Identification and Intervention for Action Planning Deficits in Children With Hemiplegic Cerebral Palsy

Swati M. Surkar
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IDENTIFICATION AND INTERVENTION FOR ACTION PLANNING DEFICITS
IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY

by

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Presented to the Faculty of
the University of Nebraska Graduate College
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Under the Supervision of Professor Max J. Kurz and
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The primary purpose of this investigation was to describe and quantify action-planning deficits during goal-directed movements in children with hemiplegic cerebral palsy (HCP). Three specific topics were addressed: brain activation, kinematics, and the use of visual input. First, we assessed prefrontal cortex (PFC) activation during complex goal-directed actions in children with HCP. The outcome suggested that children with HCP have higher PFC activation than age matched typically developing (TD) children during action planning, potentially due to the difficulty in allocating attentional resources for simultaneously processing the cognitive (i.e., attention, memory, information processing) and motor demands of the goal-directed task. Reduced task performance paralleled the increased cortical activation. Secondly, we explored the kinematics of action planning and execution of goal-directed action of children with HCP. We found that children with HCP lack forward planning capacity of sequential action, which further impacts the ability to execute action. Thirdly, we explored anticipatory visual patterns and the temporal coupling between eye and hand in children with HCP. The outcomes from this study indicate delays in anticipatory vision and impaired visuomotor coordination, potential factors responsible for the delay in motor performance in children with HCP. Moreover, we observed increased visual monitoring of the moving arm, a potential compensatory mechanism for impaired proprioception of the arm.
A secondary purpose was to evaluate whether hand arm bimanual intensive therapy (HABIT) improves action planning and subsequent action execution deficits, and improves PFC activation. After completion of 50-hours of HABIT program, children with HCP displayed reduction in PFC activation. The reduction in cortical activation was accompanied by clinically relevant improvements in bimanual coordination, affected hand function, and motor task performance. Altogether this investigation provides novel information about the action planning and subsequent action execution deficits and the influence of therapeutic interventions in reducing these deficits to optimize learning motor skills in children with HCP.
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<td>Assisting hand assessment</td>
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<td>BBT</td>
<td>Box and blocks test</td>
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<td>CNS</td>
<td>Central nervous system</td>
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<td>CIMT</td>
<td>Constraint induced movement therapy</td>
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<td>DeoxyHb</td>
<td>Deoxygenated hemoglobin</td>
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<td>DLPFC</td>
<td>Dorsolateral prefrontal cortex</td>
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<td>EEG</td>
<td>Electroencephalography</td>
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<td>fNIRS</td>
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<td>HCP</td>
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<td>IRB</td>
<td>Institutional review board</td>
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<td>MOA</td>
<td>Movement onset asynchrony</td>
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<td>MTA</td>
<td>Movement termination asynchrony</td>
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<td>MT</td>
<td>Movement time</td>
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<td>NHPT</td>
<td>Nine-hole peg test</td>
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<td>OxyHb</td>
<td>Oxygenated hemoglobin</td>
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<td>Prefrontal cortex</td>
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<td>RT</td>
<td>Reaction time</td>
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<td>TD</td>
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INTRODUCTION

Hemiplegic Cerebral Palsy

“Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain. The motor disorder of cerebral palsy is often accompanied by disturbances of sensation, perception, cognition, communication, and behavior; by epilepsy, and by secondary musculoskeletal problems” (Rosenbaum et al., 2007). Hemiplegic CP (HCP) is a common type of CP, which affects one side of the body due to brain damage that primarily affects one hemisphere (Uvebrant, 1988). The etiology of HCP is varied and includes, for example, circulatory brain lesions, cerebral hemorrhage, hypoxic ischemic encephalopathy, premature births, and traumatic causes (Uvebrant, 1988). The prevalence of HCP is approximately 1 per 1000 live births in the United States (Winter et al., 2002; Yeargin-Allsopp et al., 2008), and includes an economic burden to our society of approximately $800,000 per child (Honeycutt et al., 2003).

Due to an early brain injury to one side of the cortex, children with HCP have deviant motor output and sensorimotor dysfunction, which impairs function of the paretic hand. Since the upper extremity on the affected side is more involved than the lower extremity, children with HCP have various functional limitations, such as difficulty in using the affected extremity to reach, grasp, release, and manipulate objects. Later, these limitations also restrict the child’s participation in educational, leisure, and vocational roles (Sakzewski et al., 2009).

Previous studies on motor control in children with HCP have focused exclusively on problems related to movement execution (Chang et al., 2005; van Thiel et al., 2002; Steenbergen et al., 2000). This notion emerged based on these children’s existing
musculoskeletal impairments such as spasticity, limited range of motion, weakness, etc. Based on the assumption that movement dysfunction in children with HCP is solely due to action execution problems, the rehabilitation strategies have been focusing primarily on impairment-based approaches such as reducing spasticity, increasing range of motion, preventing deformity, and providing joint stability (Law et al., 1991; Law et al., 1997; Lowe et al., 2006; Speth et al., 2005; Wallen et al., 2007). However, the efficacy of these impairment-based rehabilitation approaches is limited (Novak et al., 2013), which in turn affects the child’s participation and amplifies the financial burden on the family in remediating the worsening dysfunctions. This may be due to the fact that the larger emphasis has been given merely to action execution problems. Although the prerequisite for successful action execution is action planning, it has been mostly overlooked in children with HCP (Steenbergen & Gordon, 2006).

**Action Planning**

Action planning is an ability to predict the future state of the motor system or the consequences of its action (Steenbergen et al., 2007). It is an integral aspect of motor control and is also essential for skilled movements (Kaller et al., 2011). Emerging evidence suggests that children with HCP have deficits in planning the actions, which potentially is detrimental in performing the activities of daily living (Steenbergen & Gordon, 2006).

**Evidence for action planning deficits in children with HCP- Object manipulation and grip selection**

While manipulating objects, a comfortable posture of the upper extremity at the end of an intended action is crucial for successfully accomplishing the task. The
comfortable end posture of the hand at the end of the action is called end-state comfort effect (Rosenbaum & Jorgensen, 1992; Rosenbaum et al., 1992). The potential advantage of end-state comfort effect is that it allows precision of movement (Rosenbaum et al., 1996). For example, if a coffee cup requires to be placed upside down, initially a biomechanically awkward handgrip is selected; however, if the task is accomplished successfully, the hand posture is comfortable at the end of the task. Overall, for anticipatory planning of a purposeful action, the perceptual-motor demands of the task need to be taken into consideration in advance in order to accomplish the action with precision.

The studies that have investigated motor planning in children with HCP using object manipulation and grip selection revealed action-planning deficits in these children (Steenbergen et al., 2000; 2004; Mutsaarts et al., 2004; 2005; 2006; Te Veldi et al., 2005). Steenbergen (2004), using a bar handling paradigm, demonstrated that comfort of the end posture of the affected as well as the unaffected hand was not optimized. Children with HCP used a comfortable grip at the beginning of the task, which resulted in a loss of end-state comfortable posture (Steenbergen et al., 2004). Similarly, while performing a biomechanically complex task of rotating a hexagonal knob, children with HCP selected a stereotyped grip pattern and failed to adjust an initial grip, which resulted in repeated task failures (Mutsaarts et al., 2005). It has also been observed that while planning an object manipulation task that involves a sequence of action, children with HCP did not plan the end goal of an action, instead action planning was directed to an early or intermediate goal (Mutsaarts et al., 2005; Steenbergen & van der Kamp, 2004). Hence, children with HCP used a step-by-step planning strategy and planning continued as the action unfolded. Collectively, results from the object manipulation studies imply that children with HCP have deficits in forward planning an
action, which ultimately results in lack of fluidity of movement and task failures.

**Evidence for action planning deficits in children with HCP - Anticipatory Scaling of Fingertip Forces**

For smooth handling of objects, anticipatory scaling of fingertip and hand forces is required to overcome the inherent delays in sensorimotor system for acquiring information about the weight and texture of the objects (Johnson-Frey et al., 2004). Anticipatory force planning is dependent on an internal model of the physical properties of the objects and such information can be obtained from the previous memory of handling such objects (Salimi et al., 2003). Healthy adults and children also acquire the information regarding the physical properties of an object by lifting it with one hand for anticipatory force scaling in subsequent lift with the other hand (Gordon et al., 1994; Johansson & Westling, 1988). Thus, anticipatory force scaling is transferred across hands.

Evidence suggests that the anticipatory fingertip forces are impaired in children with HCP (Eliasson et al., 1991, 1992, 1995; Gordon & Duff, 1999; Gordon et al., 1999; Duff & Gordon, 2003). The results of these studies demonstrated that the extent of fingertip force application with the affected hand did not reflect the physical properties of the object and an optimal fingertip force scaling occurred only after repetitively lifting the object with the affected hand (Gordon & Duff, 1999). Since these results were observed only on the affected arm, it could be speculated that the lack of fingertip force scaling is due to motor execution rather than a planning problem. However, in a follow up study Gordon et al. (1999) showed that the anticipatory scaling of fingertip forces on the affected hand improved after successive lifting of the object with the unaffected hand. These results indicate that the enriched sensory information from the unaffected hand
was transferred to the affected hand, which helped in improving anticipatory scaling forces on the affected arm (Gordon et al., 1999). Altogether, these results suggest that deficits in anticipatory scaling of fingertip forces could be due to an inability to an atypical internal representation of an object’s properties or integrate sensorimotor information, which affects the overall planning of the task.

Collectively, the results from the anticipatory grip selection and fingertip forces suggest that the deficits in anticipatory planning potentially contribute to limitations in motor performance and the activities of daily life (Steenbergen & Gordon, 2006). Although these studies are based only on behavioral observations, these findings are valuable; however, based on the behavioral observations alone, we cannot segregate whether poor motor performance is due to impaired musculoskeletal machinery (spasticity, weakness, joint torsions, limited range of motion etc.) or due to central planning deficits since cortical and subcortical structures are involved in planning the actions (Luft et al. 2002; Gallivan et al., 2011). Hence, investigating neural activation at the cortical level could potentially help in delineating the neural correlates of planning deficits in children with HCP. Such efforts would both act as a stepping-stone in understanding the neural mechanisms of planning and serve as a springboard for future novel interventions to optimize motor performance in children with HCP.

The Planning-Control Framework

There is a functional distinction between the planning and control stages of an action (Elliott et al., 1991). Glover (2004) proposed the planning-control model in which body movements are selected and executed by two temporally overlapping systems: planning and execution.
**The Planning System:** During the planning phase, which begins before the initiation of an action, cognitive and visual processes are coupled to form a motor program. Planning requires selection and initiation of an adaptive motor program. Planning is responsible for selecting an appropriate target and choosing a particular grasp for the successful completion of the intended action. Planning also determines kinematic parameters such as the timing and velocity of movement. Since planning takes cognitive and visual information into account, this information can be classified into four basic aspects of the environment and actor: “(1) the spatial characteristics of the actor and the target, including the size, shape, and orientation of the target, as well as spatial relations between the actor and the target; (2) the nonspatial characteristics of the target, including function, weight, fragility, and the coefficient of friction of its surfaces; (3) the overarching goal of the action; and (4) the visual context surrounding the target” (Glover, 2004). This information is integrated with memories of past experiences.

**The Control System:** The execution phase of an action is influenced by the control system; an efference copy of a motor command is sent to the forward model, which is quickly updated by visual and proprioceptive feedback. The control system requires minimizing spatial movement errors and it monitors and adjusts the motor programs. These adjustments are limited to spatial characteristics of the target, as these are most likely to change or to be erroneously planned. Spatial errors may arise from how the movement was planned or during the execution of the plan. For spatially accurate movement, the control system requires vision along with the proprioception and efference copy of a motor command (Glover, 2004).
Cortical Control of Action Planning

Over the past decade, neuroimaging of movement-related brain activity has substantially advanced our understanding of how adults and children plan and produce goal directed movements (Luft et al. 2002; Sahyoun et al. 2004; MacIntosh et al. 2004; Kapreli et al. 2007; Beurze et al. 2007; Gallivan et al. 2011; 2013; Valyear and Frey 2015; Kurz et al., 2016). As expected from its proposed role, the prefrontal cortex (PFC) plays a critical role in planning and monitoring evolving actions (Kaller et al., 2011; Koechlin et al., 2000; Marois, 2002; Baker et al., 1996; Owen et al., 1996). Moreover, these studies have shown that the production of goal-directed actions involves the activation of a distributed network that includes the primary sensorimotor cortices, secondary somatosensory area, parietal cortices, supplementary motor area, basal ganglia, thalamus, and cerebellum.

The prefrontal cortex, specifically the dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC), is associated with motor planning (Baker et al., 1996; Owen et al., 1996; Hanakawa et al., 2008; Marios, 2002). The DLPFC has been found to play a crucial role in the neural network for planning action sequences (Owen, 2005; Tanji et al., 2007); mental conception, evaluation, and outcomes of behavioral sequences of actions before their execution (Goel, 2002; Unterrainer & Owen, 2006); in the detection of motor errors (Halsband & Lange, 2006) and initiation of movements (Jahanshahi et al., 1995). Furthermore, the DLPFC’s is considered to be the major anatomical correlate of the central executive function and attention (Baddeley, 2003; Atsumori et al., 2010) and bilateral DLPFC activation has been reported while planning cognitive-motor tasks (Shallice, 1982). The goal-relevant information for the action control seems to be maintained and retrieved by the left VLPFC (Badre and Wagner, 2007; Souza et al., 2009).
The PFC has extensive connections with the sensorimotor cortex, premotor cortex, and DLPFC (Witt et al., 2008). This network has been associated with higher motor processing such as motor programming, motor planning, and sensory guidance of movements (Tanji, 2001). The supplementary motor area receives input from the basal ganglia and the prefrontal area and is closely related to self-paced actions as well as motor planning and preparation (Ryun et al., 2014). Combined, these networks play a vital role in movement control. The cerebellum has been shown to be active during the preparation, execution, and timing of both simple and complex movements (Habas, 2004) and the basal ganglia also has been associated with simple and complex sequential movements (Maillard, 2000). Thus, the PFC works in close communication with the cortical and subcortical regions important for movement control.

Although it is well recognized that these brain areas are involved in the control of movement, the neurophysiology literature on children with HCP has predominantly focused on identifying the structural aberrations that exist within the white matter volume and fiber track integrity. These studies are primarily related to the aberrant motor actions and did not consider the activity within the key cortical networks involved in planning and control of the action (Carr et al., 1993; Maegaki et al., 1999; Staudt et al., 2002; Vandermeeren et al., 2003a; Vandermeeren et al., 2003b; Holmstrom et al., 2010). The very few studies that have evaluated the cortical activity of children with HCP have shown that the sensorimotor cortices can be hyper-activated and may involve compensatory networks when planning and executing motor actions (Guzzetta et al., 2007; Wilke et al., 2009; Kurz et al., 2014, Manning et al., 2015; Vandermeeren et al., 2003; Walther et al., 2009). However, these insights have been gained from the evaluation of simple motor actions (i.e., knee and hand movements) that do not involve higher order cognitive decisions and maintenance of goal-relevant information.
Potentially, the evaluation of more ecologically valid complex motor tasks may accelerate our understanding of how the central processing deficits impact the motor actions seen in children with HCP.

**Role of Vision In Action Planning**

Vision is an integral part of planning and controlling goal-directed movements (Glover, 2004). Our everyday activities include reaching, grasping, and manipulation of various objects. To ensure successful movement towards the target (object), precise information about the target is mandatory. Although information about the target could be multimodal such as visual, auditory, and somatosensory, in our day-to-day activities vision is commonly used to obtain the target related information. Later, when one requires making precise movements under rapidly changing conditions, vision integrates with other somatosensory systems to initiate and guide goal-directed movements.

Vision, along with dynamic integration with various sensorimotor systems, plays a critical role in the successful execution of goal-directed actions (Goodale, 2011; Neggers & Bekkering, 1999; Land et al., 1999; Sarlegna, & Sainburg, 2009; Mackrous, & Proteau, 2016). To achieve an end goal of a goal-directed action, vision first identifies and locates the target. Later, this visual information is transformed into appropriate motor commands (Goodale, 2011). When the task is complex, the central nervous system (CNS) also needs to closely monitor the actions to update an action plan and amend action execution (Desmurget & Grafton, 2000; Franklin et al., 2012). Collectively, an efference copy motor command is sent to a forward model that anticipates sensorimotor consequences, predicts the movement endpoint, and when necessary, issues corrective motor commands to accomplish an accurate goal-directed
action (Mackrous & Proteau, 2016). The forward model is updated during movement execution by incoming proprioceptive and visual inputs (Shadmehr et al., 2010).

During the past few decades, many researchers have investigated the role of vision in planning and controlling goal-directed movements. The results of these studies suggest that the anticipatory vision/saccades are faster than the goal-directed hand movement (Abrams et al., 1990; Bekkering et al. 1994, 1995). Eyes also fixate the target before movement begins. Moreover, when visual inputs are available, movements are more accurate (Desmurget et al., 1997; Elliott et al., 1991; Ghez et al., 1995), whereas movement errors were observed when visual feedback of initial hand position was distorted (Bagesteiro et al. 2006; Holmes and Spence 2005; Sainburg et al. 2003; Sarlegna and Sainburg, 2007; Sober and Sabes 2003).

According to the planning-control model, vision is an integral part of planning as well as controlling movement (Glover, 2004). Movement and vision are represented in the inferior parietal and superior parietal lobe respectively (Glover, 2004). During the planning phase, a motor program is selected based on coupling between cognitive and visual factors, whereas during the execution phase, vision is coupled with proprioceptive feedback (Glover, 2004). Moreover, to ensure that the movement is spatially accurate, the control system requires a quickly computed visual representation. Eye movements thus seem to be temporally and spatially tightly coupled to the motor actions of the particular task. One possibility is that the eyes are mainly involved in ‘forward planning’ seeking out objects for future use and setting up the operations to be performed on them. Collectively, the results of these studies indicate that vision precedes hand movement and is a precursor for anticipatory control of goal-directed actions.

