DEVELOPMENTAL DIFFERENCES IN PREFRONTAL CORTEX ACTIVITY IN THE TOWER OF HANOI PUZZLE WITH HIGH VS. LOW MOTOR ELEMENTS IN ADULTS AND CHILDREN WITH AND WITHOUT DEVELOPMENTAL COORDINATION DISORDER

by

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A thesis submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Master of Science in Biomechanics and Movement Science

Summer 2019

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ACKNOWLEDGMENTS

First, I would like to thank my adviser, Dr. Nancy Getchell, and my committee, Dr. Christopher Knight and Dr. Anjana Bhat for their guidance, encouragement, and feedback throughout this M.S. project. I would also like to acknowledge Matthew Paul for developing the Tower of Hanoi computerized condition and Dr. Barry Bodt for developing the statistical analyses for chapters 2 & 3. Additionally, I would like to specially thank my family, supportive friends, and lab mates, Reza Koiler and Elham Bakhshipour. Reza, your enthusiasm, drive, innovation, and passion for biomedical science inspires me every day. Ella, I could not have been able to complete this project without your help in virtually every data collection, processing fNIRS data, practicing presentations, writing multiple manuscript drafts, and your constant encouragement. To my very supportive friends and family: it undoubtedly takes a village to complete a research project, thank you all for your unwavering support. Lastly, I would like to thank Dr. Mary Martin for her invaluable support and advocacy. There were more than a few roadblocks in the way to completing this project, most of which would not have been surpassed without your help and advocacy.
PREFACE

Nancy Getchell (NG) and Kimberly Milla Ceja (KMC) designed the experiment. Elham Bakhshipour (EB), Amanda Plumb (AP), NG, and KMC collected the data. Barry Bodt (BB), NG, EB, and KMC analyzed the data and prepared all figures. KMC, EB, and NG drafted the manuscripts. NG and BB provided critical revisions. All authors approved chapter 2 to be published and contributions to be included in this thesis. Chapter 2 was published on May 10th, 2019 in Frontiers of Human Neuroscience.
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ABSTRACT

The prefrontal cortex (PFC) plays an important role in executive function (EF) as well as motor planning. Recent neuroimaging research has indicated that individuals with developmental coordination disorder (DCD) demonstrate differences in their PFC activity. To explore this, we used functional near-infrared spectroscopy (fNIRS) to compare PFC activity in adults, typically developing (TD) children, and children with DCD as they performed two conditions (2D and 3D) of the Tower of Hanoi (ToH) disk-transfer task that have equivalent EF demands but different motor requirements. Overall, we sought to better understand the role of the PFC in these two conditions to detect if neural activity and behavioral performance differ as a function of ToH condition, and to identify whether any differences exist in these measures among all 3 groups. To do this, we performed 3 studies. In study 1, 20 right-handed, neurotypical adults (10M/10F, \(\bar{x} = 24.6\), SD ± 2.8 y.o.) participated. Results showed significantly larger changes in oxygenated hemoglobin, \(\Delta\text{HbO}\), for 3D compared to 2D condition (\(p = 0.0211\)) and a significant interaction between presentation order and condition (\(p = 0.0015\)). Notably, a strong correlation between performance and \(\Delta\text{HbO}\) existed between blocks 1 (B1) and 2 (B2; \(r = -0.69, r^2 = 0.473, p < 0.01\)) when the 3D condition was initially performed, in contrast to the 2D condition where no significant correlation was seen. Findings also showed a significant decrease in \(\Delta\text{HbO}\) between B1 and B2 (\(p = 0.0015\)), while performance increased significantly for both conditions (\(p < 0.005\)). In study 2, 18 TD children (5F/13M, \(\bar{x} = 11.33\), SD ± 2.41 y.o.) participated and were further separated into 2 age bands: younger (N=7, 1F/6M, \(\bar{x} = 9.02\), SD ± 1.20 y.o.) and older (N=11, 4F/7M, \(\bar{x} = 12.79\), SD ± 1.71 y.o.). In contrast to study 1, results in the TD sample did not show a significant effect when comparing
ΔHbO between 2D and 3D conditions for either younger or older children, although neural activity was larger in the 3D than in the 2D condition (p > 0.05). Likewise, a decrease in ΔHbO was seen in B2 as opposed to B1 in both conditions however the relationship was not significant for either group (p > 0.05). Lastly, performance did not significantly differ between blocks for both groups (p > 0.05). In study 3, we performed a descriptive study on 4 children with DCD (0F/4M, $x = 11.81$, SD ± 0.58 y.o.). Data displayed larger ΔHbO in the 2D as opposed to the 3D condition in 3 out of 4 participants, and a decreased ΔHbO in B2 compared to B1 for all participants. Furthermore, 2 participants performed above the average TD sample performance score (2.88 for B1 and 2.94 for B2), while one participant performed below, and the other participant performed at average levels. Lastly, 3 participants showed generalized PFC activity for both conditions, whereas one participant showed localized activity to the dorsolateral PFC during the 3D condition, but generalized activity during the 2D. Overall, we plan to use this information to guide future research into elucidating the potential points of impairment on the perception-cognition-action continuum in DCD.
Developmental Coordination Disorder (DCD) is a neuromotor developmental disability that consistently affects motor function, coordination, and the acquisition of motor skills (American Psychiatric Association, 2013; World Health Organization, 2016; Niklasson et al., 2018). It affects 4-13% of school-aged children, and it is diagnosed more in boys than in girls (Dewey & Wilson, 2001; Sugden & Chambers, 1998; Cousins & Smyth, 2003; Cairney et al., 2006; Hillier, 2007; Kirby & Sugden, 2007; Vaivre-Douret, 2014). DCD varies in severity and presents with a variety of comorbid learning disorders, which can persist through adulthood when no intervention occurs (Fox & Lent, 1996; Kirby & Sugden, 2007). Identifying the etiology of DCD is challenged by the array of symptoms, although deficits with sensorimotor integration, coordination, and motor planning are seen (Clark, Smiley-Oyen, Getchell, & Whitall, 2005). Moreover, children with DCD have difficulties using predictive control, pervasive issues with executive function, and deficits in motor imagery and planning similar to those experienced by children with mild cerebral palsy (Wilson et al., 2017).

The prefrontal cortex (PFC) has a central role in executive function, which can be defined as a set of processes fundamental to goal-directed behavior such as anticipation, goal establishment, monitoring of results, inhibition of action, and planning (Wood & Graffman, 2003; Stuss & Benson, 1986). Particularly, the PFC
houses motor planning related processes such as outlining the execution of programmed sequences of actions and planning the consequences of such actions (i.e. internal model of action sequences; Kawato, 1999). Moreover, the PFC is concerned with the active representation of future events resulting from behavioral actions within a framework of problem-solving (Mushiake et al., 2009).

Current research on DCD can only speculate on the efficacy of interventions given that an etiology for the disorder has not been identified. In attempting to resolve this uncertainty, this thesis explored patterns of activity in the PFC using functional near-infrared spectroscopy (fNIRS), a technology that indirectly measures neural activity by calculating changes in the relative ratios of oxygenated (oxy-Hb, also ΔHbO) and deoxygenated (deoxy-Hb, also ΔHbR) hemoglobin in the capillary beds of cerebral cortices. fNIRS emits photons with wavelengths within the near-infrared range of light (700 and 900 nm), where most brain tissue is relatively transparent to, except for the hemoglobin chromophores (oxy-Hb and deoxy-Hb). Therefore, the near-infrared photons can cross brain matter at the cortical level, without relatively interacting with the tissue, and reach the hemoglobin chromophores that can absorb or scatter the near-infrared light. Sensors placed in the fNIRS device can then use this optical window to measure the differences between light emitted and light absorbed or scattered, which indirectly measures neural activity through neurovascular coupling, where increases in neural activity also increase the delivery of oxygen and glucose for consumption leading to closely associated increases in blood flow (Ruocco et al., 2014). Ultimately, the increased blood flow into the capillary beds facilitates access to oxygenated hemoglobin in the local tissue, therefore resulting in a hemodynamic
response that reflects the location and magnitude of neural activity, allowing us to use ∆HbO and ∆HbR as markers for brain activity (Kim, Seo, Jeon, Lee, & Lee, 2017).

The fNIRS technology is advantageous compared to others because it can discern cognitive load and cognitive states in the PFC during activities of daily living or conditions that require movement (Masataka, Perlovsky, & Hiraki, 2015). Furthermore, fNIRS recordings can be integrated with other modalities such as EMG (Izzetoglu et al., 2005), and do not expose people to radioactive materials unlike technologies like positron emission tomography (PET). Additionally, fNIRS is more favorable to use in children given that it is less sensitive to motion artifact, it is quieter, and does not require confined positions during scanning, such as functional magnetic resonance imaging (fMRI) and PET. Lastly, fNIRS’ recordings can be visualized onto a topographic map built upon sensor geometry and a brain template based on fMRI data (Izzetoglu et al., 2005).

Overall, fNIRS is a neuroimaging tool that is non-invasive, portable, affordable and safe for continuous and repeated measurements. Along with its tolerance to motion, where head mobility is minimized (Izzetoglu et al., 2005), strong correlation with fMRI in measurements of hemodynamic responses (Ferrari & Quaresima, 2012; Kleinschmidt et al., 1996), better spatial resolution than MEG and EEG and better temporal resolution than fMRI and PET (Bunce, Izzetoglu, Izzetoglu, Onaral, & Pourrezaei, 2006; Irani, Platek, Bunce, Ruocco, & Chute, 2007). fNIRS is ideal to study cognitive activity during behavioral tasks in ecologically relevant conditions (Kim et al., 2017).
Given that children with DCD have issues with processes related to executive function and motor planning (i.e. internal modelling) as well as manual control of actions (Wilson et al., 2017), it is crucial to explore PFC activity and whether any differences exist between DCD and TD children, as well as adults, particularly in a task that allows for equal demands on executive function (i.e. problem-solving) with differing demands on motor action. Problem-solving is an intricate process of higher-order cognition that identifies problems and then generates and implements solutions to achieve a target state (Simon & Newell, 1971). It can be broken down into three fundamental, overlapping processes: problem recognition, definition and representation (Pretz, Naples, & Sternberg, 2003). Tower tests, such as the Tower of Hanoi (ToH) puzzle, are validated and frequently used in research and clinical settings to assess problem-solving and are generally comprised of three placeholders, such as pegs, which can vary in length as well as the color and size of the balls or disks being used (W. C. Culbertson, Moberg, Duda, Stern, & Weintraub, 2004; W. Culbertson & Zillmer, 1998). Following a model deconstructing problem-solving into three processes, a tower test can be defined as a specific problem (recognition) with initial and target states that clearly specify the operators and constraints (definition). Variations occur in the number of operators allowed to reach the target state and the established rules to complete the task (representation) (Ruocco et al., 2014).

Even though the parameters of Tower tests have varied among different studies (i.e. different number of disks, colors, sizes, etc.), all have resulted in PFC activity, including the anterior, inferior and dorsolateral regions. Furthermore, increasing the
difficulty task (i.e. increased number of moves necessary to reach the target state) leads to increased levels of activity, particularly in the left dorsolateral region of the PFC (dlPFC). The left dlPFC has been related to identification of information relevant to the goal and creation of an internal problem representation, whereas the right dlPFC is associated with mental transformations and working memory (Ruocco et al., 2014). Notably, the Tower of Hanoi puzzle has the advantage of being sensitive to disruption in the prefrontal cortex. (Casey, Vauss, Chused, & Swedo, 1994; Goel & Grafman, 1995; Saint-Cyr, Taylor, & Lang, 1988; Simon, 1975), a valuable characteristic in assessing potential deficits in the PFC activity of DCD children.

Therefore, this thesis aims to further explore the role of the PFC in a problem-solving task, namely the Tower of Hanoi, with high- and low-motor components in children with DCD, TD children, and adults. Chapter 2 discusses the first project conducted in a young neurotypical adult sample, followed by Chapter 3 where a second project conducted in a TD children sample is discussed. Lastly, chapter 4 explores data gathered in four children with DCD as a descriptive study. Overall, this thesis explores PFC activity during two conditions of the ToH puzzle in young adults, typically developing children, and children with developmental coordination disorder with the purpose of identifying potential developmental differences in the perception-action continuum.
Chapter 2

DOES MOVEMENT MATTER? PREFRONTAL CORTEX ACTIVITY DURING 2D VS. 3D PERFORMANCE OF THE TOWER OF HANOI PUZZLE

2.1 Abstract

In the current study, we used functional near-infrared spectroscopy (fNIRS) to compare prefrontal cortex (PFC) activity in adults as they performed two conditions of the Tower of Hanoi (ToH) disk-transfer task that have equivalent executive function (EF) but different motor requirements. This study explored cognitive workload, defined as the cognitive effort utilized during problem-solving by performance output. The first condition included a two-dimensional (2D) computerized ToH where participants completed trials using a computer mouse. In contrast, our second condition used a traditional, three-dimensional (3D) ToH that must be manually manipulated. Our aim was to better understand the role of the PFC in these two conditions to detect if PFC activity increases as a function of motor planning and to compare the use of 2D vs. 3D versions of ToH to elucidate the value of real-world actions during motor planning. Twenty right-handed, neurotypical adults (10M/10F, \( \bar{x} = 24.6, \ SD \pm 2.8 \) years old) participated in two blocks (one per condition) of three 1-min trials where they were asked to solve as many puzzles as possible. These data were analyzed using a mixed effects ANOVA with participants nested within blocks for 2D vs. 3D conditions, presentation order (leading block), individual participants, and regions and additional follow-up statistics. Results showed that changes in oxygenated hemoglobin, \( \Delta \text{HbO} \), were significantly higher for 3D compared to the 2D condition (\( p = 0.0211 \)). Presentation order and condition interacted significantly (\( p = 0.0015 \)). Notably, a strong correlation between performance and \( \Delta \text{HbO} \) existed between blocks 1 and 2 (\( r = -0.69, r^2 = 0.473, p < 0.01 \)) when the 3D condition was
initially performed, in contrast to the 2D condition where no significant correlation was seen. Findings also showed a significant decrease in ΔHbO between the first and second block (p = 0.0015) while performance increased significantly for both 3D and 2D conditions (p < 0.005). We plan to use this information in the future to narrow the potential points of impairment on the perception-cognition-action continuum in certain developmental disabilities.

