showed less BOLD signal than the TD group. Specifically, differences were noted in a broad network of regions associated with motor learning and performance, including the right inferior parietal lobule (BA 40), bilateral dorsal prefrontal cortex (DLPFC: BA 46), right middle occipitotemporal area (BA 37), lobule VI of the cerebellum, bilateral posterior cingulate, and left thalamus (Figures 4.3 and 4.4). We will first discuss our findings in light of our hypotheses and for each brain region separately; then we will offer our interpretation of our results from a more integrated, brain network perspective.
Consistent with our hypothesis, we found that children with DCD showed very little change in cerebellar activation with practice, whereas TD children demonstrated increased activation in lobule VI from early practice to retention. Activation of lobule VI has been associated with improved performance on a variety of tasks, including serial reaction time tasks,\textsuperscript{38} motor sequence learning,\textsuperscript{39} reaching tasks,\textsuperscript{40} and planned, discretely aimed arm movements.\textsuperscript{41} Further support for the importance of cerebellar cortex activity during motor learning comes from data showing a strong association between activity in lobules V/VI and the magnitude of motor correction during visuomotor learning.\textsuperscript{42}

Contrary to what we expected, children with DCD did not show a compensatory pattern of over-activity in the prefrontal and parietal regions. We will first discuss the prefrontal activations noted in our study. fMRI results in the DCD group revealed decreased activation from early practice to retention in both the left and right DLPFC. In contrast, the TD group demonstrated a significant increase in percent signal change in these regions over the same time. Activation of the DLPFC has been associated with the initial stages of explicit motor learning,\textsuperscript{43} specifically for motor\textsuperscript{44-46} and visuomotor\textsuperscript{47} sequences. While our task was not a sequencing task per se, it could be conceptualized as a sequence of motor movements, as the children were required to repeatedly trace the identical flower shape over days of practice.

The DLPFC has also been linked to attentional control,\textsuperscript{48,49} with hypoactivity in the DLPFC being associated with ADHD.\textsuperscript{50,51} While our inclusion criteria precluded inclusion of children with this commonly comorbid diagnosis, the DCD group had significantly more attentional symptoms endorsed by their parents on the CADS compared to the peer control group, ($t (12) = 2.66, p = 0.02$). This finding is consistent with other studies indicating that
children with DCD have more attentional problems than their peers. While we cannot parse out the specific influence of the DLPFC on the performance of our task (e.g., attention, motor learning, or both), Querne et al. suggest that children with DCD may have dysfunction in the attentional brain network, as evidenced by less prefrontal activity compared to controls during a go/no-go task. Taken together, the lower levels of BOLD signal in DLPFC in the present study and past work and higher scores on the CADS, suggest that poorer attentional capability may be a factor that impacts motor learning in children with DCD. Though standardized attentional testing such as the CADS did not reveal clinically significant levels of deficits in attention in our sample of children with DCD, attention is still critical for motor learning and even mild to moderate impairments may impact learning efficacy.

Activation of the right DLPFC, along with the inferior parietal lobule, has been linked to spatial working memory. In addition to lower activation in the DLPFC, the DCD group demonstrated little change in activation of the right inferior parietal lobule over time, whereas the TD group demonstrated a significant increase in activation in these regions from early practice to retention. These results suggest that spatial working memory may support learning of our trail-tracing task. A more significant factor related to greater activation in the inferior parietal lobule is this region’s role in the integration of sensory information and processing of visual feedback. Sensory feedback has been shown to play an important role in learning new motor skills. Other researchers have found parietal under-activation in children with DCD during performance of a visuomotor task and suggest that the dysfunction in motor control may be related to poor proprioceptive input.

Children with DCD also showed little change or lower activation from early practice to retention in the right middle occipitotemporal area (BA 37), left and right posterior
cingulate, and left thalamus. By contrast, the TD group shifted from negative or low BOLD signal at early practice to large positive activations at the retention test in these brain regions. These areas have been linked to visual awareness, spatial attention and sensorimotor integration respectively. While we did not predict differences between groups in these regions, it is reasonable to speculate that the learning of our trail-tracing task may be supported by increased visual-spatial attention and greater sensorimotor integration.

There was only one brain area where the DCD group showed increased activation compared to TD peers from early practice to the retention test: the claustrum/putamen. Activity in the putamen has been associated with well-learned motor movements that come in the later stages of motor learning, which is inconsistent with our findings. Neither group improved to the point of errorless or near perfect performance. While this may be related to the difficulty of the task, we surmise that both groups were still in an early learning phase. Support for this hypothesis is the increased activity in the cerebellum in the TD group; cerebellar activations have been observed at the beginning of the acquisition process but become undetectable when the task has been well learned. Activation in the cerebellum was noted in both groups at retention. A more likely explanation for increased activation of the putamen in the DCD group may be the putamen’s involvement in motor planning. Greater activation in the putamen suggests that children with DCD may be actively developing a motor plan; however, at the time of the retention test, this new plan for movement did not translate to improved performance. There may be several reasons for this: the motor plan may have been deficient (based on poor sensorimotor information, with reduced activation in this cerebello-thalamo-cortical network) or the motor plan may not have been executed as intended (as evidenced by little change in cerebellar activation with
practice). Activation of the striatum has also been linked to the early acquisition phase of motor sequence learning, when there may be greater reliance on the use of cognitive strategies and working memory. Greater activation of the putamen in children with DCD suggests that these children may be trying to rely more on the cognitive control of movement than their TD counterparts. If this were the case, we would anticipate greater activation in the DLPFC to support working memory demands. We found the opposite effect, with decreased activation in bilateral DLPFC with practice. It is possible that children with DCD may be attempting to use a cognitive strategy to support motor performance, but this compensatory strategy is ineffective because they cannot invoke the DLPFC. Further investigation is needed to confirm this speculation.