Only two studies have investigated the role of vision in planning in children with
HCP (Steenbergen et al., 1996; Verrel et al., 2008). The anecdotal observation of Steenbergen et al. (1996) study suggests that children with HCP have increased visual attentiveness to their affected arm, which could be a potential mechanism to compensate for sensorimotor arm deficits. Verrel et al. (2008) did not find evidence of anticipatory gaze deficits; however, their study results demonstrated increased visual attentiveness to the affected arm. The results of these studies cannot be generalized due to the limited sample size of the study participants. Despite the important role of vision in planning goal-directed actions, it has not been thoroughly investigated in children with HCP. It is likely that children with HCP have deficits in anticipatory visual control, which potentially contributes to impaired planning and control of the goal-directed actions.

Moreover, visual and proprioceptive information coordinate to control limb movements (Sarlegna & Sainburg, 2009). The integration of visual and proprioceptive signals from the periphery is required to estimate the position of the arm while planning a goal-directed action (Desmurget & Grafton, 2000). Vision provides extrinsic information and is used to plan spatial features of movements toward visual targets, whereas proprioception provides intrinsic information about limb configuration and movement, and transforms spatial planning into neural/motor commands (Sarlegna & Sainburg, 2009). It has been shown that the visuo-proprioceptive mapping is disturbed in children with CP (Wann, 1991). However, the evidence on eye-hand coordination in children with HCP is very sparse. Investigating visuomotor coordination will add a valuable insight in understanding the integration of sensorimotor systems and their impact on action planning and execution in children with HCP.
Therapeutic Intervention

Traditionally, upper limb rehabilitation approaches in children with HCP were impairment based and the treatments included the regulation of muscle tone, increasing the range of motion, preventing deformity, providing joint stability, stretching, strengthening, etc. However, the efficacy of these therapies in improving the upper limb function is precarious (Novak et al., 2013).

Since the past decade, intensive therapies such as constraint induced movement therapy (CIMT), bimanual training, goal-directed or task specific training have been widely used in the rehabilitation of children with HCP (Novak et al., 2013). However, the emphasis of these therapies is on action execution. Although sequential actions, which involve action planning, are practiced in these approaches, action planning is not explicitly trained. Additionally, although these interventions have shown a positive trend in the improvement of hand function in children with HCP, the effectiveness of these interventions has been limited by discrepancies in numerous factors (Eliasson et al., 2014).

Despite the evidence that action-planning deficits potentially result in movement dysfunction, therapeutic interventions emphasizing action planning deficits is sparse. Steenbergen et al. (2009) proposed motor imagery as a potential therapy measure for training motor planning in children with HCP. Motor imagery focuses on training the cognitive aspects of motor behavior. In the motor imagery training approach, active cognitive processes are used to internally reproduce the actions with the help of working memory, while overt execution of the movement plan is inhibited. In this approach, the actions are represented without confounding sensory feedback or motor output. Moreover, the imagined and executed movements have been shown to share common neural substrates (Zacks et al., 2008). Although motor imagery appears as a
promising therapeutic intervention for training action planning, feasibility of this technique in young children with HCP is uncertain. The exact age at which children can use motor imagery is not established. It has been shown that five-year-old children could not be engaged in the motor imagery process (Molina et al., 2008); hence, the engagement of young children remains questionable.

Another potential therapeutic approach for improving action planning deficits in children with HCP is hand arm bimanual intensive therapy (HABIT) (Craje et al., 2010). Only a single study has investigated the effect of intensive hand function training on action planning in children with HCP (Craje et al., 2010). HABIT is a functional training approach, which includes intensive training of bimanual activities, mostly embedded in play and a functional context (Gordon et al., 2007). Although the results of this intervention trial demonstrated that combined CIMT and bimanual training of a total dose of sixty hours improved the anticipatory planning, the focus of therapy was not explicitly on improving the action planning. Hence, whether intensive practice of bimanual functional tasks enriches the movement experience on the affected hand required to form an effective action plan is a question for further research. Finally, the conclusions of this study show that the improvements in action planning with combined CIMT and HABIT were based on improvement in the anticipatory grip selection patterns. While these behavioral observations may be accurate, there is a substantial need to further investigate the potential beneficial effects of such interventions on action planning related cortical activation and to establish a link between brain and behavior.
Purpose of Dissertation

A primary purpose of this dissertation is to gain a more complete understanding of action planning deficits in children with HCP while performing a goal-directed sequential movement. Specifically, this dissertation will investigate neural activation within the prefrontal cortices during goal-directed action with the upper extremities and seek to quantify the differences in prefrontal cortex (PFC) activation between children with HCP and typically developing (TD) children. It is hypothesized that children with HCP will show an increased amount of neural activity in the PFC due to greater utilization of cognitive resources that are required for planning and controlling the goal-directed actions. Moreover, it is hypothesized that the deficits in action planning will have an impact on the motor performance of these children. The outcomes from this main purpose will be foundational in understanding the cortical control of action planning and in enhancing our knowledge base of the contribution of action planning in motor performance of children with HCP.

The second main purpose of this dissertation is to explore the kinematic characteristics of the action planning and execution during goal-directed sequential actions in children with HCP. It is hypothesized that children with HCP do not plan the entire sequence of an action in advance, and if the final action goal is more complex, it may interfere with planning the initial action. Furthermore, it is hypothesized that notable planning deficits might impact the execution of complex actions. The outcomes of this research will provide precise insights about the mechanics of action planning and execution, and will further our understanding of the relationship of these biomechanical characteristics with behavioral outcomes.

The third main purpose of this dissertation is to explore the role of vision in planning and execution of goal-directed action in children with HCP. It is hypothesized
that children with HCP will show delays in anticipatory vision, which will further impact the ability to plan and execute the goal-directed action. Moreover, it is hypothesized that visuomotor coordination will be impaired in these children, which may be characterized as atypical temporal coupling between eye and hand. The outcomes of this study will provide a deeper understanding of the coordination of the sensorimotor system and its impact on motor performance in children with HCP.

The final purpose of this dissertation is to better target action planning and execution deficits through intensive intervention. Furthermore, this study seeks to understand the effects of hand arm bimanual intensive therapy (HABIT) on PFC activation in children with HCP. It is hypothesized that HABIT would improve action-planning ability in children with HCP, and that the improvement would be reflected through reduced PFC activation and improved motor performance during goal-directed actions. The results of this study will provide valuable insights on the effects of such intensive intervention on cortical changes.

The overall outcomes of this dissertation will provide a comprehensive understanding of action planning deficits and their potential impact on action execution in children with HCP. Additionally, they will provide foundational work on the intervention that is beneficial to improving the planning deficits and enhancing motor performance in children with HCP.
CHAPTER 1: NEURAL ACTIVATION WITHIN THE PREFRONTAL CORTEXES
DURING THE GOAL-DIRECTED ACTIONS OF CHILDREN WITH
HEMIPLEGIC CEREBRAL PALSY: AN FNIRS STUDY

Introduction

The unilateral sensorimotor dysfunction in children with hemiplegic cerebral palsy (HCP) can result in the loss of upper extremity motor control, which affects activities of daily living and restricts the child’s participation in educational, leisure and vocational roles (Sakzewski et al., 2009). Until recently, action execution problems residing in the musculoskeletal machinery were considered as primarily responsible for activity limitations in children with HCP (Boyd et al., 2001). However, emerging evidence suggests that the activity limitations and action performance problems seen in these children are not solely an action execution disorder, but might also be due to deficits in planning of the goal directed actions (Steenbergen & Gordon, 2006; Kurz et al., 2014).

Action planning is the ability to predict the future state of the motor system, and is integral for the control of skilled movements (Steenbergen & Gordon, 2006; Kaller et al., 2011). According to the planning-control model, action planning has two main components: a) pre-movement planning, and b) online monitoring and correction of the movement in order to achieve the goal state (Glover, 2004). Pre-movement planning involves processes such as goal determination, target identification, selection, analysis of object affordances, timing, and computation of the target size, shape, orientation and position relative to the body (Glover et al., 2012). Online control involves visual and proprioceptive feedback to monitor movement and minimize spatial errors (Glover et al., 2012). Behavioral studies reveal that children with HCP have a deficit at the action planning level (Mutsaarts et al., 2006; Steenbergen et al., 2004; Duff & Gordon, 2003;
Steenbergen & van der Kamp, 2004; Mutsaarts et al., 2005). This notion is based on the observation that children with HCP have task failures (Mutsaarts et al., 2006), uncomfortable grip selection, loss of the end-state-comfort effect (Mutsaarts et al., 2006; Steenbergen et al., 2004), and difficulty in anticipating grip forces (Duff & Gordon, 2003). They also take a longer time to plan sequential movements (Steenbergen & van der Kamp, 2004), and lack fluid movement (Mutsaarts et al., 2005). Consequently, the presence of an action-planning deficit likely limits the ability to successfully execute movements. While these behavioral observations may be accurate, observations alone cannot determine whether the source of aberrant movements stem from impaired musculoskeletal machinery (i.e., spasticity, muscle weakness or lack of selective control, joint torsions, contractures), faulty cognitive processes (i.e., attention, memory, information processing) or a combination of both.

Over the past decade, neuroimaging of movement-related brain activity has substantially advanced our understanding of how adults and children plan and produce goal directed movements (Luft et al. 2002; Sahyoun et al. 2004; MacIntosh et al. 2004; Kapreli et al. 2007; Beurze et al. 2007; Gallivan et al. 2011; 2013; Valyear and Frey 2015; Kurz et al., 2016). These studies have shown that the production of goal directed actions involves the activation of a distributed network that includes the primary sensorimotor cortices, secondary somatosensory area, parietal cortices, supplementary motor area, basal ganglia, thalamus and cerebellum. In addition, such studies have also highlighted that the prefrontal cortex (PFC) also plays a critical role in planning and monitoring of the evolving actions (Kaller et al., 2011; Owen, 2005). Within the PFC the dorsolateral prefrontal cortex (DLPFC) is involved in the detection of motor errors (Halsband & Lange, 2006), and initiation of movements (Jahanshahi et al., 1995), while the ventrolateral prefrontal cortex (VLPFC) is involved in the maintenance of goal
relevant information (Badre & Wagner, 2007). The DLPFC has extensive connections with the premotor and sensorimotor cortex, which plays vital role in movement control (Witt et al., 2008). Although it is well recognized that these brain areas are involved in the control of movement, the neurophysiology literature on children with HCP has predominantly focused on identifying the structural aberrations within the white matter volume and the fiber tracks that are related to aberrant actions (Staudt et al., 2002; Stashinko et al., 2009). The few studies evaluating the cortical activity of children with HCP showed that the sensorimotor cortices can be hyper-activated and may involve compensatory networks when planning and executing goal directed actions (Kurz et al., 2014; Guzzetta et al., 2007; Wilke et al., 2009; Manning et al., 2015). However, these insights have been gained from the evaluation of simple actions (i.e., knee and hand movements) that do not involve higher order cognitive decisions and maintenance of goal relevant information. Potentially, the evaluation of more ecologically valid motor tasks may improve our understanding of how central processing deficits impact the goal directed actions seen in children with HCP.

In this exploratory investigation, we used functional near infrared spectroscopy (fNIRS) to measure the PFC activation as children with HCP performed a shape-matching motor task with their upper extremities. The shape-matching task encompasses- a) pre-movement planning, which involves various cognitive processes to make a decision of appropriate shape match and to manipulate different shapes, and b) online control of movement, which involves action of reach, grasp, and orient the shapes accurately. Our primary hypothesis was that children with HCP would show an increased amount of neural activity in the PFC due to greater utilization of cognitive resources that are required for planning and control of their actions. Our secondary hypothesis was that the deficits in action planning might impair the motor performance.
Methods

Participants

The Institutional Review Board of the University of Nebraska Medical Center (UNMC) approved the study, and we obtained parental consent and child assent to participate in this investigation. The participating children with HCP were recruited from the physical therapy clinic at UNMC and TD children were recruited through word of mouth. We excluded children with frontal cortical lesions, cognitive impairments, visual deficits, musculoskeletal deformity of the hand and arm, and arm weakness due to neurological impairments such as brachial plexus injuries. Twelve children with HCP (Age = 6.8 ± 2.9 yrs; males = 7) and fifteen TD children (Age = 5.8 ± 1.1 yrs; males = 8) participated in this investigation. All children with HCP had a previously defined diagnosis of hemiplegia by a pediatric neurologist. Further details of the participating children are given in Table 1.

<table>
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<tr>
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<th>Gender</th>
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<th>AHA Score</th>
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<th>Gender</th>
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Experimental Paradigm

The task consisted of a sequential shape-matching task, which had three-complexity levels: easy, moderate, and difficult. The easy condition had the same shape types, the moderate condition had two different shape types, and the difficult condition had multiple shape types that were different from each other (Fig. 1). The three-complexity levels of the task were based on the intricacy of the shape identification, accurate selection, manipulation, and the type of grasp required based on the type, size, shape, and orientation of the shape. The children were asked to match the shapes with the corresponding template by selecting an appropriate shape and placing it accurately on a given template.

The task was performed in a block paradigm, which consisted of a 30 second rest period where the child sat still, and a 30 second active period where the child matched the shapes. To avoid anticipation of the respective complexity levels, the conditions were randomized and each task condition was repeated four times. The children performed a total of twelve blocks of the shape-matching task (3 shape complexity conditions x 4 repetitions of each condition) during the entire session. The total duration of the data collection was twelve minutes. Children with HCP performed the task with the affected and the unaffected arm, and TD children performed the task with the dominant and the non-dominant hand. We chose to evaluate both arms to explore the global nature of cognitive processes required for the movement planning and control, and to avoid the arm bias of the hemiplegic hand due to physical restrictions in performing the task in view of impairments in the affected arm.
fNIRS Data Acquisition

fNIRS is a neuroimaging technique that measures hemodynamic changes in cortical tissues continuously and non-invasively in an ecologically valid environment (Boas & Dale, 2004). fNIRS utilizes specific wavelengths of infrared light that penetrate the skull to measure the absorption characteristics of oxygenated (OxyHb) and deoxygenated (DeoxyHb) hemoglobin within the underlying neural tissues. The fNIRS device consists of a series of photon emitters and detectors. The detectors measure the refracted light, which is used to quantify the amount of OxyHb and DeoxyHb changes in local neural tissues. A greater concentration of OxyHb corresponds to a heightened amount of activity in the underlying neural tissues (Boas & Dale, 2004).

For this experiment, we used a continuous wave fNIRS system (fNIR Devices LLC, Potomac, MD) that utilized two different wavelengths (730 and 850 nm) to measure the concentration of OxyHb and DeoxyHb based on the modified Beer-Lambert law (Obrig & Villringer, 2003). The fNIRS system was composed of three
components: a flexible head piece (sensor pad), which secures the emitters and
detectors in a fixed position to allow for fast placement of the sensor pad on the
forehead; a control box for hardware; and a computer that runs the data acquisition.
The positioning of two light sources and two detectors on the sensor pad yielded a total
of four active optodes or measurement channels. According to 10-20 EEG systems, the
optodes were located lateral to the Fpz on the left and the right side of the forehead.
The sensors had a temporal resolution of 500 milliseconds per scan with 2.5 cm of light
source-detector separation, which allows for approximately 1.25 cm penetration depth.
All optodes were connected to fiber optic cables that allowed the transmission of
infrared light to the fNIRS system. We used cognitive optical brain imaging (COBI)
studio software for data acquisition and visualization (fNIR Devices LLC, Potomac, MD).

fNIRS Data Analysis

The measured OxyHb hemodynamic waveforms were low-pass filtered with a
finite impulse response filter that had an order of 20 and cut-off frequency of 0.1 Hz.
This filter was implemented to attenuate the high frequency noise, respiration, and
cardiac cycle effects (Ayaz et al., 2010). Waveforms that were saturated or had motion
artifacts were excluded from the analysis. The epochs of each trial were 60 seconds in
duration (-30 sec to +30 sec), with the presentation of the shape-matching task defined
as 0.0 seconds. The OxyHb hemodynamic waveforms for each channel were corrected
based on the average OxyHb seen in the baseline period (-25 to -5 sec), and the 4 trials
performed in each condition were subsequently averaged. The average maximum
OxyHb across the respective channels was used as the primary outcome variable. We
used OxyHb as a marker for regional brain activation since previous study findings have
shown that OxyHb is more sensitive to neural changes than DeoxyHb (Suzuki et al., 2004).

Behavioral Data Analysis

The video recorded behavioral data was used for the analysis of the motor task performance. The number of accurately matched shapes was quantified across each trial and the average performance across the four trials for each condition was used as an outcome variable. We also assessed an average number of errors in matching the shapes across all trials. A wrong match and inaccurate orientation of the shapes were considered as errors. In addition, we assessed reaction time (RT), which was determined as time to initiate the hand movement after the shape-matching task was presented. RT for the first shape in each trial was assessed, and average RT across all trials was considered for the final analysis.

Lastly, we had the children perform the nine-hole peg test (NHPT) and the box and blocks test (BBT) to assess manual dexterity and speed.

Statistical Analysis

Separate mixed model ANOVAs (group x hand x task-conditions) with group (TD and HCP) as the between-subject factor, and arm (dominant/unaffected, non-dominant/affected) and task conditions (easy, moderate and difficult) as the within-subject factors were used to determine if there were significant differences in OxyHb and task performance. Separate 2x2 mixed ANOVAs with group (TD and HCP) as the between-subject factor, and arm (dominant/unaffected, non-dominant/affected) as the within-subject factors were used to determine if there were significant differences in the RT, task errors, NHPT and BBT. Significant interaction effects were followed up with a
Least Squared Difference post-hoc analysis. All statistical analysis was performed using SPSS (Version 23.0; IBM Corporation, Armonk, NY) and $P$ values equal to or less than the 0.01 alpha levels for Least Squared Difference correction were considered significant. Results in the text and graphs are presented as a mean ± standard error of the mean and 95% confidence interval.

Results

Table 2 shows mean OxyHb ($\mu$mol) for each task conditions for TD and children with HCP.

fNIRS Results

There was a significant group main effect ($P=0.001$) for OxyHb with the children with HCP having greater OxyHb than the TD children (Fig. 2). There also was a significant condition main effect ($P=0.003$). Post-hoc analyses indicated a significant difference ($P=0.005$) in the OxyHb between easy (0.14 ± 0.02 $\mu$mol; 0.11-0.19) and difficult (0.24 ± 0.03 $\mu$mol; 0.22-0.31) conditions. The arm main effect was not significant ($P=0.12$).