2.2 Introduction

The prefrontal cortex (PFC) is a brain structure with a significant function in planning complex cognitive behavior, personality expression, decision making, and moderating social behavior (Yang and Raine, 2009). Processes underlying high-level executive function (EF) have historically been associated with the PFC (Ball et al., 2011). Furthermore researchers have identified neural networks that are active during complex executive processes and are highly interconnected between the PFC and several brain regions, such as the posterior parietal cortex, limbic and cortical areas (Selemon and Goldman-Rakic, 1988; Öngür and Price, 2000; Halgren et al., 2002; Honey et al., 2002; Schall et al., 2003; Periáñez et al., 2004; Owen et al., 2005; Simmonds et al., 2008). EF is an umbrella term encompassing the higher level cognitive processes responsible for the completion of a specific goal and its related behaviors such as anticipation, goal establishment, monitoring of results, inhibition of action, and planning (Stuss, 1986; Moriguchi and Hiraki, 2013). The role of the PFC in motor planning is to outline the execution of programmed sequences of actions and to plan the consequences of such actions, also referred to as internal modeling (Kawato, 1999). Specifically, the PFC is concerned with the active representation of future events resulting from behavioral actions within a framework of problem-
solving, with the dorsolateral PFC particularly suited to assist in the control of responses to environmental stimuli and regulation of behavior (Wood and Grafman, 2003; Mushiake et al., 2009). The experimental evidence for a better understanding of EF is the result of using different tasks such as the Stroop Task, where the ink of a word representing a color might mismatch such color (Smith et al., 2006), the Wisconsin Card Sorting Task, where participants classify cards based on different criteria (Koch et al., 2018), and the Tower of Hanoi puzzle (ToH), a disk-transfer task that requires the relocation of disks from an initial configuration to a target configuration in the least possible number of moves (Liang et al., 2016b). ToH requires participants to appropriately respond to new situations, as well as demands related to anticipatory, means-end problem-solving (Welsh and Huizinga, 2001). Moreover, it has been used for decades as a neuropsychological task for assessing EF on healthy individuals and different clinical populations (Goel and Grafman, 1995; Slomine et al., 2002; Griebling et al., 2010; Yu et al., 2016; Shuai et al., 2017). Previous research utilizing Tower tests have all resulted in PFC activity, including the anterior, inferior, and dorsolateral regions, despite the use of different parameters (i.e., the amount, size, and color of the disks used; Baker et al., 1996; Boghi et al., 2006; Wagner et al., 2006; Just et al., 2007; den Braber et al., 2008; Fitzgerald et al., 2008; Campbell et al., 2009; Zhu et al., 2010; Kaller et al., 2011; Stokes et al., 2011; de Ruiter et al., 2009; Hahn et al., 2012; Ruocco et al., 2014). Furthermore, an increase in the difficulty of the task (i.e., increased number of moves necessary to reach the target state) led to increased levels of activity, particularly in the left dorsolateral region of the PFC (dIPFC). The left dIPFC has been related to the identification of information relevant to the goal and creation of an internal problem representation, whereas the
right dlPFC has been associated with mental transformations and working memory (Ruocco et al., 2014). Notably, the ToH puzzle has the advantage of being sensitive to disruption in the PFC (Simon, 1975; Saint-Cyr et al., 1988; Casey et al., 1994; Goel and Grafman, 1995). Additionally, the activity of the PFC during the computerized version of ToH has been shown using different neuroimaging techniques such as fMRI (Head et al., 2002; Griebling et al., 2010; Crescentini et al., 2012) and EEG (Ruiz-Díaz et al., 2012; Guevara et al., 2013), in addition to functional near-infrared spectroscopy (fNIRS; Liang et al., 2016a,b). fNIRS is a neuroimaging tool that is non-invasive, portable, affordable, and safe for continuous and repeated measurements. fNIRS indirectly measures neural activity using the neurovascular coupling principle (i.e., blood flow follows neural activity). This phenomenon occurs when increases in neural activity also increase the delivery of oxygen and glucose for consumption, leading to closely associated increases in blood flow. Ultimately, the increased blood flow into the capillary beds facilitates access to oxygenated hemoglobin in the local tissue. Thus, neurovascular coupling results in a hemodynamic response that reflects the location and magnitude of neural activity, which allows us to use oxy- (∆HbO) and deoxy-Hb (∆HbR) as markers for brain activity (Kim et al., 2017). Along with its tolerance to motion, assuming movement of the head is limited (Izzetoglu et al., 2005), strong correlation with fMRI in measurements of hemodynamic responses (Kleinschmidt et al., 1996; Ferrari and Quaresima, 2012), better spatial resolution than MEG and EEG as well as better temporal resolution than fMRI and PET (Bunce et al., 2006; Irani et al., 2007), fNIRS is ideal to study cognitive activity during behavioral tasks in ecologically relevant conditions (Kim et al., 2017), including in children (Caçola et al., 2018). Therefore, it is appropriate for investigating different conditions
of the ToH including both three-dimensional (3D) and two-dimensional (2D) modalities. Our specific aim was to determine if PFC hemodynamics and behavioral performance differ as a function of ToH condition (3D vs. 2D) in neurotypical young adults. We hypothesized that there would be greater changes in $\Delta HbO$ during the 3D condition as compared to the 2D condition of the ToH task (H1). Additionally, we hypothesized that each condition would show regional areas with greater changes in oxygenation than other regions within the same condition (H2).

2.3 Materials and Methods

2.3.1 Participants

Twenty-seven neurotypical adults aged between 18 and 35 were initially recruited for this study from the University of Delaware and Newark communities. Participants were included if they were healthy, right handed, and without known neurological deficits. Three participants were not included due to being lefthanded. Exclusion criteria included any head injury within the 6 months prior to testing, an open wound on the forehead, or a seizure disorder. After data collection, an additional three participants were excluded due to incomplete data sets and one participant was excluded due to being an outlier, i.e., hemodynamic data was over two standard deviations from the mean, leaving a total of $n = 20$ neurotypical adults (10F/10M) with a mean age of 24.6 (SD $\pm$ 2.8) years old. To ensure that participants were right hand dominant, they completed the Edinburgh Handedness Inventory to assess hand preference for various tasks, such as writing (Oldfield, 1971). Participants were all right-handed and had a mean Laterality Quotient (L.Q.) of 79.2 (SD $\pm$ 19.6) with an average Decile of 5.4 (SD $\pm$ 3.3; Oldfield, 1971). Sixteen participants had no previous
experience solving the ToH puzzle, i.e were task naïve, and the remaining four were self-described beginners, meaning they have had minimal experience solving the ToH puzzle. Participants averaged 172 (± 9.61) cm in height and 73.91 (± 14.77) kg in body mass. The Institutional Review Board at the University of Delaware approved the protocol for this study and participants provided written informed consent after being educated on the study and its procedures.

2.3.2 Experimental Design

2.3.2.1 Conditions

The present study used two conditions: a 3D and a 2D modality of the ToH task. The first condition involved the use of a 3D wooden model, with three peg-holes and four graduated disks, which was physically manipulated during puzzle solving (Figure 2.1A). The second condition involved the use of a 2D computer model with custom-made opensource software (Salesforce Company, 2018), also consisting of three peg-holes and four graduated disks however manipulated through a computer mouse by clicking and dragging (Figure 2.1B). Block order (B1/B2) was randomized and counterbalanced using an online randomized integer sequence calculator (Haahr, 1998) resulting in eight participants initially performing the 3D condition (3D/B1) and 12 participants initially performing the 2D condition (2D/B1).
Figure 2.1. Different Tower of Hanoi conditions. (A) Three-dimensional (3D) condition performed by using one hand to move disks and the other hand to hold the frame. (B) Two-dimensional (2D) condition performed on a PC computer using one hand to manipulate a mouse.

2.3.2.2 Protocol

Participants became familiar with the ToH puzzle by performing a practice attempt for each condition using three disks; there were no time constraints for this practice. Following practice, participants had a 1-min rest period, in which they comfortably sat on a chair and focused their attention on a green cross on a screen in front of them, with their eyes open and sitting as still as possible. Following the initial rest period, participants attempted to solve ToH puzzles in two blocks (one per condition; block 1 = B1 and block 2 = B2), each consisting of three 1-min epochs with a 20-s rest in between to allow hemodynamic flow to return to baseline (Kuhtz-Buschbeck et al., 2003; Abibullaev et al., 2014; Yin et al., 2015; Huhn et al., 2019; Table 2.1). Using Welsh and Huizinga’s (2001) ToH-Revised list containing 22 items, 10 different puzzle configurations were created. Each puzzle had a unique combination of start and end disk positions, which in turn were ordered into two different sequences to avoid an order effect. Puzzles varied in difficulty, with the
minimum number of moves required to solve a puzzle ranging from 8 to 15 (Appendix A) show the two sequences of 10 puzzles used in this study with associated difficulty). Furthermore, puzzle sequence was randomized and counterbalanced. Each participant was presented with the same puzzle sequence for both 3D and 2D conditions, i.e., they were presented with different puzzles in each sequence but the sequence was identical for both blocks, allowing for a second attempt at a given puzzle if the previous puzzle was solved. After each block, participants had a 1-min rest period.

Table 2.1. Protocol timeline for 3D/B1 participants. Participants were introduced to the puzzle with a practice attempt for each task, followed by a one-minute rest period prior to completing 2 blocks or problem-solving. 3D = three-dimensional ToH task; 2D = two-dimensional ToH task; R = rest.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice</td>
<td></td>
</tr>
<tr>
<td>3D</td>
<td>N/A</td>
</tr>
<tr>
<td>2D</td>
<td>N/A</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
<tr>
<td>Block 1</td>
<td></td>
</tr>
<tr>
<td>3D-1</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>3D-2</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>3D-3</td>
<td>60 s</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
<tr>
<td>Block 2</td>
<td></td>
</tr>
<tr>
<td>2D-1</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>2D-2</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>2D-3</td>
<td>60 s</td>
</tr>
</tbody>
</table>
2.3.3 Experimental Device

A 16-channel continuous-wave functional near-infrared (fNIRS) device (Ayaz et al., 2012, 2013) was utilized to collect data from the PFC of all participants (fNIR Devices LLC, Potomac, MD, USA). The sensor included 10 photo detectors and four light emitters (16 optodes total), each releasing light at 730–850 nm wavelengths and separated by 2.5 cm, which allowed for a penetration depth of about 1.2 cm (Ayaz et al., 2011). The fNIRS sensor band was placed on top of the participants’ forehead such that the center of the sensor’s horizontal axis was aligned to the center of the participants’ head (symmetry axis of the head). The sensor’s vertical axis was positioned in the Fp1 and Fp2 locations in accordance to the international 10-20 system of cerebral electrode placement (Homan et al., 1987; Ayaz et al., 2006). **Figure 2.2** depicts the fNIRS sensor band used in this study (fNIR Devices LLC, Potomac, MD, USA) and **Figure 2.3** shows an fMRI-based topographic map of the brain (Ayaz et al., 2018).
Figure 2.2. fNIR® sensor pad used for data collection. Written informed consent was obtained from the individual to publish this image.
Figure 2.3. (A) Brain template with data from sample participant depicting prefrontal regions under investigation. (B) Brain activity presented in 16 measurements locations (optodes) for the same participant. Data was further analyzed in clusters of 8 regions (C), and 4 regions (D). Figures B-D depict opposite laterality from figure A, i.e. the right side of the figure corresponds to the right hemisphere and vice versa.
2.3.4 Data Acquisition and Analysis

fNIRS data were sampled at 2 Hz and acquired using Cognitive Optical Brain Imaging (COBI) studio software (Ayaz et al., 2011). Data were processed using fNIRSoft Software (Version 4.9, Ayaz et al., 2018) and represents the mean activation during all three 1-min blocks for each condition. The device was initiated and the first 10 s were utilized as baseline prior to task initiation. During this time, the participant remained still and focused on a green cross located in a computer screen across from the participant. Before placing the sensor band, an alcohol swab was used to clean the forehead of the participants and the light in the testing room was subsequently reduced. Researchers were careful to exclude any hair between the sensors and the participants’ forehead to obtain optimal signal acquisition. Raw light intensities were visually inspected and individual optodes rejected when data did not reflect hemodynamic activity due to lack of proper contact between the sensors and the forehead or placement on top of hair. Researchers also visually inspected the data and manually removed optodes in accordance to Ayaz et al. (2011). Then, a finite impulse response (FIR) filter (20th order, Hamming window) was used to low-pass filter the raw light intensity data at 0.1 Hz to remove input from physiological signals, such as respiration and heartbeat. Data were subsequently converted to changes in concentration using the modified Beer-Lambert law (Cope and Delpy, 1988) and depicted into four outcome measures: change in oxygenated hemoglobin (ΔHbO), change in deoxygenated hemoglobin (ΔHbR), total change in hemoglobin (ΔHbT) and total change in oxygenation (ΔOxy). We restricted our analysis to ΔHbO because our preliminary analysis showed high correlation among ΔHbO, ΔHbT, and ΔOxy, in
addition to ΔHbO having stronger and more wide-spread signals than those from ΔHbR and ΔHbT (Zhang et al., 2011), including in the ToH task (Liang et al., 2016a,b). Furthermore, it has been shown that ΔHbO has a strong correlation to BOLD signal whereas ΔHbR has a weak correlation (Strangman et al., 2002), in addition to better signal-to-noise ratio (SNR) than ΔHbR (Hoshi, 2007; Zhang et al., 2010). Finally, data depicting changes in concentration were processed using the detrending filter, which removes a drift in the data using linear parameters that convert the slope of the baseline to zero. Hemodynamic data for 20 participants were included in the analyses and reflected a mean activation of the three 1-min epochs for each condition. Furthermore, performance data for 17 participants were included in the analyses, defined as the number of puzzles a participant attempted to solve within each block out of 10 potential puzzles. Due to data collection error, performance data were not obtained for three participants.

2.3.5 Statistical Analysis

Data were analyzed in JMP Pro 13.1.0. The effects of 2D vs. 3D conditions, presentation order (leading block), individual participants, and regions were examined using a mixed effects ANOVA with participants nested within blocks. A separate analysis was conducted for each of four representations of the optodes based on the sensor layout (Figures 2.3B–D). Those four representations depicted data for the complete PFC (overall), a division of the PFC into four regions (left lateral, left medial, right medial, and right lateral), a division of the PFC into eight regions (left lateral dorsal and ventral, left medial dorsal and ventral, right medial dorsal and ventral, and right lateral dorsal and ventral), and a division of the PFC into 16 regions, i.e., data for each of the individual optodes. An exploratory analysis subsequent to
ANOVA investigated the significance of conditions by considering paired differences between 2D and 3D for each participant and each optode representation in Tukey mean difference plots. A regression analysis showed the association between performance (puzzles attempted) and ΔHbO.

2.4 Results

2.4.1 ΔHbO in 2D vs. 3D Conditions

A mixed-effects ANOVA based on a mean ΔHbO response over all optodes was performed with conditions, presentation order, participants within blocks, and region as factors. As predicted, overall ΔHbO was significantly higher for the 3D condition compared to the 2D (Figure 2.4, p = 0.0211). In addition, a significant interaction existed between the order of presentation and condition (Figure 5, p = 0.0015), with those participants who started with 3D in block 1 (3D/B1) showing a much larger change in ΔHbO than those who started with 2D (2D/B1). Additionally, participant responses to experimental conditions were not universal: there were significant interactions between condition and participant (p = 0.0013), region and participant (p = 0.0124), and there was a three-way interaction of participant × region × block × order (p < 0.0001).
Figure 2.4. Changes in oxygenated hemoglobin, ΔHbO (µM) as a function of condition. The 3D condition showed significantly higher activity, p = 0.0207. Error bars show standard error values.

2.4.2 ΔHbO and Regional Analysis

With a similar mixed-effect ANOVA analysis using individual optode recordings for ΔHbO, no significant differences were seen in regional activity using the 16, 8, or 4 optode model with this particular group (p > 0.05). In other words, specific sets of optodes did not show higher ΔHbO activity within a condition.

2.4.3 ΔHbO and Performance on ToH

ΔHbO decreased significantly between the first and second block (p = 0.0015); at the same time, the total number of puzzles solved increased significantly for both 3D and 2D conditions (B1 = 3.56, B2 = 4.50, p < 0.005). Furthermore, there was a negative correlation between the number of puzzles solved and ΔHbO (r = -0.37), suggesting that participants learned the ToH task and could perform it with less cognitive effort in the second block.
Notably, when the 3D condition was performed in block 1 (3D/B1), a significant negative correlation between performance and ∆HbO existed ($r = -0.69$, $r^2 = 0.473$, $p < 0.01$, Figure 2.5). In contrast, when participants started with the 2D condition, there was no significant correlation between B1 and B2 ($r = -0.177$, $r^2 = 0.0313$, $p > 0.05$) when the 2D condition was performed in block 1 (2D/B1, Figure 2.6). Due to the significant interaction found between conditions (2D vs. 3D) and condition order (leading block) along with the correlation differences, we followed up with an analysis of relative neural efficiency (Paas and Van Merriënboer, 1993; Paas et al., 2003). Both groups improved relative neural efficiency from B1 to B2, but the amount of change differed substantially. The calculated relative neural efficiency for 3D/B1 participants was -5.82 for block 1 and 5.64 for block 2. In contrast, the 2D/B1 participants had a relative neural efficiency of -1.37 for block 1 and 1.44 for block 2 (Figure 2.7).

![Figure 2.5](image_url)

Figure 2.5. Mean ∆HbO (μM) as a function of presentation order. Condition changes from first (B1) to second (B2) block. Significantly lower mean ∆HbO was seen in B2 with respect to B1 for participants that initially performed the 3D condition, $p=0.0015$, shown as 3D first (3D/B1 group). Error bars show standard error values.
2.6 Correlations between performance (# of puzzles attempted to solve) and prefrontal activity (ΔHbO, μM). Regression line shows the strong correlation, r² = 0.473, found in participants that initially performed the 3D condition, shown as 3D first (3D/B1 group).

