BRAIN ACTIVATION FOLLOWING CONSTRAINT-INDUCED MOVEMENT THERAPY USING FUNCTIONAL NEAR INFRARED SPECTROSCOPY IN STROKE PATIENTS

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DEDICATION

This dissertation is dedicated to my late grandmother, Khanam Safia Suleman. Thank you for always believing in me, even at times when I did not believe in myself. Your remembrance was my inspiration for the intense effort put forth during the completion of this project. I am forever grateful for the impact your support and encouragement had on my educational career.

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ABSTRACT

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BRAIN ACTIVATION FOLLOWING CONSTRAINT-INDUCED MOVEMENT THERAPY USING FUNCTIONAL NEAR INFRARED SPECTROSCOPY IN STROKE PATIENTS

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Based on the learned non-use theory, constraint-induced movement therapy (CIMT) is a rehabilitation technique that is utilized with stroke patients to regain function of an affected extremity. CIMT provides patients the resources to help enhance their reliance on an impaired limb while constraining the intact limb. Over time, the impaired limb gains strength and is able to effectively challenge its learned non-use during daily living tasks (Grotta et al., 2004; Taub, Uswatte, & Pidikiti, 1999). Research suggests the use of CIMT has shown to be significantly effective in chronic stroke patients' ability to improve function in the use of an impacted limb (Grotta et al., 2004; Kunkel et al., 1999; Liepert et al., 1998). In addition, neuroimaging studies have demonstrated that CIMT influences the reorganization of the brain (Levy, Nicholas, Schmalbrock, Keller, & Chakeres, 2001).

Functional Near-Infrared Spectroscopy (fNIRS) is an novel method of mapping the brain by using light to measure changes in oxygenated and de-oxygenated hemoglobin concentration in cortical tissue (Nishimura, Rapoport, Wubbels, Downs, & Downs, 2010). Research employing imaging technology to investigate functional and

neurological recovery following brain injury is essential in understanding the implication of various neurorehabilitation methods. Furthermore, additional research is necessary to validate the sensitivity of fNIRS in detecting changes in brain activity, such as the motor cortex. The purpose of this study was to utilize fNIRS to explore cortical activation patterns in stroke patients before and after neurorehabilitation. More specifically, the study examined hemoglobin signal among patients who experienced hemiparesis after a left middle cerebral artery (MCA) stroke. Participants' upper extremity motor functioning following two weeks of CIMT was examined to determine if CIMT during stroke rehabilitation is associated with changes in neural activity.

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CHAPTER I

INTRODUCTION

According to the World Health Organization (1971, p. 6), a stroke is defined as "the sudden onset of a focal neurological deficit due to a local disturbance in blood supply to the brain." It is also the third leading cause of disability in the world (Murray et al., 2012). Each year, approximately 795,000 people experience a stroke in the United States. Between 2000 and 2010, mortality from stroke decreased 22.8%, and the relative proportion of death dropped 35.8%. It has been suggested the reduction in stroke mortality is due to a decline in the number of incidents and an improvement in interventions that address the management of risk factors related to stroke (Go et al., 2014).

The manifestation of stroke is presented as various neurological symptoms that depend upon the extent and affected areas of the brain. The presentation of stroke can prolong for a few seconds to indefinitely. The long-term effects of stroke vary depending on the size and area(s) of the blockage and the amount of recovery. As a result, patients experience a variety of cognitive and physical conditions that affect their ability to live independently (Dombovy, Sandock, & Basford, 1986; Garraway & Akhtar, 1978; Langhorne, Bernhardt, & Kwakkel, 2011). Several neuroimaging studies have examined cortical activity following stroke rehabilitation (Eliassen et al., 2008; Nishimura et al., 2010; Schaechter et al., 2002; Sheng & Lin, 2009), which enables researchers to explore and map how the brain reorganizes and recovers following insult.

Rehabilitation Following Stroke

Although effective at enhancing functional recovery, intensive rehabilitation treatments can be time-consuming and costly (Dombovy et al., 1986; Feigenson, 1979). The average care spending for hospitalized stroke patients is $20,000. In addition, post-inpatient rehabilitation costs about $17,000 and approximately $5,000 for medication (Godwim, Wasserman, & Ostwald, 2011; Wang et al., 2014). Research suggests inpatient care from a multidisciplinary team (e.g., stroke care unit) is more cost-effective than home care, conventional care, and general medical facilities (Kalra et al., 2005; Langhorne, Williams, Gilchrist, & Howie, 1993; Moodie et al., 2006; Saka, Serra, Samyshkin, McGuire, & Wolfe, 2009). These costs are also influenced by need, or the extent of disability post-stroke, which is resolved more quickly in stroke care units and results in a shorter length of stay (van Exel, Koopmanschap, van Wijngaarden, & Reimer, 2003).

Recovery after stroke is multifaceted and can involve a number of learning-dependent and spontaneous processes (Langhorne et al., 2011). Meta-analyses and systematic reviews suggest specialized stroke treatment is more effective than conventional therapy (Foley, Teasell, Bhogal, Speechly, & Hussein, 2013). The Stroke Unit's Trailists' Collaboration (2013) published similar results after investigating patient outcomes in inpatient stroke units. Their findings suggest participants who received treatment in a stoke unit had a better likelihood of regaining independence, returning home, and surviving than patients in contemporary conventional care (typically a medical facility).

Research conducted by Kwakkel, Kollen, and Lindeman (2004) suggests there are four mechanisms that could possibly influence functional recovery, particularly when insults occur to motor brain areas: restitution of non-infarcted penumbral areas (when damaged cortical tissue survives for a small amount of time, but is unable to fulfill its role or communicate), resolution of diaschisis (the neural networks that compensate for functional reduced motor areas caused by insults), tissue repair (cortical plasticity), and behavior compensation. Usually, stroke rehabilitation consists of a repeated procedure that includes (1) an evaluation to classify and measure a patient's weaknesses; (2) establishing reasonable goals for improvement; (3) developing an intervention to attain goals; and (4) reassessing progress in regards to the patient's goals. While recovery outcomes and patterns vary per patient, the ability to regain motor function can be calculated during the initial days post-stoke (Langhorne et al., 2011).