![Fig. 2: Mean difference in OxyHb between TD and children with HCP](image)
Table 2: Mean ensemble of fNIRS data for TD and children with HCP

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<th>OxyHb (Dominant)</th>
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<td>0.22</td>
</tr>
<tr>
<td>HCP 2</td>
<td>0.61</td>
<td>0.73</td>
</tr>
<tr>
<td>HCP 3</td>
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<td>0.35</td>
</tr>
<tr>
<td>HCP 4</td>
<td>0.62</td>
<td>0.73</td>
</tr>
<tr>
<td>HCP 5</td>
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<td>0.02</td>
</tr>
<tr>
<td>HCP 6</td>
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<td>0.51</td>
</tr>
<tr>
<td>HCP 7</td>
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<td>0.38</td>
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<tr>
<td>HCP 8</td>
<td>0.03</td>
<td>0.08</td>
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<tr>
<td>HCP 9</td>
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<tr>
<td>HCP 10</td>
<td>0.42</td>
<td>0.59</td>
</tr>
<tr>
<td>HCP 11</td>
<td>0.6</td>
<td>0.1</td>
</tr>
<tr>
<td>HCP 12</td>
<td>0.13</td>
<td>0.38</td>
</tr>
<tr>
<td>Average</td>
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<td>0.347</td>
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There was a significant group by arm interaction ($P=0.005$). Post-hoc analyses revealed a significant difference ($P=0.001$) in OxyHb when the task was performed with the affected arm of children with HCP and the non-dominant arm of TD children. Similarly, there was a significant ($P=0.003$) difference in OxyHb concentration when the task was performed with the unaffected arm of children with HCP and the dominant arm of TD children. There was also a significant difference ($P=0.03$) in OxyHb between the affected and the unaffected arm of children with HCP (Fig. 3). None of the other interaction terms were significant ($P > 0.05$).

![Fig.3: Comparison of the arm specific differences in OxyHb between TD and children with HCP](image)

**Task Performance**

There was a significant group main effect ($P=0.001$) for the number of shapes matched, with TD children matching more shapes (8.02 ± 0.2 shapes; 7.6-8.5) than the children with HCP (5.2 ± 0.3 shapes; 4.7-5.7).

There was a significant condition main effect ($P=0.001$). Post-hoc analyses indicated that children matched a greater number of shapes in easy (8.13 ± 0.3 shapes; 8.0-8.2) and hard (4.6 ± 0.3 shapes; 4.2-5.0) conditions.
9.1-10.7) than moderate (6.53 ± 0.3 shapes; 5.5-7.3; \(P=0.001\)) and difficult (5.10 ± 0.3 shapes; 5.4-6.9; \(P=0.001\)) conditions.

There was a significant arm main effect (\(P=0.001\)), indicating that the number of shapes matched by the dominant/unimpaired arm (7.28 ± 0.3 shapes; 6.7-7.7) was greater than what was completed by the non-dominant/impaired arm (6.21 ± 0.3 shapes; 5.5-6.5).

There also was a significant group by arm interaction (\(P=0.004\)). Post-hoc analyses revealed significant difference (\(P=0.001\)) in the number of shapes matched by the affected arm of children with HCP (4.1 ± 0.4 shapes; 3.4-4.8) was less than what was matched by the non-dominant arm of TD children (7.9 ± 0.4 shapes; 7.3-8.6). Similarly, the number of shapes matched with the unaffected arm of children with HCP (6.3 ± 0.4 shapes; 5.5-7.0) was significantly less (\(P=0.004\)) than the number completed by the dominant arm of TD children (8.1 ± 0.4 shapes; 7.5-8.7). Lastly, for the children with HCP the number of shapes matched by the affected arm (4.1 ± 0.4 shapes; 3.4-4.8) was significantly (\(P=0.0001\)) less than the number of shapes completed for the unaffected arm (6.3 ± 0.4 shapes; 5.5-7.0). None of the other interaction terms were significant (\(P>0.05\)).

**Reaction Time**

There was a significant group main effect for RT (\(P=0.001\)), indicating that overall the TD (0.9 ± 0.05 seconds; 0.6-1.2) had a faster reaction time than the children with HCP (2.31 ± 0.3 seconds; 2.0-2.7). None of the other main effects or interaction terms were significant (\(P>0.05\)).
**Task Errors**

There was a significant group main effect ($P=0.001$), indicating that the TD children (1.4 ± 0.2 errors; 0.77-2.0) had fewer errors during the shape-matching tasks than children with HCP (4.6 ± 0.5 errors; 4.0-5.4).

There also was a significant hand main effect ($P=0.01$). However, post-hoc analysis only revealed a trend for a difference ($P=0.07$) in task errors exhibited by the dominant/unaffected (2.26 ± 0.39 errors; 1.5-3.1) and the non-dominant/affected arms (3.44 ± 0.52 errors; 2.4-4.5). None of the other main effects or interaction terms were significant ($P>0.05$).

**Nine-hole Peg Test (NHPT)**

There was a significant group main effect ($P=0.001$), showing that the TD children (41.03 ± 1.9 seconds; 27.9-55.0) were faster at completing the NHPT than the children with HCP (96.1 ± 12.0 seconds; 81.2-111.0). There also was a significant arm main effect ($P=0.007$) indicating that the NHPT was completed faster with the dominant/unaffected arm (54.56 ± 7.13 seconds; 40.2-68.9) than the non-dominant/affected arm (82.93 ± 7.02 seconds; 68.8-97.0).

There was a significant group x arm interaction ($P=0.01$). Post-hoc analyses revealed children with HCP were significantly ($P=0.001$) slower at the NHPT when they used affected arm (123.3 ± 10.47 seconds; 102.3-144.4) compared with when the TD children used their non-dominant arm (42.6 ± 9.4 seconds; 23.7-61.4). Similarly, the children with HCP were significantly slower ($P=0.004$) when they used unaffected arm (68.8 ± 10.4 seconds; 47.8-89.9) compared with when the TD children used their dominant arm (40.28 ± 9.7; 20.8-59.8 seconds). In addition, the children with HCP
performed the NHPT significantly (P=0.03) slower with their affected arm compared with their unaffected arm.

**Box and Blocks Test (BBT)**

There was significant group main effect (P=0.001) indicating that overall the TD children (33.03 ± 1.3 blocks; 29.4-36.7) moved more blocks than and children with HCP (20.5 ± 2.7 blocks; 16.4-24.6). There was no significant arm main effect (P=0.11) or interaction (P=0.06).

**Discussion**

The results of this novel investigation suggest that children with HCP have higher PFC activation while performing a shape-matching motor task with their impaired upper extremities. Interestingly, the greater PFC activation was also seen when the children with HCP performed the shape-matching motor task with the unaffected hand. The heightened activity seen within the PFC was accompanied by reduced behavioral performance during the shape-matching task, the BBT and NHPT. Taken together, these results suggest that the atypical actions seen in children with HCP may be partially related to the greater demands placed on the PFC when planning and executing a goal directed movement with the upper extremities.

The increased activation seen in the PFC implies that children with HCP may have difficulty allocating attentional resources for simultaneously processing the cognitive (i.e., attention, memory, information processing) and motor demands required for completing the shape-matching task. Based on this notion, the children with HCP may have greater activation in the PFC because competing neural resources are needed for orchestrating the degrees of freedom of the impaired arm and the cognitive
processes required for the selection of the object, decision making for an accurate match, and object manipulation. Thus, children with HCP may have inefficient capacity to allocate necessary attentional resources for simultaneously processing the motor and cognitive task demands. Our study results corroborate with the other studies, which demonstrated that children with HCP have deficits in cognitive processing (Murias et al., 2014).

The children with HCP also had a heightened amount of activity within the PFC when using their unaffected arm. This implies that the perinatal brain insult has a pervasive effect on the overall cortical processing. Prior research has shown that in some children with HCP the ipsilateral homologue cortices often assumes the role of the damaged contralateral cortices that would normally be involved in the control of movement (Staudt et al., 2002). This has been suggested to result in an increased burden on the contra-lesional hemisphere because it must account for the control of both limbs. Based on this notion, we suspect that the dual responsibilities of the contra-lesional hemisphere may have influenced the PFC processing demands while performing the shape-matching task with the unaffected arm.

The children with HCP matched a fewer number of shapes, had longer RT, and more shape matching errors compared with the TD children. Altogether these behavioral results indicate that the shape-matching task was more difficult for the children with HCP. It could be argued that the ability to match a fewer number of shapes potentially originates from faults in the musculoskeletal machinery (i.e., spasticity, weakness, joint contractures). Although plausible, this argument is weak because the ability to match the shapes was also confounded in the unaffected arm of the children with HCP. This finding may imply that the musculoskeletal impairments are
not solely responsible for reduced motor performance; rather, deficient cognitive processing may underlie the uncharacteristic motor performance.

The motor impairments seen in the children with HCP while performing the shape matching tasks were further confirmed by the outcomes of the BBT and NHPT. Children with HCP completed fewer blocks during the BBT and took longer time to complete the NHPT. Thus, the children with HCP had reduced manual speed and dexterity bilaterally, which corresponds to the finding that the children with HCP matched fewer numbers of shapes and had increased shape-matching errors.

One of the major limitations of the present study is that a limited number of optodes were used, and it was restricted to the PFC. Moreover, the other areas associated with action planning such as the fronto-parietal cortical areas, basal ganglia and cerebellum were not evaluated simultaneously. Potentially, deficits in these cortical and subcortical areas may have a larger influence on the action-planning deficits seen in children with HCP. Secondly, we did not have electromyographic or kinesiological data to measure the motor impairments that may reside in musculoskeletal system. Therefore, our study results are inadequate in partitioning whether the uncharacteristic motor performance seen in children with HCP is due to impaired musculoskeletal machinery and/or aberrant cortical processes. Addressing these limitations should be taken into consideration in future studies that are directed at understanding the action-planning deficits in children with HCP.

**Conclusion**

Our study results show that children with HCP have increased activation in the PFC while performing a shape-matching motor task with their affected and unaffected upper extremities. This suggests that the children with HCP may utilize greater
cognitive and attentional resources to plan and execute their goal directed motor actions. In addition, our results indicate that the children with HCP have slower reaction times and generate more errors during their goal directed motor actions, even in the unaffected extremity. These parallel results imply that the motor performance problems seen in children with HCP could be due to an underlying cognitive processing and action-planning deficits associated with the PFC. Therefore; therapeutic interventions focusing on improving the cognitive processing demands may subsequently improve the ability of children with HCP to learn new motor skills.
CHAPTER 2: A KINEMATIC ANALYSIS OF ACTION PLANNING AND EXECUTION IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY

Introduction

Hemiplegic cerebral palsy (HCP), a leading cause of childhood disability, affects almost one out of every thousand live births in the United States (Yeargin-Allsopp et al., 2008). Due to early brain injury to one side of the cortex, children with HCP may have a variety of sensorimotor impairments that result in functional limitations, particularly limitations of reaching, grasping, releasing, and manipulating objects with the affected upper extremity. Later, these limitations also restrict the child’s participation in educational, leisure, and vocational roles (Sakzewski et al., 2009). Until recently, action execution problems residing in the musculoskeletal machinery were considered as primarily responsible for activity limitations in children with HCP (Boyd et al., 2001). The motor output responsible for movement execution problems was characterized by the number of movement subunits, (Chang et al., 2005), variability of hand trajectories (e.g., van Thiel et al., 2002), compensatory movements (van Roon et al., 2005; Steenbergen et al., 2000), reduced movement speed, discontinued movement strategy, and fragmented movements (Trombly, 1992; Roby Brami et al., 1997). However, emerging evidence suggests that activity limitations and action performance problems seen in these children are not solely an action execution disorder, but might also be due to deficits in the ability to plan goal-directed actions (Steenbergen and Gordon, 2006; Kurz et al., 2014).

Action planning is defined as the ability to anticipate forthcoming perceptual-motor demands of an action goal, or to anticipate the future state of the motor system (Mutsaarts et al., 2006; Johnson-Frey, 2004); it is a crucial capacity for performing all
skilled movements (Kaller, 2011). Various activities of daily living, such as holding a cup, manipulating objects, dressing and undressing, putting a shoe on and tying shoe laces require action planning before the final execution of the movement, and recent studies reveal that children with HCP have deficient action planning abilities (Mutsaarts et al., 2006; Creje, 2010a, 2010b; Steenbergen and Gordon, 2006; Steenbergen & van der Kamp, 2004). This conclusion is primarily based on the observation that children with HCP exhibit atypical grip selection and loss of comfort of the end-posture. Moreover, evidence also reveals that children with HCP have difficulty in anticipating necessary grip force (Duff & Gordon, 2003), that they require a longer time to plan sequential movements (Mutsaarts et al., 2005), and that they do not achieve fluid movement (Mutsaarts et al., 2005). Thus, the consequences of an action-planning deficit likely limit the ability of the child with HCP to successfully execute movements.

In the past decade, end-state comfort effect has been used to assess movement planning in children with HCP (Adalbjornsson et al., 2008; Janssen et al., 2009). The end-state comfort effect is a tendency to maximize comfortable hand and arm postures at the end of the object manipulation tasks (Adalbjornsson et al., 2008). End-state comfort also indicates movement efficiency with the potential for subsequent movement (Rosenbaum et al., 1992, 1996). Studies that have used manipulation of a variety of objects, such as cubical block, hexagon, bar, or sword, have shown that children with HCP use a atypical grasp pattern at the beginning of the task; and also lack the ability to achieve the end-state comfort effect. Children with HCP have also showed lack of flexibility in grip adaptation to the changing task context, which resulted in biomechanically awkward hand posture at the end of the task and subsequently resulted in task failures (Steenbergen et al. 2000, 2004; Mutsaarts et al., 2004, Craje et al., 2010).
Children with HCP also lack forward planning of goal-directed action. Children with HCP have been observed to perform tasks using a step-by-step method of action planning. Mutsaarts et al., (2005, 2006) investigated action planning of a biomechanically complex task, and found that children with HCP who had to rotate a hexagon in 60°, 120° or 180°, in a clockwise or a counterclockwise direction, did not plan initial grip selection by considering the end goal of these biomechanically complex rotations. Rather, these children selected an initial grip that was unsuitable for the end goal, and thereby often failed to perform the task. Children with HCP also did not complete the planning process before the onset of movement. Instead, they used a step-by-step planning process, reflected through increased reaction and movement time to accomplish the end goal of the given action. These findings support the idea of impaired action planning in children with HCP, which might be responsible for impaired task execution.

For successful execution of functional tasks, a sequence of movements must be planned together, rather than each action determined individually. However, it should be noted here that most studies that assessed action planning in children with HCP were based on behavioral assessments of discrete tasks performed with the unaffected arm. It is therefore currently unknown whether or not discrete motor planning deficits have a cascading effect on the ability of children with HCP to plan and execute a sequence of movements.

In this study, we explored the biomechanics of complex sequential prehension movements. These consisted of initially reaching for an object (movement sequence 1), followed by grasping and placing the object in one of six possible target positions of varying endpoint complexity (movement sequence 2). The primary purposes were to: 1) determine differences in kinematic characteristics of sequential action planning and
execution between TD children and children with HCP; 2) assess whether task complexity affects initial planning in TD and HCP children; and 3) assess the impact of action planning on action execution in children with HCP compared to TD children.

Our first hypothesis was that there would be notable differences in kinematic characteristics of planning and execution phases of TD and children with HCP. Our second hypothesis was that planning of the initial action would be hindered if the final movement in the sequence was more complex than the previous movements, because attention might be directed toward an upcoming target in the second movement sequence stage, and that this would create further interference with the planning of the first motor action. Our third hypothesis was that notable planning deficits might impact the execution of movement. Due to their lack of ability to perform forward planning, children with HCP might continue planning the action in the second movement sequence, and this would be reflected in the execution phase of the movement.

Methods

Participants

The study participants consisted of thirteen children with HCP (Age = 6.6 ± 2.9 yrs; males = 7) and fifteen TD children (Age = 5.8 ± 1.1 yrs; males = 8). All children with HCP had a previously defined diagnosis of hemiplegia by a pediatric neurologist. We excluded children with cognitive impairments, frontal cortical lesions, visual deficits, musculoskeletal deformity of the hand and arm, recent arm surgery, botulinum toxin injection in the past 1 year, and arm weakness due to neurological impairments such as brachial plexus injuries. All TD children were right handed, per the Edinburgh handedness inventory (Oldfield, 1971). Further details of the participants are given in Table 3. The children with HCP were recruited from the physical therapy clinic at
UNMC, and TD children were recruited by word-of-mouth. The Institutional Review Board of the University of Nebraska Medical Center (UNMC IRB) approved the study, and we obtained parental consent and child assent for participation in this study.

Table 3: Demographic details of the participating TD and children with HCP

<table>
<thead>
<tr>
<th>HCP</th>
<th>Gender</th>
<th>Age (yrs)</th>
<th>Hemiplegia</th>
<th>MACS</th>
<th>AHA</th>
<th>Diagnosis</th>
<th>TD</th>
<th>Gender</th>
<th>Age (yrs)</th>
</tr>
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<tr>
<td>HCP 1</td>
<td>M</td>
<td>4.5</td>
<td>L</td>
<td>V</td>
<td>7</td>
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</tr>
<tr>
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<td>4.6</td>
<td>R</td>
<td>I</td>
<td>85</td>
<td>Perinatal stroke</td>
<td>TD 2</td>
<td>F</td>
<td>6.6</td>
</tr>
<tr>
<td>HCP 3</td>
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<td>R</td>
<td>V</td>
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<td>4.1</td>
</tr>
<tr>
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<td>L</td>
<td>III</td>
<td>59</td>
<td>Perinatal stroke</td>
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</tr>
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<td>L</td>
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</tr>
<tr>
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<td>L</td>
<td>III</td>
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<td>R</td>
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<td>L</td>
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<td></td>
<td></td>
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**Experimental Paradigm**

The experimental task used in this study was originally developed by Craje et al., (2010), to assess anticipatory action planning in children. It is a valid action-planning task and has higher precision demands (Jongbloed-Pereboom et al., 2016). The task consists of initially reaching and grasping an object placed at a fixed position, followed by placing it in one of the six possible target positions of varying endpoint complexity (Fig. 4). The orientations of the target positions are $0^\circ$, $90^\circ$, $135^\circ$, $180^\circ$, $225^\circ$ and $270^\circ$. $0^\circ$ is a simple target condition and does not require any biomechanically complex hand
position. In our test, with zero as a starting position, the $90^\circ$, $135^\circ$, and $180^\circ$ were oriented clockwise, whereas the $270^\circ$, $225^\circ$, and $180^\circ$ positions were oriented counterclockwise. The clockwise positions were considered more complex for the right arm, and the counterclockwise positions more complex for the left arm. The complexity of target positions was determined based on the biomechanically greater compromised final hand position was required to place the object at the final target position.