2.5 Discussion

2.5.1 Changes in Oxyhemoglobin as a Function of Puzzle Type

As we hypothesized, ΔHbO was significantly higher for the 3D condition compared to the 2D condition overall (Figure 2.4). This suggests that the 3D condition placed higher cognitive demands on the participants in order to solve the puzzle, which may be due to greater demands on perceptual decision-making processes (object identification, selection, and localization) due to the integration of increased spatial and tactile sensory processing (Wong et al., 2015). Additionally, higher demands on motor planning, i.e., increased demands on abstract kinematics, action selection, and movement (Wong et al., 2015), would be imposed by the 3D condition with respect to the 2D condition.
Furthermore, participant responses to experimental conditions varied on the basis of condition, presentation order, and region, as demonstrated by the significant interactions (condition and participant, region and participant, participant \( \times \) region \( \times \) presentation order). These results provide further support for individual differences in EF (Ackerman, 1987, 1988; Miyake et al., 2000; Osaka et al., 2004; Miyake and Friedman, 2012; Smith et al., 2019) since participants had different levels and patterns of neural activity for each condition between each other (interpersonal differences) and amongst themselves (intrapersonal differences). Given that performance in the ToH task has been associated to inductive reasoning as well as other aspects of fluid intelligence (Welsh et al., 1999; Devine et al., 2001; Lock et al., 2002), the study done by Dunst et al. (2014) is of relevance. Brain activity between ‘‘brighter’’ and ‘‘less bright’’ participants was compared as they worked on a number-series task taken from the numerical-inductive reasoning (Arendasy and Sommer, 2012) of the intelligence structure-battery (INSBAT, Arendasy, 2008). They found significant differences in brain activity within eight regions (particularly left inferior frontal, left middle frontal, and right middle frontal), when the task difficulty was not standardized, i.e., adjusted for each participant according to their ability based on intelligence scores. Our study did not standardize the ToH task difficulty based on participants’ ability, thus individual differences can be partially explained by ability in terms of fluid intelligence. Moreover, it has been suggested by Simon (1975) that the restrictions of the ToH task lead to the creation of various problem-solving strategies with varying effectiveness and that can account for individual differences, particularly for performance. Furthermore, Simon (1975) proposes the recursive guiding solution method as the optimal problem-solving strategy since it decreases the demands placed
on working memory, planning, and inhibition (all executive processes) by the inherent complexity of the ToH puzzle. The recursive guiding solution begins with moving the largest disk to the end-goal position, followed by moving the smaller disk out of the way and in the open peg (subpyramid stack of smaller disks), and then restarting the process by moving the largest disk in the subpyramid to the end-goal position and repeating all steps until reaching the solution (Simon, 1975).

2.5.2 Prefrontal Cortex: Overall vs. Regional Differences

Contrary to our hypothesis and despite previous studies demonstrating that hemodynamic responses can be used to reliably quantify cognitive state and load levels in the bilateral PFC (Basso Moro et al., 2013; Fishburn et al., 2014; Unni et al., 2015; Bonetti et al., 2019), the present study did not find significant differences among optodes when parsed into different regions. Although the lack of regional differences is important, it is worthwhile to note that fNIRS’ spatial resolution is limited by the optical source-detector distance, which is normally 2–3 cm, despite the technology having high temporal resolution (Tak et al., 2016). This relatively low spatial resolution, compared to fMRI, may cause difficulties in localizing different regions of the brain. Additionally, this study analyzed regional differences based on the layout of the device (4, 8, and 16 regions), which may not have been appropriate to parse out the functional activity of the PFC.

Moreover, the present study did not stratify participants based on individual differences shown to reflect distinct brain activity, such as fluid intelligence and spatial ability (Lamm et al., 2001; Neubauer and Fink, 2009; Dunst et al., 2014). The presence of individual differences, as described above, might have precluded our
ability to detect regional differences. Lastly, previous research has shown that restricting the processing time during a cognitive task can affect the magnitude and patterns of neural activity (Porebski, 1954; McCarthy and Wood, 1985; Van Breukelen and Roskam, 1991; Haig et al., 1997; Gulliksen, 2013), and even increase the demand for neural resources (Lamm et al., 2001). It could be that restricting the time to complete puzzles to 1-min epochs affected our study in unexpected ways. Other analysis techniques that take into consideration temporal aspects of each epoch, such as a time-series analysis, might lead to identification of differences.

2.5.3 Associations Between Brain and Behavior

There may have been a learning effect across the blocks, as ΔHbO decreased significantly between B1 and B2 while the total number of puzzles solved increased significantly, regardless of condition order. Since prior knowledge reduces the cognitive load inherent to task complexity, also known as the intrinsic load (Kalyuga et al., 2004; Sweller, 2008), having solved the same puzzles in B1 as in B2 likely reduced this intrinsic load placed by the puzzle in B2. This shift in cognitive load from B1 to B2 led to an approximation of the ‘‘ideal’’ load for the task, also known as germane cognitive load, thereby reducing the amount of neural resources needed to solve the puzzle (Sweller, 2008; Taylor, 2013). This is further supported by the negative correlation seen between the number of puzzles solved and ΔHbO, suggesting that participants may have progressively learned to solve the ToH task and could perform it with less cognitive effort in B2 due to a more efficient use of neural resources.
Our results support evidence from previous studies in neural efficiency, listed in the review by Neubauer and Fink (2009), where a negative relationship between brain activation and task performance has been consistently seen on tasks of low to medium difficulty or complexity, indicating a potential association between performance and cognitive load. Likewise, our results further support previous evidence where practice has led to a significant negative correlation between performance and neural activation, indicating a more discriminating activity of neural circuitry in B2 due to a sharpened cognitive strategy gained during B1 (Haier et al., 1988, 1992).

As previously mentioned, presentation order (leading block) and condition interacted significantly (Figure 2.5), showing a significant negative correlation between performance and ΔHbO (Figure 2.6) for 3D lead participants (3D/B1 group) as opposed to 2D lead participants (2D/B1 group). A relative neural efficiency analysis (Figure 2.7, Paas and Van Merriënboer, 1993; Paas et al., 2003) showed that while both groups improved relative neural efficiency from B1 to B2, the magnitude of change was considerably different, with those starting with the 3D condition showing increases in neural efficiency that were five times greater than those starting with 2D. This suggests that learning the ToH using the 3D puzzle, while more difficult, leads to higher cognitive efficiency in subsequent trials. Because of the task design, it is unclear if this improvement in neural efficiency would occur if the participants continued to perform the task manually.
As previously mentioned, 2D/B1 participants did not show a significant correlation between B1 and B2. Since a significant negative correlation between performance and neural activity indicates a shift towards higher neural efficiency, it can be concluded that participants in the 2D/B1 group did not learn the task, at least not as well as 3D/B1 participants. While this is an immediate effect given our study’s paradigm, our results are consistent with the study by Kantak et al. (2017) where they found that practicing a complex skill improves the long-term performance of the unpracticed simpler goal-directed task. The complex task presents the participant with higher motor and/or cognitive load, which in turn increases neuroplastic changes across the cognitive-motor network, essential for learning and its transfer (Nudo et al., 1996; Plautz et al., 2000; Meehan et al., 2011; Lefebvre et al., 2015; Wadden et al., 2015).
The improvement in neural efficiency in the 3D/B1 group may be a result of a contextual interference effect, where initial high contextual interference during skill acquisition leads to an initial decrement in performance followed by better performance once the skill is learned, as compared to a low interference task (Lee et al., 1992). In this study’s paradigm, the change in performance from B1 to B2 was greater when the 3D ToH condition was performed, along with the highest overall ∆HbO and subsequent lowest overall ∆HbO in the 2D ToH condition. Thus, having a more complex modality of a task, i.e., a 3D puzzle, would place higher demands on sensory information processing in addition to motor planning demands, which can be seen as interfering with the task itself and therefore increasing cognitive load. This result is analogous to that of Welsh and Huizinga (2005) where two sets of participants were administered either a blocked schedule of increasingly difficult ToH puzzles, or a random schedule with randomized order of puzzle difficulty. They found that as expected, the blocked group had a decrease in performance, whereas the random group increased their accuracy thereby evidencing a learning effect (Welsh and Huizinga, 2005).

2.5.4 Limitations and Future Directions

One limitation to this study is that participants were not stratified by individual differences, particularly differences that have been shown to reflect distinct brain activity such as fluid intelligence and spatial ability (Lamm et al., 2001; Neubauer and Fink, 2009; Dunst et al., 2014). Future work can address this limitation by creating distinct groups based on relevant individual differences amongst the participants. Additionally, future work can utilize other analysis techniques that take into
consideration temporal aspects of each epoch, in order to further assess for regional
differences, and expand analysis by using a system that allows to visualize more
regions of the brain.

2.6 Conclusion

To our knowledge, this is the first study that investigated the neural activity of
the PFC while controlling the cognitive component and manipulating movement,
using a 3D and 2D modality of the ToH puzzle. To answer the question posed by our
title, it appears that, in fact, movement does matter. Our results showed higher
oxyhemoglobin concentration for the 3D condition compared to the 2D condition,
suggesting a higher complexity for the 3D condition due to increased demands on
sensory processing and integration as well as motor planning. Practice and the order of
presentation contributed to a learning effect, where oxyhemoglobin decreased and
performance increased from B1 to B2 overall, however, the relationship was
significant for the 3D/B1 group unlike the 2D/B1 group. This suggests that not only
practice is important for performance, but also the complexity of the task first
performed which in turn leads to a refined cognitive strategy as shown by the
considerable decrease in oxyhemoglobin concentration from B1 to B2 in the 3D/B1
group. Overall, our results further support previous evidence by showing that neural
efficiency eases demands on EF, although it is contingent on task constraints. Our
results also provide further evidence in the importance of practicing a more complex
version of a task prior to executing a simpler version for learning and performance.
We plan to expand our exploration of PFC activity between the two- and three-
dimensional ToH conditions to children to narrow the potential points of impairment
on the perception-cognition-action continuum in certain developmental disabilities.
Chapter 3

DEVELOPMENTAL DIFFERENCES IN PREFRONTAL CORTEX ACTIVITY IN THE TOWER OF HANOI TASK WITH HIGH VS. LOW MOTOR ELEMENTS

3.1 Abstract

Our group has characterized hemodynamic activity in the prefrontal cortex (PFC) during the Tower of Hanoi (ToH) task in adults, however to our knowledge this has not been investigated in children. In study 2, we examined PFC activity in typically developing (TD) children using functional Near-Infrared Spectroscopy (fNIRS) as they solved the ToH puzzle, a validated and extensively used executive function task. Two conditions were presented to participants; the first condition utilized a traditional 3D model requiring manual manipulation. The second condition used a 2D computerized model that presented equivalent executive function demands yet with diminished motor requirements. Our aim was to further understand the PFC role in these two ToH conditions (high vs. low motor elements), and to characterize PFC activity in TD children during a cognitive-motor task. Eighteen TD children (5F/13M, $\bar{x} = 11.33$, SD ± 2.41 y.o.) participated in this study and were further separated into 2 age bands: younger (N=7, 1F/6M, $\bar{x} = 9.02$, SD ± 1.20 y.o.) and older (N=11, 4F/7M, $\bar{x} = 12.79$, SD ± 1.71 y.o.). These data were analyzed using a mixed effects ANOVA with participants nested within blocks for 2D vs 3D conditions, presentation order (leading block), individual participants, and regions in addition to follow-up statistics. In contrast to study 1, results in the TD sample did not show a significant effect when comparing $\Delta$HbO between 2D and 3D conditions for either younger or older children, although neural activity was larger in the 3D than in the 2D condition ($p > 0.05$). Likewise, a decrease in $\Delta$HbO was seen in B2 as opposed to B1.
in both conditions however the relationship was not significant for either group (p > 0.05). Lastly, performance did not significantly differed between blocks for both groups (p > 0.05). In conclusion, while the trends shown by the data suggest similar effects seen in adults, our results are not significant and therefore inconclusive. This information warrants further exploration to continue parsing developmental differences in PFC activity to guide future research into developmental disabilities, such as DCD, and probably points of impairment.

3.2 Introduction

In this study, we continue to investigate the hemodynamic activity of the prefrontal cortex (PFC) during the Tower of Hanoi (ToH) puzzle, however in typically developing (TD) children. Our research group has characterized PFC activity in adults while performing three-dimensional (3D) and two-dimensional (3D) variations of the ToH puzzle, thereby implementing a task with equivalent cognitive demands but distinct motor requirements (high vs. low; Milla et al., 2019).

Executive function (EF) is an umbrella term that encloses higher-order cognitive processes underlying modulation of thoughts, attention, and actions (Fuster, 2015; Wiebe & Karbach, 2018). The top model of EF emphasizes both the unity and variety that executive processes display (Miyake et al., 2000; Miyake & Friedman, 2012). Specifically, EF includes various processes such as attention shifting, goal monitoring and establishment, working memory updating, response inhibition, completion of goals, monitoring of results, and planning of actions, among others (Stuss & Benson, 1986; Moriguchi & Hiraki, 2013; Wiebe & Karbach, 2018).
EF is closely associated to the frontal lobes, particularly the PFC, a cerebral area critical to associating and integrating sensory inputs, thoughts, and actions that are relatively novel or changing fast (Grant & Berg, 1948; Shallice, 1982; Miller & Cohen, 2001; Stuss & Levine, 2002; Ball et al., 2011). Additionally, the PFC is critical to decision making, moderating social behavior, and planning complex cognitive behavior, such as outlining the execution of programmed sequences of actions and its consequences (Kawato, 1999; Yang & Raine, 2009; Selemon & Goldman-Rakic, 1988; Ongur & Price, 2000; Halgren, et al., 2002; Honey et al., 2002; Schall et al., 2003; Perianez et al., 2004; Owen et al., 2005; Simmonds et al., 2008).

Functional neural networks in the PFC underlying various EF processes become more distinct and separable throughout development (Tsujimoto, 2008). In other words, EF follows a protracted developmental trajectory that evolves over the life span of the individual and corresponds to the frontal lobes maturation and degeneration (Hedden & Gabrieli, 2004; Casey, et al., 2005; Moriguchi, 2018; West, 2018). Thus, the architecture of EF becomes more intricate through childhood and adolescence (Wiebe et al., 2008; Lee et al., 2013; Chevalier & Clark, 2018), with a subsequent deterioration in late adulthood (de Frias et al., 2009; Li et al., 2018).

This protracted development leads EF to be the last cognitive function to reach adult-like performance and the first one to decline (Li et al., 2004), in addition to amplifying EF’s susceptibility to environmental impact and experience, therefore magnifying exposure to both risks and interventions (Karbach & Unger, 2014; Hackman, Gallop, Evans, & Farah, 2015; Wass, 2015; Hughes & Devine, 2018; Finch
& Obradović, 2018). At the beginning stages of EF’s development trajectory, we see that infants are able to engage in simple goal-directed behaviors that provide the basis for the protracted development of executive control through childhood and adolescence (e.g., Cuevas & Bell, 2014; Cuevas, Rajan, & Bryant, 2018). As EF continues to develop, it experiences deep changes in early and middle childhood and evolves to sustain progressively more adaptive and flexible behavior that encourages independence (Chevalier & Clark, 2018).

Working memory, an important piece of EF, is defined as the ability to sustain a representation at a given time to assist in goal-directed activities (Cowan, 2015; Chevalier & Clark, 2018). Tasks requiring working memory place various demands on processes related to executive management, ranging from simply maintaining information in early childhood (i.e. forward digit span and spatial delay tasks), to concurrently manipulating information supported by processes such as updating, inhibition, and transformation in adulthood (i.e. counting span, self-ordered pointing, or listening span tasks; Linares, Bajo, & Pelegrina, 2016). Working memory progressively develops throughout childhood and into adolescence (e.g., Hitch, et al., 1989; Luciana & Nelson, 1998; Beveridge et al., 2002; DeLuca et al., 2003; Brocki & Bohlin, 2004; Gathercole et al., 2004; Luna et al., 2004; Luciana et al., 2005). Specifically, performance on elementary measures of spatial memory maintenance rise throughout early and middle childhood and reach plateau by early adolescence (Gathercole et al., 2004; Luciana et al., 2005). In turn, performance in complex working memory updating tasks, where retrieval of previously relevant information is needed, markedly progress in middle childhood and early adolescence and continue to
develop through late adolescence (e.g., Carriedo, Corral, Montoro, Herrero, & Rucián, 2016).