Motor Recovery

The most common and documented disability resulting from stroke is an impairment of motor functions, which affects approximately 80% of patients (Langhorne, Coupar, & Pollock, 2009). An evaluation of systematic reviews identified 19 categories of motor recovery interventions that target upper and lower limb functions. Rehabilitation techniques with the greatest amount of research support and the most number of randomized controlled trials include biofeedback, electrostimulation, fitness training, robotics, and constraint-induced movement therapy (CIMT). Intensive, repetitive task-specific practice showed the most promise, indicating this aspect of rehabilitation is an effective component in motor recovery following stroke (Langhorne et al., 2009). Notably, high-intensity, repetitive task-specific techniques is the foundation to the theoretical principle of CIMT.

Constraint-Induced Movement Therapy (CIMT). Developed by Dr. Edward Taub (1980), CIMT provides patients the ability to enhance reliance on an impaired limb while restraining the intact limb. To train and facilitate motor recovery of an impaired limb, he incorporated a method called shaping which was found to be most effective. Shaping is a behavioral technique "in which a motor or behavioral objective is approached in small steps by successive approximations" (Taub, 2012, p. 162), and incorporates repetitive task practice to facilitate an improvement in motor function. Few materials are requirement to conduct CIMT, making it cost-effective and easily accessible for patients to carry out in the home setting. A literature review that describes the development, theoretical foundation, and efficacy of CIMT in stroke patients is detailed in Chapter 2.

Neuroimaging Technology in Stroke Rehabilitation

One way to investigate the effect of rehabilitation on the brain's ability to repair damaged areas and re-establish neuronal connections is through imaging. Human and animal research suggests the structural and functional reorganization of the brain occurs weeks to months after an insult. The severity and site of insult, as well as the structural connections between neighboring regions, influence the reorganization of injured neural networks (Green, 2003). More specifically, the reorganization of cortical tissue within the surrounding areas of injured tissue has been shown to occur in the functional recovery of stroke (Cramer et al., 2002). Imaging technology, such as structural neuroimaging, can be utilized to examine changes of the brain in vivo as well as the degree and site of an injury. In addition, neuroimaging provides researchers the ability to observe cortical function in relation to particular activation levels and its adaptation to injury (Seitz, Lindenberg, & Schlaug, 2010).

Various imaging devices can offer information regarding how brain areas compensate and relearn its functions due to damage from injury (Seitz et al., 2010). A relatively new technology introduced in the late 1900s called Near-Infrared Spectroscopy (NIRS) uses light to calculate oxygenated and deoxygenated hemoglobin levels as a measure of cortical activity. In order to map this data to determine the localization of cortical activity, functional NIRS was created. Interestingly, this device is portable, non-invasive, and allows for movement, making it ideal to use when studying motor recovery (Ferrari & Quaresima, 2012). The development and clinical use of NIRS in experimental research is explained in Chapter 2.

Neuroimaging research supports that patients who receive CIMT demonstrate cortical reorganization in the lateral and contralateral cortex and new activation in areas of the brain related to limb function (Puh, 2012; Ro et al., 2006; Wang et al., 2012). Not only does CIMT lead to significant improvements in motor function of an impaired limb, this rehabilitation technique also facilitates neuronal plasticity (Wang et al., 2012). Chapter 2 reviews the imaging studies that investigate changes in brain activity following CIMT.

Purpose and Significance of Study

The purpose of this study was to utilize functional Near-Infrared Spectroscopy (fNIRS) to investigate brain activity in stroke patients before and after rehabilitation. More specifically, the study examined oxygenated hemoglobin signal among patients who exhibited hemiparesis after a left middle cerebral artery (MCA) stroke. Participants' upper extremity motor functioning following two weeks of constraint-induced movement therapy (CIMT) was also assessed.

The following research questions were addressed in this study:

(1) What are the differences in hemoglobin signal before and after patients undergo two weeks of CIMT?

(2) What is the association between upper extremity hemiparesis and hemoglobin signal among patients who experienced a left MCA stroke?

Findings from this study provide researchers a deep understanding of the implications of rehabilitation on brain plasticity and neuronal recovery. The results confirm previous research and the use of CIMT as an effective method of treatment to improve motor abilities in an impaired limb. In addition, this study provides key information regarding the underlying mechanism of rehabilitation techniques that promote cortical reorganization of brain areas that control motor movement (Wang et al., 2012).

CHAPTER II

LITERATURE REVIEW

Constraint induced movement therapy (CIMT) has gained increased recognition due to its efficacy in helping stroke patients to regain motor function (Krakauer, 2006). Several studies have used neuroimaging techniques, such as functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), and electroencephalogram (EEG), to examine cortical changes following stroke rehabilitation (Eliassen et al., 2008; Schaechter et al., 2002; Sheng & Lin, 2009). Functional Near Infrared Spectroscopy (fNIRS) is a novel neuroimaging device that can map the brain by using light to measure cortical activity (Nishimura et al., 2010). This chapter reviews the biological characteristics of stroke, as well as the development and clinical use of CIMT as a rehabilitation treatment for stroke patients. In addition, the use of neuroimaging technology to examine brain activity of the motor cortices following stroke rehabilitation is discussed.

Neurobiology of Stroke

The brain consists of numerous blood vessels that supply it with oxygen which promotes cortical function and growth (Riggs, 2012).The internal carotid and vertebral arteries are vessels that arise from the dorsal aorta and provide blood to the brain. The internal carotid arteries branch into the middle and anterior cerebral arteries (Figure 1). Together, the middle and anterior cerebral arteries create the anterior circulation that supplies blood to the forebrain. In addition to the cortex, these cerebral arteries supply blood to the basal surface of the brain, including the internal capsule, thalamus, and basal ganglia. The vertebral arteries, along with the 10 medullary arteries, supply the spinal cord with increased blood flow. The left and right vertebral arteries join at the pons to form the midline basilar artery, which connects the blood supply from the internal carotid arteries in the form of a ring toward the bottom of the brain called the circle of Willis (Purves et al., 2001).

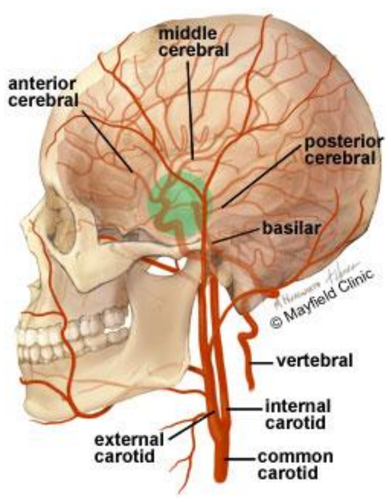


Figure 1. The internal carotid artery (bottom) divides into several arteries, including the middle cerebral artery [Mayfield Clinic, 2016].