The last brain area where we found a significant interaction between groups and across time is the left middle and inferior temporal gyri (BA 20). While this area has been associated with visual recognition and learning, the pattern of activation we observed is difficult to interpret. The TD group went from positive activation at early practice to a negative BOLD signal at retention, whereas the DCD group showed a less negative BOLD response with practice. We hesitate to speculate on the meaning of this finding.

Taken together, our results suggest that children with DCD may have a deficit in forming an internal model of movement. Successful motor control is thought to result from an internal model that accurately predicts the sensory consequences of motor command. The cerebellum has been proposed as a key structure to forming an internal model; support for this hypothesis has been derived from neurophysiology, imaging, and patient studies. Theoretical models of motor learning posit that the cerebellum receives an efference copy of the motor command and compares the predicted movement with the
actual movement; if there is a mismatch, the cerebellum sends an error signal as feedback to create a more accurate movement the next time.\textsuperscript{78} Given the under-activity in the cerebellum of children with DCD in this study, we hypothesize that they may have difficulty in updating, and thus forming, the internal model. This hypothesis is consistent with our results and with the clinical presentation of children with DCD; they appear to benefit little from practice,\textsuperscript{17} perhaps because the error signal is not being generated or correctly interpreted.

Other researchers have proposed an internal modeling deficit in children with DCD.\textsuperscript{10,11,18-20} Using a visuomotor adaptation paradigm, Kagerer et al.\textsuperscript{10,11} surmised that the deficit in motor learning in children with DCD was related to cerebellar dysfunction, given the cerebellum’s role in providing the error signal in response to visuomotor distortion to update the internal model. Wilson et al.\textsuperscript{19,20} hypothesized that deficient formation of the internal model was related to parietal lobe involvement. They based this hypothesis from their studies using a mental rotation paradigm; children with DCD demonstrated similar deficits in motor imagery to patients with lesions in the posterior parietal cortex.\textsuperscript{88} Our results lend support for both of these hypotheses; children with DCD demonstrated decreased activation in both the cerebellum and parietal regions, albeit in the inferior parietal lobule, not the posterior parietal cortex. Although Kashiwagi et al.\textsuperscript{21} highlighted parietal dysfunction in DCD, they dismissed the role of the cerebellum. Given that the inferior parietal lobule receives projections from the cerebellum,\textsuperscript{57} it is likely that both of these regions are implicated in the presentation of DCD.

Our results are supported by neuroimaging studies conducted by Allen et al.,\textsuperscript{89} who confirmed through magnetic resonance imaging that the cerebellum is connected to the inferior parietal lobule and DLPFC. Under-activation of all these areas in children with DCD
suggests that the cerebello-cortical loop is affected in this disorder. We cannot determine from our study if it is the afferent (cerebello-thalamo-cortical pathway) or efferent (cortico-ponto-cerebellar pathway) part of the loop that is implicated; we suspect the former given the under-activation of the thalamus, but diffusion tensor imaging would be necessary to confirm this hypothesis.

In summary, our results suggest that children with DCD may be deficient in updating an internal model of movement through under-activation of the cerebellum and/or the cerebello-thalamo-cortical pathway involving the thalamus, inferior parietal lobule, and DLPFC. To compensate for decreased cerebellar activation, children with DCD may be using the cortico-striatal network to support their motor performance.

Results of our study provide an important contribution to our understanding of DCD, but they are not without limitations. The small sample size limits generalizability of the results, but provides data to calculate sample sizes for future fMRI studies of children with DCD. We allowed more head motion than what is considered ideal, as we did not want to lose participants from our small sample. Although motion can affect interpretation of fMRI results, our areas of significant brain activation are consistent with previous literature given the nature of the task. Our experimental trail-tracing task may have been too difficult or the practice dose too short to achieve error-free performance and reach later stages of motor learning. Greater practice time may have yielded more robust findings and a greater likelihood of detecting differences between the DCD and TD groups. Although we had children complete tracing practice in sitting to allow data collection in community settings for family convenience, our design could have been improved by completing practice sessions in supine-lying; this may have promoted greater transfer from practice to post-test
for children with DCD. Despite these potential weaknesses, the study design allowed us to capture differences in motor learning and brain activation between the two groups under equivalent practice conditions.

4.5. Conclusion

To our knowledge, this study is the first to examine patterns of brain activation in children with DCD while learning a trail-tracing task. Consistent with their clinical presentation, children with DCD did not show an improvement in motor accuracy with equivalent practice to TD children. Our results indicate that differences in brain activation may be related to differences in motor learning. Compared to TD peers, the DCD group demonstrated under-activation in the cerebellum and in brain areas associated with the cerebello-thalamo-cortical network. We hypothesize that children with DCD have a deficit in updating internal models of movement, and that they may use the cortico-striatal network to support their motor performance. Further neuroimaging studies linking motor performance and brain activation in this population are needed to better understand the neurobiology of the disorder and should include diffusion tensor imaging to assess the integrity of neural networks in children with DCD.
Table 4.1. Demographic and clinical characteristics of children with developmental coordination disorder (DCD) and typically-developing (TD) comparison children

<table>
<thead>
<tr>
<th></th>
<th>DCD</th>
<th>TD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>10.8</td>
<td>10.9</td>
</tr>
<tr>
<td>MABC-2 (percentile)</td>
<td>6.9**</td>
<td>48.29**</td>
</tr>
<tr>
<td>DCDQ</td>
<td>36.0**</td>
<td>65.86**</td>
</tr>
<tr>
<td>KBIT-2</td>
<td>112.6</td>
<td>106.71</td>
</tr>
<tr>
<td>CADS</td>
<td>57.6*</td>
<td>47.86*</td>
</tr>
</tbody>
</table>