Likewise, inhibitory control increases throughout childhood and into adolescence, reaching adult-like levels of performance between 12 years old (Ridderinkhof & Van der Molen, 1995; Bédard et al., 2002; Bunge et al., 2002; Durston et al., 2002; Van den Wildenberg & Van der Molen, 2004), and early adolescence (Williams et al., 1999). Inhibitory control has also been shown to predict performance in the ToH task in a young-adult sample (Miyake et al., 2000).

Tower tests, such as the ToH and Tower of London (ToL), are extensively used neuropsychological tasks that assess EF in healthy individuals and several clinical populations (Goel & Grafman, 1995; Slomine et al., 2002; Griebling et al., 2009; Shuai et al., 2017; Yu et al., 2016), and remain valid to assess EF even when its parameters, such as the amount, size, and color of the disks used, differ (Baker et al., 1996; Boghi et al., 2006; Wagner et al., 2006; Just et al., 2007; Den Braber et al., 2008; Fitzgerald et al., 2008; Campbell et al., 2009; Zhu et al., 2010; De Ruiter et al., 2011; Kaller et al., 2011; Stokes, 2011; Hahn et al., 2012, Ruocco et al., 2014). Moreover, the ToH task requires performers to adequately respond to novel situations utilizing anticipatory, means-end problem-solving (Welsh & Huizinga, 2001), and has the advantage of being receptive to deficits in the PFC (Casey et al., 1994; Goel et al., 1995; Saint-Cyr et al., 1988; Simon, 1975).
Utilizing the ToL task, children have been shown to need more movements to successfully reach the end-goal (Kirk & Kelly, 1986; Welsh et al., 1991; Anderson et al., 1996; Baker et al., 2001; Lehto et al., 2003; Lehto, 2004), similarly to patients with PFC deficits (Owen et al., 1990; Morris et al., 1993; Carlin et al., 2000; Andres & Van der Linden, 2001). Moreover, Huizinga and colleagues (2006) showed a developmental improvement in the performance of the ToL leading to adult-like levels between the ages of 11-15. The percentage of perfect solutions improved into young-adulthood, in accord to previous studies (Welsh et al., 1991; Baker et al., 2001; Lehto, 2004; Anderson et al., 2005).

The aforementioned qualities of the Tower tests make the ToH puzzle a well-suited task to explore differences in motor-planning related EF in the prefrontal cortex of typically developing children. Furthermore, PFC activity during both 3D and 2D versions of the ToH has been investigated through various neuroimaging techniques such as EEG (Ruiz-Díaz et al., 2012; Guevara et al., 2013), fMRI (Griebling et al., 2009; Head et al., 2002; Crescentini et al., 2012), and fNIRS (Liang et al., 2016), with the latter being ideal to explore paradigms in ecologically valid settings and children populations due to being safe, non-invasive, portable, and tolerant to motion artifact (Kim et al., 2017; Caçola et al., 2018; Izzetoglu et al., 2005; Ayaz et al., 2011).

With this study, we aimed to determine if PFC hemodynamics in TD children differ as a function of 1) ToH condition (3D vs 2D), and 2) regions. We hypothesized that there would be greater changes in ΔHbO during the 3D condition as compared to the 2D condition of the ToH task in both age bands (H1). We also expected to see
regional areas with greater changes in ΔHbO than other regions within the same condition, also in both age bands (H2). Lastly, we describe differences observed between the 2 age bands of TD children and adult data from chapter 2 (Milla et al., 2019), to further explore associations between behavior and neural markers of EF activity.

3.3 Materials and Methods

3.3.1 Participants

Twenty four typically developing (TD) children (7F/17M) with a mean age of 11.29 (SD ± 2.36) years old were initially recruited for this study, twelve from the University of Delaware and Newark communities and twelve from the Federation University Australia and Ballarat communities. Results from a paired two-sample for means t-test showed that the two samples’ cognitive activity was not statistical significant from each other (p = 0.77). Participants were included if they were healthy and without known neurological deficits. Exclusion criteria included any head injury within the 6 months prior to testing, an open wound on the forehead, or a seizure disorder. After data collection, two participants were not included due to being left-handed and four participants were excluded due to incomplete data sets, leaving a total of n = 18 TD children (5F/13M, \( \bar{x} = 11.33 \), SD ± 2.41 years old), which were then separated into 2 age bands: younger children (7.00 – 10.99 y.o., n = 7) and older children (11.00 – 16.99 y.o., n = 11; see table 3.1 for further demographic details).
To assess hand dominance, participants completed the Edinburgh Handedness Inventory to assess hand preference for various tasks, such as writing, opening lids, and using utensils (Oldfield, 1971). Sixteen participants were all right-handed and had a mean Laterality Quotient (L.Q.) of 82.96 (SD ± 22.22) with an average Decile of 6.69 (SD ± 4.05; Oldfield, 1971). Researchers were unable to collect handedness information for the other participants. The Institutional Review Board at the University of Delaware and Federation University Australia approved the protocol for this study and participants provided written informed assent, in addition to parents providing written parental consent, after being educated on the study and its procedures.

3.3.2 Movement Assessment Battery for Children 2nd Edition

Children’s motor development was assessed using the Movement Assessment Battery for Children 2nd edition (MABC-2) specific to their age band (Henderson, Sugden, & Barnett, 2007). The MABC-2 consists of a checklist and a performance test; in this study we utilized the performance test which evaluates three different motor abilities: manual dexterity, aiming and catching skills, and balance. Each category includes 3-4 tests, which evolve in difficulty and are associated with quantitative scores that represent percentiles in motor performance. Children scoring a percentile at or less than 15th are considered “at risk” for Developmental Coordination Disorder (DCD), whereas children scoring at or below the 5th percentile are considered to have DCD (Henderson & Sugden, 2007). All children included in this study scored at or above the 16th percentile in the overall MABC-2 score, as depicted in Table 3.1.
Table 3.1. Average scores for the overall MABC-2 score and its 3 subcategories: manual dexterity (MD), aiming and catching (A&C), and balance (Bal). Values are depicted for the overall sample.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age</th>
<th>Overall MABC-2</th>
<th>MD</th>
<th>A&amp;C</th>
<th>Bal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>18</td>
<td></td>
<td>56.00 (± 20.97)</td>
<td>47.50 (± 26.00)</td>
<td>62.17 (± 24.41)</td>
<td>60.33 (± 27.54)</td>
</tr>
<tr>
<td>(5F/13M)</td>
<td></td>
<td>11.33 ± 2.41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger</td>
<td>7</td>
<td></td>
<td>58.71 (± 27.21)</td>
<td>42.00 (± 30.72)</td>
<td>61.43 (± 31.63)</td>
<td>66.29 (± 22.70)</td>
</tr>
<tr>
<td>(1F/6M)</td>
<td></td>
<td>9.02 ± 1.20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older</td>
<td>11</td>
<td></td>
<td>54.27 (± 18.41)</td>
<td>51.00 (± 24.82)</td>
<td>62.64 (± 21.72)</td>
<td>56.55 (± 31.86)</td>
</tr>
<tr>
<td>(4F/7M)</td>
<td></td>
<td>12.79 ± 1.71</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.3.3 Experimental Design

3.3.3.1 Conditions

The present study used two conditions: a 3D and a 2D modality of the ToH task. The first condition involved the use of a 3D wooden model, with three peg-holes and four graduated disks, which was physically manipulated during puzzle solving (Figure 3.1A). The second condition involved the use of a 2D computer model with custom-made opensource software (Salesforce Company, 2018), also consisting of three peg-holes and four graduated disks however manipulated through a computer mouse by clicking and dragging (Figure 3.1B). Block order (B1/B2) was randomized and counterbalanced using an online randomized integer sequence calculator (Haahr, 1998) resulting in 10 participants initially performing the 3D condition (3D first) and 8
participants initially performing the 2D condition (2D first). Figure 3.1 panel C shows the experimental set up.

![Figure 3.1](image1.png)

**Figure 3.1.** Different Tower of Hanoi conditions. **(A)** Three-dimensional (3D) condition performed by using one hand to move disks and the other hand to hold the frame. **(B)** Two-dimensional (2D) condition performed on a PC computer using one hand to manipulate a mouse. **(C)** Shows the experiment set up.

### 3.3.3.2 Protocol

Participants became familiar with the ToH puzzle by performing a practice attempt for each condition using three disks; there were no time constraints for this practice. Following practice, participants had a 1-min rest period, in which they
comfortably sat on a chair and focused their attention on a green cross on a screen in front of them, with their eyes open and sitting as still as possible. Following the initial rest period, participants attempted to solve ToH puzzles in two blocks (one per condition; block 1 = B1 and block 2 = B2), each consisting of three 1-min epochs with a 20-s rest in between to allow hemodynamic flow to return to baseline (Kuhtz-Buschbeck et al., 2003; Abibullaev et al., 2014; Yin et al., 2015; Huhn et al., 2019; Table 3.2). Using Welsh and Huizinga’s (2001) ToH-Revised list containing 22 items, 10 different puzzle configurations were created. Each puzzle had a unique combination of start and end disk positions, which in turn were ordered into two different sequences to avoid an order effect. Puzzles varied in difficulty, with the minimum number of moves required to solve a puzzle ranging from 8 to 15 (Appendix A) show the two sequences of 10 puzzles used in this study with associated difficulty).

Furthermore, puzzle sequence was randomized and counterbalanced. Each participant was presented with the same puzzle sequence for both 3D and 2D conditions, i.e., they were presented with different puzzles in each sequence but the sequence was identical for both blocks, allowing for a second attempt at a given puzzle if the previous puzzle was solved. After each block, participants had a 1-min rest period. Lastly, performance was utilized as a measure of behavior and defined as the number of puzzles participants attempted to solve throughout a condition.
Table 3.2. Protocol timeline for 3D/B1 participants. Participants were introduced to the puzzle with a practice attempt for each task, followed by a one-minute rest period prior to completing 2 blocks or problem-solving. 3D = three-dimensional ToH task; 2D = two-dimensional ToH task; R= rest.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice</td>
<td></td>
</tr>
<tr>
<td>3D</td>
<td>N/A</td>
</tr>
<tr>
<td>2D</td>
<td>N/A</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
<tr>
<td>Block 1</td>
<td></td>
</tr>
<tr>
<td>3D-1</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>3D-2</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>3D-3</td>
<td>60 s</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
<tr>
<td>Block 2</td>
<td></td>
</tr>
<tr>
<td>2D-1</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>2D-2</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>2D-3</td>
<td>60 s</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
</tbody>
</table>

3.3.4 Experimental Device

A 16-channel continuous-wave functional near-infrared (fNIRS) device (Ayaz et al., 2012, 2013) was utilized to collect data from the PFC of all participants (fNIR Devices LLC, Potomac, MD, USA). The sensor included 10 photo detectors and four light emitters (16 optodes total), each releasing light at 730–850 nm wavelengths and separated by 2.5 cm, which allowed for a penetration depth of about 1.2 cm (Ayaz et al., 2011). The fNIRS sensor band was placed on top of the participants’ forehead such that the center of the sensor’s horizontal axis was aligned to the center of the
participants’ head (symmetry axis of the head). The sensor’s vertical axis was positioned in the Fp1 and Fp2 locations in accordance to the international 10-20 system of cerebral electrode placement (Homan et al., 1987; Ayaz et al., 2006).

**Figure 3.2** depicts the fNIRS sensor band used in this study (fNIR Devices LLC, Potomac, MD, USA) and **Figure 3.3** shows an fMRI-based topographic map of the brain (Ayaz et al., 2018).

![fNIR® sensor pad used for data collection. Written informed consent was obtained from the individual to publish this image.](image-url)
Figure 3.3. (A) Brain template with data from sample participant depicting prefrontal regions under investigation. (B) Brain activity presented in 16 measurements locations (optodes) for the same participant. Data was further analyzed in clusters of 8 regions (C), and 4 regions (D). Figures B-D depict opposite laterality from figure A, i.e. the right side of the figure corresponds to the right hemisphere and vice versa.
3.3.5 Data Acquisition and Analysis

fNIRS data were sampled at 2 Hz and acquired using Cognitive Optical Brain Imaging (COBI) studio software (Ayaz et al., 2011). Data were processed using fNIRSoft Software (Version 4.9, Ayaz et al., 2018) and represents the mean activation during all three 1-min blocks for each condition. To obtain optimal signal acquisition, LED Current and Gain were adjusted until raw wavelength signal was verified to be between 40-4000 mV. The device was initiated and the first 10 s were utilized as baseline prior to task initiation. During this time, the participant remained still and focused on a green cross located in a computer screen across from the participant. Before placing the sensor band, an alcohol swab was used to clean the forehead of the participants and the light in the testing room was subsequently reduced. Researchers were careful to exclude any hair between the sensors and the participants’ forehead to obtain optimal signal acquisition. Raw light intensities were visually inspected and individual optodes rejected when data did not reflect hemodynamic activity due to lack of proper contact between the sensors and the forehead or placement on top of hair. Researchers also visually inspected the data and manually removed optodes in accordance to Ayaz et al. (2011). Then, a finite impulse response (FIR) filter (20th order, Hamming window) was used to low-pass filter the raw light intensity data at 0.1 Hz to remove input from physiological signals, such as respiration and heartbeat. Data were subsequently converted to changes in concentration using the modified Beer-Lambert law (Cope and Delpy, 1988) and depicted into four outcome measures: change in oxygenated hemoglobin (ΔHbO), change in deoxygenated hemoglobin (ΔHbR), total change in hemoglobin (ΔHbt) and total change in oxygenation (ΔOxy). We restricted our analysis to ΔHbO because our preliminary analysis showed high correlation among ΔHbO, ΔHbt, and ΔOxy, in addition to ΔHbO having stronger and
more wide-spread signals than those from ΔHbR and ΔHbT (Zhang et al., 2011), including in the ToH task (Liang et al., 2016a,b). Furthermore, it has been shown that ΔHbO has a strong correlation to BOLD signal whereas ΔHbR has a weak correlation (Strangman et al., 2002), in addition to better signal-to-noise ratio (SNR) than ΔHbR (Hoshi, 2007; Zhang et al., 2010). Finally, data depicting changes in concentration were processed using the detrending filter, which removes a drift in the data using linear parameters that convert the slope of the baseline to zero. Hemodynamic data for 18 participants were included in the analyses and reflected a mean activation of the three 1-min epochs for each condition. Furthermore, performance data for 17 participants were included in the analyses, defined as the number of puzzles a participant attempted to solve within each block out of 10 potential puzzles.

3.3.6 Statistical Analysis

Data were analyzed in JMP® Pro 13.1.0. As previously mentioned, participants were grouped into 2 age bands: younger children (7.00 – 10.99 y.o.) and older children (11.00 – 16.99 y.o). The effects of 2D vs 3D conditions, presentation order (leading block), regions, and age bands were examined using a mixed effects ANOVA with participants nested within blocks. A separate analysis was conducted for each of four representations of the optodes based on the sensor layout (Figure 3.3.B-D). Those four representations depicted data for the complete PFC (overall), a division of the PFC into 4 regions (left lateral, left medial, right medial, and right lateral), a division of the PFC into 8 regions (left lateral dorsal and ventral, left medial dorsal and ventral, right medial dorsal and ventral, and right lateral dorsal and ventral), and a division of the PFC into 16 regions, i.e. data for each of the individual optodes. An exploratory analysis subsequent to ANOVA investigated the significance of
conditions by considering paired differences between 2D and 3D for each participant and each optode representation in Tukey mean difference plots.

3.4 Results

3.4.1 ΔHbO in 2D vs. 3D Conditions

A mixed-effects ANOVA based on a mean ΔHbO response over all optodes was performed with conditions, presentation order, participants within blocks, and region as factors. Contrary to our prediction, ΔHbO was higher but not significantly for the 3D condition as opposed to the 2D condition in the overall sample (p = 0.0724), younger nor older groups (p > 0.05). However the trend seen in the data (Figure 3.4) suggests 2D vs. 3D is important overall. While not significant (p = 0.09865, Figure 3.5), the overall sample showed a higher ΔHbO response in block 1 (B1) for participants that began the protocol with the 3D condition (3D first), as compared to B2 where they completed the 2D condition. Participants that began the protocol with the 2D condition (2D first) had similar levels of ΔHbO in both blocks.