The middle cerebral artery (MCA) has branches of vessels that extend to the lateral areas of the brain on both hemispheres. Functions associated with these areas include swallowing, speech, and language. In addition, branches of the MCA form lenticulostraite arteries that supply blood to the thalamus and basal ganglia. More specifically, the left MCA supplies blood to the angular gyrus, Heschle’s gyrus, and

Broca's and Wernicke's areas. The sensory and motor regions responsible for the head and neck also receive blood from the left MCA (McCaffery, 2014; Purves et al., 2001).

Stroke is described as a neurological impairment caused by an acute vascular focal insult in the central nervous system. A stroke occurs when a blood vessel ruptures in the brain or when the blood supply to the brain is interrupted by a clot. The focal insult can be a result of intracerebral hemorrhage, cerebral infarction, or subarachnoid hemorrhage (Centers for Disease Control [CDC], 2015; Sacco et al., 2013). The functional deficits resulting from stroke can be temporary or long-lasting, and patients may or may not recover (Caplan, 2006). According to the Centers for Disease Control and Prevention (CDC, 2015), approximately 795,000 people each year suffer from a stroke in the United States. Furthermore, stroke is a primary cause of serious long-term disability among Americans (Morbidity and Mortality Weekly Report, 2009). Risk factors of having a stroke include age, ethnicity, and gender; however, various factors such as smoking, lack of exercise and high blood pressure can increase one's risk for having a stroke (CDC, 2015).

There are three main categories of strokes: ischemic, hemorrhagic, and transient ischemic attack (TIA). Eighty-seven percent of all stroke cases are ischemic. Ischemic strokes occur when a clot or obstruction in an artery blocks the blood supply to the brain. The clot or obstruction is typically a result of fatty substances along the blood vessel wall. Hemorrhagic strokes occur when a blood vessel in the brain ruptures. As a result, blood is leaked into the brain causing pressure, and eventually damage, to the cells. TIA, also referred to as a mini stroke, is also caused by a clot; however, the obstruction is temporary. TIAs typically last about one minute and do not lead to permanent brain damage (American Heart Association [AHA], 2015a, 2015b; CDC, 2013)

Although rare (1.3% of stroke cases), a stroke affecting the anterior cerebral artery (ACA) primarily results in cardioembolism. Motor and sensory deficits, including limb weakness and aphasia, as well as speech disturbance are also seen in patients with this type of stroke (Arboix et al., 2009). Vertebral-basilar strokes can affect the brain stem and/or the cerebellum. Also less common, clinical symptoms of patients with a stroke affecting the brain stem vary depending on the site of the stroke. A vertebral-basilar stroke can lead to hemiparesis, double vision, slurred speech, abnormal respiration, and impaired swallowing. Cerebellar strokes typically affect coordination and balance. Symptoms of cerebellar strokes include headaches, vomiting, and vertigo (Tocco, 2011).

The MCA is the most common location to exhibit cerebral blockage (Tocco, 2011). A distinct feature of a MCA stroke involves arm weakness that is characterized by paralysis or hemiplegia. MCA strokes typically affect the arms and face significantly more than the legs. A MCA stroke that results in injury to the left or dominant hemisphere can cause expressive and/or receptive aphasia, whereas unilateral neglect may be seen in patients with a MCA stroke that results in injury to the right or nondominant hemisphere (Tocco, 2011). Damage to the right or left MCA can result in hemianopsia (inability to see in half of the visual field) in both eyes. In addition, patients with MCA stroke may experience sensory difficulties affecting the head and neck (McCaffery, 2014). Because motor deficits are the most profound symptoms following stroke, functional recovery tends to be the focus of treatment. Within the last 30 years, various neurorehabilitation methods have been created to enhance motor function following brain injury (Faralli, Bigoni, Mauro, Rossi, & Carulli, 2013; Stinear, Ackerley, & Byblow, 2013).

Rehabilitation in Stroke Patients with Motor Sequelae

The amount of injury to the corticospinal tract is associated with motor recovery (Ward & Cohen, 2004). According to He, Dum, and Strick (1993), a disruption in the connection between the primary motor cortex and motor neurons in the spinal cord results in an increased involvement of the secondary motor areas; this suggests secondary motor areas may participate in novel roles following recovery (Ward & Cohen, 2004). Furthermore, research suggests several cortical areas, particularly pre-injured tissue, are involved in initiating the cerebral reorganization that promotes functional recovery (Green, 2003; Nathan & Smith, 1973). Longitudinally, injured brain areas may use unaffected neural networks and cortical areas that are able to generate any kind of motor connection to the motor neurons in the spinal cord. In addition, rehabilitation treatment can facilitate the reorganization of neighboring healthy tissue following stroke (Ward & Cohen, 2004). For example, a systematic literature review (Kokotilo, Eng, & Boyd, 2009) that investigated cortical reorganization during forced-use tasks following stroke found increased activation in motor regions, including the contralateral (unaffected) hemisphere. Notably, as recovery progresses, the utilization of these additional motor areas typically reduce (Kokotilo et al., 2009).

The adaptive changes that occur in the brain following focal injury provide several different approaches to stroke rehabilitation to help patients regain motor function (Ward & Cohen, 2004). A common condition seen in stroke patients is paresis of a limb and the motor function of, for example, a paretic hand may be affected by various rehabilitation strategies. Pharmacological interventions affecting dopaminergic and adrenergic neurotransmitters, such as d-amphetamine, may significantly improve recovery based on the brain's use-dependent plasticity following motor training (Buterfisch et al., 2002; Ward & Cohen, 2004). Neurofacilitatory approaches to rehabilitation have employed sensory stimulations, such as tapping, vibration, and quick stretch, to help restore motor movement in stroke patients (Brunstorm, 1966; Duncan, 1997). Other commonly used interventions include functional electrical stimulation and biofeedback; however, meta-analyses have concluded mixed findings in the efficacy of biofeedback as a rehabilitation treatment (Duncan, 1997; Glanz et al., 1995; Schleenbaker & Mainous, 1993).

Research suggests decreasing somatosensory input of an anesthesized hand has resulted in better motor function of the nonanesthesized hand in healthy individuals (Werhahn, Mortenson, Van Boven, Zeuner, & Cohen, 2002). Similar findings have shown that chronic stroke patients demonstrate motor improvements of their affected hand when cutaneous anesthesia is administered to their unaffected hand (Floel et al., 2004). Improvement in stroke patients' motor function resulting from a decrease in somatosensory input of their unaffected limb aligns with the underlying principle of constraint induced movement therapy (CIMT; Ward & Cohen, 2004). CIMT is a relatively new rehabilitation technique that utilizes the idea of forced use to regain motor function of stroke patients' impaired limb.