* p < 0.05    **p < 0.001

CADS, Conners ADHD DSM-IV Scale; DCD, developmental coordination disorder; DCDQ, Developmental Coordination Disorder Questionnaire; KBIT-2, Kaufman Brief Intelligence Test-2; MABC-2, Movement Assessment Battery for Children -2; TD, typically-developing children.
Table 4.2. Means, standard deviations, and effect sizes for behavioural task comparisons

<table>
<thead>
<tr>
<th></th>
<th>Early Practice Mean (SD)</th>
<th>Retention Mean (SD)</th>
<th>Within Group Effect</th>
<th>Between Group Effect DCD - TD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DCD</td>
<td>TD</td>
<td>Retention - Early Practice</td>
<td>Early Retention Practice</td>
</tr>
<tr>
<td>Number of Traces</td>
<td>5.54 (2.07)</td>
<td>6.44 (2.06)</td>
<td>0.47&lt;sup&gt;a&lt;/sup&gt;</td>
<td>-0.20&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>6.51 (2.02)</td>
<td>6.07 (1.79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time Per Trace [sec]</td>
<td>22.84 (10.58)</td>
<td>19.14 (6.23)</td>
<td>-0.54&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>18.36 (5.17)</td>
<td>19.41 (5.34)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tracing Error</td>
<td>196.92 (138.35)</td>
<td>178.67 (116.65)</td>
<td>0.09</td>
<td>-0.31&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>211.13 (169.25)</td>
<td>148.58 (76.54)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> small effect size  <sup>b</sup> moderate effect size

DCD, developmental coordination disorder; TD, typically-developing children
Table 4.3. Coordinates for significant activation Group x Time ANOVA
(corrected, \( p < 0.01 \))

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>BA</th>
<th>Volume</th>
<th>Talairach coordinates (peak activation)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(µl)</td>
<td>( x )</td>
</tr>
<tr>
<td>R inferior parietal lobule</td>
<td>40</td>
<td>3034</td>
<td>-41</td>
</tr>
<tr>
<td>L claustrum and putamen</td>
<td>1409</td>
<td>26</td>
<td>-6</td>
</tr>
<tr>
<td>R middle occipital and middle temporal gyrus</td>
<td>37</td>
<td>1365</td>
<td>-42</td>
</tr>
<tr>
<td>R middle frontal gyrus</td>
<td>46</td>
<td>841</td>
<td>-43</td>
</tr>
<tr>
<td>L posterior cingulate gyrus</td>
<td>31</td>
<td>549</td>
<td>-3</td>
</tr>
<tr>
<td>L middle and inferior temporal gyrus</td>
<td>20</td>
<td>336</td>
<td>48</td>
</tr>
<tr>
<td>L middle and inferior frontal gyrus</td>
<td>46</td>
<td>264</td>
<td>40</td>
</tr>
<tr>
<td>L thalamus</td>
<td>239</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>L cerebellar lobule VI</td>
<td>229</td>
<td>16</td>
<td>75</td>
</tr>
</tbody>
</table>


Figure 4.1. Flower-shaped trail-tracing task
Figure 4.2. Behavioural data from early practice to retention

A represents the number of traces, B displays average time per trace, and C demonstrates tracing error.

DCD, developmental coordination disorder; TD, typically-developing
Figure 4.3. Significant activations from Group [DCD, TD] x Time [baseline, retention] ANOVA (corrected, $p < 0.01$)
Figure 4.4. Significant activations from Group [DCD, TD] x Time
[baseline, retention] ANOVA (corrected, $p < 0.01$)
4.6. References


87. Smith MA, Shadmehr R. Intact ability to learn internal models of arm dynamics in Huntington’s disease but not cerebellar degeneration. *J Neurophysiol*. 2005;93:2809-2821.


Chapter Five: Discussion and Future Direction

5.1. Overview

This thesis explored several questions related to the neurobiology of developmental coordination disorder (DCD) and the patterns of brain activation related to motor performance and motor learning in children with this disorder. First, I conducted a comprehensive review of the literature to examine the hypothesized neural correlates of DCD. Then, I conducted a behavioural and neuroimaging study to explore differences in motor behaviour and brain activation patterns of children with and without DCD, before and after practice on a trail-tracing task. This design allowed me to compare the differences between motor performance and motor learning in children with DCD. In this chapter, I will first review the main research findings of the thesis and highlight how these findings contribute to theory and evidence related to what is known or suspected in children with DCD. I will then discuss the strengths and limitations of the work, suggest directions for future research, and share some final thoughts.

5.2. Support for a Cerebellar Hypothesis for Developmental Coordination Disorder

Findings from Chapter Two suggest that, although there are likely several neural correlates of DCD, the cerebellum is a probable source of the dysfunction associated with this disorder.\(^1\) Support for this hypothesis comes largely from behavioural studies\(^2-4\) and research on common co-morbid disorders.\(^5-8\) Neuroimaging evidence from this thesis lends support to the cerebellar hypothesis for DCD. Results from Chapter Three indicated that there were no significant differences in cerebellar activation between children with DCD and typically-developing (TD) children during performance of a fine-motor task. While this
finding is contrary to what we hypothesized, it is consistent with our behavioural data, i.e., there were no significant differences in tracing accuracy between the two groups. However, differences emerged with a shift from motor performance (first attempts at the task) to motor learning (after practice). In Chapter Four, significant differences between groups were noted in cerebellar activation, with the DCD group showing little change in activation from early practice to retention and the TD group showing increased blood oxygen level-dependent (BOLD) response in the cerebellum at retention. Relative to TD peers, the DCD group demonstrated under-activation of the cerebellum. These findings are consistent with our behavioural data, in that children with DCD showed essentially no change in tracing accuracy with practice, and their tracing accuracy at retention was poorer than that of TD children.