When looking at the younger and older groups, we see an interaction effect however not significant (p = 0.0586). All trends show a visible decrease in ΔHbO from B1 to B2 when the 3D condition is performed first, however the older children show lower changes in ΔHbO for the 2D first participants compared to the younger children and similarly to the adults (Figure 3.6).
Figure 3.4. Mean overall PFC activity in 3D vs. 2D trials represented by \( \Delta \text{HbO} \) (\( \mu \text{M} \)). While the 3D condition has visibly higher activity than the 2D condition, the relationship was not significant at the \( p = 0.05 \) level (\( p = 0.0724 \)). Error bars show standard error values.

Figure 3.5. Changes in \( \Delta \text{HbO} \) as represented by a Least Squares Means Plot (LS Means), where the blue lines represent the 3D condition and the red lines represent the 2D condition. While not significant at the \( p = 0.05 \) level, visibly higher \( \Delta \text{HbO} \) response in block 1 was seen for participants that began the protocol with the 3D condition (3D first), as compared to B2 where they completed the 2D condition.
Figure 3.6. Mean overall PFC activity in 3D first vs. 2D first participants represented by ΔHbO (µM). All 3 groups show a visible decrease in ΔHbO from B1 to B2 in 3D first participants, however the relationship was not significant at the p = 0.05 level (p = 0.0724). Older children show patterns of activity more similar to adults than younger children do. Error bars show standard error values.
3.4.2 $\Delta$HbO and regional analysis

With a similar mixed-effect ANOVA analysis using individual optode recordings for $\Delta$HbO, no significant differences were seen in regional activity using the 16, 8, or 4 optode model with this particular group ($p > 0.05$). In other words, specific sets of optodes did not show higher $\Delta$HbO activity within a condition.

3.4.3 $\Delta$HbO and Performance on ToH

We did not observe significant interactions between $\Delta$HbO and performance for neither group nor the overall sample ($p > 0.05$), in contrast to the results seen in adults for the 3D first group (Figure 3.7). $\Delta$HbO and performance showed a weak positive correlation from B1 to B2 in younger children, however the relationship became more negative for older children and was significantly negative in adults when the 3D condition was initially performed.
Figure 3.7. Correlations between ΔHbO and performance for all 3 groups. Neither the younger nor older children groups showed significant interactions for both 3D and 2D first. As shown in chapter 2, the adult sample showed a significant correlation for the 3D first participants (p < 0.01).
3.5 Discussion

3.5.1 Changes in oxyhemoglobin as a function of puzzle type

While the relationships were not significant at the p < 0.05 level, ∆HbO was higher for the 3D condition compared to the 2D condition (Figure 3.4), and for 3D first participants as opposed to 2D first participants (Figure 3.5). These trends suggest that the level of movement and order of presentation implicated in a motor-cognitive task, such as the ToH puzzle, are important in executive function processes in children. Furthermore, having lower cognitive activity in B2 compared to B1 when completing the 3D condition first, suggests that initially performing the most movement-enriched condition, i.e. 3D ToH puzzle, creates a shift towards a more efficient use of cognitive resources in children, similarly to adults (Milla et al., 2019), and would warrant further exploration.

Younger and older children did not show a significant interaction effect between conditions and block 1 (p = 0.0586), however Figure 3.6 visibly shows a decrease in ∆HbO from B1 to B2 in the 3D first participants for both groups. Notably, older children show changes in ∆HbO for the 2D first participants closer to baseline, as opposed to younger children whose ∆HbO was equally as high for 2D and 3D first. Therefore, we observe that patterns of PFC activity resemble more closely those of adults as children’s PFC and EF matures. In other words, patterns of activity observed in older children are more similar to that of adults than those observed in younger children, likely due to EF’s protracted development (Casey et al., 2005; Hedden & Gabrieli, 2004; Moriguchi, 2018; West, 2018) and PFC’s functional neural networks refinement throughout development (Tsujimoto, 2008).
3.5.2 Prefrontal cortex: Overall vs. regional differences

Contrary to our hypothesis but in accord to results in an adult sample (Milla et al., 2019), no significant differences were found in ∆HbO among optodes when explored into different regions (16, 8, and 4) for either each condition or block. As discussed in Milla et al. (2019) this could be due to fNIRS’ limited spatial resolution that is constrained by a 2-3 cm distance between the optical source and detector (Ayaz et al., 2011; Scarapicchia et al., 2017), as well as evaluating regional activity based on the default optode layout of the device. Additionally, individual differences such as fluid intelligence and spatial ability display distinct neural activity (Lamm et al., 2001; Neubauer and Fink, 2009; Dunst et al., 2014), which were not factored into our study and could have affected the results in unforeseen ways.

3.5.3 Associations Between Brain and Behavior

Despite previous evidence seen in adults were a significant negative correlation between ∆HbO and performance was found for 3D first participants, our study did not find any significant relationships for neither the younger nor the older sample (Figure 3.7). ∆HbO and performance showed a weak positive correlation from B1 to B2 in younger children, although the relationship became more negative throughout the development (i.e. in older children) until reaching significance with adults, this in 3D first participants.

We suspect that the differences between younger and older children, as well as adults, are due to PFC’s protracted development and EF’s concomitant evolution. The
absence of a shift towards higher neural efficiency (i.e. reduced cognitive load as indicated by ∆HbO with an increased performance) in both younger and older children groups when the 3D condition is initially performed could be due to children and adolescents being deficient in planning skills, with processes such as managing multiple spatial units and self-organization developing towards later adolescence (Luna et al., 2004; Luciana et al., 2005). Expanding this study to more participants and further breaking down the age range could potentially show this trend in later adolescence/young adulthood participants.

3.6 Conclusion

While the results from a children sample follow similar trends as those seen in an adult sample, i.e. higher cognitive activity in the 3D vs. the 2D ToH conditions as well as in B1 compared to B2 in 3D first vs. 2D first, the relationships are not significant and therefore results from this study are inconclusive and warrant further exploration. Future research could expand on this study by including a larger number and wider age range of participants, particularly participants considered in late adolescence/young adulthood, in order to identify when patterns of neural efficiency begin to resemble those in adults.
4.1 Abstract

Developmental coordination disorder (DCD) is a neuromotor disorder that affects motor coordination and the capacity to learn as well as to acquire motor skills in 5-8% of school-aged children. Despite evidence of difficulties with sensorimotor integration and motor planning, the etiology of the disorder is still unknown. A critical issue for therapeutic intervention is determining where dysfunction exists within the cerebral cortex that results in impaired movement. If dysfunction is related to motor planning, this would implicate areas such as the prefrontal cortex (PFC). However, if it is related to motor execution, this would implicate either the primary motor cortex or lower order motor structures. By examining the activity in the PFC during a problem-solving task that can be performed with high- and low- motor planning requirements, we hope to begin to decipher the role of the PFC in this disorder. To examine PFC activity, we used functional near-infrared spectroscopy (fNIRS), a technique that measures changes in hemoglobin oxygenation as an indirect measure of cortical activity. Previous studies have used fNIRS to examine cortical activity during executive function tasks, such as the Tower of Hanoi (ToH) puzzle. However, to our knowledge no study has examined the differences in prefrontal activity between a computerized (2D) and a manual (3D) version of the ToH puzzle in children with and without DCD. Thus, the aim of this exploratory study was to investigate differences in PFC hemodynamics between DCD and typically developing (TD) children in 2 versions of the Tower of Hanoi task. Four children (0F/4M) aged between 11 – 12 (\(\bar{x}\))
= 11.81, SD ± 0.58) years old were recruited for this study and classified with or at-risk for DCD if their Movement Assessment Battery 2n Edition (MABC-2) overall score was at or below 15th percentile, with a mean overall MABC-2 percentile of 4.78 (± 3.15). fNIRS data were collected while participants attempted to solve as many puzzles as possible during two blocks of three, one-minute epochs. Data were then analyzed using fNIRSoft software and the change in oxygenated hemoglobin (ΔHbO) was used to evaluate differences in cognitive activity. The gathered descriptive information showed larger ΔHbO in the 2D condition as opposed to the 3D condition for three out of 4 participants, as well as smaller ΔHbO in block 2 as opposed to block 1 for all participants. Furthermore, two participants performed above the average TD sample performance score (2.88 for B1 and 2.94 for B2), while one performed below and the other performed at the average TD performance score. Lastly, three participants showed generalized PFC activity for both conditions, whereas one participant (S3) showed localized activity to the dorsolateral PFC during the 3D condition, but generalized activity during the 2D condition. Overall, the descriptive information gathered in this study shows contrary findings to those seen in adults and TD children, in regards to PFC activity differences between 2D and 3D conditions. However, this information supports previous findings related to the effect of practice (B1 vs. B2) and generalized (i.e., lack of regional differences) activity. We hope to use this information as a starting point to further explore the role of the PFC in children with DCD, and elucidate the potential sources of dysfunction originating deficits in executive function and motor planning related processes.
4.2 Introduction

Developmental Coordination Disorder (DCD) is a neurodevelopmental motor disability that persistently affects coordination, fine and gross motor function, and the acquisition of motor skills in children without an obvious medical or intellectual origin (American Psychiatric Association, 2013; World Health Organization, 2016; Niklasson et al., 2018). The prevalence of this disorder is dependent on the assessment used and values have been found to be 4-5% in mainstream schools, according to Wright and Sugden (1996) two-step approach assessment, 6% for children aged 5-11 according to the American Psychiatric Association, and 5-13% of school-aged children worldwide (APA; Cousins & Smyth, 2003; Cairney et al., 2006; Hillier, 2007; Kirby & Sugden, 2007; Vaivre-Douret, 2014). Moreover, DCD is more often diagnosed in boys than in girls, with calculations varying from small differences to 3-4 times more (Sugden & Chambers, 1998; Dewey & Wilson, 2001; Kirby & Sugden, 2007). DCD severity varies and can persist through adulthood when no intervention occurs (Fox & Lent, 1996; Kirby & Sugden, 2007), in addition to often presenting with a variety of comorbid learning disorders, such as ADHD (Kadesjö and Gillberg, 1998; Pitcher et al., 2003; Watemberg et al., 2007), emotional problems (De Raeymaecker, 2006; Cairney et al., 2010), as well as speech, reading, and writing difficulties (Visser, 2003).

The heterogeneity of symptoms makes it challenging to identify the etiology of the disorder, however evident difficulties with sensorimotor integration, motor planning, and coordination are seen (Clark et al., 2005). Furthermore, children with DCD have difficulty using predictive control, pervasive issues with executive function and similar deficits in motor imagery and planning, similarly to children with mild
cerebral palsy (Wilson et al., 2017), all of which deficits in either motor execution or motor planning. The prefrontal cortex (PFC) has a crucial role in executive function, which can be defined as a set of processes underlying goal-directed behavior such as anticipation, goal establishment, monitoring of results, inhibition of action, and planning (Stuss & Benson, 1986; Wood & Graffman, 2003). Furthermore, the PFC is involved in motor planning related processes, such as outlining the execution of programmed sequences of actions and planning the consequences of such actions, also referred to as internal modeling (Kawato, 1999). Specifically, the PFC is concerned with the active representation of future events resulting from behavioral actions within a framework of problem-solving (Mushiake et al., 2009).

Neuroimaging studies using Diffusion Tensor Imaging (DTI) as well as structural and functional Magnetic Resonance Imaging (MRI and fMRI) have identified potential neurophysiological substrates of DCD that include the cerebellum (Zwicker et al. 2010 & 2011; Debrabant et al., 2013 & 2016), basal ganglia (Querne et al., 2008; Zwicker et al. 2012; McLeod et al., 2014; Debrabant et al., 2016), parietal lobe (Querne et al. 2008; Kashiwagi et al., 2009; Zwicker et al., 2010 & 2011; Debrabant et al., 2013 & 2016; McLeod et al., 2014; Licari et al., 2015), and regions of the frontal lobe (Langevin et al., 2015), such as the medial orbitofrontal cortex (Caeyenberghs et al., 2016) and notably, the dorsolateral PFC (Debrabant et al., 2013) which has been suggested as an exceptional neural correlate of DCD given its role in executive function and cognitive processes (Biotteau et al. 2016).
Furthermore, behavioral studies have also provided evidence of issues in anticipatory control of movement (Williams et al., 2011 & 2013; Noten et al., 2014; Fuelscher et al., 2015; Reynolds et al., 2015; Ferguson et al., 2015; Adams et al., 2016), basic processes of motor learning in more complex tasks (Jarus et al., 2015; Jelsma et al., 2015), and cognitive control (Shu et al., 2012; Asonitou et al., 2012; Pratt et al., 2014; Leonard et al., 2015; Asonitou & Koutsouki, 2016; Wilson et al., 2017). Notably, evidence has been shown that school-age children with DCD are the most challenged in executive function tasks with a visuospatial or motor load (Leonard et al., 2015), and adults with DCD have displayed consistent executive function deficits of moderate size even when participants were at-risk for DCD (Saban et al., 2012 & 2014).

Therefore, it is of interest to investigate the role of the PFC in children with DCD, specifically executive function and motor planning related processes. In attempting to resolve this uncertainty, the study utilized functional near-infrared spectroscopy (fNIRS), a technology that indirectly measures neural activity by calculating changes in the relative ratios of oxygenated (oxy-Hb, also ∆HbO) and deoxygenated (deoxy-Hb, also ∆HbR) hemoglobin in the capillary beds of cerebral cortices. The fNIRS technology is advantageous because it can discern both cognitive load and states in the PFC during activities of daily living or that require movement (Masataka, Perlovsky, & Hiraki, 2015), in addition to being non-invasive, portable, affordable, and safe for continuous and repeated measurements. Moreover, it is ideal to study cognitive activity during behavioral tasks in ecologically relevant conditions (Kim et al., 2017) given that fNIRS is tolerant to motion, assuming head mobility is
minimized (Izzetoglu et al., 2005), has a strong correlation with fMRI in measurements of hemodynamic activity (Ferrari & Quaresima, 2012; Kleinschmidt et al., 1996), has a better temporal resolution than fMRI and PET and a better spatial resolution than MEG and EEG (Bunce, Izzetoglu, Izzetoglu, Onaral, & Pourrezaei, 2006; Irani, Platek, Bunce, Ruocco, & Chute, 2007).

Given that the deficits displayed by children with DCD encompass processes related to executive function and motor planning (i.e. internal modelling) as well as manual control of actions (Wilson et al., 2017), it is crucial to explore PFC activity and whether any differences exist between DCD and TD children, particularly in a task that allows for equal demands on executive function (i.e. problem-solving) with differing demands on motor action. Tower tests, such as the Tower of Hanoi (ToH) puzzle, are validated and frequently used in research and clinical settings to assess problem-solving. The Tower of Hanoi puzzle is particularly useful since it is sensitive to disruption in the PFC (Casey, Vauss, Chused, & Swedo, 1994; Goel & Grafman, 1995; Saint-Cyr, Taylor, & Lang, 1988; Simon, 1975).

Thus, this study aims to further explore the role of the PFC in an executive function task with high- and low-motor components in children with DCD, and to compare with TD children to identify potential differences.
4.3 Materials and Methods

4.3.1 Participants

Four children (0F/4M) aged between 11 – 12 (\( \bar{x} = 11.81, \) SD ± 0.58, table 4.1) years old were recruited for this study, one from the University of Delaware and Newark communities, and three from the Federation University Australia and Ballarat communities. Children were administered the Movement Assessment Battery 2nd edition (MABC-2) and classified as DCD if their overall score fell at or below 15th percentile. Exclusion criteria included any head injury within the 6 months prior to testing, an open wound on the forehead, or a seizure disorder. Participants completed the Edinburgh Handedness Inventory to assess hand preference for various tasks, such as writing, opening lids and using utensils (Oldfield, 1971). Two participants were right-handed and had a mean Laterality Quotient (L.Q.) of 56.65 (SD ± 33.02) with an average Decile of 3.00 (SD ± 2.83), whereas one participant was left-handed and had a Laterality Quotient (L.Q.) of -100.00 with a Decile of 10.00 (Oldfield, 1971). Researchers were unable to gather handedness data for participant S3. The Institutional Review Board at the University of Delaware and Federation University Australia approved the protocol for this study and participants provided written informed assent, in addition to parents providing written parental consent, after being educated on the study and its procedures.
Table 4.1. Summary of participants age and overall MABC-2 scores. ± P2 and P3 are twin siblings.