Constraint Induced Movement Therapy

CIMT was developed by Dr. Edward Taub (1980) to provide patients the means to enhance their reliance on an impaired limb while restraining the intact limb. Intensive behavioral training of the impaired limb is conducted simultaneously to facilitate an improvement in motor functioning. Over time, the impaired limb gains strength and is able to effectively contest its learned non-use during daily living tasks (Grotta et al., 2004; Taub et al., 1999; van der Lee, 2003).

CIMT is based on clinical studies conducted in the field of neuroscience and behavioral psychology (Taub, Crago, & Uswatte, 1998). Research suggests the use of CIMT is effective in chronic stroke patients' ability to regain and improve the functioning of their impaired limb (e.g., arm), and that such improvements show long-term effects (Grotta et al., 2004; Kunkel et al., 1999; Liepert et al., 1998; Wolf, Lecraw, Barton, & Jann, 1989). In addition, there are neurological effects of CIMT, such as the reorganization of various neural networks and structures that facilitate motor function.

Neuroanatomy Underlying CIMT and Learned Nonuse. Several processes are involved when the central nervous system (CNS) receives sensory feedback from the environment. The spinal cord receives afferent input (sensory information relayed to the CNS) via the dorsal root of the spinal nerves (Cheprasov, n.d.; Taub, 1976). When the dorsal root is severed (dorsal rhizotomy), there are sensory, reflect, and anatomical consequences; however, the supply of motor nerves are left intact. Taub’s (1976) animal research concluded that the amount of damage to the dorsal root is correlated to the functional use of a deafferented limb. For example, monkeys exhibit minor motor deficits when at least one major dorsal root is left unsevered (known as bilalteral deaffrentation) compared to every dorsal root fiber. Although monkeys with total dorsal rhizotomy do not use their affected limb in free situations (Taub, 1976), they demonstrate functional use of their affected limb when they are placed in constricting situations (Taub, 1980). Interestingly, monkeys are able to learn how to efficiently utilize their deafferented limb when put in a condition to avoid electric shock; however, they revert to nonuse of that limb when taken out of the constricting situation (Knapp, Taub, & Berman, 1963).

The use of a deafferented limb often results in pain and unpleasant consequences, such as falling and incoordination, which facilitates suppression in using the limb (Taub, 1976, 1980). Furthermore, animal research suggests monkeys demonstrate adequate function of daily living with three intact limbs and, therefore, do not utilize their deafferented one. As a result, movement of their deafferented limb is suppressed, a behavior known as learned nonuse (Taub, 1980; Taub et al., 1998). The idea of forced use is the foundation of how CIMT was developed as a rehabilitation technique, particularly for stroke patients.

The Development of CIMT. In order to facilitate purposive movement of a deafferented limb, constraint of that limb is required (Taub, 1980). By restricting the unaffected limb in animals, they are forced to use their deafferented limb to complete daily living tasks. This leads to an increased motivation to surpass their learned nonuse of the deafferented limb and promote its motor functioning (Taub et al., 1994; Taub et al., 1998). These treatment strategies are based on Taub's (1976) animal research utilizing operant conditioning to facilitate the use of an affected forelimb in monkeys (as described in the previous section). It was believed that conditioned-response situations gave animals the ideal opportunity to utilize any motor function their deafferented limb had left post-surgery. Such conditioned-responses provided animals the motivation to increase the utilization of their deafferented limb while the motor involvement could be controlled to a minimum. Therefore, an unusable forelimb could be transformed into one that is able to conduct purposeful movement (Taub, 1976).

Taub's (1980) CIMT protocol incorporates various treatment strategies that involve shaping and emphasizing repeated practice utilizing an affected limb while restraining the use of the non-affected limb in the clinical and home setting (Morris, Crago, DeLuca, Pidikiti, & Taub, 1997; Taub et al., 1998). To train and facilitate motor recovery of an impaired limb, shaping, a behavioral technique "in which a motor or behavioral objective is approached in small steps by successive approximations" (Taub, 2012, p. 162), was found to be most effective. To effectively carry out shaping tasks, patients meet a minimum motor criteria at the wrist and fingers: greater than 10 degrees extension of the wrist, 10 degrees abduction of the thumb, and 10 degrees extension of any two other fingers. Participants must repeat this procedure three times within 1 minute to fulfill this criterion (Taub et al., 1993; Taub et al., 1998).

Taub's CIMT protocol recommends patients receive 6-7 hours of CIMT a day over the course of 10 consecutive treatment days. Patients also wear a mitten on the unaffected upper extremity for approximately 90% of waking hours for two weeks to ensure the affected limb is consistently utilized (Taub et al., 1993). A particular emphasis is placed on massed practice following CIMT to facilitate the patient's use of their affected limb in their daily life (Taub, 1980). In addition, a "transfer package" is a set of activities that are carried out throughout the CIMT treatment regimen to outline patient expectations and provide structure for each session. The transfer package includes a behavioral contract between the patient and therapist, a Motor Activity Log (MAL) that provides information regarding how often the patient utilized their affected limb each day, home skills assignments to reinforce practiced use of the affected limb, and one month of post-treatment weekly telephone calls (Taub, 2012).

Efficacy of CIMT in Humans. Ince (1969) and Halberstam, Zaretsky, Bruckers, and Gutman (1971) were the first researchers to apply CIMT in humans. Ince (1969) applied the concept of operant conditioning utilized in primate research as a rehabilitation treatment for three chronic stroke patients with paresis in their upper extremity. To avoid an electrical shock, the stroke patients had to stretch their affected arm while their unaffected arm was restrained. Although motor functioning in two of the three stroke patients did not improve, the third patient demonstrated a substantial increase in muscle strength following treatment and in daily living tasks (Ince, 1969; Taub et al., 1998). Halberstam and colleagues (1971) conducted a similar study with 20 brain injured patients and 20 aged matched controls. To avoid a mild electrical shock, the patients had to produce a motor response by stretching their affected arm in a vertical and horizontal direction when provided an auditory stimulus. Although their unaffected arm was not restrained, all participants displayed improved speed and distance in their motor response after CIMT (Halberstam et al., 1971).