For the experiment, the child was seated in an appropriately sized chair, with upright back and hips, knees flexed to $90^\circ$, shoulder slightly flexed, elbow flexed to $90^\circ$, forearm pronated, wrist neutral, and palms placed at a marked starting position. The task began with lighting up an LED light in one of the six target positions, randomly ordered. The time between lighting up the LED and initiation of hand movement served as the individual metric for the child’s pre-movement planning phase. Children were instructed to reach for the object (Movement Sequence 1) (Fig. 5 A), grasp it, and place it in a target position (Movement Sequence 2) (Fig. 5 B) identified by an LED, and then to place the hand back at the starting position. Children were instructed to initiate arm movement as soon as possible after the appearance of the LED starting cue to reach for the object and place it at the goal position.

We chose to evaluate both arms to explore the global nature of cognitive processes required for movement planning and control, and to avoid arm bias for the hemiplegic hand resulting from physical restrictions in performing tasks and in view of compensations already in place due to impairments in the affected arm. As noted, and to avoid anticipation of the target position, targets were randomized and each target condition was repeated three times. The children performed both movement sequences for a total of eighteen times (6 target conditions x 3 repetitions of each condition) during the entire session. The average all performances was used as the outcome metric.
Children with HCP performed the task with the affected and the unaffected arm, and TD children performed the task with the dominant and the non-dominant hand.

Figure 4. Experimental set up consisted of a hand starting position (blue box in lower corners) and a series of targets where an object was to be placed. The target for the respective trial was indicated by an LED. The target directly under the object in the figure was $0^\circ$, followed by $90^\circ$, $135^\circ$, $180^\circ$, $225^\circ$, and $270^\circ$ in a clockwise direction.

Fig. 5 A): Movement sequence 1
Reaching for the object, indicates online control of movement

Fig. 5 B): Movement sequence 2
Grasping and placing the object in one of the six target positions ($225^\circ$ here), indicates movement execution
Data Acquisition and Analysis

A single reflective marker was placed on the dorsum of the hand. An eight-camera motion capture system was used to record the resultant trajectory of the reflective marker (VICON Motion Systems Ltd.). The sampling frequency was 120 Hz, with a pre-adjusted sampling time of 2 seconds.

The raw data was stored in a computer, digitized using Nexus 2.1, and then converted into 3D (x, y, z) coordinates. Events of interest for the first and the second movement sequences were determined. The data was later analyzed using customized MATLAB programs (The Mathworks, Inc., Natick, MA, USA). In addition to kinematic measurements, behavioral data was recorded using two video cameras, which captured the sagittal and frontal views of each task trial. Datavyu, video coding, and a data visualization tool were used to assess RT, end-state-comfort effect, and task failures.

Outcomes

1. Pre-movement planning

   Reaction time (RT): The time between the appearance of starting cue (lighting up an LED light) and initiation of the hand movement.

2. Online control (Movement sequence 1)

   a) Reach time: The time between the initiation of hand movement and reaching to the object.

   b) Reach trajectory: The path length between the starting position and the object.

   c) Reach deviation: The average deviation of the path length of the hand trajectory between the starting position to reaching to the object, and the actual hand path length.
d) **Reach acceleration:** The peak of the change in hand velocity while reaching for the object.

3. **Execution (Movement sequence 2)**

   a) **Movement time:** The time between grasping the object and placing it at the target position.

   b) **Movement trajectory:** The path length between the object and the target position.

   c) **Movement deviation:** The average deviation of the path length of the hand trajectory between grasping the object and placing it at the target position, and the actual hand path length.

   d) **Movement acceleration:** The peak of the change of hand velocity while placing the object at the target position.

4. **Behavioral measures**

   a) **End-state comfort effect:** The biomechanically comfortable hand position at the end of the target position (Fig 6 A and B).

   ![](image)

   **Fig 6:** End-state comfort effect. A) TD child: the grasp demonstrates biomechanically comfortable end-posture of the hand. At the end of the task, the supinated position of the hand at the end of placing the object at the 270° target position is biomechanically comfortable and offers advantage for further action of releasing the object.

   B) Child with HCP: the grasp demonstrates biomechanically uncomfortable end-posture of the hand. The child with HCP shows pronated hand position at the end of placing the object at the 270° target position. Such end-posture of the hand is biomechanically uncomfortable and disadvantageous for the further action, for example, releasing the object.

   b) **Number of task failures:** The inability to place the object at the target position due to inappropriate grip selection, lack of end-state comfort effect, perseveration errors, etc.
**Statistical Analysis**

To determine if there were significant differences in RT and all kinematic variables in movement sequence I, II, and the number of task failures, separate mixed model ANOVAs (group x hand x target positions) with group (TD and HCP) as the between-subject factor, and arm (dominant/unaffecte, non-dominant/affected) and target positions (0°, 90°, 135°, 180°, 225°, and 270°) as the within-subject factors were used. Chi-square test was used to assess end-state comfort effect. Significant interaction effects were followed up with a Least Squared Difference post-hoc analysis.

We also performed simultaneous multiple linear regression, with movement deviation as a dependent variable, and RT, reach time, reach path, reach deviation, and reach acceleration as independent variables.

All statistical analysis was performed using SPSS (Version 23.0; IBM Corporation, Armonk, NY); P values equal to or less than 0.01 alpha levels corrected for the Least Squared Difference were considered significant. Results in the text and graphs are presented as a mean ± standard error of the mean.

**Results**

**Differences in kinematic characteristics**

**Pre-Movement Planning Phase**

1) Reaction Time (RT)

There was a significant group main effect for RT (P=0.01), indicating that overall the TD children (591.66 ± 606.79 ms) had shorter movement time than the children with HCP (2579.87 ± 565.35 ms).

No other main effects or interactions were significant.
On-line control Phase

First Movement in Sequence

1) **Reach Time:** There was a significant group main effect ($P=0.03$) for reach time, indicating that children with HCP took longer to reach for the object (TD=0.97 $\pm$ 0.17 sec; HCP=3.28 $\pm$ 0.18 sec). None of the other main effects or interaction terms were significant ($P>0.05$).

2) **Reach Trajectory:** There was a significant group main effect ($P=0.004$) for the reach trajectory, indicating the children with HCP had an extended reach path (TD=27.0 $\pm$ 4.88 cm; HCP=85.3 $\pm$ 5.25 cm). None of the other main effects or interaction terms were significant ($P>0.05$).

3) **Reach Deviation:** There was a significant group main effect for reach deviation ($P=0.001$), indicating that children with HCP had larger deviations in reach (TD=4.72 $\pm$ 3.7 cm; HCP=49.21 $\pm$ 3.9 cm). None of the other main effects or interaction terms were significant ($P>0.05$).

4) **Reach Acceleration:** There was a significant group main effect for acceleration during the reach ($P=0.001$), signifying that children with HCP had slower reach accelerations (TD=2.4 $\pm$ 0.08 m/sec$^2$; HCP=0.73 $\pm$ 0.09 m/sec$^2$).

   There was a significant hand main effect ($P=0.001$). Post-hoc analysis revealed the non-dominant/affected (0.69 $\pm$ 0.12 m/sec$^2$) arm had significantly ($P=0.001$) reduced reach accelerations compared to the dominant/unaffected (2.7 $\pm$ 0.13 m/sec$^2$) arm.

   There was a significant group x hand interaction ($P=0.001$). Post-hoc analysis revealed a significant difference in reach acceleration between the non-dominant arm of TD children (4.25 $\pm$ 0.14 m/sec$^2$) and the affected arm of children with HCP (0.67 $\pm$ 0.13 m/sec$^2$) (Fig. 7).
Execution Phase

Second Movement in Sequence

1) Movement Time: There was a significant group main effect ($P=0.001$) for movement time, indicating that children with HCP took longer to complete the movement sequence (TD=1.74 ± 0.12 sec; HCP=2.59 ± 0.14 sec).

There was a significant hand main effect ($P=0.01$). Post-hoc analysis revealed the non-dominant/affected (2.33 ± 0.13 sec) arm required significantly ($P=0.001$) longer time to complete the movement sequence compared to the dominant/unaffected (1.93 ± 0.13 sec) arm.

There also was a significant group x arm ($P=0.02$) interaction. Post-hoc analysis revealed a significant difference ($P=0.001$) between the non-dominant arm of TD children (1.79 ± 0.18 sec) and the affected arm of children with HCP (3.03 ± 0.2 sec), indicating that the affected arm of children with HCP required a longer time to complete the movement.
2) **Movement Trajectory:** There was a significant group main effect ($P=0.001$) for movement trajectory, indicating that children with HCP took a longer movement path to reach for the target ($TD=24.06 \pm 12.1\text{ cm}; HCP=31.02 \pm 13.09\text{ cm}$).

There was a significant hand main effect ($P=0.02$). Post hoc analysis revealed that the non-dominant/affected ($29.18 \pm 1.30\text{ cm}$) arm had a significantly ($P=0.03$) longer movement trajectory compared to the dominant/unaffected ($25.36 \pm 1.25\text{ cm}$) arm.

3) **Movement Deviation:** There was a significant group main effect ($P=0.001$) for movement deviation, indicating that the movement of children with HCP while reaching to the target was more deviated as compared to TD children ($TD=16.20 \pm 2.03\text{ cm}; HCP=42.42 \pm 2.19\text{ cm}$).

There was a significant hand main effect ($P=0.01$). Post-hoc analysis revealed that the movement of the non-dominant/affected arm ($31.39 \pm 2.36\text{ cm}$) was significantly ($P=0.05$) more deviated than the dominant/non-affected arm ($25.21 \pm 2.28\text{ cm}$).

4) **Movement Deceleration:** There was a significant group main effect ($P=0.04$) for the average deceleration, indicating the children with HCP had greater decelerations in their arm trajectories ($HCP = -9.5 \pm -5.1\text{ m/sec}^2; TD= -3.9 \pm 0.4\text{ m/sec}^2$) compared to TD children.

None of the other main effects or interaction terms were significant ($P>0.05$).
**Task failures**

There was a significant group main effect ($P=0.001$), indicating that the TD children ($1.1 \pm 0.1$ errors; $0.67-1.3$) had fewer task failures than children with HCP ($6.6 \pm 0.9$ errors; $4.0-7.6$).

None of the other main effects or interaction terms were significant ($P>0.05$).

**End-state comfort effect**

There was a significant difference in end-state comfort effect between TD and children with HCP ($P=0.001$). All TD children showed 100% end-state comfort effect. In children with HCP, however, 20% of children could not perform the task with their affected hand because of severe impairments. Among the remaining 80%, 38.8% of children with HCP did not show end-state comfort with the affected hand, and 16.7% did not show it with the unaffected side.

**Discussion**

In this study we investigated kinematics of planning and execution of goal-directed sequential complex prehensile action in children with HCP. The results of this investigation suggest that children with HCP have longer RT during planning phase. Our study results also indicate that during the first sequence of movement, children with HCP had longer reach time, extended reach trajectory, increased reach deviation, and reduced acceleration, indicating that children with HCP may have deficits in online control of sequential action. Moreover, during the second movement sequence, children with HCP had longer movement time, increased movement trajectory and deviation, as well as reduced deceleration, indicating deficits in movement execution. Altogether these results suggest that children with HCP have deficits in planning and executing a
sequential action. We also further explored whether planning deficits affect action
execution in children with HCP. Our results demonstrated lack of end-state comfort
effect and an increased number of task failures during the second sequence of
movement in children with HCP. These results potentially indicate that deficits in initial
planning impacted the execution and resulted in task failures. Moreover, reach time and
reach deviation in the control phase predicted movement deviation in the execution
phase. This association indicates that deficits in action planning potentially impact the
action execution.

According to the planning-control model, action planning has two main
components: a) pre-movement planning, and b) online monitoring and correction of
movement in order to achieve the goal state (Glover, 2004). Pre-movement planning
involves processes such as goal determination, target identification, selection, analysis
of object affordances, timing, and computation of the target size, shape, orientation, and
position relative to the body (Glover et al., 2012). Online control involves visual and
proprioceptive feedback to monitor movement and minimize spatial errors (Glover et al.,
2012). Our study results are discussed in view of the planning-control model of
movement performance.

Our study results demonstrated that children with HCP had increased RT, which
suggests that children with HCP had delays in processing the information required for
movement planning. Our results are consistent with the findings of previous studies that
showed increased RT and lack of forward planning in children with HCP (Mutsaarts et
al, 2005; 2006; Steenbergen et al., 2007; Steenbergen & Van der Kamp, 2004).

During the first sequence of movement, the task was to reach and grasp the
object. Our study results indicate that children with HCP had longer reach time, longer
reach trajectories, more reach deviation, and reduced acceleration. The first movement
sequence in our experimental paradigm required online control and correction of movement to achieve the predetermined action goal of reaching and grasping the object. However, longer reach time and reach trajectory potentially indicates that children with HCP lacked online control and monitoring of movement. Moreover, increased reach deviation and longer reach trajectory also indicate that children with HCP potentially have a reduced capacity to detect spatial errors; hence, these children showed more deviation while reaching for the target. Children with HCP also had reduced acceleration while reaching for the target. Amplitude of peak accelerations is associated with motor planning and is indicative of feed-forward processes in planning and controlling a movement (Seidler et al.; 2004). A lack of smoother, faster, and straight reaching movements in children with HCP potentially indicates planning deficits, which could be due to deficits in internal model of movement (Wolpert, 2000). Moreover, the reduced online control of movement could be related to lack of feedback control, which involves modification of ongoing movement using information from sensory receptors (Seidler, 2004). Previous studies have shown that children with HCP have aberrant sensory processes, which likely interfere with planning and detection of errors during online control of action (Kurz, 2014; Duff et al., 2003).

During the second sequence of movement the task was to grasp and place the object in biomechanically complex positions. During this execution phase, children with HCP showed longer movement time, increased movement trajectory and movement deviation, as well as reduced deceleration. These results indicate that children with HCP have deficits in executing a sequential action. Our results are consistent with the previous studies that have shown action execution deficits in children with HCP (Butler et al., 2010; Mackey et al., 2005; Rönnqvist & Rösblad, 2007). Although, these findings from the planning, control, and execution phases support our first hypothesis and
confirms the action planning and execution deficits in children with HCP.

We were interested in exploring whether the complexity of the task would affect initial planning of an action in children with HCP. Contrary to the second hypothesis, our study results revealed that complexity of the target did not delay the RT, which indicates that higher perceptual-motor demands of the biomechanically complex position did not interfere with the initial planning process. These results also imply that potentially children with HCP do not plan the entire sequence of an action in advance and may use the step-by-step planning; hence, the complexity of the target position did not affect the initial planning of these children.

Our study results showed reduced end-state comfort effect and an increased number of task failures in children with HCP. During the second sequence of movement clockwise and counterclockwise positions of object placement were complex for the dominant and the non-dominant hand, and both required ongoing planning while executing the task. Reduced end-state comfort effect indicates deficits in planning the action in children with HCP (Craje et al. 2009; Steenbergen et al., 2004). As noted, the reduced end-state-comfort effect in the second movement sequence indicates that children with HCP might have continued planning during the execution phase of action. Moreover, children with HCP might have used a problem solving strategy later as the movement unfolded. Therefore, deficits in planning the action may have contributed to movement execution deficit in the second state of movement.

Our argument that action-planning deficits impact action execution is supported by our study analysis, which shows that movement time was affected by reach deviation and reach trajectory. These results indicate that the execution of movement was largely influenced by kinematic indices during the planning stage of movement. Moreover, observational analysis indicates that the trials led to task failures and
ultimately did not result in end-state comfort effect. Overall, these study findings indicate that action-planning deficits affected action execution in children with HCP.

One of the major limitations of the present study is that the participating children with HCP were heterogeneous in terms of age, severity, and side of hemiplegia. Although there are equivocal findings regarding the age of development of action planning and the side of hemiplegia, inclusion of younger children with HCP who had severity levels ranging from mild to severe, and who had left as well as right hemiplegia, may limit the generalization of study our results. The composition of the participant group may also warrant cautious interpretation of our study findings. Secondly, our kinematic analysis was based on tracking of a single hand marker, which limits detailed analysis of biomechanical indices. Finally, our study has a relatively small sample size, which might be inadequate in detecting the impact of target complexity on biomechanical indices.

**Conclusion**

Our study results suggest that children with HCP have deficits in planning complex sequential actions. Therefore, these children plan a step-by-step action rather than planning an entire sequence of movement, which potentially interferes with action execution. Action planning problems potentially contribute to reduced functional capacity of children with HCP. Focusing on the movement planning component during therapeutic intervention, rather than solely focusing on movement execution strategies, could potentially improve the functional motor outcomes of children with HCP.
CHAPTER 3: ANTICIPATORY VISUAL PATTERNS AND VISUOMOTOR COORDINATION IN CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY

Introduction

Hemiplegic cerebral palsy (HCP) is one of the most common forms of cerebral palsy, with a prevalence of almost one in a thousand live births in the United States (Yeargin-Allsopp et al., 2008). Due to various sensorimotor dysfunctions, children with HCP have difficulty in using the affected upper extremity for activities of daily living, specifically involving reaching, grasping, releasing, and manipulating objects. Along with sensory deficits such as proprioception and tactile perception (Cooper et al., 1995; Valvano & Newell, 1999; Sarlegna & Sainburg, 2009), children with HCP have central deficits in integrating sensorimotor and visuo-perceptual modalities, which potentially affect the ability to execute motor actions (Gordon et al., 2006; Wann, 1991). Emerging evidence also suggests that impaired motor performance in children with HCP may be related to impaired forward control and deficits in planning goal-directed actions (Steenbergen & Gordon, 2006; Kurz et al., 2014).