Support for a cerebellar hypothesis for DCD comes from the finding that these children may have a deficit in updating internal models of movement.\(^3,4,9-11\) This hypothesis will be further discussed in Section 5.4, but is mentioned here to highlight indirect evidence for cerebellar involvement in DCD. The cerebellum has been proposed as a structure that is key to forming internal models of movement:\(^12,13\) neurophysiological,\(^14,15\) imaging,\(^16\) and clinical studies\(^17-21\) support this assertion. Behavioural and neuroimaging results from Chapter Four contribute to this body of literature and lend support for cerebellar involvement in the updating of internal models of movement. This thesis has integrated evidence from motor learning and neuroscience with findings from DCD clinical research, thus providing converging evidence to support a cerebellar hypothesis for DCD.
5.3. Children with Developmental Coordination Disorder Activate Different Brain Regions than Typically-developing Children to Support Motor Performance

Results from Chapter Three indicated that, despite similar motor performance, children with DCD employed a very different network of brain regions than TD children when completing the same fine-motor task. This finding is clinically important, as similar results have been reported in individuals with Parkinson disease (PD). Dagher et al.\textsuperscript{22} found that people with mild PD performed similarly to controls on a Tower of London task, but that they activated a completely different neural network to complete this motor and planning task. It is hypothesized that individuals with mild PD are recruiting a compensatory network to overcome deficits in the basal ganglia, the primary source of dysfunction in PD. This same hypothesis may be true for children with DCD; they may be activating a different network to compensate for decreased cerebellar function. If children with DCD are using brain areas not typically associated with motor planning or motor learning to support their motor performance, these brain regions may not be available for other motor or cognitive operations.\textsuperscript{23} This may partially explain why children with DCD have difficulty under dual-task conditions\textsuperscript{24} and will be further discussed in Section 5.5.

Findings from Chapter Three showed that children with DCD activated eight brain regions that were significantly different than those activated by TD peers and represented twice as many brain regions as those recruited by the TD group. Because the amount of effort required for task performance can be inferred from the amount of brain activation,\textsuperscript{25} this finding implies that the children with DCD had to direct more effort to achieve motor performance similar to their peers. This study provides the first neuroimaging evidence to support the clinical observation that children with DCD seem to exert great effort and
experience fatigue with motor-based activities.\textsuperscript{26,27} To date, fatigue in children with DCD has been attributed to physical fatigue, such as the fatigue resulting from fixing joints to reduce degrees of freedom.\textsuperscript{28,29} This thesis contributes evidence to suggest that children with DCD may also experience cognitive fatigue, related to the effort in planning, executing, and learning of movement.

Evidence from this thesis and recent work of others\textsuperscript{30,31} indicate that children with DCD exhibit differences in neural networks and patterns of brain activation relative to same-age peers. This is the first experimental evidence to indicate potential sources of neuropathology underlying DCD. These studies will set the groundwork for future neuroimaging studies, which will further contribute to our understanding of DCD.

\section*{5.4. Children with Developmental Coordination Disorder May Have Difficulty Forming an Internal Model for Motor Learning}

As discussed in Chapter One, several authors have hypothesized that an internal modeling deficit may account for the motor learning challenges experienced by children with DCD.\textsuperscript{3,4,9-11} Chapter Four provided the first neuroimaging evidence that this, indeed, may be the case. Relative to TD peers at the retention test, children with DCD demonstrated under-activation in the cerebellum and in regions connected by the cerebello-thalamo-cortical pathway [thalamus, inferior parietal lobule, and dorsolateral prefrontal cortex (DLPFC)].\textsuperscript{32} The children with DCD were also less accurate than TD children on the trail-tracing task, showing little change from early practice to retention. Taken together, these results are consistent with the theoretical models demonstrating failures of the internal model for motor learning.\textsuperscript{14} Two types of internal models have been proposed to exist in the cerebellum; forward internal models predict the sensory consequences of movement from efference copies
of issued motor commands, whereas inverse internal models calculate necessary feed-forward motor commands to alter motor output.\textsuperscript{14} While results of this study (Chapter Four) cannot distinguish which internal model may be implicated, other DCD researchers have surmised that children with DCD have poor feed-forward control,\textsuperscript{11,33} thus, suggesting dysfunction in the forward model component. In the forward internal model, the cerebellum is thought to receive an efference copy of the motor command and then compare the predicted movement with the actual movement; if there is a mismatch, the cerebellum sends an error signal as feedback to create a more accurate movement on subsequent occasions.\textsuperscript{14} It is not clear from the results in Chapter Four if children with DCD are able to generate this error signal, or if the signal is based on faulty or deficient information. Lower activation in several regions linked in the cerebello-thalamo-cortical pathway in children with DCD suggests that afferent input to the cerebellum may be affected. Alternatively, evidence from motor adaptation studies reviewed in Chapter Two suggests that children with DCD are able to generate an error signal, but only under conditions of abrupt (and not gradual) visual distortion.\textsuperscript{2-4}