Taub and colleagues (1993) compared stroke patients' motor functioning following CI therapy to an attention-comparison group. After receiving two weeks of CI therapy, the stroke patients demonstrated a significant improvement in the quality of motor function in their affected arm, which was sustained at a two-year follow-up. Similar findings have been published in a number of studies (e.g., Milter, Bauder, Sommer, Dettmers, & Taub, 1999; Taub, Pidikiti, DeLuca, & Crago, 1996). Compared to standard occupational therapy, stroke patients showed significant improvements in upper extremity dexterity, strength, and coordination as measured by the Action Research Arm Test when CIMT was added to their acute rehabilitation regimen (Dromerick, Edwards, & Hahn, 2000). When CIMT is solely the rehabilitation regimen, chronic stroke patients continue to demonstrate a significant improvement in their affected upper extremity (Levy et al., 2001). CIMT has led to significant improvements in the functional ability, quality of movement, and task completion time of an impaired upper extremity, as well as a significant increase in its use in everyday life (Kunkel et al., 1999). Boake and colleagues (2007) conducted the first randomized controlled trial that examined the neurophysiological and long-term effects of CIMT in subacute stroke patients. Although there were no significant differences in the long-term progression in motor performance between patients who received CIMT and traditional therapy, a significant increase in the quality of movement of the CIMT group's affected extremity during daily living tasks was reported. Furthermore, patients exhibited a significantly greater improvement on a motor performance test following two weeks of CIMT (Boake et al., 2007).

A systematic review (Peurala et al., 2011) was conducted to evaluate participants who received CIMT and modified versions of CIMT. Both the original and modified version of the therapy improved motor functions in stroke patients with upper extremity impairment. Notably, patients who received the original CIMT (60-70 hours for two weeks) demonstrated even better mobility on motor outcome measures such as the Wolft Motor Function Test (Peurala et al., 2011). A meta-analysis (Shi, Tian, Yang, & Zhao, 2011) that compared outcomes of stroke patients who received modified CIMT to traditional rehabilitation included 13 randomized controlled trials between 2000 and 2009. The results from the 13 studies that were analyzed included a total of 287 stroke patients with upper extremity impairment. Patients who received modified CIMT as a rehabilitation treatment demonstrated better improvements on several outcome measures, including the Action Research Arm Test, Fugl Meyer Assessment, and Motor Activity Log, than those who received traditional rehabilitation. Patients who received modified

CIMT appeared to use their affected upper extremity more in their daily living and improved the automaticity of motor movement in their affected upper extremity (Shi et al., 2011). A more recent meta-analysis (Thrane, Friborg, Anke, & Indredavik, 2014) reviewed the efficacy of CIMT as a stroke rehabilitation treatment in 22 studies involving 906 stroke patients between 1999 and 2012. A small but significant post-treatment effect was found for arm motor function, and a moderate effect was found post-treatment and at a 3-6 month follow up for arm motor activity (Thrane et al., 2014). These results further signify the short and long-term efficacy of CIMT as a rehabilitation method for stroke patients with upper extremity paresis.

Animals in primate research as well as human patients who receive CIMT have shown to generalize the use of their affected arm in other settings (Taub et al., 1994; Taub, Uswatte, Mark, & Morris, 2006). Improvements in motor function post-CIMT are also correlated with increased brain activity in the motor cortices of the uninjured hemisphere (Schaechter et al., 2002). CIMT's influence of cortical reorganization may be facilitated by the brain's ability to utilize unaffected neural networks to assist in motor recovery during CIMT (Ward & Cohen, 2004).

Overview of Neuroimaging Research

Neuroimaging studies that examined cortical activation following CIMT have shown this rehabilitation technique influences the reorganization of the brain (Levy et al., 2001). For example, using functional magnetic resonance imaging (fMRI), Sheng and Lin (2009) found significant differences in activation of the ipsilateral and contralateral cerebral cortex, particularly in the frontal lobe, in stroke patients following two weeks of CIMT. A similar study using fMRI found increased activation patterns of the motor cortices, specifically in the ipsilateral hemisphere and contralateral cerebellum, of stroke patients following two weeks of CIMT (Schaechter et al., 2002). Wittenberg and colleagues (2003) found increased cortical activity in the primary and supplementary motor areas and the cerebellum using positron emission tomography (PET) scans before and after 10 days of CIMT among patients who experienced a stroke. Another study examined brain activity utilizing transracial magnetic stimulation (TMS) in chronic stroke patients before and after receiving two weeks of CIMT. When particular upper extremity muscles were stimulated, patients experienced increased neuronal activation in the affected hemisphere, which facilitated cortical plasticity in the motor cortex (Liepert et al., 1998).

A case study (Park, Butler, Cavalheiro, Alberts, & Wolf, 2004) that employed functional near infrared spectroscopy (fNIRS) in addition to fMRI and TMS assessed hemodynamic changes while a stroke patient received CIMT. Results indicated a shift in oxygenated hemoglobin levels in the motor cortex from the unaffected to the affected hemisphere throughout therapy sessions. During the final CIMT sessions, the stroke patient demonstrated a general decrease in oxygenated hemoglobin in the left and right hemisphere, suggesting an overall reduction in neuronal signal. According to the authors, this reduction may be due to a decreased necessity of synaptic activity associated with the CIMT tasks. A similar pattern was shown in the control participant; however, the reduction occurred following the first assessment session, suggesting an intervention effect of CIMT for the stroke patient. NIRS is a relatively new neuroimaging instrument used to measure cortical activity and has shown its usefulness in rehabilitation by enabling researchers to study the relationship between cortical processes and functional abilities (Ferrari & Quaresima, 2012; Park et al., 2004)

Near Infrared Spectroscopy

Functional near infrared spectroscopy (fNIRS) provides researchers an innovative method of mapping the brain by using near infrared (NIR) light to measure changes in cerebral oxygenation and hemoglobin concentration in cortical tissue (Nishimura et al., 2010). FNIRS is a type of brain imaging technology that is portable, non-invasive, and provides continuous physiological monitoring. NIR instruments also provide the capability for movement, making it a particularly useful tool when studying responses to various stimuli (Ferrari & Quaresima, 2012).

The Development of Near Infrared Spectroscopy. In the 18th century, astronomer William Herschel discovered radiation existed further beyond red light. This finding occurred when he utilized a glass prism to scatter sunlight onto three thermometers that held carbon blackened bulbs. The resulting radiance or heat is known as “NIR radiation” and its range as “NIR spectrum” (Aenugu, Kumar, Srisudharson, Parthiban, Ghosh, & Banji, 2011; Fouad, Amin, El-Bandary, & Hassanien, 2014; Herschel, 1800). In the early 20th century, W. W. Coblentz measured and recorded the NIR spectra, which consisted of hundreds of compounds in the 1- to 15- μm wavelength vicinity. Through this, Colbentz provided scientists a new instrument, called spectroscopy, in which information regarding the structures of compounds could be acquired. Colleagues of Colbentz began to develop novel instrumental designs that are the foundation of today's spectroscopy (Hindle, 2008).