Action planning is the ability to anticipate forthcoming perceptual-motor demands of an action goal (Kaller et al., 2011), and involves higher levels of cognitive and visual processes (Glover, 2004; Glover et al., 2012). Studies investigating planning deficits in children with HCP have for the most part been based on object manipulation and anticipatory fingertip forces (Gordon et al., 2006; Gordon & Duff, 1999). These studies suggested possible deficits in the integration of sensory information, such as vision, with motor output in children with HCP. Although vision plays a critical role in planning an action, it has been largely overlooked in children with HCP.

Vision, along with dynamic integration with various sensorimotor systems, plays
a critical role in the successful execution of goal-directed actions (Goodale, 2011; Neggers & Bekkering, 1999; Land et al., 1999; Sarlegna & Sainburg, 2009; Mackrous & Proteau, 2016). To achieve the end goal of a goal-directed action, visual scanning is first required for identification and location of a target. This visual information then contributes to appropriate motor commands. When the task is complex, vision is engaged to closely monitor actions, update an action plan, and amend action execution (Desmurget & Grafton, 2000; Franklin et al., 2012). Collectively, a motor command is sent to a forward model that anticipates sensorimotor consequences, predicts the movement endpoint, and, when necessary, issues corrective motor commands to accomplish an accurate goal-directed action. The forward model is updated during movement execution by incoming proprioceptive and visual inputs (Shadmehr et al., 2010).

Visual and proprioceptive information contributes to the control of limb coordination (Sarlegna & Sainburg, 2009). Integration of visual and proprioceptive signals from the periphery is required to estimate the position of the arm while planning a goal-directed action (Desmurget & Grafton, 2000). Vision provides extrinsic information and is used to accommodate the spatial features of movements toward visual targets, whereas proprioception provides intrinsic information about limb configuration and movement and transforms the spatial plan into neural/motor commands (Sarlegna & Sainburg, 2009).

One such example of visual and proprioceptive coupling is eye-hand coordination. Studies on eye-hand coordination of visual targets in healthy adults have shown that saccadic eye movements are much shorter and quicker than goal-directed hand movements, and that eyes first fixate on the target before hand movement begins (e.g., Abrams et al. 1990; Bekkering et al. 1994, 1995). Moreover, movements are more
accurate when the person is able to see while making them (Desmurget et al. 1997; Elliott et al. 1991; Ghez et al. 1995; Desmurget et al. 1998); furthermore, movement errors occur when visual feedback of the initial position is distorted (Bagesteiro et al. 2006; Holmes & Spence 2005; Sainburg et al. 2003; Sarlegna & Sainburg, 2007; Sober & Sabes 2003). The results of these studies indicate that vision precedes hand movement and is a precursor for anticipatory control of goal-directed actions. To ensure that movement is spatially accurate, the control system requires quickly computed visual representation. Eye movements thus seem to be tightly coupled, both temporally and spatially, to the motor actions of a specific task. One possibility is that the eyes are mainly involved in “forward planning,” or seeking out objects for future use and setting up the operations to be performed on them.

It has been shown that forward planning is affected in children with HCP (Mutsaarts et al., 2005, 2006; Duff & Gordon, 2003). However, studies investigating the contribution of vision in action planning deficits in children with HCP are very limited. Studies that have investigated eye-hand coordination demonstrated that children with HCP closely monitor the actions of the affected hand during object manipulation and transportation (Verrel et al., 2008). Steenbergen and colleagues also anecdotally noted increased visual attention to the affected hand (Steenbergen et al., 1996). These observations suggest that online visual monitoring of movements is potentially used to compensate for underlying sensorimotor deficits. Although a strategy of close visual monitoring might be beneficial for online control of action, such a strategy may compromise the planning process as a whole, because the eyes are not free to scan the visual scene and identify task-relevant landmarks in advance, and this ability is necessary for appropriate prospective control of an action. Therefore, investigating anticipatory visual strategies in children with HCP is crucial to understanding the nature
of planning deficits in children with HCP.

The purpose of this study was a) to determine differences in anticipatory visual patterns in children with HCP compared to typically developing (TD) children and b) to assess visuomotor coordination in children with HCP. Our first hypothesis was that children with HCP would have delayed anticipatory gaze patterns, which may impact action planning and execution of goal-directed action. Our second hypothesis was that children with HCP would exhibit atypical eye and hand coordination.

**Methods**

**Participants**

The study participants consisted of thirteen children with HCP (Age = 6.8 ± 2.9 yrs; males = 7) and fifteen TD children (Age = 5.8 ± 1.1 yrs; males = 8). All children with HCP had a previously defined diagnosis of hemiplegia by a pediatric neurologist. We excluded children with visual deficits such as nystagmus, strabismus, cognitive impairments, frontal cortical lesions, musculoskeletal deformity of the hand and arm, recent arm surgery, botulinum toxin injection in the past 1 year, and arm weakness due to neurological impairments such as brachial plexus injuries. All TD children were right handed per the Edinburgh handedness inventory (Oldfield, 1971). Further details of participating children are given in Table 4. The children with HCP were recruited from the physical therapy clinic at UNMC, and TD children were recruited through word of mouth. The Institutional Review Board of the University of Nebraska Medical Center (UNMC) approved the study, and we obtained parental consent and child assent to participate in this investigation.
Table 4: Demographic details of the participating TD and children with HCP

<table>
<thead>
<tr>
<th>HCP</th>
<th>Gender</th>
<th>Age (yrs)</th>
<th>Hemiplegia</th>
<th>MACS</th>
<th>AHA</th>
<th>Diagnosis</th>
<th>TD</th>
<th>Gender</th>
<th>Age (yrs)</th>
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Setup and procedure

Fig. 8 shows the experimental setup. The experimental task used in this study is a valid upper extremity action-planning task (Jongbloed-Pereboom; 2016). For the experiment, the child sat in an appropriately sized chair, with upright back and hips and knees flexed to 90°, shoulder slightly flexed, elbow flexed to 90°, forearm pronated, wrist neutral and palms placed at a marked starting position. The task consisted of initially reaching and grasping an object placed at a fixed position (Fig. 9 A), followed by placing the object in one of six possible target positions with varying endpoint complexity as directed by a cue (Fig. 9 B). The orientations of the target positions were 0°, 90°, 135°, 180°, 225°, and 270°. 0° was a biomechanically simple target condition and served as starting gaze fixation target. With zero as a starting position, the 90°, 135°, and 180° positions were oriented clockwise, and the 270°, 225°, and 180°
positions were oriented counterclockwise. The clockwise positions were considered more complex for the right arm, and the counterclockwise more complex for the left. The complexity of the target positions was determined based on a biomechanically more compromised final hand position required to place the object at final target position. One experimenter sat facing the child to supervise the task, and the second experimenter controlled the online eye tracker data recording. The first experimenter manipulated task trials by starting and ending the task cues.

The task began with lighting up an LED panel in one of the six target positions in a random order and served as a target cue for placing the object at that target position. The task was divided between the planning and execution phases. The planning phase was the time between lighting up an LED cue and the initiation of hand movement. The execution phase consisted of two movement sequences: a) movement sequence 1 (time between hand initiation to reaching at the object); and b) movement sequence 2 (time between grasping and placing the object at a target position). Each trial started with the hand resting at the starting position and gaze at a fixation target. Later, children were instructed to complete the task sequence, specifically to move the arm as soon as possible after the appearance of the starting cue, to reach at the object, grasp and place the object at the target position identified by the LED light, and return the hand to the starting position (Fig. 9A and B). Gaze and arm movements were recorded during the entire task sequence.

To avoid anticipation of the target position, targets were randomized and each target condition repeated three times. The children performed both movement sequences with each arm for a total of eighteen times (6 target conditions x 3 repetitions of each condition) during the entire session, and the average performance of each condition was used as an outcome metric. Children with HCP performed the task
with the affected and the unaffected arm, and TD children performed the task with the
dominant and the non-dominant hand. We evaluated both arms to explore the global
nature of cognitive processes required for movement planning and control, and to avoid
arm bias toward the hemiplegic hand due to physical restrictions in performing the task
in view of impairments in the affected arm.

Fig. 8: Experimental set up consisted of a hand starting position (blue box in lower
corners) and a series of targets where an object was to be placed. The target for the
respective trial was indicated by an LED. The target directly under the object in the
figure was $0^\circ$, followed by $90^\circ$, $135^\circ$, $180^\circ$, $225^\circ$, and $270^\circ$ in a clockwise direction.

Fig. 9 A): Movement sequence 1
Fig. 9 B): Movement sequence 2
Data acquisition

Head-Mounted Eye Tracker

Visual patterns were assessed using an ultra-light, head-mounted eye-tracker (Positive Science) with a sampling frequency of 30 Hz (Fig. 10). The headgear consisted of two miniature cameras mounted on a flexible, padded band that rested above the child’s eyebrows and stayed firmly in place with Velcro straps attached to an adjustable cap. An infrared LED attached to the headgear illuminated the child’s right eye for tracking the dark pupil and creating a corneal reflection. An infrared eye camera at the bottom right of the visual field recorded eye movements (bottom left arrow in Fig. 10A and B) and a second scene camera attached at eyebrow level faced out and recorded the task (top left arrow in Fig. 10A and B).

The eye-tracker transmitted videos of the participant’s right eye and field of view to a computer running Yarbus software (Positive Science). The software calculated gaze angle based on pupil location and corneal reflection, and superimposed a crosshair over the scene camera view to indicate gaze direction. The crosshairs indicated point of gaze on the scene camera video based on the locations of the corneal reflection and the center of the pupil. The gaze video (scene video with superimposed point of gaze) and eye-camera video were recorded for later coding (Fig. 10C). The temporal resolution of the eye-tracker was 33.3 ms (one video frame) and the spatial resolution was 1.5°.
Fig. 10: A) Child wearing head-mounted eye tracker, B) Eye tracker headgear with scene and eye camera, C) Image from the scene camera with the child’s point of gaze indicated by a purple crosshair. Inset shows image from the eye camera.

**Calibration of the Eye Tracker**

We created a calibration board with a grid of five 5x5 inch square-shape windows with each window placed at the right and the left upper and lower corners and one at the center of the calibration board. Children sat on a chair in front of the task. We presented a squeaky small toy through the window to draw the child’s attention and gaze at the toy. To calibrate the system, we asked the child to look at the toy presented through each of these five windows. The gaze on the squeaky toy in real time was used as a calibration point. Since the calibration was performed online, another experimenter who controlled the eye-tracker registered the five calibration points on a computer.
screen, running the eye tracker setup. When all five-calibration points were accomplished, the experimenter verified the calibration by transforming the recorded gaze to a 2D signal by projecting it to the xy-plane. If calibration was not accurate within 2-3°, the eye camera was adjusted and the calibration process repeated until an accurate calibration was obtained.

**Eye tracker Coding and Analysis**

Behavioral data was recorded using the two video cameras, which captured the sagittal and frontal views of each task trial. Gaze and sagittal and frontal videos were synchronized using a flashlight beam as a synchronizing cue. The primary coder first identified the main events, including pre-movement planning and movement sequences 1 and 2. Approximate fixations were computed as the intersection of gaze direction with plane parallel to xy-plane, containing the center of the object and the target location (Fig. 10C). DataVyu, video coding and a data visualization tool recording onset, offset, duration, and frequencies of behavior were used to assess the temporal characteristics of gaze and arm movements.

**Outcomes**

**Visual Anticipatory Pattern**

1. **Anticipatory Gaze Time:** Time lag between appearance of a starting stimulus and first gaze at the stimulus.

   Anticipatory gaze time = [gaze onset time] - [starting stimulus time]
Eye-Hand Coordination

1. **Movement Onset Asynchrony (MOA):** Time lag between the first gaze to the starting stimulus and hand initiation.
   
   \[ \text{MOA} = \text{[Hand initiation time]} - \text{[gaze onset time]} \]

2. **Movement Termination Asynchrony (MTA):** Time lag between the object placement and gaze at the target.
   
   \[ \text{MTA} = \text{[gaze at the target time]} - \text{[time of the object placement at the target]} \]

3. **Frequency of gaze shift:** Number of times the gaze moved in each sequence of movement.

Action Planning

**Reaction Time:** Time lag between the first gaze to the starting stimulus and hand initiation.

Action Execution

**Movement time:** Time to complete each movement sequence.

Statistical Analysis

Separate mixed-model ANOVAs (group x hand x target positions) with group (TD and HCP) as the between-subject factor, and arm (dominant/unaffected, non-dominant/affected) and target positions (0°, 90°, 135°, 180°, 225°, and 270°) as the within-subject factors were used to determine if there were significant differences in all outcome variables. Least Squared Difference post-hoc analysis was used to assess interaction effect. All statistical analysis was performed using SPSS (Version 23.0; IBM Corporation, Armonk, NY); \( P \) values equal to or less than 0.01 alpha levels corrected for
Least Squared Difference were considered significant. Results in text and graphs are presented as a mean ± standard error of the mean.

Results

Visual Anticipatory Pattern

a) Anticipatory Gaze Time

There was a significant group main effect for anticipatory gaze time (P=0.001), indicating that; overall, the TD children (341.12 ± 82.18 ms) had faster anticipatory gaze time than the children with HCP (878.44 ± 76.58 ms) (Fig. 11).

No other main effects or interactions were significant.

![Graph showing difference in anticipatory gaze timing between TD and children with HCP](image)

Fig. 11: Difference in anticipatory gaze timing between TD and children with HCP

Eye-Hand Coordination

a) Movement Onset Asynchrony (MOA) during planning phase

There was a significant group main effect for MOA (P=0.001), indicating overall that the TD children (250.17 ± 115.90 ms) had smaller latency between gaze timing and hand initiation than the children with HCP (764.81 ± 107.99 ms) (Fig. 12).

No other main effects or interactions were significant.
b) Movement Onset Asynchrony (MOA) during execution phase

Movement sequence 1: There was a significant group main effect for MOA in sequence 1 ($P=0.001$), indicating that overall the TD children (153.53 ± 65.11 ms) had smaller latency between gaze to the fixation target and the first hand movement than the children with HCP (480.01 ± 60.66 ms) (Fig. 13).

No other main effects or interactions were significant.
Movement sequence 2:
There was a significant group main effect for MOA in sequence 2 ($P=0.01$), indicating that overall the TD children ($121.03 \pm 51.11$ ms) had smaller latency between gaze leaving the fixation target and starting to move toward the final target than did the children with HCP ($-220.19 \pm 56.60$ ms) (Fig. 14).

c) Movement termination asynchrony (MTA)
There was a significant group main effect for MTA in sequence 2 ($P=0.01$), indicating that overall the TD children ($189.03 \pm 45.66$ ms) had quicker and shorter anticipatory gaze time than the children with HCP ($356.10 \pm 51.1$ ms) (Fig. 14).

![Fig. 14: Difference in movement onset asynchrony (MOA) between TD and children with HCP during the beginning and end of the second movement sequence of the execution phase](image)

d) Frequency of gaze shift
There was a significant group main effect ($P=0.01$) for frequency of gaze shift, indicating that the TD children ($7.2 \pm 2.3$) had fewer gaze shifts than children with HCP ($15.6 \pm 4.1$).
**Action Planning**

a) Reaction Time (RT)

There was a significant group main effect for RT ($P=0.01$), indicating that overall the TD children ($591.66 \pm 606.79$ ms) had shorter movement time than the children with HCP ($2579.87 \pm 565.35$ ms).

No other main effects or interactions were significant.

**Action Execution**

a) Movement Time (MT)

**Movement sequence 1**

There was a significant group main effect for the time to complete the movement sequence 1 ($P=0.001$), indicating that overall the TD children ($640.19 \pm 92.26$ ms) had shorter movement time than the children with HCP ($1153.91 \pm 89.69$ ms).

No other main effects or interactions were significant.

**Movement sequence 2**

There was a significant group main effect for the time to complete the movement sequence 2 ($P=0.001$), indicating that overall the TD children ($1342.88 \pm 345.21$ ms) had shorter movement time than the children with HCP ($3729.60 \pm 321.63$ ms).

No other main effects or interactions were significant.

**Discussion**

The main purpose of this study was to investigate the role of vision in relation to action planning and task execution in children with HCP. Specifically, we were interested in understanding the anticipatory visual patterns and temporal coupling of eye and hand during the performance of a complex sequential action. The results of this
investigation indicate that children with HCP have prolonged anticipatory gaze timing, which indicates deficits in anticipatory vision. Moreover, children with HCP showed prolonged MOA during action planning as well as during the execution phases, which indicates impaired temporal coupling between eye and hand. Interestingly, our study results demonstrated negative MOA and increased frequency of gaze shift during the beginning of execution phase, which suggests increased visual monitoring of the moving arm. These results were parallel with increased RT and MT in children with HCP. Collectively, results of this investigation revealed that children with HCP may have deficits in anticipatory vision required for planning and executing a goal-directed action. Moreover, our study results also indicate impaired visuomotor coordination in children with HCP.

The prolonged anticipatory gaze timing that was seen suggests that children with HCP have a delay in gaze latency on a starting stimulus. It also indicates that gaze patterns were less anticipatory in children with HCP. Prior studies have shown that gaze is shorter and quicker, and that eyes attend to the target more quickly during goal-directed actions (Land et al., 1999; Bekkering et al. 1994, 1995; Saavedra et al., 2009). For accurate movement, visual attention to the target is a necessary pre-condition (Neggers & Bekkering, 2000). Task-specific eye movements are also shown to be linked to the planning and control aspect of manual action (Flanagan & Johansson, 2003; Glover, 2004). Since vision precedes motor actions, quick gaze thus appears as one of the precursors for completing an accurate motor action. Our study results revealed that children with HCP have a visual delay in attending to a target after the appearance of a starting cue. This delay in gaze timing potentially contributed to the deficit in goal-directed action planning in children with HCP, given that predictive vision is required for planning and control of goal-directed actions (Land, 2009; Glover 2000).
Moreover, because vision precedes motor action, a delay in gaze timing or visual attention to a target potentially followed the delay in motor action. We speculate that the anticipatory visual deficit is one of the crucial components of action planning and the execution deficits that are typically seen in children with HCP (Steenbergen et al., 2000, 2004; te Velde et al., 2003; Gordon and Steenbergen, 2006). Our study results contradict the results of Verell et al. (2008) where deficits in anticipatory gaze control in children with HCP were not found. However, their study design did not manipulate the starting cue, and therefore they could not assess gaze latency. Our study design is novel in that we could systematically assess gaze timing and visual attentiveness to the cue as soon as the starting stimulus was presented. Our study is the first to report a delay in visual anticipatory patterns in children with HCP.