Under-activation of the cerebellum, combined with the finding that children with DCD showed no learning of the experimental motor task, suggests that the internal modeling deficit likely explains the motor learning difficulties noted in children with DCD. Additional neuroimaging studies with larger sample sizes and longer task practice are needed to confirm this hypothesis. Such future studies would contribute not only to our understanding of DCD, but also will provide more evidence regarding the theory of internal models of movement. Neuroscientists may discover that children with DCD are an appropriate population within which to study this neurocognitive view of motor learning.
5.5. Thesis Findings Contribute to Alternative Hypotheses of Developmental Coordination Disorder

As described in Chapter One, the automatization deficit hypothesis should also be considered as a possible mechanism underlying DCD. This hypothesis has been tested primarily using a dual-task paradigm. Findings from these studies suggest that children with DCD have difficulty performing a task when a second task makes use of the same “pool” of cognitive or motor resources. While the study in Chapter Four was not designed to test the automatization deficit hypothesis, findings from this study seem to both support and refute this hypothesis. For example, authors have speculated that the cerebellum is a likely source of this automatization deficit. Given the known role of the cerebellum for movement automaticity, under-activation of the cerebellum in children with DCD relative to TD peers lends support for this hypothesis.

Contrary to the automatization deficit hypothesis are other fMRI results from Chapter 4. Compared with TD peers at retention, children with DCD showed significantly greater activation in the putamen and significantly lower activation in the DLPFC; this pattern of activation has been associated with later stages of motor learning and movement automaticity in healthy young adults. It is unclear why this pattern of activation emerged in the children with DCD. Clearly, these children had not automatized their movement, as they showed essentially no change in tracing accuracy with practice. Discrepancies between our results and previous work may be related to task differences or ages of the participants. Alternatively, the pattern of greater activation in the putamen and lower activation in the DLPFC in children with DCD may not be related to automaticity, but to two other reasons for these activations. Each of these will be discussed in turn.
Activation in the putamen has been linked to motor planning.\textsuperscript{44} Greater activation of the putamen in the DCD group (Chapter Four) suggests that these children may be able to form a motor plan, but not be able to execute it. This suspected intact ability of children with DCD to form a motor plan is also evident in greater activation of the posterior parietal cortex (BA 7) during early practice (Chapter Three); this brain region has been associated with motor planning and movement.\textsuperscript{45} These fMRI results, in combination with under-activation of the cerebellum, suggest that children with DCD may be able to form a motor plan, but the plan may be deficient or not executed as intended.\textsuperscript{42} These results are consistent with the observation that children with DCD have difficulty with movement execution.\textsuperscript{46}

Lower activation of the DLPFC in the DCD group as compared to the TD group (Chapter Four) could also be related to attentional differences between groups. Relative to the TD group, the children with DCD in our sample had significantly more parent-reported symptoms of ADHD, despite none of the children having this diagnosis. Hypoactivity in the DLPFC has been associated with ADHD,\textsuperscript{47-49} which is consistent with significantly lower activation in the DLPFC in the DCD group compared to TD children. Thus, attentional differences, and not a later stage of motor learning, may account for lower activation of the DLPFC in children with DCD.

Results of this thesis research cannot provide direct support for the automatization deficit hypothesis, but findings suggest that this hypothesis warrants further investigation. Neuroimaging may be helpful in future studies designed to test the automatization deficit hypothesis by comparing performance and brain activation patterns of children with DCD under single-task and dual-task conditions.
An alternative hypothesis that has not been explored in the DCD literature is a possible deficit in the default-mode network of the brain. The study in Chapter Three showed that lower activation of the posterior cingulate gyrus was positively correlated with the number of traces completed by the TD children, suggesting that this brain region may be important in the motor performance of our experimental task. This same relationship was not observed for children with DCD. The posterior cingulate gyrus is one of several regions that form the default-mode network, which also includes the superior frontal gyrus, parietal regions (retrosplenial and lateral parietal areas and angular gyrus), regions of the temporal lobe, and the parahippocampal gyrus.\textsuperscript{50} While the precise function of the default-mode network is unknown,\textsuperscript{50} this network has been shown to be active at rest, with deactivation associated with engagement in attention-demanding tasks.\textsuperscript{51,52} Interestingly, children with DCD showed the opposite pattern of activation in regions linked in this network; the DCD group showed significantly greater activation than TD peers in the supramarginal gyrus, posterior cingulate gyrus, parahippocampal gyrus, and superior frontal gyrus (Chapter Three). While speculative, this finding suggests that motor performance of children with DCD may be related to dysfunction in the default-mode network of the brain. Future studies will need to test this hypothesis.

5.6. Thesis Findings Contribute Behavioural and fMRI Evidence for Prevailing Thoughts about Motor Learning and Response Inhibition in Children with Developmental Coordination Disorder

Past research has shown that children with DCD rely heavily on visual feedback to guide task performance during early learning stages,\textsuperscript{53-55} and that this reliance on vision is observed well beyond the age at which TD children rely on vision to control movement.\textsuperscript{53,56,57}
The neuroimaging results presented in Chapter Three further suggest that children with DCD tend to use visual and spatial processing to support their motor performance; when performing the experimental trail-tracing task, children with DCD showed greater activation than TD peers in brain areas associated with visual-spatial attention and memory, including the supramarginal gyrus, superior parietal lobule, posterior cingulate gyrus, lingual gyrus, and parahippocampal gyrus.\textsuperscript{58-63}

As mentioned in Chapter Four, our experimental trail-tracing task may have been too difficult or the practice dose too short to achieve error-free performance and reach later stages of motor learning for both the DCD and TD groups. Neither group improved to the point of errorless or near perfect performance and both groups showed activation of the cerebellum at retention (Chapter Four). Cerebellar activations have been observed at the beginning of the acquisition process\textsuperscript{64,65} but become undetectable when the task has been well learned.\textsuperscript{42,66,67} As such, our study cannot distinguish differences between groups in terms of early versus late motor learning; however, the DCD group showed essentially no change in motor behaviour or cerebellar activation with practice. These results, combined with greater reliance on visual-spatial processing, provide further support for the suggestion that children with DCD remain in the early stages of motor learning far longer than their peers.\textsuperscript{53}