During the early 1900s, infrared spectroscopy was used very little and few scientists had access to the available instruments. At the time, the primary use of NIR spectra was to investigate organic compounds. It is suggested that F. E. Fowle was the first to utilize quantitative NIR measurement when he studied the atmospheric moisture at the Mount Wilson observatory (Fowle, 1912; Hindle, 2008). In 1938, NIR measurement was used to examine water molecules in gelatin (Ellis & Bath, 1938). Approximately 65 years after Colbentz's work, custom NIR measurement was introduced. In the 1950s, there was an increased demand for quick, quantitative measurement of moisture, protein, and oil. In the early 1970s, NIR laboratory instrument sectors started to emerge in U.S. facilities such as Neoec and Technicon (Hindle, 2008).

Jöbsis (1977; 1999) was the first to utilize NIRS in animal models. NIR light was shown to be effectively transmitted through biological tissue and adequately continuously monitor oxygen levels. Later with his colleagues (Brazy, Lewis, Mitnick, & Jöbsis, 1985), Jöbsis used NIRS to monitor cerebral oxygenation in preterm infants. The optical device used was called the near infrared oxygen sufficiency scope (NIROS-SCOPE). NIROS-SCOPE is a transcutaneous instrument that is able to measure a comparative amount of oxygenated and deoxygenated hemoglobin as well as changes in the oxidation-reduction state of cytochrome a,a_3, an enzyme involved with the cellular metabolism of oxygen. When the appropriate NIR wavelengths are chosen, alterations in light absorption can be utilized to measure changes in the supply of hemoglobin and in the oxidation-reduction state of cytochrome a,a_3. Together, it provides information on tissue blood volume that allows researchers the ability to examine how the brain utilizes oxygen and processes its delivery. The successful use of NIR in sick newborns provided an avenue for researchers to employ a noninvasive method to effectively assess cerebral oxygenation in humans (Brazy et al., 1985; Jöbsis, 1977).

The first quantitative assessment of different hemodynamic and oxygenated specifications was described by David Delpy in 1984 (Ferrari & Quaresima, 2012; Wyatt, Cope, Delpy, Wray, & Reynolds, 1986). Delpy and his colleagues created a new NIR device that was able to measure changes in hemodynamics and cerebral oxygenation, including cerebral blood flow and volume, in sick infants. To do so, changes in light intake from the laser optodes at various wavelengths were transformed into oxygenated hemoglobin, reduced hemoglobin, and cytochrome a,a_3 concentration (Wyatt et al., 1986). Then in 1989, Hamamatsu Photonics K.K. (Hamamatsu City, Japan) developed the first commercial NIR system called the NIRO-1000. Between 1980 and 1995, nine other companies were involved with building NIRS prototypes, including Hitachi Ltd. Central Research Laboratories (Tokyo, Japan) and American Edwards Laboratories in conjunction with Duke University (Ferrari & Quaresima, 2012).

Characteristics of Near Infrared Spectroscopy. Cortical activity in the brain is related to several physiological changes such as fluctuations in optical characteristics of brain tissue (Ferrari & Quaresima, 2012). When photons are emitted through biological tissue, their diffusion depends upon several processes that include scattering, reflectance, and absorption. Scattering and absorption depend on wavelength, whereas reflectance refers to the light beam angle from the NIRS device to the tissue surface of the brain. For example, as the number of photon wavelengths increases, scattering decreases and results in the distribution of infrared light. These processes lead to differences in the effectiveness of photon distribution through tissue among the infrared and ultraviolet range. A considerable quantity of emission can be efficiently distributed through biological tissue that is within a 700-1300 nm range of NIR light. Because the brain heavily relies on oxygen for healthy functioning, there is minimal intrusion of overlapping tissue in the brain, which allows NIRS to easily access information on cerebral oxygenation (Jöbsis, 1977).

Within the NIR spectral range (650-1000 nm), human biological tissue is fairly translucent to and permeable by NIR light. Because blood vessels are able to fully consume light, NIRS is highly unresponsive to them; therefore, NIRS primarily gathers information regarding the changes in oxygenation that take place within the venous compartment. The amount of hemoglobin that is absorbed by NIR light is dependent on the level of oxygenation within the optical surface area. NIRS uses laser optodes, also called diodes, which are light producing sources and detectors that cover an optical surface area of 650 and 1000 nm (Ferrari & Quaresima, 2012).

The laser optode sources transmit NIR light through cortical tissue and its receiving detectors. The spatial placement of NIR light is explained by photon migration simulation research on how NIRS processes brain activity (Ferrari & Quaresima, 2012; Okada & Delpy, 2003; Okada et al., 1997). As light emits through tissue by the optode sources, it diffuses in all directions including the scalp and subarachnoid part of the cerebrospinal fluid. The spatial sensitivity of every pair of optode source and detector creates a crescent moon shaped pathway (Figure 2; Naseer & Hong, 2015). Because light scatters as it passes through different layers of cortical tissue, the distance of NIR light that penetrates through tissue is deeper than the physical length between the sources and detectors. To obtain adequate depth penetration, it has been suggested that the distance between the sources and detectors be approximately 3 centimeters (Ferrari & Quaresima, 2012). A source-detector distance less than 2.5 centimeters is only able to gather information from a small amount of tissue. Although light is emitted deeper into brain tissue when a source-detector distance is greater than 4 centimeters, a minimal amount of light is received by the detector (Gratton et al., 2006).

Various NIRS devices employ different techniques to process infrared light that are based on a particular form of illumination. The type of information that is collected depends upon which NIRS device and technique is selected. The continuous wave (CW) technique processes light depletion through the skull. The frequency domain (FD) technique processes light depletion and phase delay of developing light. The time domain (TD) technique illuminates the skull with brief pulses of light and identifies the form of the pulses following its transmission through brain tissue. The most widely used CW-based NIRS device collects information on changes in oxygenated and deoxygenated hemoglobin, whereas the FD- and TD-based devices describe the optical elements of biological tissue and provide absolute measures of oxygenated and deoxygenated hemoglobin concentrations (Ferrari & Quaresima, 2012).