Our study results also indicate longer duration of MOA (latency between hand initiation and onset of gaze) during the action-planning phase in children with HCP. This suggests that after directing gaze to the starting stimulus, there was a significant delay in initiating the arm movement. Delay in initiating a goal-directed movement after visually locating the target further indicates that there is a potential delay in information processing or integrating sensory information with motor output, an indicator of planning deficit (Wong et al., 2015). Prior studies on action planning have demonstrated deficits in integrating sensorimotor information in children with HCP (Gordon et al.). Initially there was seen to be a delay in gaze onset on a starting cue; however, after visually attending the cue a delay in initiating the motor action was also observed. These results indicate that children with HCP might have deficits at the visual as well as sensorimotor integration levels, which might have an impact on visuomotor coordination. MOA on the affected arm has been reported in a single study in children with HCP (Verell et al., 2008). However, our study results suggest the presence of MOA on the affected as well
as unaffected arm during the planning phase of a goal-directed action, and this supports our supposition about the global nature of planning deficits in children with HCP.

During the execution phase, our study results demonstrated negative MOA as soon as the hand began to move to the final target. We saw positive movement termination asynchrony (MTA) when approaching that target. These results suggest that the child visually monitored the arm movement when the arm began moving toward the target, not afterward, which indicates a potential strategy to compensate for sensory and proprioceptive deficits of the affected arm. However, when the arm began to approach the target, gaze was directed to the target before the arm completed the goal-directed movement. These results indicate that during the execution phase, vision guided the arm by increasing gaze attention to the arm, first to potentially compensate for sensorimotor deficits, and later to direct the arm to the appropriate target. These results of increased visual monitoring of the arm in children with HCP were in contrast to the visual patterns seen in TD children. In TD children gaze moved to the final target and movement did not require visual monitoring of the arm. Altogether during the movement execution phase, there was an overall increased visual attention to the moving arm, which might have jeopardized visual ability to scan the environment for accurate action execution in children with HCP. Our study results are consistent with other studies that demonstrated increased visual attentiveness to the arm during object transport phase in children with HCP (Verell, 2008; Steenbergen, 2000; Steenbergen & Van der Kamp, 2004). Earlier studies also have shown difficulty in encoding visual and proprioceptive information into a common egocentric frame (Wann, 1991). In these studies, it has been shown that gaze leads arm movements and that eye movements support hand-movement planning and control (Johansson et al., 2001). Gaze thus may
be viewed as part and parcel of the overall motor program for the task (Land & Furneaux, 1997). Our study results of impaired eye and hand coordination indicate potential deficits in integration of vision and proprioception and may support our argument of impaired visuomotor coordination in children with HCP.

Our study results also indicate increased frequency of gaze shift in children with HCP. Moreover, our observation suggests that gaze shift was in the direction of the moving arm during action planning and in the execution phases. These results complement the results of our study, suggesting increased visual monitoring of the moving arm. Increased gaze frequency in children with HCP also indicates lack of smooth pursuit movements, reported as an indicator of planning deficits. Increased frequency of saccades with increased latency has also been shown to be associated with reduced motor performance (Chen et al., 2016). In addition to a lack of visual anticipatory patterns, RT and MT were prolonged during the planning and execution phases of children with HCP, and this indicates deficits in planning as well as execution. Although our results indicate that children with HCP have problems integrating the visual and motor systems.

**Conclusion**

Our study results show that children with HCP have delayed visual anticipatory patterns, impaired visuomotor coordination, and increased visual monitoring of the moving arm. Since vision plays a crucial role in planning and controlling a goal-directed action, impaired vision and visuomotor coordination might impact planning and execution of goal-directed actions of children with HCP. Hence, therapeutic interventions focusing on improving visuomotor coordination may improve the motor performance in children with HCP.
CHAPTER 4: HAND ARM BIMANUAL INTENSIVE THERAPY IMPROVES PREFRONTAL CORTEX ACTIVATION DURING GOAL-DIRECTED ACTIONS OF CHILDREN WITH HEMIPLEGIC CEREBRAL PALSY

Introduction

Children with hemiplegic cerebral palsy (HCP) have various sensorimotor dysfunctions that result in functional limitations and restrict the child’s participation in educational, leisure, and vocational roles (Sakzewski et al., 2009). Until recently, action execution problems residing in the musculoskeletal machinery were considered to be primarily responsible for activity limitations in children with HCP (Boyd et al., 2001). However, emerging evidence suggests that activity limitations and action performance problems seen in these children are not solely an action execution disorder, but that they might also be due to deficits in the planning of goal-directed actions (Steenbergen & Gordon, 2006; Kurz et al., 2014).

Action planning is the ability to anticipate forthcoming perceptual-motor demands of an action goal, and is crucial for control of skilled movements (Kaller et al., 2011). Various activities of daily living, such as holding a cup, manipulating objects, dressing and undressing, putting a shoe on, and tying shoe laces require a series of information processing such as pre-movement planning, online monitoring, and control of goal-directed actions, before the final execution of these actions takes place (Glover, 2004; Glover et al, 2012). Thus, before accomplishing an action goal, a great deal of cognitive, sensorimotor, and visual information integrates to plan a goal-directed action. Recent studies have shown that children with HCP have deficient motor planning (Mutsaarts et al., 2005; Steenbergen et al., 2006; Duff & Gordon, 2003). Consequently, the presence of an action-planning deficit likely limits the ability to successfully execute
movements (Gordon & Steenbergen, 2006). While these observations may be accurate, therapeutic interventions in children with HCP have specifically focused on motor execution problems (Boyd et al., 2001).

The most commonly used therapeutic approaches in children with HCP are constraint-induced movement therapy (CIMT), hand/arm bimanual intensive therapy (HABIT), and task-specific training (Novak et al., 2013). These approaches have been effective in improving the paretic hand function and bimanual coordination in children with HCP. The cortical changes related to therapy are based on a reorganization of the sensorimotor cortex, an increase in white matter volume, and maintaining the integrity of the corticospinal tract fiber tract (Carr et al., 1993; Maegaki et al., 1999; Staudt et al., 2002; Vandermeeren et al., 2003a; Vandermeeren et al., 2003b; Holmstrom et al., 2010, Weinstein et al., 2015). However, these studies have largely overlooked action-planning problems in children with HCP.

The prefrontal cortex (PFC) plays a critical role in planning and monitoring actions as they evolve (Kaller et al, 2011). The PFC works in close communication with the cortical and subcortical regions important for movement control (Luft et al., 2002). Within the PFC, the dorsolateral prefrontal cortex (DLPFC) is involved in detection of motor errors (Halsband et al., 2006) and initiation of movements (Jahanshahi et. al., 1995), whereas the ventrolateral prefrontal cortex (VLPFC) is involved in maintaining information relevant to the goal (Badre et al., 2007). The DLPFC is extensively connected to the premotor and sensorimotor cortex, and plays a vital role in movement control (Witt et al., 2008). Neuroimaging studies have demonstrated activation while planning a motor task specifically within the PFC and distributed motor networks (Owen et al., 1996; Baker et al., 1996; Tanji, 2007), and activation within the DLPFC and VLPFC during preparatory activity of a sequential action (Pochon et al., 2001; Toni et
A few neuroimaging studies have demonstrated evidence of action planning deficits in children with HCP (Chinier et al., 2014; Van Elk et al., 2010; Guzzetta et al., 2007; Wilke et al., 2009; Kurz et al., 2014; Manning et al., 2015; Vandermeeren et al., 2003; Walther et al., 2009). The results of these studies showed that children with HCP have reduced activation in their bilateral fronto-parietal networks and in the dorsal posterior cingulate cortex, that they have hyper-activated sensorimotor cortices, and that they have developed compensatory networks when planning and executing motor actions.

Although behavioral and neuroimaging studies indicate that children with HCP have impaired action planning and that this potentially results in movement dysfunction, to date only a single study has evaluated the effects of intensive hand function training on action planning in children with HCP (Craje et al., 2010). The results of this intervention trial demonstrated that combined CIMT and bimanual training improved anticipatory planning, with conclusions based on improvement in anticipatory grip selection patterns. Although these behavioral observations may be accurate, further investigation is needed about the potential beneficial effects of interventions on action planning and cortical activation. Such investigation will establish a link between brain and behavior.

In this investigation we used functional near-infrared spectroscopy (fNIRS) to assess PFC activation when children with HCP performed shape-matching motor tasks. The rationale in using fNIRS is that it allows assessment of an ecologically valid motor task. The primary purpose of this novel exploratory investigation was to determine changes in PFC activation following hand arm bimanual intensive therapy (HABIT). Our rationale in using HABIT was that it allows intensive practice of bimanual tasks and enriches movement experience on the hand chosen to form an effective motor plan and
has shown as one of the most effective interventions in improving bimanual coordination in children with HCP. We hypothesized that HABIT would improve action planning ability and associated cortical activation in children with HCP, and that improvement would be reflected through reduced PFC activation during goal-directed actions. Secondary purposes of this study were: 1) to determine whether 50 hours of HABIT improves affected hand function and bimanual coordination; and 2) to determine whether there is a relationship between PFC activation and motor task performance in children with HCP.

**Methods**

**Participants**

Nine children with HCP (ages 4.8 ± 0.9 yrs; 4 males) were included in this investigation. Fifteen TD children (ages 5.9 ± 1.2 yrs; 8 males) also participated in this study and served as a comparison group. Further details of participating children with HCP are given in Table 5. All children with HCP were previously diagnosed with hemiplegia by a pediatric neurologist. We excluded children with frontal cortex lesions, cognitive impairments, visual deficits, musculoskeletal deformity of the hand and arm that restrict the motor performance, and arm weakness due to other neurological impairments such as brachial plexus injuries. The Institutional Review Board of the University of Nebraska Medical Center (UNMC) approved the study. We obtained parental consent and child assent to participate in the study. The participating children with HCP were recruited from the physical therapy clinic at UNMC.
Table 5: Characteristics of study participants

<table>
<thead>
<tr>
<th>Participants</th>
<th>MACS Level</th>
<th>Age (yrs)</th>
<th>Paretic Hand</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Participants</th>
<th>Gender</th>
<th>Age (yrs)</th>
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<tr>
<td>HCP 1</td>
<td>V</td>
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<td>M</td>
<td>Perinatal stroke</td>
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Total=9 I=2, III=5 V=2 Average L=6 M=4

Total=15 M=6 Average F=9 5.8 yrs

Functional Near Infrared Spectroscopy (fNIRS)

fNIRS is a neuroimaging technique that measures hemodynamic changes in cortical tissues continuously and non-invasively in an ecologically valid environment (Boas et al., 2004). fNIRS uses specific wavelengths of light and is based on absorption characteristics of oxygenated (OxyHb) and deoxygenated (DeoxyHb) hemoglobin, both indicators of cortical activation. A series of photon emitters and detectors in the fNIRS device measures regional brain activity by quantifying changes in hemoglobin concentration. The emitters produce infrared light, which penetrates the skull and cortical tissues and is absorbed or refracted by hemoglobin in the underlying neural tissues. The detectors measure the refracted light used to quantify the amount of
OxyHb and DeoxyHb changes in local neural tissues. A greater concentration of OxyHb corresponds to a greater degree of activity in the underlying neural tissues (Boas et al., 2004). During neural activation, there is an increase in OxyHb and a decrease in DeoxyHb as detected by a typical fNIRS signal. The advantages of fNIRS are that it is safe, non-invasive, affordable, portable, and offers good spatial resolution. It is also less susceptible to head movements, is quiet, and does not require the participant to be confined or remain motionless in the supine position. A previous optical imaging study showed that as the skill of complex bimanual coordination task develops, frontal cortex activation reduces (Andrew-Perez et al., 2016). Based on this novel insight, we hypothesized that in children with HCP, as the skill of bimanual tasks develops with intensive practice using HABIT, PFC activation will reduce due to decreased dependence on cognitive resources used to accomplish complex motor tasks.

**HABIT Protocol**

We conducted 50 hrs of the HABIT program in a summer camp based on the HABIT protocol developed by Gordon et al., 2007. Children practiced bimanual activities for 5 hrs per day (4 hours on-site and 1 hour home exercise program each day), 5 days per week, for two consecutive weeks. In our HABIT trials, therapy goals were determined based on pre-intervention assessments and interviews with the children and parents. Based on individual therapy goals, two trained interventionists per child guided and continuously monitored each child’s activities. Various bimanual goal-directed activities and functional training were delivered in a play context. We incorporated age-appropriate fine motor and manipulative gross motor activities requiring the use of both hands. Specific bimanual activities were based on the role of the involved limb in the activity (for example, stabilizer, manipulator, active/passive
assisting). Bimanual activities were made progressively more complex by increasing task difficulty, and task demands graded so that the activities were successful. Positive reinforcement and knowledge of performance were used to motivate and reinforce target movements. The emphasis of therapy was on structured practice of various skilled bimanual activities. The repetitive practice sessions were incorporated into whole- and part-task practice. The goal of whole-task practice was to improve task skill by manipulating the temporal and spatial components of the task. Part-task practice focused on improving speed of the task. Interventionists progressively emphasized completing each movement with the involved upper extremity so as to increase the use of the affected arm in bimanual activities. Functional training was tailored to each child’s goals and activities practiced for 20-30 min per session. Each child also performed one-hour bimanual task practice in a functional context at home. Parents kept daily activity logs to monitor compliance. Make-up sessions were conducted when a child was not able to participate any day during the camp.

**Experimental Paradigm**

The task consisted of sequential shape matching, with three complexity levels: easy, moderate, and difficult. The easy condition had the same shape types, the moderate had two different shape types, and the difficult had multiple different shape types (Fig. 15). The three complexity task levels were based on intricacy of shape identification, accurate selection, manipulation, and type of grasp required based on type, size, shape, and orientation of shape. Children were asked to match shapes with their corresponding templates by selecting a shape and placing it accurately on a template.
Each task was performed in a block paradigm consisting of a 30-sec rest period when the child sat still, and a 30-sec active period when the child matched shapes to templates. To avoid anticipation of the complexity levels, conditions were randomized and each task condition repeated four times. The children performed a total of twelve blocks of the shape-matching task (3 shape complexity conditions x 4 repetitions of each condition) for the full session. The total duration of data collection was twelve minutes. Children with HCP performed the task with the affected and the unaffected arm, and TD children performed the task with the dominant and the non-dominant hand. We chose to evaluate both arms to explore the global nature of cognitive processes required for movement planning and control, and to avoid arm bias for physical restrictions in the hemiplegic hand due accommodations that might already have been developed in performing tasks given impairments in the affected arm.

Fig. 15: Experimental task conditions. A- Easy, B-Moderate, C- Difficult
**fNIRS Data Acquisition**

For this experiment, we used a continuous wave fNIRS system (fNIR Devices LLC, Potomac, MD) that employed two different wavelengths (730 and 850 nm) to measure the concentration of OxyHb and DeoxyHb based on the modified Beer-Lambert law (Obrig & Villringer, 2003). The fNIRS system had three components: a flexible head piece (sensor pad), which secures emitters and detectors in a fixed position for fast placement of the sensor pad to the forehead; a control box for hardware; and a computer to run data acquisition. Two light sources and two detectors on the sensor pad yielded a total of four active optodes (measurement channels). According to 10-20 EEG systems, optodes were located lateral to the Fpz on the left and right sides of the forehead. Sensors had a temporal resolution of 500 milliseconds per scan, with 2.5 cm of separation between light source and detector, allowing for approximately 1.25 cm penetration depth. All optodes were connected to fiber optic cables for transmission of infrared light to the fNIRS system. We used cognitive optical brain imaging (COBI) studio software for data acquisition and visualization (fNIR Devices LLC, Potomac, MD).

**fNIRS Data Analysis**

The measured OxyHb hemodynamic waveforms were low-pass filtered, including a finite impulse response filter with an order of 20 and a cut-off frequency of 0.1 Hz. This filter was used to attenuate high frequency noise, respiration, and cardiac cycle effects (Ayaz et al., 2010). Waveforms that were saturated or had motion artifacts were excluded from analysis. The epochs of each trial lasted 60 seconds (-30 sec to +30 sec), with presentation of the shape-matching task defined as 0.0 seconds. The OxyHb hemodynamic waveforms for each channel were corrected based on the
average OxyHb seen in the baseline period (-25 to -5 sec), and the 4 trials performed in each condition were then averaged. The average maximum OxyHb across respective channels was used as the primary outcome variable. We used OxyHb as a marker for regional brain activation because previous study findings showed OxyHb is more sensitive to neural changes than DeoxyHb (Suzuki et al., 2004).

**Behavioral Data Analysis**

The behavioral data recorded on video was used for the analysis of motor task performance. The number of accurately matched shapes was quantified across each trial and the average performance across the four trials for each condition was used as an outcome variable. We also assessed an average number of errors in matching the shapes across all trials. A wrong match and inaccurate orientation of the shapes were considered errors. We also assessed reaction time (RT), determined as the amount of time needed to initiate hand movement after the shape-matching task was presented. RT for the first shape in each trial was assessed, and average RT across all trials was considered for the final analysis.

**Clinical Outcomes**

Lastly, we asked the children to perform the Assisting Hand Assessment (AHA, Version 5.0) for bimanual coordination (Krumlinde-Sundholm, 2007), and the nine-hole peg test (NHPT) and the box and blocks test (BBT) for manual dexterity and speed.

**Statistical Analysis**

Separate mixed model ANOVAs (intervention x hand x task-conditions) with intervention (pre- and post-HABIT) as the between-subject factor, and arm (unaffected
and affected) and task conditions (easy, moderate and difficult) as the within-subject factors were used to determine whether there were significant differences in OxyHb and task performance pre- and post-intervention. Separate 2x2 mixed ANOVAs with intervention (pre- and post-HABIT) as the between-subject factor, and arm (unaffected and affected) as the within-subject factors were used to determine if there were significant differences in the RT, task errors, NHPT, and BBT. Significant interaction effects were followed up with a Least Squared Difference post-hoc analysis. Paired t-test assessed the pre- and post-HABIT changes in the AHA.