Greater activation of the DLPFC in the DCD group relative to the TD group during early practice (Chapter Three) suggests that the DCD group may have been more reliant on cognitive strategies to support motor performance, another indication of early motor learning.\textsuperscript{58} Greater activation of the DLPFC was significantly related to slower motor performance in the DCD group. A myriad of studies have shown that children with DCD perform slower than their peers,\textsuperscript{68-74} and this study provides neuroimaging evidence as a
possible reason for this consistent finding. Interestingly, children with DCD showed faster tracing speeds than TD children at retention. This may be related to lower activation of the DLPFC in the DCD group from early practice to retention (Chapter Four). Taken together, these results suggest that the DLPFC has a role in the speed of movement of children with DCD, but not in the accuracy of their motor performance. This suggestion is consistent with neuropsychological findings that showed response inhibition in children with DCD was related to speed of movement, and not to decreased accuracy. Although this finding was attributed to the cerebellum, neuroimaging evidence presented here suggests that the DLPFC may also be involved. In the Piek et al. study, children with DCD performed more poorly than control children on the Trailmaking/Memory Updating task, a task that is thought to measure working memory and behavioural inhibition, both of which have been linked to the DLPFC.

Decreased activation in the DLPFC may also explain the observation that children with DCD make more failure-to-inhibit errors than typical children. However, Mandich et al. did not control for potential co-morbid ADHD in the children with DCD in their sample, which may also account for the inhibition deficits observed. Because poor inhibition and hypoactivity in the DLPFC have been associated with ADHD, the influence of attentional difficulties in our study and Mandich et al.’s work cannot be overlooked.

5.7. Implications for the Treatment of Children with Developmental Coordination Disorder

Although this thesis was not designed to evaluate intervention for children with DCD, our findings may influence how we think about interventions for children for DCD and provide direction for future study. For example, children with DCD did not show any
improvement in tracing accuracy, whereas the TD group showed improved tracing accuracy with the equivalent amount of practice. Because both groups still had a large number of errors at the retention test, more practice was needed to better assess differences in motor learning. In our study, no verbal feedback or cognitive strategies were given to support motor behaviour; given current motor learning theory\textsuperscript{83} and intervention approaches for DCD,\textsuperscript{84-87} the next logical step is to assess whether feedback and/or strategy use influence motor learning and patterns of brain activation in children with DCD.

Currently, it is not known how much practice is required to induce a change in motor behaviour in children with DCD. While this study (Chapter Four) did not address this question, the practice schedule was insufficient to create change for children with DCD, but was adequate for the TD group to show increases in tracing accuracy. This implies, at the very least, that children with DCD may need more practice than TD peers to improve motor performance. As noted in Chapter One, the amount of repetition and intensity of training are critical in order to induce neuroplasticity.\textsuperscript{88}

Several reviews of treatment approaches for DCD have been conducted, with current evidence favouring task-specific over deficit-oriented interventions.\textsuperscript{89-92} Treatments aimed at reducing the motor impairment underlying DCD have been rejected,\textsuperscript{90,92,93} as they were based on outdated neuromaturational and hierarchical theories\textsuperscript{91,92} and produced either little benefit or inconclusive results.\textsuperscript{90,91,94} Results from Chapter Four, and work from others,\textsuperscript{3,4,9-11} suggest that children with DCD may have difficulty in forming and updating internal models of movement, which is a more recent understanding of neural mechanisms of motor learning. Future work could investigate whether task-specific interventions and the use of cognitive
strategies result in updating of internal models of movement and neuroplastic change in children with DCD.

5.8. Strengths and Limitations of the Studies

The studies contained within this thesis represent unique and novel contributions to our understanding of DCD. Chapter Three is one of only two studies\textsuperscript{31} to explore brain activation and motor performance in children with DCD. The study presented in Chapter Four is the first of its kind, as no other study has examined patterns of brain activation associated with motor learning in children with and without DCD. Both of these studies, together with recent work of others,\textsuperscript{30,31} provide the first lines of evidence to show that children with DCD are neurobiologically different from their TD peers.

In selecting participants with DCD, every effort was made to include children who met the diagnostic criteria for the disorder.\textsuperscript{95} With this goal in mind, we included measurement of motor impairment, confirmation that the motor coordination difficulties interfered with activities of daily living and/or school performance, and an estimate of intelligence. Participants were also screened for co-morbid ADHD, something that is often neglected in studies of children with DCD.\textsuperscript{96} As per the Leeds Consensus,\textsuperscript{97} selection criteria could have been stricter by including only children who scored at or below the 5\textsuperscript{th} percentile on the MABC-2. Given the exploratory nature of these thesis studies, the broader criterion of below the 16\textsuperscript{th} percentile was set, which is in keeping with inclusion criteria used in most other studies of DCD.\textsuperscript{96}

Small sample sizes limit the generalizability of findings across the two studies (Chapters Three and Four) and might have prevented detection of significant differences in motor behaviour between the DCD and TD groups. Despite the small sample, significant
differences between groups ($p < 0.01$) in patterns of brain activation were noted at both early practice (Chapter 3) and retention (Chapter 4). A replication study with a larger sample size would increase confidence in these results. These studies provide data for sample size calculations for such future work.