<table>
<thead>
<tr>
<th>Participants</th>
<th>Age</th>
<th>MABC-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCD N = 4, 0F/4M</td>
<td>11.81 ± 0.58</td>
<td>4.78&lt;sup&gt;th&lt;/sup&gt; ± 3.15</td>
</tr>
<tr>
<td>P1</td>
<td>12.5</td>
<td>9&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>± P2</td>
<td>11.33</td>
<td>5&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>± P3</td>
<td>11.33</td>
<td>5&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>P4</td>
<td>12.08</td>
<td>0.1&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

4.3.2 Movement Assessment Battery for Children 2<sup>nd</sup> Edition

Children’s motor development was assessed using the Movement Assessment Battery for Children 2<sup>nd</sup> edition (MABC-2) specific to their age band (Henderson, Sugden, & Barnett, 2007). The MABC-2 consists of a checklist and a performance test; in this study we utilized the performance test which evaluates three different motor abilities: manual dexterity, aiming and catching skills, and balance. Each category includes 3-4 tests, which evolve in difficulty and are associated with quantitative scores that represent percentiles in motor performance. Children scoring a percentile at or less than 15<sup>th</sup> are considered “at risk” for Developmental Coordination Disorder (DCD), whereas children scoring at or below the 5<sup>th</sup> percentile are considered to have DCD (Henderson & Sugden, 2007). All children included in this exploratory study scored at or below the 15<sup>th</sup> percentile in the overall MABC-2 score, as depicted in Table 4.2.
Table 4.2. Average scores for the overall MABC-2 score and its 3 subcategories: manual dexterity (MD), aiming and catching (A&C), and balance (Bal).

<table>
<thead>
<tr>
<th>Overall MABC-2</th>
<th>MD</th>
<th>A&amp;C</th>
<th>Bal</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.78 (± 3.15)</td>
<td>4.65 (± 4.35)</td>
<td>34.88 (± 34.34)</td>
<td>8.75 (± 4.49)</td>
</tr>
</tbody>
</table>

4.3.3 Experimental Design

4.3.3.1 Conditions

The present study used two conditions: a 3D and a 2D modality of the ToH task. The first condition involved the use of a 3D wooden model, with three peg-holes and four graduated disks, which was physically manipulated during puzzle solving (Figure 4.1A). The second condition involved the use of a 2D computer model with custom-made opensource software (Salesforce Company, 2018), also consisting of three peg-holes and four graduated disks however manipulated through a computer mouse by clicking and dragging (Figure 4.1B). Block order (B1/B2) was randomized and counterbalanced using an online randomized integer sequence calculator (Haahr, 1998) resulting in eight participants initially performing the 3D condition (3D first) and 12 participants initially performing the 2D condition (2D first). Figure 4.1 panel C shows the experimental set up.
Figure 4.1. Different Tower of Hanoi conditions. (A) Three-dimensional (3D) condition performed by using one hand to move disks and the other hand to hold the frame. (B) Two-dimensional (2D) condition performed on a PC computer using one hand to manipulate a mouse. (C) Shows the experiment set up.

4.3.3.2 Protocol

Participants became familiar with the ToH puzzle by performing a practice attempt for each condition using three disks; there were no time constraints for this practice. Following practice, participants had a 1-min rest period, in which they comfortably sat on a chair and focused their attention on a green cross on a screen in front of them, with their eyes open and sitting as still as possible. Following the initial
rest period, participants attempted to solve ToH puzzles in two blocks (one per condition; block 1 = B1 and block 2 = B2), each consisting of three 1-min epochs with a 20-s rest in between to allow hemodynamic flow to return to baseline (Kuhtz-Buschbeck et al., 2003; Abibullaev et al., 2014; Yin et al., 2015; Huhn et al., 2019; Table 4.3). Using Welsh and Huizinga’s (2001) ToH-Revised list containing 22 items, 10 different puzzle configurations were created. Each puzzle had a unique combination of start and end disk positions, which in turn were ordered into two different sequences to avoid an order effect. Puzzles varied in difficulty, with the minimum number of moves required to solve a puzzle ranging from 8 to 15 (Appendix A) show the two sequences of 10 puzzles used in this study with associated difficulty).

Furthermore, puzzle sequence was randomized and counterbalanced. Each participant was presented with the same puzzle sequence for both 3D and 2D conditions, i.e., they were presented with different puzzles in each sequence but the sequence was identical for both blocks, allowing for a second attempt at a given puzzle if the previous puzzle was solved. After each block, participants had a 1-min rest period. Lastly, performance was utilized as a measure of behavior and defined as the number of puzzles participants attempted to solve throughout a condition.
Table 4.3. Protocol timeline for 3D/B1 participants. Participants were introduced to the puzzle with a practice attempt for each task, followed by a one-minute rest period prior to completing 2 blocks or problem-solving. 3D = three-dimensional ToH task; 2D = two-dimensional ToH task; R= rest.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Practice</td>
<td></td>
</tr>
<tr>
<td>3D</td>
<td>N/A</td>
</tr>
<tr>
<td>2D</td>
<td>N/A</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
<tr>
<td>Block 1</td>
<td></td>
</tr>
<tr>
<td>3D-1</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>3D-2</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>3D-3</td>
<td>60 s</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
<tr>
<td>Block 2</td>
<td></td>
</tr>
<tr>
<td>2D-1</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>2D-2</td>
<td>60 s</td>
</tr>
<tr>
<td>R</td>
<td>20 s</td>
</tr>
<tr>
<td>2D-3</td>
<td>60 s</td>
</tr>
<tr>
<td>Rest</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>60 s</td>
</tr>
</tbody>
</table>

4.3.4 Experimental Device

A 16-channel continuous-wave functional near-infrared (fNIRS) device (Ayaz et al., 2012, 2013) was utilized to collect data from the PFC of all participants (fNIR Devices LLC, Potomac, MD, USA). The sensor included 10 photo detectors and four light emitters (16 optodes total), each releasing light at 730–850 nm wavelengths and separated by 2.5 cm, which allowed for a penetration depth of about 1.2 cm (Ayaz et al., 2011). The fNIRS sensor band was placed on top of the participants’ forehead such
that the center of the sensor’s horizontal axis was aligned to the center of the participants’ head (symmetry axis of the head). The sensor’s vertical axis was positioned in the Fp1 and Fp2 locations in accordance to the international 10-20 system of cerebral electrode placement (Homan et al., 1987; Ayaz et al., 2006).

**Figure 4.2** depicts the fNIRS sensor band used in this study (fNIR Devices LLC, Potomac, MD, USA) and **Figure 4.3** shows an fMRI-based topographic map of the brain (Ayaz et al., 2018).

![fNIR® sensor pad used for data collection. Written informed consent was obtained from the individual to publish this image.](image)
Figure 4.3. (A) Brain template with data from sample participant depicting prefrontal regions under investigation. (B) Brain activity presented in 16 measurements locations (optodes) for the same participant. Data was further analyzed in clusters of 8 regions (C), and 4 regions (D). Figures B-D depict opposite laterality from figure A, i.e. the right side of the figure corresponds to the right hemisphere and vice versa.
4.3.5 Data Acquisition and Analysis

fNIRS data were sampled at 2 Hz and acquired using Cognitive Optical Brain Imaging (COBI) studio software (Ayaz et al., 2011). Data were processed using fNIRSoft Software (Version 4.9, Ayaz et al., 2018) and represents the mean activation during all three 1-min blocks for each condition. To obtain optimal signal acquisition, LED Current and Gain were adjusted until raw wavelength signal was verified to be between 40-4000 mV. The device was initiated and the first 10 s were utilized as baseline prior to task initiation. During this time, the participant remained still and focused on a green cross located in a computer screen across from the participant. Before placing the sensor band, an alcohol swab was used to clean the forehead of the participants and the light in the testing room was subsequently reduced. Researchers were careful to exclude any hair between the sensors and the participants’ forehead to obtain optimal signal acquisition. Raw light intensities were visually inspected and individual optodes rejected when data did not reflect hemodynamic activity due to lack of proper contact between the sensors and the forehead or placement on top of hair. Researchers also visually inspected the data and manually removed optodes in accordance to Ayaz et al. (2011). Then, a finite impulse response (FIR) filter (20th order, Hamming window) was used to low-pass filter the raw light intensity data at 0.1 Hz to remove input from physiological signals, such as respiration and heartbeat. Data were subsequently converted to changes in concentration using the modified Beer-Lambert law (Cope and Delpy, 1988) and depicted into four outcome measures: change in oxygenated hemoglobin (ΔHbO), change in deoxygenated hemoglobin (ΔHbR), total change in hemoglobin (ΔHbT) and total change in oxygenation (ΔOxy). We restricted our analysis to ΔHbO because our preliminary analysis showed high correlation among ΔHbO, ΔHbT, and ΔOxy, in addition to ΔHbO having stronger and
more wide-spread signals than those from ΔHbR and ΔHbT (Zhang et al., 2011), including in the ToH task (Liang et al., 2016a,b). Furthermore, it has been shown that ΔHbO has a strong correlation to BOLD signal whereas ΔHbR has a weak correlation (Strangman et al., 2002), in addition to better signal-to-noise ratio (SNR) than ΔHbR (Hoshi, 2007; Zhang et al., 2010). Finally, data depicting changes in concentration were processed using the detrending filter, which removes a drift in the data using linear parameters that convert the slope of the baseline to zero. Hemodynamic data for 4 participants were included in the analyses and reflected a mean activation of the three 1-min epochs for each condition. Furthermore, performance data for 4 participants were included in the analyses, defined as the number of puzzles a participant attempted to solve within each block out of 10 potential puzzles.

### 4.4 Results

#### 4.4.1 Summary of results

Overall, participants had the highest levels of cognitive activity (ΔHbO) in the first block as opposed to the second block. Three out of the 4 participants performed the 2D condition first, and as mentioned above, all had lowers levels of ΔHbO in the second block, irrespective of which condition was done first. Only one participant improved their performance score (P4) coupled with a decrease in ΔHbO, therefore showing a shift towards higher neural efficiency. All other participants either remained at the same level of performance or worsen, with the notable observation that all participants lowered their ΔHbO in the second block from the first block (Figure 4.4). A summary of these results is shown in Table 4.4.
Table 4.4. Summary of results for the overall DCD sample and each participant

<table>
<thead>
<tr>
<th>Group</th>
<th>3D vs. 2D (ΔHbO)</th>
<th>ΔHbO &amp; Performance: B1 vs. B2</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>2D↑</td>
<td>↓ ΔHbO, ↓ Performance</td>
</tr>
<tr>
<td>P2</td>
<td>2D↑</td>
<td>↓ ΔHbO, = Performance</td>
</tr>
<tr>
<td>P3</td>
<td>3D↑</td>
<td>↓ ΔHbO, = Performance</td>
</tr>
<tr>
<td>P4</td>
<td>2D↑</td>
<td>↓ ΔHbO, ↑ Performance</td>
</tr>
<tr>
<td>DCD</td>
<td>Not different, B1 &gt; B2 for all</td>
<td>Neural efficiency ≈ for 3 participants, ↑ for 1 and ↓ for 1</td>
</tr>
</tbody>
</table>

Figure 4.4. Association between neural activity, ΔHbO, and performance (number of puzzles attempted to solve). Only one participant improved their performance (P4), whereas 2 participants remained the same (P2 and P3) and one worsen (P1).
4.4.2 Participant 1

The first participant (P1) was a male with a chronological age of 12 years and 6 months at the time of testing. P1 had an overall MABC-2 score of 9\textsuperscript{th} percentile and scores of 9\textsuperscript{th}, 5\textsuperscript{th}, and 16\textsuperscript{th} for the Manual Dexterity (MD), Aiming & Catching (A&C), and Balance (Bal) sub-categories respectively. P1 was right-handed with a laterality quotient (L.Q.) of 33.3 and a Decile of 1. Furthermore, P1 initially performed the 2D condition and had a performance score of 4 for block 1 (B1), followed by a performance score of 3 in block 2 (B2). This fared poorly compared to the TD sample average performance score of 2.88 (± 1.36) for B1, and was similar to the average performance score of 2.94 (± 1.14) for B2.

As portrayed on Figure 4.5, P1 had a smaller change in activity in the 3D condition ($\Delta$HbO = 0.0030) as opposed to the mean activity seen in the TD sample ($\Delta$HbO = 0.3334). The change in neural activity was larger in the 2D condition ($\Delta$HbO = -0.2348) compared to that of the TD sample ($\Delta$HbO = -0.0063). When comparing 2D vs. 3D, $\Delta$HbO was smaller for 3D (0.0030) compared to 2D (-0.2348), opposing results seen in TD children (3D $\Delta$HbO = 0.3334 vs. 2D $\Delta$HbO = -0.0063).

The change in neural activity was larger in the first block as opposed to the second block (B1 $\Delta$HbO = -0.2348 vs. B2 $\Delta$HbO = 0.0030), similarly to the TD sample (B1 $\Delta$HbO = 0.3382 vs B2 $\Delta$HbO = -0.0111, Figure 4.6). Lastly, P1 showed generalized activity in the PFC for both conditions, similarly to the TD sample.
Figure 4.5. Topographs hemodynamic activity for each condition (2D and 3D) for the TD sample and P1.
Figure 4.6. Topographs portraying mean PFC hemodynamic activity for blocks 1 & 2 (B1 & B2) for the TD sample and P1.
4.4.3 Participant 2

The second participant (P2) was a male with a chronological age of 11 years and 4 months at the time of testing. P2 had an overall MABC-2 score of 5th percentile and scores of 0.5th, 84th, and 9th for the MD, A&C, and Bal sub-categories respectively. P2 was right-handed with a L.Q. of 80.0 and a Decile of 5. Furthermore, P2 initially performed the 2D condition and had a performance score of 4 in B1, followed by a performance score of 3 in B2. The TD sample had an overall average performance score of 2.88 (± 1.36) for B1 and of 2.94 (± 1.14) for B2.

As portrayed on Figure 4.7, P2 had smaller change in activity (ΔHbO = 0.0782) in the 3D condition as opposed to the mean activity seen in the TD sample (ΔHbO = 0.3334). Activity in the 2D condition was visibly larger (ΔHbO = 0.6718) than the mean activity seen in the TD sample (ΔHbO = -0.0063). When comparing 2D vs. 3D, ΔHbO was smaller for 3D (0.0782) compared to 2D (0.6718), opposing results seen in TD children (3D ΔHbO = 0.3334 vs. 2D ΔHbO = -0.0063).

Furthermore, activity was visibly lower in the second block as opposed to the first block (B1 ΔHbO = 0.6718 vs. B2 ΔHbO = 0.0782), similarly to the TD sample (B1 ΔHbO = 0.3382 vs B2 ΔHbO = -0.0111, Figure 4.8). Lastly, P2 showed generalized activity in the PFC for both conditions, similarly to the TD sample.
Figure 4.7. Topographs portraying mean PFC hemodynamic activity for each condition (2D and 3D) for the TD sample and P2.
Figure 4.8. Topographs portraying mean PFC hemodynamic activity for blocks 1 & 2 (B1 & B2) for the TD sample and P2.
4.4.4 Participant 3

The third participant (P3) was a male with a chronological age of 11 years and 4 months at the time of testing and a twin sibling of P2. P3 had an overall MABC-2 score of 5th percentile and scores of 9th, 50th, and 5th for the MD, A&C, and Bal sub-categories respectively. P3 initially performed the 3D condition and had a performance score of 1 in B1, followed by a performance score of 1 in B2, which fared poorly compared to the TD sample overall average performance score of 2.88 (+1.36) for B1 and of 2.94 (± 1.14) for B2.

As portrayed on Figure 4.9, P3 had visibly larger activity (ΔHbO = 0.6420) in the 3D condition as opposed to the mean activity seen in the TD sample (ΔHbO = 0.3334). Activity in the 2D condition was higher (ΔHbO = 0.3460) than the mean activity seen in the TD sample (ΔHbO = -0.0063). When comparing 2D vs. 3D, ΔHbO was larger for 3D (0.6420) compared to 2D (0.3460), similarly to results seen in TD children (3D ΔHbO = 0.3334 vs. 2D ΔHbO = -0.0063).