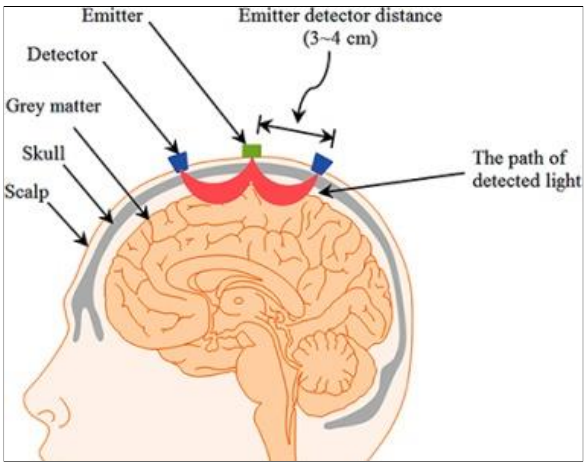


Figure 2. NIR light is emitted by sources (emitters) through the scalp and skull, and is received by detectors in a crescent moon shaped pathway [Naseer & Hong, 2015].

Functional Near Infrared Spectroscopy. In 1992, hemodynamic and oxygenation variations in the brain led researchers to utilize NIRS to examine functional cortical activity. FNIRS, also called near-infrared imaging or optical topography, primarily identifies changes in optical characteristics of the brain from different measurement locations simultaneously. The key characteristic that distinguishes fNIRS from typical NIRS instruments is that the measurement data can be demonstrated onto a brain map and display where significant hemoglobin activity occurred within a particular area of the brain. Within a single-site of activation, an increase in oxygenated hemoglobin and a decrease of deoxygenated hemoglobin can occur. This change in hemoglobin demonstrates an increase in arteriolar vasodialation of the surrounding area, resulting in neurovascular coupling (an increase of blood flow and volume in the brain). The increased amount of oxygen within the activation site usually surpasses the local neuronal ratio at which oxygen is used; therefore, an overabundance of oxygenation is presented in the activated area that is measured by fNIRS (Ferrari & Quaresima, 2012).

In late 1991 and early 1992, a group of research institutions conducted the first fNIRS studies that utilized single-site measurements in humans (Ferrari & Quaresima, 2012). One of these studies examined changes in the oxygenation of hemoglobin in the frontal cortex of healthy volunteers while they completed mental tasks. Younger-aged participants (22-30 years) demonstrated a significant increase in oxygenated and total hemoglobin concentration while they completed problems they perceived as difficult, whereas those who completed the problems without difficulty displayed no change in hemoglobin. Older-aged participants (31-47 years) showed a decrease in oxygenated hemoglobin and an increase in deoxygenated hemoglobin concentration during the mental tasks. With age, participants demonstrated a decrease in the rate of oxygen consumption and an overall decline in cerebral blood flow (Hoshi & Tamura, 1993a). Another study that utilized fNIRS to examine oxygenated and deoxygenated hemoglobin variations for the first time in the visual cortex of patients while receiving and after photic stimulation (PS) treatment. An increase in oxygenated hemoglobin following PS and a minimal change in deoxygenated hemoglobin were found in the visual cortical areas; however, there were no changes observed in the frontal area (Kato, Kamei, Takashima, & Ozaki, 1993). Results from these studies demonstrate the need for measuring and mapping cerebral oxygenation and hemodynamics concurrently among different regions of the brain (Ferrari & Quaresima, 2012).

Hoshi and Tamura (1993b) conducted a study in which various cortical areas of patients' blood volumes and hemoglobin oxygenations were examined during auditory and visual stimulations and mental tasks. Cortical activation indicated that changes in oxygenated hemoglobin varied between brain regions, specifically in the temporal and frontal areas. While there was an increase in oxygenated hemoglobin and total hemoglobin concentration in the temporal and frontal areas, deoxygenated hemoglobin decreased in the frontal area. Furthermore, deoxygenated hemoglobin initially showed no change in the temporal area, followed by an increase with an additional rise in total hemoglobin concentration. Such fluctuations suggest the amount of overcompensation of oxygenation in the frontal area was more than the temporal area. As a result, the hemoglobin oxygenation state differed between and within various cortical areas during activation (Hoshi & Tamura, 1993a).

Several test-retest studies have demonstrated that fNIRS outcomes can be reliably repeated, particularly when utilized with a group of participants and multiple wavelength channels (Ferrari & Quaresima, 2012; Plitchta et al., 2006; Plichta et al., 2007;

Schecklmann, Ehlis, Plichta, & Fallgatter, 2008). Simultaneous fMRI and NIRS measurement studies have confirmed the validity of fNIRS results in that such findings significantly coincide with fMRI outcomes (Ferrari & Quaresima, 2012). Currently, a standardized method to analyze the measurement data from multichannel devices for creating topographical maps or for defining the statistical significance of changes in cerebral oxygenation and hemodynamic responses has not been well-established (Elwell & Cooper, 2011).

Application in clinical populations. The first utilization of NIRS in a clinical population was in 1994 when Okada and colleagues studied the hemodynamic and oxygenation state of the forebrain among healthy volunteers and patients with schizophrenia during a mirror-drawing task (MDT; Ferrari & Quaresima, 2012; Okada, Tokumitsu, Hoshi, & Tamura, 1994). The majority of healthy volunteers demonstrated an increase in oxygenated and a decrease in deoxygenated hemoglobin simultaneously during the MDT. Interestingly, this hemodynamic pattern differed between hemispheres for men and women. Most women exhibited activation in both hemispheres due to increases in hemoglobin while completing the MDT. Most men primarily exhibited activation in the dominant hemisphere, which was indicated by significantly more concentration of hemoglobin in the right hemisphere than the left. The patients with schizophrenia showed a dysfunctional response pattern between hemispheres and lack of activity in the dominant hemisphere, which was not otherwise observed in the healthy volunteers. Patients with schizophrenia who showed a dysfunctional response pattern exhibited the illness for a longer period of time than the patients who showed dysregulated blood flow patterns. These results suggest that the deterioration of cerebral oxygenation and the hemodynamics between hemispheres is a characteristic of how schizophrenia neurologically progresses (Okada et al., 1994). Notably, this study was the first to establish the importance and effectiveness of NIRS in the field of psychiatry (Ferrari & Quaresima, 2012).