As indicated in Chapter Four, the duration of tracing practice was too short for children to achieve few tracing errors, an indication of a later stage of motor learning. A greater practice dose may have induced stronger motor learning effects and helped to better highlight differences in motor learning between the DCD and TD groups. The trail-tracing task may also have been too difficult to master with the amount of practice provided. This choice of task, however, offered more ecological validity than other commonly used motor tasks in fMRI studies (e.g., tapping a sequence); tracing within the lines of the flower-shaped trail demanded fine-motor control that is consistent with the difficulty experienced by children with DCD.\textsuperscript{98}

A common limitation in fMRI research is extraneous head motion, a limitation experienced also within our studies. Corrections for head motion were made and runs with excessive motion were excluded; however, we retained data with more than ideal motion so as to not lose participants from our small sample. Although head motion can affect interpretation of fMRI results, the areas of significant brain activation we observed were consistent with previous literature for the type of motor task we used (discussed in Chapter Four). To limit head motion in future studies, a mock scanner could be used to train subjects prior to fMRI data collection.\textsuperscript{99}
5.9. Directions for Future Research

Neuroimaging has great potential to inform our understanding of the neurobiology of DCD and to evaluate interventions for children with this disorder. This thesis has set the stage for a trajectory of research to address unanswered questions about DCD. For example, although under-activation of the cerebellum in children with DCD was observed, it is not known if the issue is within the cerebellum itself, or with information getting to or from the cerebellum. A neuroimaging technique known as diffusion tensor imaging (DTI)\textsuperscript{100} could be used in future studies to assess the integrity of the white matter tracts in children with DCD. This information might have clinical significance, in that treatment approaches may differ if pathways are disrupted versus if the cerebellum itself is underdeveloped or malfunctioning. A problem with the cerebellum (as opposed to white matter tracts) is likely to result in a better outcome from treatment, as neuroplasticity has been shown to occur in gray matter when learning a new motor skill.\textsuperscript{101,102}

Despite efforts to exclude children with co-morbid ADHD, the DCD group in our sample had significantly more attentional difficulties (as measured by the Conners ADHD DSM-IV Scale\textsuperscript{103}) in comparison with the control group. The impact of attention on motor learning needs to be further investigated, especially because almost half of children with DCD may have co-morbid ADHD.\textsuperscript{104,105} To assess the relative contribution of attention and motor abilities to motor learning, the study in Chapter Four could be replicated with four groups of children: DCD only, ADHD only, DCD with co-morbid ADHD, and TD children. Differences in brain activation and motor learning could also be assessed in children with DCD who have co-morbid conditions other than, or in addition to, ADHD.
A critical next step is to assess the effectiveness of cognitive-based treatments for DCD using fMRI. While positive outcomes from therapy interventions have been reported, none of the current intervention approaches for DCD have been examined using neuroimaging. Because fMRI allows for the measurement of patterns of brain activation associated with motor performance, it has the potential to measure if and how therapeutic interventions stimulate neuroplastic change. Future studies could extend the present work to explore how other parameters that impact motor learning affect skill acquisition and patterns of brain activation; these may include focus of attention, cognitive strategy use, extrinsic feedback, and contextual interference. Use of fMRI, along with other neuroimaging techniques, can inform our thinking about how interventions shape patterns of brain activity and lead to improved function in children with DCD.

5.10. Final Thoughts

This thesis has made several important and novel contributions to our understanding of children with DCD. First, it has shown unequivocally that children with DCD are neurobiologically different than their TD peers, lending credence to the legitimacy of DCD as a developmental disorder. Second, this work has suggested support for several hypotheses related to DCD, such as the involvement of the cerebellum in the disorder and suspected deficits in forming or updating internal models of movement. Third, neuroimaging results have suggested an alternative hypothesis worthy of further investigation: children with DCD may have a deficit in the default-mode network of the brain. Fourth, our behavioural and fMRI results have lent support to previous findings related to motor performance and motor learning in children with DCD. Finally, work from this thesis has set the stage for a trajectory
of research to better understand the neuropathology of DCD and to assess the propensity for neuroplastic change in association with rehabilitation interventions for children with DCD.
5.11. References


Appendix A: UBC Research Ethics Board Certificates of Approval
ETHICS CERTIFICATE OF FULL BOARD APPROVAL

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INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

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Other locations where the research will be conducted:

To confirm the diagnosis of developmental coordination disorder and rule out other medical conditions, children may need to be assessed by a physician. Dr. Freeman and Dr. Weiss (psychiatrists) have written letters of support for this study and may be involved in this capacity. Children may see Dr. Freeman in his physician's office or Dr. Weiss at the ADHD clinic at BC Children's Hospital.

CO-INVESTIGATOR(S):

- Susan R. Harris
- Jill G. Zwicker

SPONSORING AGENCIES:

- British Columbia Medical Services Foundation

PROJECT TITLE:

- Neuroimaging and Quality of Life of Children with Developmental Coordination Disorder

THE CURRENT UBC CREB APPROVAL FOR THIS STUDY EXPIRES: December 11, 2008

The full UBC Clinical Research Ethics Board has reviewed the above described research project, including associated documentation noted below, and finds the research project acceptable on ethical grounds for research involving human subjects and hereby grants approval.

REB FULL BOARD MEETING

REVIEW DATE: December 11, 2007

DOCUMENTS INCLUDED IN THIS APPROVAL:

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**CERTIFICATION:**

**In respect of clinical trials:**
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The documentation included for the above-named project has been reviewed by the UBC CREB, and the research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved by the UBC CREB.