Similarly, two Separate mixed model ANOVAs (group x hand x task-conditions) with group (TD and pre-intervention/ TD and post-intervention) as the between-subject factor, and arm (dominant/unaffected, non-dominant/affected) and task conditions (easy, moderate and difficult) as the within-subject factors were used to determine if there were significant differences in OxyHb and task performance. Separate 2x2 mixed ANOVAs with group (TD and pre-intervention/ TD and post-intervention) as the between-subject factor, and arm (dominant/unaffected, non-dominant/affected) as the within-subject factors were used to determine if there were significant differences in the RT, task errors, NHPT and BBT. Significant interaction effects were followed up with a Least Squared Difference post-hoc analysis.

All statistical analysis was performed using SPSS (Version 22.0; IBM Corporation, Armonk, NY) and P values equal to or less than the corrected 0.01 alpha levels were considered significant. Results in the text and graphs are presented as a mean ± standard error of the mean.
Results

Patient Flow

Fig. 16 shows patient recruitment. We screened 32 children, of whom 10 participated in the two HABIT camps (July 2015: n=6; July 2016: n=4). 8 children completed all the assessments.

Treatment Characteristics

All children completed 50 hours of HABIT. Our activity logs showed that for 94.6% of the time, children were engaged in bimanual activities. On average, they spent 74.2% of time in whole-task practice, 10.2% in part-task practice, and 12% in functional training. All the children had good compliance (9.8 ± 0.33 hrs) for the home exercise program. There were no adverse events reported during the course of either HABIT camp. Children did not receive any additional therapy (OT/PT) during the course of the HABIT camp.
32 children were assessed for eligibility

16 excluded

6 unwilling to participate

A total 10 children participated in the two HABIT camps

6 children participated in the first HABIT camp

All six completed the 50 hrs HABIT

Assessments-
1. All 6 children completed the behavioral assessments
2. 5 children completed the fNIRS assessment

6 children (2 children from the previous year’s HABIT camp) participated in the second HABIT camp

All six completed the 50 hrs HABIT

Assessments-
1. Remaining 3 children completed the behavioral and fNIRS assessments

2 children from previous year were not included in the fNIRS and final analysis

1 child could not complete the post-HABIT testing

Figure 16. Patients’ flow diagram showing progress through the stages of the study, including flow of participants, withdrawals, and inclusion in analyses. A total of 32 individuals were screened via telephone/e-mail, and 16 of these were excluded for the following reasons: too old (n = 4), too young (n = 3), poor cognition (n = 3), diagnosis other than hemiplegia (n = 3), uncontrollable seizures (n = 2), recent hemispherectomy surgery (n = 1). A total of 16 children met the study criteria and were invited to undergo physical screening; 2 parents chose not to undergo physical screening. Of the remaining 14 individuals, 4 could not participate due to time constraint (n=2) and fear of physical stress to the child (n=2). A total 10 children participated in the HABIT camp (6- first year/ 6- second year (2-children repeated the HABIT from the previous year and hence, were not included in the analysis). Out of 10 children, all completed the 50 hours of HABIT. Out of 10 children, one could not complete the post-HABIT testing. Out of remaining 9 children, all completed the behavioral assessments. However, one could not complete the fNIRS assessments (crying). Therefore our final analysis consists of 8 children.
fNIRS Results

Table 6 highlights the pre- and post-HABIT changes in primary outcomes and table 7 shows pre- and post-HABIT mean OxyHb changes for each task condition for children with HCP, and mean OxyHb for TD children.

Table 6: Pre- and post-HABIT changes in primary outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Pre-HABIT</th>
<th>Post-HABIT</th>
<th>Significance (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyHb</td>
<td>0.33 ± 0.04</td>
<td>0.15 ± 0.02</td>
<td>0.001</td>
</tr>
<tr>
<td>Task Performance</td>
<td>4.3 ± 0.4</td>
<td>5.2 ± 0.3</td>
<td>0.01</td>
</tr>
<tr>
<td>AHA</td>
<td>54.66 ± 9.3</td>
<td>64.22 ± 9.7</td>
<td>0.001</td>
</tr>
<tr>
<td>RT</td>
<td>2.23 ± 0.29</td>
<td>1.35 ± 0.17</td>
<td>0.006</td>
</tr>
<tr>
<td>Task Errors</td>
<td>4.88 ± 0.61</td>
<td>2.55 ± 0.42</td>
<td>0.002</td>
</tr>
</tbody>
</table>

a. Pre- and post-intervention

There was a significant intervention (pre/post) main effect (P=0.001), with children having greater OxyHb pre- than post-intervention (pre: 0.33 ± 0.04 µmol/post: 0.15 ± 0.02 µmol; δ²=0.2) (Fig. 17).

There was a significant condition main effect (P=0.005). Post-hoc analyses indicated a significant difference (P=0.01) in OxyHb between easy (0.17 ± 0.04 µmol) and difficult (0.33 ± 0.04 µmol) conditions.

There was a significant arm main effect (P=0.03) with greater OxyHb when children with HCP performed the task with the affected (0.28 ± 0.04 µmol) than the unaffected arm (0.20 ± 0.03 µmol). None of the other main effects or interaction terms were significant (P>0.05).
Table 7: Mean ensemble of fNIRS data for children with HCP and TD children

<table>
<thead>
<tr>
<th></th>
<th>HCP OxyHb Affected_Pre</th>
<th>HCP OxyHb Affected_Post</th>
<th>HCP OxyHb Unaffected_Pre</th>
<th>HCP OxyHb Unaffected_Post</th>
<th>OxyHb Unaffected_Post</th>
<th>OxyHb Unaffected_Post</th>
<th>OxyHb Unaffected_Post</th>
<th>OxyHb Unaffected_Post</th>
<th>OxyHb Unaffected_Post</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
<td></td>
</tr>
<tr>
<td>HCP 1</td>
<td>0.15       0.22        0.42       0.26</td>
<td>0.06       0.08        0.09       0.08</td>
<td>0.14       0.19        0.2        0.18</td>
<td>0.01       0.02        0.06       0.029</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 2</td>
<td>0.63       0.73        0.76       0.71</td>
<td>0.27       0.6          0.73       0.53</td>
<td>0.01       0.12        0.43       0.22</td>
<td>0.02       0.06        0.06       0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 3</td>
<td>0.32       0.35        0.43       0.37</td>
<td>0.05       0.2          0.45       0.23</td>
<td>0.24       0.25        0.5        0.33</td>
<td>0.02       0.17        0.38       0.25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 4</td>
<td>0.63       0.73        0.76       0.71</td>
<td>0.07       0.17         0.16       0.13</td>
<td>0.02       0.07        0.12       0.09</td>
<td>0.04       0.04        0.02       0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 5</td>
<td>0.04       0.12        0.43       0.16</td>
<td>0.12       0.1          0.3        0.17</td>
<td>0.02       0.07        0.12       0.09</td>
<td>0.04       0.07        0.12       0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 7</td>
<td>0.11       0.17        0.2        0.16</td>
<td>0.02       0.06         0.05       0.04</td>
<td>0.02       0.07        0.12       0.09</td>
<td>0.04       0.07        0.12       0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 8</td>
<td>0.05       0.11        0.13       0.10</td>
<td>0.02       0.06         0.06       0.05</td>
<td>0.02       0.07        0.12       0.09</td>
<td>0.04       0.07        0.12       0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCP 9</td>
<td>0.04       0.08        0.14       0.09</td>
<td>0.02       0.06         0.05       0.04</td>
<td>0.02       0.07        0.12       0.09</td>
<td>0.04       0.07        0.12       0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>0.245      0.30039      0.40797    0.32</td>
<td>0.08       0.1642       0.23464    0.16</td>
<td>0.088      0.16385      0.26613    0.17</td>
<td>0.06       0.1432      0.17272     0.12</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>TD OxyHb (Non-dominant hand)</th>
<th>TD OxyHb (Dominant hand)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TD</td>
<td>Easy       Moderate     Difficult  Average</td>
<td>Easy       Moderate     Difficult  Average</td>
</tr>
<tr>
<td>TD 1</td>
<td>0.01       0.02        0.19       0.19</td>
<td>0.08       0.14        0.16       0.16</td>
</tr>
<tr>
<td>TD 2</td>
<td>0.14       0.3         0.04       0.04</td>
<td>0.18       0.5         0.34       0.34</td>
</tr>
<tr>
<td>TD 3</td>
<td>0.03       0.14        0.05       0.05</td>
<td>0.04       0.009       0.05       0.05</td>
</tr>
<tr>
<td>TD 4</td>
<td>0.12       0.04        0.09       0.09</td>
<td>0.09       0.17        0.23       0.23</td>
</tr>
<tr>
<td>TD 5</td>
<td>0.002      0.05        0.08       -0.06</td>
<td>-0.06      -0.02       0.02       0.02</td>
</tr>
<tr>
<td>TD 6</td>
<td>0.04       0.01        0.01       0.01</td>
<td>0.08       0.21        0.13       0.13</td>
</tr>
<tr>
<td>TD 7</td>
<td>0.03       0.16        0.29       -0.04</td>
<td>0.09       0.1         0.1       0.1</td>
</tr>
<tr>
<td>TD 8</td>
<td>0.01       0.05        0.17       0.07</td>
<td>0.07       0.0008      0.12       0.12</td>
</tr>
<tr>
<td>TD 9</td>
<td>0.05       0.14        0.14       0.14</td>
<td>0.06       0.19        0.15       0.15</td>
</tr>
<tr>
<td>TD 10</td>
<td>0.02       0.04        -0.05      0.13</td>
<td>0.13       0.1         0.16       0.16</td>
</tr>
<tr>
<td>TD 11</td>
<td>0.06       0.12        0.18       0.07</td>
<td>0.07       0.05        0.19       0.19</td>
</tr>
<tr>
<td>TD 12</td>
<td>0.19       0.04        0.1        0.05</td>
<td>0.05       0.2         0.14       0.14</td>
</tr>
<tr>
<td>TD 13</td>
<td>0.06       0.03        0.03       0.26</td>
<td>0.26       0.28        0.31       0.31</td>
</tr>
<tr>
<td>TD 14</td>
<td>0.15       0.15        0.22       0.2</td>
<td>0.2        0.1         0.15       0.15</td>
</tr>
<tr>
<td>TD 15</td>
<td>0.24       0.19        0.16       0.09</td>
<td>0.09       0.14        0.16       0.16</td>
</tr>
<tr>
<td>Average</td>
<td>0.076      0.098       0.11       0.086</td>
<td>0.14       0.16        0.16       0.16</td>
</tr>
</tbody>
</table>
b. Pre-intervention and TD

There was a significant group main effect ($P=0.001$), with children with HCP having greater OxyHb pre-intervention than TD children (pre: $0.33 \pm 0.04 \mu\text{mol}$/post: $0.11 \pm 0.01 \mu\text{mol}$) (Fig. 17).

There was a significant condition main effect ($P=0.002$). Post-hoc analyses indicated a significant difference ($P=0.001$) in OxyHb between easy ($0.17 \pm 0.02 \mu\text{mol}$) and difficult ($0.29 \pm 0.02 \mu\text{mol}$) conditions.

There was a significant ($P=0.001$) group-by-arm interaction. Post-hoc analysis revealed a significant difference ($P=0.001$) in OxyHb between the affected arm ($0.40 \pm 0.05 \mu\text{mol}$) of children with HCP and the non-dominant arm ($0.18 \pm 0.03 \mu\text{mol}$) of TD children. There also was a significant difference ($P=0.02$) in OxyHb between the unaffected arm of children with HCP ($0.26 \pm 0.04 \mu\text{mol}$) and the dominant arm of TD children ($0.13 \pm 0.02 \mu\text{mol}$).
c. Post-intervention and TD

There were no significant group ($P=0.06$) (Fig. 17) and arm ($P=0.8$) main effects. There was a significant condition main effect ($P=0.001$). Post-hoc analyses revealed a significant difference ($P=0.008$) between easy (0.08 ± 0.01 μmol) and difficult (0.17 ± 0.02 μmol) conditions.

Task performance

a. Pre- and post-intervention

There was a significant intervention (pre/post) main effect ($P=0.01$), with children matching 21% more number of shapes post-intervention than pre-intervention (pre: 4.3 ± 0.4/post: 5.2 ± 0.3 shapes) (Fig. 18).

There was a significant condition main effect ($P=0.001$). Post-hoc analyses indicated that children matched a greater number of shapes in easy (6.17 ± 0.33 shapes) than moderate (4.38 difficult ± 0.33 shapes) and difficult conditions (3.71 ± 0.33 shapes; $P=0.01$).

There was a significant arm main effect ($P=0.001$), with the affected (4.1 ± 0.28 shapes) arm matching 24% fewer number of shapes than the unaffected arm (5.4 ± 0.31 shapes).

![Fig. 18: Comparison of task performance between pre- and post- HABIT, and TD children](image)
**b. Pre-intervention and TD**

There was a significant group main effect ($P=0.001$): children with HCP ($4.28 \pm 0.31$ shapes) matched 47% fewer number of shapes than TD children ($8.03 \pm 0.25$ shapes) (Fig. 18).

There was also a significant condition main effect ($P=0.001$). Post-hoc analysis showed a significant difference ($P=0.001$) between easy ($8.29 \pm 0.43$ shapes), moderate ($6.57 \pm 0.37$ shapes) and difficult ($5.0 \pm 0.33$ shapes) conditions.

There was a significant arm main effect ($P=0.02$), with the dominant/unaffected (6.5 ± 0.22 shapes) arm matching an 11% higher number of shapes than the non-dominant/affected arm ($5.8 \pm 0.22$ shapes).

**c. Post-intervention and TD**

There was a significant group main effect ($P=0.001$), with children with HCP ($5.23 \pm 0.30$ shapes) matching 35% fewer number of shapes than TD ($8.03 \pm 0.25$ shapes) children (Fig. 18).

There was a significant condition main effect ($P=0.001$). Post-hoc analysis showed that children matched more shapes in easy ($8.7 \pm 0.38$ shapes) than moderate ($6.77 \pm 0.33$ shapes) and difficult ($5.4 \pm 0.29$ shapes; $P=0.001$) conditions.

There was a significant arm main effect ($P=0.02$), with the dominant/unaffected arm ($7.27 \pm 0.31$ shapes) matching a 9% higher number of shapes than the non-dominant/affected ($6.67 \pm 0.31$ shapes) arms.

**Assisting Hand Assessment (AHA)**

There was significant improvement in AHA score ($P=0.001$, $\delta^2=3.5$) between pre-HABIT ($54.66 \pm 9.3$) and post-HABIT ($64.22 \pm 9.7$) assessments.
Reaction Time (RT)

a. Pre- and post-intervention

There was a significant intervention main effect ($P=0.006; \delta^2=0.2$), with a 39.5% reduction in RT between pre- ($2.23 \pm 0.29$ seconds) and post-intervention ($1.35 \pm 0.17$ seconds).

There was a significant arm main effect ($P=0.003$) in RT between the affected ($2.27 \pm 0.29$ seconds) and the unaffected arm ($1.32 \pm 0.15$ seconds).

b. Pre-intervention and TD

There was a significant group main effect ($P=0.001$), with 59.1% longer RT in children with HCP ($2.23 \pm 0.29$ seconds) than TD children ($0.91 \pm 0.05$ seconds).

There was a significant arm main effect ($P=0.002$), with the dominant/unaffected arm ($1.13 \pm 0.11$ seconds) having faster RT than the non-dominant/affected arm ($1.68 \pm 0.25$ seconds).

There was a significant group by arm interaction ($P=0.01$). Post-hoc analysis showed a significant difference ($P=0.004$) between the affected arm of children with HCP ($2.86 \pm 0.45$ seconds) and the non-dominant arm of TD children ($0.97 \pm 0.1$ seconds). Similarly, there was a significant difference ($P=0.001$) between the unaffected arm of children with HCP ($1.61 \pm 0.24$ seconds) and the dominant arm of TD children ($0.85 \pm 0.04$ seconds).

c. Post-intervention and TD

There was a significant group main effect ($P=0.002$) with 32.6% longer RT in children with HCP ($1.35 \pm 0.17$ seconds) than TD children ($0.91 \pm 0.05$ seconds).
There was a significant arm main effect \( (P=0.005) \). Post-hoc analysis showed significant difference \( (P=0.02) \) in RT between the non-dominant/affected \( (1.24 \pm 0.13 \text{ seconds}) \) and dominant/unaffected \( (0.91 \pm 0.05 \text{ seconds}) \) arms. There was a significant group by arm interaction \( (P=0.05) \). Post-hoc analysis showed a significant difference \( (P=0.007) \) between the affected \( (1.68 \pm 0.26 \text{ seconds}) \) and non-dominant arm of TD children \( (0.97 \pm 0.1 \text{ seconds}) \). There was no significant difference \( (P=0.1) \) between the unaffected arm \( (1.02 \pm 0.13 \text{ seconds}) \) of children with HCP and the dominant arm of TD children \( (0.85 \pm 0.04 \text{ seconds}) \).

**ERRORS**

**a. Pre- and post-intervention**

There was a significant intervention main effect \( (P=0.002) \), with a 47.7% reduction in shape-matching errors pre- \( (4.88 \pm 0.61) \) and post-intervention \( (2.55 \pm 0.42) \).

There was a significant arm main effect \( (P=0.006) \), with a higher number of errors in the non-dominant/affected arm \( (4.47 \pm 0.47) \) than in the dominant/unaffected arm \( (2.72 \pm 0.47) \).

**b. Pre-intervention and TD**

There was a significant group main effect \( (P=0.001) \), with 248.5% higher number of errors in children with HCP \( (4.88 \pm 0.61) \) than TD children \( (1.4 \pm 0.22) \).

There was a significant arm main effect \( (P=0.01) \) with a higher number of errors in the non-dominant/affected arm \( (3.83 \pm 0.36) \) than in the dominant/unaffected arm \( (2.45 \pm 0.36) \).
c. Post-intervention and TD

There was a significant group main effect ($P=0.006$) with 82% higher number of errors in children with HCP ($2.55 \pm 0.42$) than TD children ($1.40 \pm 0.21$).