Furthermore, activity was lower in the second block as opposed to the first block (B1 ΔHbO = 0.6420 vs. B2 ΔHbO = 0.3460), similarly to the TD sample (B1 ΔHbO = 0.3382 vs B2 ΔHbO = -0.0111, Figure 4.10). Lastly, P3 showed focalized activity in the bilateral dorsolateral regions of the PFC during the 3D condition, unlike the TD sample, but generalized activity in the PFC during the 2D condition, similar to the TD sample.
Figure 4.9. Topographs portraying mean PFC hemodynamic activity for each condition (2D and 3D) for the TD sample and P3.
Figure 4.10. Topographs portraying mean PFC hemodynamic activity for blocks 1 & 2 (B1 & B2) for the TD sample and P3.
4.4.5 Participant 4

The fourth, and last, participant (P4) was a male with a chronological age of 12 years and 1 month at the time of testing. P4 had an overall MABC-2 score of 0.1\textsuperscript{th} percentile and scores of 0.1\textsuperscript{th}, 0.5\textsuperscript{th}, and 5\textsuperscript{th} for the MD, A&C, and Bal sub-categories respectively. P4 was left-handed with a L.Q. of -100 and a Decile of 10. Furthermore, P4 initially performed the 2D condition and had a performance score of 2 in B1, followed by a performance score of 3 in B2, which was similar to the TD sample overall average performance score of 2.88 (± 1.36) for B1 and of 2.94 (± 1.14) for B2.

As portrayed on Figure 4.11, P4 had lower activity ($\Delta$HbO = 0.0249) in the 3D condition as opposed to the mean activity seen in the TD sample ($\Delta$HbO = 0.3334). Activity in the 2D condition was higher ($\Delta$HbO = 0.1990) than the mean activity seen in the TD sample ($\Delta$HbO = -0.0063). When comparing 2D vs. 3D, $\Delta$HbO was lower for 3D (0.0249) compared to 2D (0.1990), opposing results seen in TD children (3D $\Delta$HbO = 0.3334 vs. 2D $\Delta$HbO = -0.0063).

Furthermore, activity was lower in the second block as opposed to the first block (B1 $\Delta$HbO = 0.1990 vs. B2 $\Delta$HbO = 0.0249), similarly to the TD sample (B1 $\Delta$HbO = 0.3382 vs B2 $\Delta$HbO = -0.0111, Figure 4.12). Lastly, P4 generalized activity in the PFC for both conditions, similar to the TD sample.
Figure 4.11. Topographs portraying mean PFC hemodynamic activity for each condition (2D and 3D) for the TD sample and P4.
Figure 4.12. Topographs portraying mean PFC hemodynamic activity for blocks 1 & 2 (B1 & B2) for the TD sample and P4.
4.5 Discussion

Overall, three of the four participants (P1, P2, & P4) described in this study had larger changes in oxyhemoglobin, ΔHbO, in the 2D condition as opposed to the 2D condition, which is contrary to the trend seen in TD children, albeit not significant, and the significant main effect seen in the adult sample. This can be due to those three participants initially performing the 2D condition, followed by the 3D condition in block 2. Therefore, they spent the most cognitive effort when solving ToH puzzles for the first time, i.e. block 1, even if the condition required reduced levels of movement, i.e. 2D condition. Therefore, all four participants had larger changes in oxyhemoglobin in block 1 compared to block 2, in accord to the trend seen in the TD sample and the significant main effect seen in the adult sample.

When it comes to performance, two (P1 & P2) participants scored above the average performance score of the TD sample ( > 2.88) for block 1, while the other two scored below the average performance score of the TD sample. In block 2, two participants (P1 & P2) worsen their score from block 1 but remained at the average for the TD sample, while one participant (P4) improved their score by one unit to reach average TD levels, and one participant (P3) remained at a performance score of 1. Interestingly, the participant with the lowest performance scores (P3) did not have the lowest manual dexterity (MD) percentile, while the participant with the lowest MD percentile (P4) performed around the average TD scores. While these data are exploratory, the differences in performance align with evidence showing that the magnitude and patterns of control issues displayed by children with DCD is dependent on the type of tasks and their complexity (Noten et al., 2014; Adams et al., 2016a,b). Furthermore, certain study paradigms utilized to explore internal modelling deficits
have shown children with DCD performing similarly to TD children (Wilson et al., 2017).

Lastly, regional activity did not seem to differ within a given condition, with three out of four participants visibly showing generalized PFC activity (P1, P2, & P4). One notable exception was that of participant P3, which visibly showed focalized activity in the bilateral dorsolateral PFC in the condition requiring more movement (3D condition), but generalized activity in the condition with lower movement requirements (2D condition). The lack of discernible differences could be due to the ToH task including end-state planning, which has been shown to results in less discernible distinctions in children with DCD (Noten et al., 2014; Adams et al., 2016), or the severity of DCD (Wilson et al., 2017).

### 4.6 Conclusion

Overall, the descriptive information gathered from four subjects classified as DCD shows contrary findings to those seen in adults and TD children, in regards to PFC activity differences between 2D and 3D conditions. However, this information supports previous findings related to the effect of practice (B1 vs. B2) and generalized (i.e., lack of regional differences) activity. We hope this information serves as starting point to further explore the role of the PFC in children with DCD, and elucidate the potential sources of dysfunction originating deficits in executive function and motor planning related processes.
Chapter 5

GENERAL CONCLUSIONS

Our goal with this thesis was to explore PFC activity in an EF task with high- and low- motor components across adults, typically development children, and children with DCD to better understand motor development and the potential source of deficits in children with DCD. Listed below are general conclusions and its implications grouped by topic as well as a table summarizing results from each study.

Table 5.1. Summary of results from each study. * indicates significant relationship.

<table>
<thead>
<tr>
<th>Group</th>
<th>3D vs. 2D (ΔHbO)</th>
<th>ΔHbO vs. Performance</th>
<th>B1/Condition interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 2: Adults</td>
<td>3D &gt; 2D, *p = 0.0211</td>
<td>↓ ΔHbO, ↑ Performance, *p &lt; 0.01</td>
<td>3D/B1 – B2 sig. different than 2D/B1 – B2, *p = 0.0015</td>
</tr>
<tr>
<td>Chapter 3: TD Children</td>
<td>3D &gt; 2D, p = 0.072</td>
<td>↑ΔHbO &amp; Performance for Y in 3D; ↓ΔHbO, ↑Performance for O, p &gt; 0.05</td>
<td>3D/B1 – B2 different than 2D/B1 – B2 between Y and O children p = 0.0586</td>
</tr>
<tr>
<td>Chapter 4: DCD Children</td>
<td>Not different, B1 &gt; B2 for all</td>
<td>Neural efficiency remain ≈ for most participants</td>
<td>B1 &gt; B2 for all</td>
</tr>
</tbody>
</table>
5.1 Changes in Oxyhemoglobin as a Function of Puzzle Type

In our study on neurotypical adults (chapter 2), we learned that movement matters when it comes to performance of a motor-cognitive task. Particularly, the performance of adult participants benefitted the most by first introducing the condition with the most “enriched” movement environment, i.e. the 3D condition, as shown by a shift towards higher neural efficiency (lower ΔHbO, and higher performance) in the second block. We learned that indeed, performing the 3D condition of the ToH puzzle places higher cognitive demands than the 2D condition, and that practice can reduce those cognitive demands.

In chapter 3, we shifted our focus towards typically developing children and while the results were inconclusive (i.e. relationships were not statistically significant at p = 0.05 level), the trends seen in the data suggest that the amount of movement (3D favored over 2D), and order of presentation (3D first instead of 2D first), also matters in children when it comes to cognitive demands (lower ΔHbO).

5.2 Prefrontal Cortex: Overall vs. Regional Differences

We observed a surprising result throughout our 3 studies: the lack of significant differences in regional activity, or generalized PFC activity. This can likely be explained by constraints in our neuroimaging device (i.e. fNIRS limited spatial resolution due to the optical source-detector distance), our analysis (i.e. parsing PFC regions based on the sensor layout), unaccounted individual differences (i.e. intelligence and spatial ability), or in the case of DCD children, the nature of the task and severity of the disorder. Future studies can replicate our study utilizing more
advanced fNIRS devices such as the ETG 4100 Hitachi fNIRS Device, which would also collect information from other cortical areas along the PFC.

5.3 Developmental Associations Between Brain and Behavior

In chapter 3, we observed a lack of significant correlations between ΔHbO and performance for both younger and older children, although the initially seen weak correlation becomes more negative throughout development and reaches significance in adulthood when the 3D condition is performed first (Chapter 2, Milla et al., 2019). These differences appear to follow the protracted development of the PFC and EF, and the lack of improvements in neural efficiency in children as likely due to their documented deficits in planning skills which develop towards later adolescence (Luna et al., 2004; Luciana et al., 2005). Expanding this study to more participants and further breaking down the age range could potentially show this trend in later adolescence/young adulthood participants.

5.4 DCD implications

In chapter 4 we evaluated data on four children with DCD through a descriptive study and found that contrary to findings in adults and TD children, cognitive activity was the largest in the 2D condition for 3 out of 4 participants. However, it must be kept in mind that those three participants performed the 2D condition in block 1, thereby practice likely factors into this trend (cognitive activity decreased in B2 as compared to B1 in all DCD participants).
Furthermore, we saw that only one participant improved their performance score coupled with a decrease in ΔHbO therefore shifting towards higher neural efficiency. All other participants either remained at the same level of performance or worsen, with the notable observation that all participants lowered their ΔHbO in the block 2, indicating that the task became too challenging for the participants and therefore cause a loss of motivation as evidence by both lower cognitive activity and equal or lower performance. Future studies could adapt our current paradigm to reduce the challenge in the ToH puzzles by either reducing the number of disks or presenting puzzles easier to solve (i.e. less number of moves necessary to reach the end-goal) and thus assess when children with DCD shift towards higher neural efficiency and if beginning the protocol with the 3D condition is more beneficial to their performance as opposed to the 2D condition.

5.5 Clinical and practical implications

Our paradigm could be used for EF training geared towards populations with known EF deficits, such as children at-risk or with DCD, ADHD, and even intellectual disabilities (Rueda et al., 2005; Titz & Karbach, 2014; Kirk et al., 2015). Our findings should be considered in this intervention and present the more “movement enriched” condition (i.e. the 3D condition) first before moving onto the less complex condition. While this was not done in our paradigm, the difficulty of the ToH puzzles can be adapted to the training needs of the individual to reduce the challenge by presenting puzzles that require a lower amount of moves to be solved, or reducing the number of disks from 4 to 3. Likewise, the puzzle itself can be very challenging regardless of its modality, as it was the case of children with DCD seen in chapter 4. In that case, EF
training can be accomplished by simply performing the 2D version of the task and again, adjusting the challenge of the puzzles to the individual’s needs in order to maintain motivation and therefore lead to increases in neural efficiency.

Lastly, our paradigm could also be used to assess a baseline level prior to an intervention, as well as a subsequent treatment response measure to evaluate the effectiveness of such intervention in an occupational or physical therapy setting.

5.6 Limitations and future directions

The spatial resolution of our fNIR device and software limited the detection of regional differences, thus future research could replicate our study utilizing more advanced fNIRS devices such as the ETG 4100 Hitachi Device, which would also collect information from other cortical areas in addition to the PFC.

Despite observing relationships in our TD sample similar to those in our adult sample, our results were not significant at the p = 0.05 level and therefore the evidence drawn from chapter 3 is inconclusive and warrants further exploration. Future research could replicate and expand this study by evaluating a larger number and wider age range of participants, to parse out developmental differences, particularly to identify the point at which adolescents’ neural efficiency resembles more closely that of adults.

In chapter 4, we observed that children with DCD found our paradigm too challenging and loss motivation, as evidenced by 3 out of 4 participants either remaining at the same level of performance or worsening in block 2 compared to
block 1, along with a decrease in cognitive activity (ΔHbO) for all 4 participants. Future studies could adapt our current paradigm to reduce the challenge in the ToH puzzles by either reducing the number of disks or presenting puzzles easier to solve (i.e. less number of moves necessary to reach the end-goal) and thus assess when children with DCD shift towards higher neural efficiency and if beginning the protocol with the 3D condition is more beneficial to their performance as opposed to the 2D condition.

While the TD and DCD children studies provided inconclusive and exploratory data respectively, we hope to utilize the information gained on PFC activity and concomitant performance to continue exploring the PFC’s role in motor-cognitive tasks, particularly to elucidate the potential source of dysfunction in DCD originating deficits in EF and motor planning related processes.


Appendix A

SUPPLEMENTARY MATERIALS

Figure A1. Sequence 1 containing the ten ToH puzzles utilized in this study. ToH puzzle sequences were created based on Welsh and Huizinga’s (2001) Tower of Hanoi-Revised list containing 22 items. Start = starting position, End = end goal position.
Figure A2. Sequence 2 containing the ten ToH puzzles utilized in this study. Start = starting position, End = end goal position.
Table A1. Difficulty for each ToH puzzle represented as the minimum number of moves necessary to reach the solution (end goal position). Both sequences contain the same puzzles but presented in a different order.

<table>
<thead>
<tr>
<th>Sequence 1</th>
<th>Sequence 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Puzzle number</strong></td>
<td><strong>Puzzle number</strong></td>
</tr>
<tr>
<td><strong>Minimum # moves to solution</strong></td>
<td><strong>Minimum # moves to solution</strong></td>
</tr>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
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<tr>
<td>6</td>
<td>13</td>
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<td>7</td>
<td>13</td>
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<td>8</td>
<td>15</td>
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<td>9</td>
<td>8</td>
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<tr>
<td>10</td>
<td>11</td>
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<tr>
<td>1</td>
<td>11</td>
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<tr>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
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<tr>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>15</td>
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<tr>
<td>6</td>
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<tr>
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<td>13</td>
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</tr>
<tr>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>
Appendix B

STUDY FORMS

B.1 Demographics form

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>Weight</td>
</tr>
<tr>
<td>Date of birth</td>
<td>Sex</td>
</tr>
<tr>
<td>Dominant hand</td>
<td>R</td>
</tr>
</tbody>
</table>

Please circle one answer:

1. Have you had a head injury within the last 6 months? I.e. concussion, etc.
   No       Yes

2. Have you ever had a seizure?
   No       Yes

3. Have you ever been diagnosed with any mental disorders or learning disabilities?
   No       Yes
   a. If yes, please list all of them:

4. Have any of your family members ever been diagnosed with any mental disorders?
   No       Yes
   a. If yes, please list all of them:

5. Do you have previous experience solving the Tower of Hanoi puzzle?
   No       Yes
   a. If yes, please rate your level of expertise:
      Beginner       Moderate       Expert
### B.2 Edinburgh Handedness Inventory

<table>
<thead>
<tr>
<th>Activity</th>
<th>Left</th>
<th>Right</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Writing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Drawing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Throwing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Scissors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Toothbrush</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Knife (without fork)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Spoon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Broom (upper hand)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Striking Match (match)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Opening box (lid)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Additional Questions**

i. Which foot do you prefer to kick with?

ii. Which eye do you use when using only one?

L.Q. Leave the spaces blank.

DECLE.
Appendix C

IRB CONSENT, ASSENT, AND PARENTAL CONSENT FORMS

C.1 Consent form

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Title of Project: Performance of the Tower of Hanoi and its relationship to activations in the prefrontal cortex in children with and without developmental coordination disorder

Principal Investigator(s): Dr. Nancy Gates

You are being invited to participate in a research study. This consent form tells you about the study including its purpose, what you will be asked to do if you decide to take part, and the risks and benefits of being in the study. Please read the information below and ask us any questions you may have before you decide whether or not you want to participate.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to learn whether your brain works differently in performing different types of tasks. You will play two types of disk-transfer games, one on a computer with specific rules, and one with a wooden set of disks with specific rules.

You will be one of approximately 50 participants in this study.

WHY ARE YOU BEING ASKED TO PARTICIPATE?

You are being asked to participate because you are a healthy adult without a history of mental illness. You will be excluded if you have 1) previous head injury, 2) open wound on forehead, and 3) seizure disorder.

WHAT WILL YOU BE ASKED TO DO?