---

Approval of the Clinical Research Ethics Board by one of:

Dr. Gail Bellward, Chair
The University of British Columbia  
Office of Research Services  
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC  
V5Z 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL:  
AMENDMENT

PRINCIPAL INVESTIGATOR:  
Lara Boyd

DEPARTMENT:  
UBC/Medicine, Faculty of Physical Therapy

UBC CREB NUMBER:  
H07-02474

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

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Other locations where the research will be conducted: Vancouver (excludes UBC Hospital)

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CO-INVESTIGATOR(S):
Susan R. Harris  
Jill G. Zwicker

SPONSORING AGENCIES:
- British Columbia Medical Services Foundation - "Motor learning in children with developmental coordination disorder: proof of concept for rehabilitation"
- Sick Kids Foundation - "Motor learning in children with developmental coordination disorder: proof of concept for rehabilitation? and health-related quality of life of children with developmental coordination disorder: a pilot study"

PROJECT TITLE:
Motor Learning in Children with Developmental Coordination Disorder: Proof of Concept for Rehabilitation?

REMINDER: The current UBC CREB approval for this study expires: December 11, 2008

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AMENDMENT APPROVAL DATE:  
May 5, 2008
CERTIFICATION:

In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The amendment(s) for the above-named project has been reviewed by the Chair of the University of British Columbia Clinical Research Ethics Board and the accompanying documentation was found to be acceptable on ethical grounds for research involving human subjects.

Approval of the Clinical Research Ethics Board by:

Dr. James McCormack,
Associate Chair
ETHICS CERTIFICATE OF EXPEDITED APPROVAL:
AMENDMENT

PRINCIPAL INVESTIGATOR: Lara Boyd
DEPARTMENT: UBC/Medicine, Faculty of/Physical Therapy
UBC CREB NUMBER: H07-02474

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CO-INVESTIGATOR(S):
Susan R. Harris
Jill G. Zwicker

SPONSORING AGENCIES:
- British Columbia Medical Services Foundation - “Motor learning in children with developmental coordination disorder: proof of concept for rehabilitation”

PROJECT TITLE: Motor Learning in Children with Developmental Coordination Disorder: Proof of Concept for Rehabilitation?

REMANDER: The current UBC CREB approval for this study expires: December 11, 2008

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AMENDMENT APPROVAL DATE: October 20, 2008

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
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The amendment(s) for the above-named project has been reviewed by the Chair of the University of British Columbia Clinical Research Ethics Board and the accompanying documentation was found to be acceptable on ethical grounds for research involving human subjects.

Approval of the Clinical Research Ethics Board by

Dr. Stephen Hopton Cann,  
Associate Chair
The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue, Vancouver, BC
VSZ 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL

PRINCIPAL INVESTIGATOR:
Lara Boyd

DEPARTMENT:
UBC/Medicine, Faculty of Physical Therapy

UBC CREB NUMBER:
07-02474

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

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CO-INVESTIGATOR(S):
Susan R. Harris
Jill G. Zwicker

SPONSORING AGENCIES:
- British Columbia Medical Services Foundation - “Motor learning in children with developmental coordination disorder: proof of concept for rehabilitation”

PROJECT TITLE:
Motor Learning in Children with Developmental Coordination Disorder: Proof of Concept for Rehabilitation?

EXPIRY DATE OF THIS APPROVAL: November 18, 2009

APPROVAL DATE: November 18, 2008

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The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds for research involving human subjects and was approved for renewal by the UBC Clinical Research Ethics Board.

Approval of the Clinical Research Ethics Board by

Dr. Stephen Hopein Cann, Associate Chair
ETHICS CERTIFICATE OF EXPEDITED APPROVAL:
AMENDMENT

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PROJECT TITLE:
Motor Learning in Children with Developmental Coordination Disorder: Proof of Concept for Rehabilitation?

REMINDER: The current UBC CREB approval for this study expires: November 18, 2009

AMENDMENT(S):
Addition of Study Site.

AMENDMENT APPROVAL DATE:
December 5, 2008

CERTIFICATION:
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Approval of the Clinical Research Ethics Board by:
Dr. James McCormack,
Associate Chair
**ETHICS CERTIFICATE OF EXPEDITED APPROVAL:**

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**CO-INVESTIGATOR(S):**

Susan R. Harris
Jill G. Zwerger

**SPONSORING AGENCIES:**

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**PROJECT TITLE:**

Motor Learning in Children with Developmental Coordination Disorder: Proof of Concept for Rehabilitation?

**REMinDeR:** The current UBC CREB approval for this study expires: November 18, 2009

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Approval of the Clinical Research Ethics Board by one of:

Dr. Peter Loewen, Chair  
Dr. James McCormack, Associate Chair  
Dr. John Russell, Associate Chair  
Dr. Caron Strahliendorf, Associate Chair
ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL

PRINCIPAL INVESTIGATOR:  Lara Boyd  
DEPARTMENT:  UBC/Medicine, Faculty of/Physical Therapy  
UBC CREB NUMBER:  H07-02474  

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Jill G. Zwicker  

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PROJECT TITLE:  
Motor Learning in Children with Developmental Coordination Disorder: Proof of Concept for Rehabilitation?

EXPIRY DATE OF THIS APPROVAL:  November 6, 2010

APPROVAL DATE:  November 6, 2009

CERTIFICATION:  
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Approval of the Clinical Research Ethics Board by one of:  
Dr. Peter Loewen, Chair  
Dr. James McCormack, Associate Chair
Appendix B: fMRI Procedure for Chapters 3 and 4
Appendix C: Method for Chapter 4

Assessed motor learning

Day 1  Days 2 - 4  Day 5

Early Practice  Task Practice  Retention
4 runs x 2 min

Within 2 weeks