There was a significant arm main effect ($P=0.006$) with the higher number of errors in children with HCP ($2.55 \pm 0.28$) than TD children ($1.40 \pm 0.28$).

Nine-hole Peg Test (NHPT)

a. Pre- and post-intervention

There was no significant intervention main effect ($P=0.1$). However, there was a trend in reduction of NHPT time between pre- (112.86 $\pm$ 11.41 seconds) and post-intervention (86.50 $\pm$ 11.41 seconds).

There was a significant arm main effect ($P=0.001$), with longer time to complete the NHPT with the affected arm (130.64 $\pm$ 12.10 seconds) and the unaffected arm (68.72 $\pm$ 10.67 seconds).

b. Pre-intervention and TD

There was a significant group main effect ($P=0.001$) with a longer time to complete the NHPT in children with HCP (112.9 $\pm$ 7.75 seconds) and TD children (41.03 $\pm$ 5.62 seconds).

There was a significant arm main effect ($P=0.001$) with more time to complete the NHPT with the non-dominant/affected arm (95.37 $\pm$ 7.04 seconds) than with the dominant/unaffected arm (58.52 $\pm$ 6.49 seconds).

There was significant group by arm interaction ($P=0.001$). Post-hoc analysis showed a significant difference ($P=0.001$) in NHPT time between the non-dominant arm of TD children (39.46 $\pm$ 2.88 seconds) and the affected arm of children with HCP.
(151.29 ± 26.22 seconds). Similarly, there was a significant difference ($P=0.001$) between the dominant arm of TD children (42.60 ± 2.62 seconds) and the unaffected arm of children with HCP (74.44 ± 10.35 seconds).

c. Post-intervention and TD

There was a significant group main effect ($P=0.001$) with longer time to complete the NHPT in children with HCP (86.50 ± 11.41 seconds) and TD children (41.03 ± 4.37 seconds).

There was a significant arm main effect ($P=0.001$) with longer time to complete the NHPT with the non-dominant/affected arm (74.73 ± 5.47 seconds) and the dominant/unaffected arm (52.80 ± 5.04 seconds).

There was significant group by arm interaction ($P=0.001$). Post-hoc analysis showed significant difference ($P=0.001$) in NHPT time between the non-dominant arm of TD children (39.46 ± 2.88 seconds) and the affected arm of children with HCP (110.0 ± 17.92 seconds). Similarly, there was a significant difference ($P=0.02$) between the dominant arm of TD children (42.60 ± 2.62 seconds) and the unaffected arm of children with HCP (63.0 ± 10.10 seconds).

Box and Blocks Test (BBT)

a. Pre- and post-intervention

There was no significant intervention main effect ($P=0.5$); however, there was a trend for improvement in the BBT between pre- and post-HABIT (pre:14.8 ± 2.4 blocks, post: 17.1 ± 2.4 blocks). There was a significant hand main effect ($P=0.01$) with 43.5% fewer number of blocks moved with the affected (11.55 ± 2.01 blocks) than with the unaffected hand (20.44 ± 2.47 seconds).
b. Pre-intervention and TD

There was significant group main effect \((P=0.001)\), with 55\% fewer number of blocks moved by children with HCP \((14.88 \pm 2.49\) blocks) than by TD children \((33.03 \pm 1.27\) blocks).

c. Post-intervention and TD

There was significant group main effect \((P=0.001)\) with 48.2\% fewer number of blocks moved by children with HCP \((17.11 \pm 2.46\) blocks) than by TD children \((33.03 \pm 1.27\) blocks).

Discussion

The results of this investigation suggest that post-HABIT, PFC activation while performing a shape-matching motor task decreased in children with HCP. Decrease in PFC activation was parallel to an improvement in bimanual coordination. Motor performance and skill also improved, as illustrated by enhanced behavioral performance during the shape-matching task, reduction in shape-matching errors, and reduction in RT. These results suggest that HABIT has the potential to reduce the burden on PFC associated with the higher cognitive demands placed on children with HCP while planning and executing shape-matching motor tasks that use the upper extremities, and that this reduction in PFC burden potentially improved both motor performance and motor skill acquisition.

Post-HABIT reduction in PFC activation implies improvement in allocation of attentional resources for simultaneous processing of cognitive (attention, memory, information processing) and motor demands required to complete a shape-matching task. The PFC plays a crucial role in modulating attentional demands of new motor
tasks (Lacourse et al, 2005) and has been shown to enhance activation during motor tasks that demand attention (Owen et al., 1997). The attenuation in PFC activation may be associated with: 1) reduction in attention to the motor task, which could be due to the practice related "automaticity" of cognitively challenging motor tasks after the HABIT intervention (Ono et al., 2015); 2) reduction in competition between neural resources needed for orchestrating attentional resources and the cognitive demands of the motor task and physical constraints of the impaired arm; 3) improvement in the functional cost of sharing cognitive and motor resources, which potentially enhanced economy of movement; and 4) increased neuronal efficiency or efficient use of neuronal circuits required for modulating planning and control of goal-directed actions. Overall, due to the acquisition of efficient action planning and execution strategies post-HABIT, functional reorganization may have occurred and may have resulted in reduced activation within the PFC. Our study results also corroborate the fMRI study that demonstrated attenuation in PFC activation following both motor skill learning (Jueptner et al 1997; Floyer-Lea & Matthews 2004; Hill et al., 2006) and practice-dependent plasticity in the PFC during bimanual coordination tasks and complex motor skill acquisition (Dabaere et al., 2004; Leff et al., 2008).

Our study results also demonstrated improvement in bimanual coordination and manual dexterity post-HABIT. The improvement in bimanual coordination is confirmed by the post-HABIT increase in AHA scores, which exceeded the minimal clinically important difference of 5 AHA units (Krumlinde-Sundholm, 2012). An intensive practice of providing a variety of bimanual tasks in variable contexts may have improved bimanual coordination. Our results are consistent with other studies that demonstrated improvement in bimanual coordination for children after they participated in the HABIT (Green et al., 2013; Hung et al., 2011; Gordon et al., 2007). Moreover, our study results
showed trends in improvement in manual dexterity and speed as indicated by NHPT time and the BBT. Intensive practice of spatial-temporal domains of goal-oriented gross and fine motor tasks may have contributed to improvements in manual dexterity and speed. These results suggest that 50 hrs of HABIT is efficacious in improving bimanual coordination and in improving affected hand function in young children with HCP.

Our study results also indicate that post-HABIT, children matched a higher number of shapes and that shape-matching errors were reduced. These results suggest improvement in motor task performance and accuracy after participating in the HABIT. We speculate that these improvements could be due to improvement in the internal model of movement that underlies action planning.

Our study results also demonstrated post-HABIT reduction in RT, which clearly indicates that children had improved cognitive processing. Since RT is associated with movement planning (Wong et al., 2015), our study results indicate potential improvement in action planning following HABIT.

One of the limitations of the present study is the lack of a control group that received either other forms of intensive therapy or conventional therapy. This would have enhanced our understanding of changes in PFC activation specific to particular therapies. A control of this kind would also have enhanced our understanding about whether our claim that HABIT improves planning capacity in children with HCP is specific to the HABIT intervention, or whether this improvement is secondary to motor skill acquisition. Secondly, a limited number of optodes were used, and these were restricted to the PFC. Also, the other areas associated with action planning, such as the fronto-parietal cortical areas, basal ganglia, and cerebellum, were not evaluated simultaneously. We thus could not assess the effects of HABIT on these cortical and subcortical structures. HABIT may have a larger potential influence on the activation of
these areas. Thirdly, we did not have electromyographic or kinesiological data to measure those motor impairments that may reside in the musculoskeletal system. Thus, our study results are inadequate in their ability to determine whether reduction in PFC is due to improvement in musculoskeletal machinery or if it follows from impaired cognitive processing. These limitations should be addressed in future studies directed at understanding the effects of interventions in improving action-planning deficits in children with HCP.

**Conclusion**

HABIT, a child friendly functional bimanual training approach, which incorporates age appropriate tasks in play context, may be a promising intervention to improve the capacity for action planning in children with HCP. HABIT also has the potential to improve neural efficiency of the PFC during planning and execution of a goal-directed action. Fifty hours of HABIT participation is also adequate to improve bimanual coordination and affected hand function in children with HCP. These improvements in action planning deficits will likely result in enhanced future motor task performance. Clinicians should consider the focus of intervention as improving cognitive processing in children with HCP to improve their learning of new motor skills.
DISCUSSION

Prefrontal Cortex Activation

The first purpose of this dissertation was to gain a comprehensive understanding of the neural basis of planning of goal-directed action in children with HCP. Moreover, this dissertation sought to assess the cortical control of action planning, and the relationship between action planning and execution in children with HCP. This dissertation specifically quantified the prefrontal cortex (PFC) activation and its potential impact on motor performance of an ecologically valid task in children with HCP. The first hypothesis exhibited was that children with HCP might have higher PFC activation due to a greater utilization of cognitive resources while planning and executing a goal-directed action. The second hypothesis was that increased cortical activation would be associated with reduced motor performance in children with HCP. The outcomes of this study enhanced our understanding of the abnormal cortical activation associated with planning and executing the goal-directed action. This finding is further helpful in developing therapeutic intervention that can target action-planning deficits and enhance motor performance in these children.

The results of this study demonstrated that the children with HCP in our study had higher PFC activation while performing a motor task with their impaired as well as unimpaired upper extremities. Increased PFC activation indicates an increased burden on the PFC for simultaneous processing of cognitive and motor demands of the goal-directed action. This finding highlights the importance of the cognitive control of motor actions, which potentially governs movement economy during normal movement control. The increased PFC activation seen in children with HCP in our study potentially signifies disturbed movement economy due to competing neural resources required for the motor and cognitive control of the impaired arm. The presence of higher PFC
activation while performing the task with the unimpaired arm was surprising; however, it
denotes that our results are not confounded by the motor deficits of the impaired limb,
and further strengthens the idea of the global nature of planning deficits in children with
HCP. These results are corroborated by previous behavioral studies that have
demonstrated evidence of planning deficits when the task was performed with the
unimpaired arm (Steenbergen & Gordon, 2006; Steenbergen et al., 2004; Mutsaarts et
al., 2004; Mutsaarts et al., 2005; Verrel et al., 2008). Moreover, our study provides
evidence of a neural basis for the behavioral findings that indicated impaired action
planning in the earlier studies. Additionally, increased cortical activation was associated
with reduced motor task performance and increased task failures in children with HCP.
These results indicate that deficient cognitive processing potentially underlies the
uncharacteristic motor performance in children with HCP. Altogether, these results
provide a foundation for a neural basis of action planning deficits in children with HCP.

**Sequential Action Planning**

The second purpose of this dissertation was to assess the biomechanical
differences in action planning and execution of complex sequential prehensile action in
children with HCP. The results of Chapter 2 suggest that children with HCP have
deficits in planning the entire sequence of an action in advance. Indeed, these children
use a step-by-step planning strategy to complete the sequence of a goal-directed action
and planning continues as the further sequence of movement unfolds.

The results of a kinematic analysis showed an increased reaction time (RT)
during the planning phase of children with HCP. It indicates that these children have a
delay in processing the task related information. Earlier studies have shown that a
longer RT indicates action-planning deficits and has been found in children with HCP (Steenbergen et al., 2004).

In addition, during the action control phase, these children had a longer reach time, longer reach path, larger reach deviation, and slower speed of reaching. During the execution phase, there was a longer movement time, longer movement path, larger movement deviation, and greater deceleration of the arm. These results also were associated with increased task errors and a reduced end-state comfort effect. The reach path and reach deviation were strong predictors of movement deviation seen in these children.

Altogether, these results suggest that children with HCP lack forward planning and control of goal-directed movement. Our study results indicate that a larger variability in reach trajectory and reach deviation was likely accountable for movement deviation. It indicates that impaired action control potentially affects the action execution. These results are in accordance with other behavioral studies that have shown a lack of end-state comfort effect and task failure stemming from action planning deficits in children with HCP (Steenbergen et al., 2004; Steenbergen & van der Kamp, 2004; Mutsaarts et al., 2004; Mutsaarts et al., 2005). However, our study provided a detailed biomechanical analysis for the planning, control, and execution phases of sequential goal-directed action, which would be further valuable in quantifying the changes in action planning and execution after therapeutic intervention.

**Anticipatory Vision and Visuo-motor Coordination**

The third purpose of this dissertation was to investigate the role of vision in planning and execution of goal-directed action in children with HCP. This dissertation
sought to assess anticipatory visual patterns and temporal couplings between eye and hand while children with HCP performed the goal-directed sequential action.

The results from Chapter 3 indicated that children with HCP have a longer latency of gaze onset after the starting stimulus appeared. These results indicate that the gaze is less anticipatory in children with HCP. Various studies have shown that the gaze is faster and vision locates the target first before the hand initiates movement during goal-directed action (Land et al., 1999; Bekkering et al. 1994, 1995; Frens & Erkelens 1991; Johnson et al., 2000; Saavedra et al., 2009). Our study results showed that children with HCP have a typical pattern of onset of gaze first, followed by hand onset to the target; however, as compared to TD children, the anticipatory gaze is delayed. We speculate that the delay in gaze timing might have contributed to the deficit in planning the action since prior studies suggest that predictive vision is required for planning and control of goal-directed actions (Land, 2008; Glover, 2000). We also suspect that the delay in anticipatory gaze timing potentially follows the delay in the motor action, and may be a reason for the delay seen in action execution in children with HCP in our study.

The results from Chapter 3 also indicate eye-hand coordination problems in children with HCP. The study’s findings suggest movement onset asynchrony (MOA) during planning as well as execution phases, which indicates a longer time lag between the initiation of the hand movement and the onset of the gaze on the target. We suspect that the delay in initiating a goal-directed movement after visually locating the target could be due to the difficulty in integrating sensory (visual) information with the motor output. Hence, we argue that children with HCP have visuomotor coordination problems. Furthermore, our findings also suggest increased visual monitoring at the beginning of moving the object to the target location. Our study results are consistent
with the other studies that demonstrated increased visual monitoring of the impaired arm (Verell et al., 2008). Although our study results did not exhibit arm specific differences in visual monitoring, we speculate that increased visual monitoring is one of the compensatory strategies for the proprioceptive deficit of the moving arm. Moreover, this compensatory strategy might have been used to visually guide the moving arm to the final target location.

**Therapeutic Intervention**

This fourth purpose of this dissertation was to evaluate the effects of intensive bimanual therapy in improving action planning and execution in children with HCP. This attempted to build upon the knowledge gained from the studies completed for the first three chapters. Specifically, the first hypothesis of this part of the dissertation was that the hand arm bimanual intensive therapy (HABIT) would not only improve action-planning capacity but would also improve action execution in children with HCP. Additionally, it was hypothesized that post-HABIT there would be a reduction in the PFC activation. The outcomes from this study will provide foundational information about the intervention program to improve action-planning and consequent action execution deficits in children with HCP.

The outcomes from this investigation indicated a post-HABIT decrease in the PFC activation. Also, there was a subsequent improvement in bimanual coordination and the affected arm function. More importantly, the post-HABIT reduction in PFC activation was comparable with TD children. Furthermore, post-HABIT, there was an enhanced task performance and a reduced number of task errors, which indicate improvement in motor performance. To our knowledge, this is the first investigation that has demonstrated a reduction in PFC activation and a subsequent improvement in
bimanual coordination in children with HCP. We suspect that the reduction in the PFC could be secondary to the improvement in action planning or allocation of attentional resources for simultaneous processing of cognitive and motor demands of the given task. However, based on our study design, it is difficult to comment whether the improvement in motor execution was essentially due to the improvement in action planning or whether it was secondary to motor skill learning following intensive bimanual tasks practice. Our study is limited in addressing the direct association between the reduction in PFC activation and improvement in motor performance because HABIT did not exclusively incorporate the action planning strategies. Earlier studies have shown that practice of the task with the unimpaired arm helps in improving the action plan of the impaired arm (Duff & Gordon, 1999). Therefore, an enriching experience of bimanual activities with HABIT might have helped in improving the action plan on the impaired arm through intensive practice of bimanual activities between the impaired and the unimpaired arm. Future investigations should focus on the interventions specifically incorporating action-planning strategies and should compare the effects of such intervention on PFC activation. Such studies will highlight the relationship between action planning and execution.
Limitations

One limitation in this dissertation is that of a small sample size. Specifically, the assessment of the impact of the task’s complexity on motor planning and execution in Chapter 2 and 3 was limited due to the small sample size. Potentially having more TD children and children with HCP in each group would have augmented the differences between the task conditions. Additionally, larger sample sizes may have produced more robust relationships between the complexity of the task conditions and the difficulty of action planning and execution. Moreover, the children with HCP in our study were heterogeneous in terms of the severity of hemiplegia. Although the impact of the severity of hemiplegia on action planning deficits is not known, we speculate that the motor limitations of children with higher severity levels of HCP might have confounded the ability to plan the action. Finally, we did not consider the side of hemiplegia. A separate analysis of right versus left hemiplegia would have been meaningful in order to distinguish the differences in planning and execution based on the side of cortical lesion in these children. Future investigations should take into account the severity and side of hemiplegia to have a more comprehensive understanding of action planning deficits in children with HCP.
Conclusions

In conclusion, this dissertation built upon the current literature, which suggests an action-planning deficit as a contributing factor to action execution and motor performance problems in children with HCP. The outcomes of the studies determined that children with HCP have abnormal cortical activation, delayed anticipatory vision, impaired visuomotor coordination, and atypical biomechanical characteristics during the planning and execution of a goal-directed action. Moreover, these outcomes in the cortical, visual, and motor domains are related to reduced task performance and task failures, which reveal a potential link between action planning and execution in children with HCP. Finally, the dissertation discovered that hand arm bimanual intensive therapy (HABIT) normalizes the cortical activation and promotes improvement in action planning and execution in children with HCP. Altogether, these results provide clinicians and researchers with new information concerning various potential factors responsible for motor performance problems and for redirecting the focus of therapeutic intervention to optimize learning new motor skills in children with HCP.
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