As part of this study you will be asked to come to our lab one time for about 45 minutes. You will need to complete an exclusion criteria questionnaire, sign the informed consent form, and fill out a handedness inventory. Then, we will explain how to play the disk-transfer game called the Tower of Hanoi. The Tower of Hanoi has three pegs and 4 disks. The goal of the game is to move disks from a starting state to a goal state following specific rules. You will have an opportunity to practice. In our study, there will be up to 10 different puzzles of the Tower of Hanoi that you need to solve. We will show you either a picture or a wooden model of a puzzle to you. You will see both the starting state and the goal state. You need to figure out how to move the disks from the starting state to the goal state on the picture. After you finish one puzzle, we will give you another puzzle until one minute of solving puzzles is completed. Then you will have 20 seconds to rest followed by more puzzles until three, one-minute intervals of solving puzzles are completed. Next we will show you the picture of the following puzzle, up to a total of 10 different puzzles. You will solve these puzzles with a wooden set of the Tower of Hanoi, and also on a computer. The puzzles you will play on a computer and with a wooden set of the Tower of Hanoi are the same but may show up in different orders.

Participant's Initials: 

Page 1 of 4
The wooden set of the Tower of Hanoi (left). The Tower of Hanoi on the computer (right).

We want to know how your brain works so we will use a device to study your brain. We will clean your forehead with an alcohol swab. A pad will be placed on your forehead like you are wearing a headband. The pad will project light on your forehead and let us see your brain. All you need to do is playing disk-transfer games with the sensor pad on your forehead like the lady in the picture below. We will take videos while you are playing disk-transfer games so that we can know how you move the disks and solve the puzzles.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Possible risk of participating in this research study is minimal. fNIRS has been used in research with adults, children and even infants. It carries minimal risks to the participants. You might feel a cold sensation after we use alcohol swabs to clean your forehead but the cold sensation should not last too long. Also, the sensor pad on your forehead could make your skin red but the marks should go away in few hours. You could feel frustrated while you are trying to solve the puzzles but we believe that you can complete the puzzles eventually.

WHAT ARE THE POTENTIAL BENEFITS?

You will not benefit directly from taking part in this research. However, the knowledge gained from this study may contribute to our understanding of how a mature brain works in controlling different type of tasks.
NEW INFORMATION THAT COULD AFFECT YOUR PARTICIPATION:

During the course of this study, we may learn new information that could be important to you. This may include information that could cause you to change your mind about participating in the study. We will notify you as soon as possible if any new information becomes available.

HOW WILL CONFIDENTIALITY BE MAINTAINED? WHO MAY KNOW THAT YOU PARTICIPATED IN THIS RESEARCH?

Your participation in this study will be kept confidential. Personal information of you will be documented on paper and available to researchers only. No information identifying you will be released without your permission unless it is subject to a subpoena or a court order. If the results of the study are published or presented at scientific meetings, your name will not be revealed.

The paper document of your participation will be stored in a locked cabinet in the Developmental Motor Control Lab at the University of Delaware for 5 years then destroyed. The data file we collect will be identified by codes only, for example: S01. No personal information will be saved in the data file. The data file we collect will be stored in password protected computers in the Developmental Motor Control Lab in the Human Performance Lab at the University of Delaware for 5 years then destroyed. The data will be available to the researchers only.

You may withdraw consent and/or stop participation in the study at any time without penalty. If you withdraw, you can ask us to destroy all previously collected data. The results will be reported in group averages. The videos we will take are for researchers of this study only.

The confidentiality of your records will be protected to the extent permitted by law. Your research records may be viewed by the University of Delaware Institutional Review Board, which is a committee formally designated to approve, monitor, and review biomedical and behavioral research involving humans. Records relating to this research will be kept for at least three years after the research study has been completed.

WILL THERE BE ANY COSTS TO YOU FOR PARTICIPATING IN THIS RESEARCH?

There are no costs associated with participating in the study.

WILL YOU RECEIVE ANY COMPENSATION FOR PARTICIPATION?

There is no compensation for your participation.

DO YOU HAVE TO TAKE PART IN THIS STUDY?

Taking part in this research study is entirely voluntary. You do not have to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide not to participate or if you decide to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which you are otherwise entitled.

Participant's Initials ________
Your decision to stop participation, or not to participate, will not influence current or future relationships with the University of Delaware. As a student, if you decide not to take part in this research, your choice will have no effect on your academic status or your grade in the class.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact the Principal Investigator, Dr. Nancy Getchell at (302) 831-6682 or getchell@udel.edu.

If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at irb-research@udel.edu or (302) 831-2137.

Your signature on this form means that: 1) you are at least 18 years old; 2) you have read and understand the information given in this form; 3) you have asked any questions you have about the research and those questions have been answered to your satisfaction; 4) you accept the terms in the form and volunteer to participate in the study. You will be given a copy of this form to keep.

Printed Name of Participant: ______________________ Sign of Participant: ______________________ Date: ________

Person Obtaining Consent: ______________________ Person Obtaining Consent: ______________________ Date: ________

(PRINTED NAME) (SIGNATURE)

OPTIONAL CONSENT TO BE CONTACTED FOR FUTURE STUDIES:

Do we have your permission to contact you regarding participation in future studies? Please write your initials next to your preferred choice.

_______ YES  ________ NO

Participant’s Initials: ________
C.2 Assent form

ASSENT TO PARTICIPATE IN RESEARCH

Title of Project: Performance of the Tower of Hanoi and its relationship to activations in the prefrontal cortex in children with and without developmental coordination disorder

Investigator(s): Dr. Nancy Getchell

I am asking if you want to be part of a research study. This form tells you what the study is about, what you will be asked to do if you want to be in the study, and the possible bad and good things about this study. Please read this paper and ask us any questions you have.

WHAT IS THE PURPOSE OF THIS STUDY?

This research study is to help us learn about how your brain works while you are playing disk-transfer games. You will play two types of disk-transfer games and we believe your brain works differently in each type of games.

We are asking you if you want to be in it because you are between 8 to 16 years old and we want to learn about children in this age range.

WHAT WILL YOU BE ASKED TO DO?

If you want to participate we will ask your parents to bring you to our lab one time for about 75 minutes. First, we will test how you move. Next, you will play a computer and wooden disk game called Tower of Hanoi. The goal is to move disks from a starting point on one peg to a finish point on a different peg following some specific rules. You will have a chance to practice. In our study, there will be up to 10 different puzzles of the Tower of Hanoi that you need to solve. We will show you either a picture or a wooden model of a puzzle to you. You need to figure out how to move the disks from one peg to another. Then we will show you the picture of the next puzzle, up to a total of 10 puzzles. The ten puzzles will be the same but may show up in different orders.

The wooden set of the Tower of Hanoi (left). The Tower of Hanoi on the computer (right).

Page 1 of 3

Participant's Initials _____________
We want to know how your brain works so we will use a device to study your brain. We will clean your forehead with an alcohol swab. A pad will be placed on your forehead like you are wearing a headband. The pad will project light on your forehead and let us see your brain activity. All you need to do is playing disk-transfer games with the sensor pad on your forehead like the lady in the picture below. We will take video while you playing the disk-transfer games so that we can know how you move disks and solve the puzzles.

WHAT ARE THE POSSIBLE BAD THINGS ABOUT THIS RESEARCH?

There are a few things about this study that could make you uncomfortable or hurt you. When we place the pad on your forehead, we will clean your forehead using alcohol swabs. Your forehead might feel cold from the alcohol, but this should not last too long. Also, the sensor pad on your forehead could make your skin red. These the marks should go away in few hours. Solving the puzzle might feel hard, and you could feel frustrated while you are trying to solve the puzzles. We want you to do your best, and believe that you can eventually finish the puzzles.

WHAT ARE THE POTENTIAL GOOD THINGS ABOUT IT?

There is no potential benefit to you and you will not benefit directly from being in the study. We hope to learn new things during this study that would help to better teach other children how to use their brain to solve problems.

WHO MAY KNOW THAT YOU PARTICIPATED IN THIS RESEARCH?

No one other than the investigators will know that you were in this study. If we tell other people about the research we will not use your name. We will use the video we take only to understand how you play and we will not show the videos to other people.

We also must let you know that if you tell us that someone has done or is doing bad things to you or other children, we will tell people who can help.

WILL YOU RECEIVE ANY COMPENSATION FOR PARTICIPATION?

There is no compensation.
CAN YOU CHANGE YOUR MIND ABOUT BEING IN THE STUDY?

You do not have to say yes. Taking part in this research study is up to you. If you choose to take part, you can change your mind and stop at any time. If you decide not to participate or if you decide to stop taking part in the research later, nothing bad will happen to you and no one will be upset with you. If, at any time, you decide to stop please let us know by telling one of the researchers.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please tell Dr. Nancy Getchell at (302) 831-6682 or getchell@udel.edu.

If you have any questions or concerns about your rights as a research participant, you may contact the University of Delaware Institutional Review Board at irb-research@udel.edu or (302) 831-2137.

If you want to participate, and we have answered all of your questions about it, please sign below.

Printed Name of Participant ___________________________ Signature of Participant ___________________________ Date ________

______________________________ ___________________________ ___________________________ ___________________________ ___________________________
Person Obtaining Consent Person Obtaining Consent Date

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Participant’s Initials: ___________________________
C.3 Parental Consent Form

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Title of Project: Performance of the Tower of Hanoi and its relationship to activations in the prefrontal cortex in children with and without developmental coordination disorder

Principal Investigator(s): Dr. Nancy Getchell

Your child is being invited to participate in a research study. This consent form tells you about the study including its purpose, what you and your child will be asked to do if you decide to take part, and the risks and benefits of being in the study. Please read the information below and ask us any questions you may have before you decide whether or not to allow your child to participate.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this study is to learn how the brain works in performing different types of tasks. Your child will play two types of disk-transfer games, one on a computer with specific rules, and one with a wooden set of disks with specific rules.

Your child will be one of approximately 50 participants in this study.

WHY IS YOUR CHILD BEING ASKED TO PARTICIPATE?

Your child is being asked to participate because your child is 8 to 16 years old. Your child will be excluded if he/she has 1) previous head injury, 2) open wound on forehead, 3) seizure disorder, and 4) family history of mental diseases.

WHAT WILL YOUR CHILD BE ASKED TO DO?

As part of this study you will be asked to bring your child to our lab one time for about 75 minutes. You will need to complete an exclusion criteria questionnaire, sign the inform consent form, and fill out a handedness inventory for your child. We will test your child’s motor development with the movement assessment battery (M-ABC) at the beginning of the session and then we will explain to your child how to play the disk-transfer game called the Tower of Hanoi. The Tower of Hanoi has three pegs and 4 disks. The goal of the game is to move disks from a starting state to a goal state following specific rules. Your child will have an opportunity to practice. In our study, there will be up to 10 different puzzles of the Tower of Hanoi that your child needs to solve. We will show either a picture or a wooden model of a puzzle to your child. Your child will see both the starting state and the goal state. Your child needs to figure out how to move disks from the starting state to the goal state on the picture. After finishing one puzzle, we will give your child another puzzle until one minute of solving puzzles is completed. Then your child will have 20 seconds to rest followed by more puzzles until three, one-minute intervals of solving puzzles are completed. Your child will solve these puzzles with a wooden set of the Tower of Hanoi, and also on a computer. The puzzles: your child will play on a computer and with a wooden set of the Tower of Hanoi are the same but they may show up in different orders.

Parent/guardian’s Initials ________
The wooden set of the Tower of Hanoi (left). The Tower of Hanoi on the computer (right).

We want to know how the brain works so we will use a device to measure your child’s brain. We will clean their forehead with an alcohol swab. A pad will be placed on their forehead like wearing a headband. The pad will project light on their forehead and let us see their brain activity. All your child needs to do is playing disk-transfer games with the sensor pad on their forehead like the lady in the picture below. We will take videos while your child playing disk-transfer games so that we can know how he/she moves disks and solve the puzzles.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Possible risk of participating in this research study is minimal. fNIRS has been used in research with adults, children and even infants. It carries minimal risks to the participants. Your child might feel a cold sensation after we use alcohol swabs to clean their forehead but the cold sensation should not last too long. Also, the sensor pad on their forehead could make their skin red but the marks should go away in few hours. Your child could feel frustrated while he/she is trying to solve the puzzles but we believe that your child can complete the puzzles eventually.

Parent/guardian’s Initials ________
WHAT ARE THE POTENTIAL BENEFITS?

Your child will not benefit directly from taking part in this research. However, the knowledge gained from this study may contribute to our understanding of how the brain works in controlling different type of tasks.

NEW INFORMATION THAT COULD AFFECT YOUR PARTICIPATION:

During the course of this study, we may learn new information that could be important to your child. This may include information that could cause you to change your mind about participating in the study. We will notify you as soon as possible if any new information becomes available.

HOW WILL CONFIDENTIALITY BE MAINTAINED? WHO MAY KNOW THAT YOUR CHILD PARTICIPATED IN THIS RESEARCH?

Your child’s participation in this study will be kept confidential. Personal information of your child will be documented on paper and available to researchers only. No information identifying your child will be released without your permission unless it is subject to a subpoena or a court order. If the results of the study are published or presented at scientific meetings, your child’s name will not be revealed.

The paper document of your child’s participation will be stored in locked cabinet in the Developmental Motor Control Lab at the University of Delaware for 5 years then destroyed. The data file we collect will be identified by codes only, for example: S01. No personal information will be saved in the data file. The data file we collect will be stored in password protected computers in the Developmental Motor Control Lab in the Human Performance Lab at the University of Delaware for 5 years then destroyed. The data will be available to the researchers only. The results will be reported in group averages. The videos we will take are for researchers of this study only.

The confidentiality of your child’s records will be protected to the extent permitted by law. Your child’s research records may be viewed by the University of Delaware Institutional Review Board, which is a committee formally designated to approve, monitor, and review biomedical and behavioral research involving humans. Records relating to this research will be kept for at least three years after the research study has been completed.

WILL THERE BE ANY COSTS TO YOU FOR PARTICIPATING IN THIS RESEARCH?

There are no costs associated with participating in the study.

WILL YOU RECEIVE ANY COMPENSATION FOR PARTICIPATION?

There is no compensation.

DOES YOUR CHILD HAVE TO TAKE PART IN THIS STUDY?

Parent/guardian’s Initials ________
Taking part in this research study is entirely voluntary. You do not have to agree to allow your child to participate in this research. If you choose to take part, you have the right to stop at any time. If you decide not to participate or if you decide to stop taking part in the research at a later date, there will be no penalty or loss of benefits to which you are otherwise entitled.

Your decision to stop participation, or not to participate, will not influence current or future relationships with the University of Delaware.

WHO SHOULD YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

If you have any questions about this study, please contact the Principal Investigator, Dr. Nancy Getchell at (302) 831-6682 or getchell@udel.edu.

If you have any questions or concerns about your child’s rights as a research participant, you may contact the University of Delaware Institutional Review Board at hrpb-research@udel.edu or (302) 831-2137.

You are making a decision whether or not to have your child participate in this study. Your signature indicates that you have read the information provided above and decided to allow your child to participate.

(P) (S) (D)

(Printed Name of Parent/Guardian) (Signature of Parent/Guardian) (Date)

Person Obtaining Consent Person Obtaining Consent Date

(P) (S)

(PRINTED NAME) (SIGNATURE)

OPTIONAL CONSENT TO BE CONTACTED FOR FUTURE STUDIES:

Do we have your permission to contact you regarding participation in future studies? Please write your initials next to your preferred choice.

_______ YES ________ NO

Parent/guardian’s Initials ________
ADULT MODEL RELEASE

Adult Model Release
University of Delaware - Photo Services,
Digital Content and Social Media

For valuable consideration received, I hereby give the University of Delaware the absolute and irrevocable right and permission, with respect to the video, social media and/or photographs that they have taken of me or in which I may be included with others.

To copyright the same in their own name or any other name they may choose.

To use, re-use, publish and re-publish the same, in whole or in part, individually or in conjunction with other photographs, in any medium and for any purpose whatsoever, including (but not by way of limitation) illustration, promotion and advertising and trade and to use my name in connection therewith if they so choose.

I hereby release and discharge the University of Delaware from any and all claims and demands arising out of, or in connection with, the use of the photographs, including any and all claims for libel.

This authorization and release shall also ensure to the benefit of the legal representatives, licensees and assigns of the University of Delaware as well as the person(s) for whom they took the photographs, video or posted social media.

I am over the age of eighteen. I have read the foregoing and I fully understand the contents thereof.

PLEASE PRINT

Date  10/05/2018

Name  REZA Koiler

Signature

Address  235 Hope st West

City, State, ZIP  Bear, Delaware 19701

Phone  302-561-5241

Witness

Event  Journal Picture