Following Okada et al's (1994) findings, two studies were conducted with Alzheimer patients and employed NIRS to examine cortical activity during various neuropsychological tasks. One study assessed hemodynamics in the frontal and parietal regions of 19 patients with Alzheimer's disease (AD) and 19 healthy controls during cognitive tasks. Increases in oxygenated and total hemoglobin and a slight decrease in deoxygenated hemoglobin occurred in healthy participants shortly after starting the tasks, whereas AD patients showed a decrease in oxygenated and total hemoglobin concentration in the parietal region, particularly during a verbal fluency task. A possible explanation for these results may be due to a general decrease of oxygenated hemoglobin in deteriorating brain regions that lead to changes in cerebral functional organization, particularly during mental tasks (Hock et al., 1996).

The second study (Fallgatter et al., 1997) compared metabolic changes of 10 dementia with Alzheimer-type (DAT) patients to 10 healthy participants during verbal fluency tasks. The healthy participants showed significant changes in oxygenated hemoglobin concentration in the left hemisphere; however, this pattern was not observed in the DAT group. The DAT patients showed a decrease in oxygenation in the frontal lobe and an overall poor performance on the fluency tasks. DAT patients also demonstrated a loss in physiological asymmetry, or hemispheric lateralization, during the fluency tasks. This group exhibited global activation of the same areas in the left hemisphere as the healthy participants did in the right hemisphere (Fallgatter et al., 1997). A similar study later compared hemodynamic responses in nine depressed patients and10 healthy volunteers (Matsuo, Kato, Fukuda, & Kato, 2000). Participants performed a series of cognitive and physiological tasks while a NIRS device collected data on oxygenated and deoxygenated hemoglobin concentration in the left frontal region. The healthy volunteers showed a significant increase in oxygenated hemoglobin and a significant decrease in deoxygenated hemoglobin while completing a verbal fluency task, whereas the depressed patients showed slight, yet not significant, hemodynamic changes. Both groups had an average and similar performance on the fluency task. These outcomes indicate that the lack of cortical activation in the left frontal region of the depressed patients while performing the fluency task was not a result of vascular distensbility. In addition, all participants did not show a significant change in oxygenated and deoxygenated hemoglobin during a verbal repetition task. When asked to hyperventilate (i.e., breathe deeply), participants in both groups showed a significant increase in deoxygenated hemoglobin and significant decrease in oxygenated hemoglobin (Matsuo et al., 2000). More recently, researchers have extended the application of NIRS in examining cortical activity to the medical population, including patients with seizures

(Nguyen et al., 2013), traumatic brain injury (Amyot et al., 2012), and concussion (Kontos et al., 2014).

Ehlis, Schneider, Dresler, and Fallgatter (2014) reviewed the application of fNIRS in the field of neuropsychiatry; results from the review suggested fNIRS is a valid instrument to examine the underlying neural processes in patients with neuropsychiatric disorders. A majority of the studies were completed in psychiatric settings that examined cortical activity in the prefrontal cortex and the effect of mental illness on daily living (Ehlis et al., 2014). For example, patients with unipolar and bipolar depression completed cognitive tasks while fNIRS collected hemodynamic changes in the prefrontal cortex (Schecklmann et al., 2011). Healthy controls showed differences in oxygenated and deoxygenated hemoglobin levels, which suggested increased activity in the dorso-lateral prefrontal, ventro-lateral, and superior frontal cortex during various working memory tasks. Patients with unipolar and bipolar depression demonstrated reduced cortical activity across all working memory tasks (Schecklmann et al., 2011).

More recently, fNIRS has been studied in pediatric clinical populations, including children with learning and developmental disabilities such as attention-deficit hyperactivity disorder (Serap, Tapsin, & Akin, 2009). Sela, Izzetoglu, Izzetoglu, and Onaral (2014) used fNIRS to investigate hemodynamic changes in the frontal lobe of typical children and young adult readers compared to young adults with dyslexia. Participants completed the Lexical Decision Task, which required them to identify presented stimuli as either a pseudo or high-frequency word. During the pseudo word condition, adult dyslexic readers demonstrated lower activity in the upper left frontal lobe compared to typical adult readers. The children demonstrated this same pattern of activity during the word condition task; this suggests the upper left frontal lobe may signify a developmental trend in lexical decision-making (Sela et al., 2014).

Kurz, Wilson, and Arpin (2014) found increased cortical activity in the superior parietal and sensorimotor regions in children with spastic diplegic cerebral palsy while walking on a treadmill. Findings from the fNIRS data during their gait performance suggested the extent of brain activity is linked to differences in gait kinematics (Kurz et al., 2014). The use of fNIRS with hemiplegic stroke patients following various rehabilitation techniques has sparked a relatively recent interest in the field, which has led to several cross-sectional and longitudinal research projects (Lin, Lin, Penny, & Chen, 2008).

Application in stroke rehabilitation. The first study to examine oxygenation changes in the motor cortex was conducted by Colier and colleagues (1997). Six healthy participants performed a finger opposition task while wearing a NIRS head device placed over the primary motor cortex of the left hemisphere. Five of the participants showed an increase in oxygenated hemoglobin concentration followed by a slight decrease in deoxygenated hemoglobin during the motor tasks, whereas one participant showed significant hemodynamic changes following the completion of the task (Colier et al., 1997). Colier, Quaresima, Oeseburg, and Ferrari (1999) conducted a similar study that investigated oxygenated and deoxygenated hemoglobin concentration in the motor cortex of six healthy participants while they performed easy and difficult motor tasks involving the hand and foot. The NIRS instrument demonstrated the ability to measure the time course of brain activity during cyclic movement tasks. Although there were no significant differences in the time course of hemodynamic response patterns between the easy and difficult tasks, all participants showed changes in hemoglobin concentration during their performance (Colier et al., 1999).

Since then, several research studies have applied NIRS in examining changes in cortical activity in stroke patients before and after rehabilitation. Saitou, Yanagi, Hara, Tsuchiya, and Tomura (2000) examined cerebral oxygenation and hemodynamic changes in the frontal cortex of healthy volunteers and hemiplegic stroke patients. For the stroke patients, significant changes in blood and oxygen volumes indicated an increase in cortical activation during various rehabilitation tasks, whereas the healthy volunteers showed a variety of change patterns. Active tasks and complex exercises, such as reading and ergometer training, as opposed to passive tasks and simple exercises, were effective in facilitating cortical activity in the prefrontal cortex (Saitou et al., 2000).

Using fNIRS, cortical activation before and after eight stroke patients received gait rehabilitation was investigated (Miyai et al., 2003). Changes in activation of the medial primary sensory motor cortex significantly correlated to improvements in gait performance. Furthermore, an increase in oxygenated hemoglobin concentration from the unaffected to the affected hemisphere was demonstrated before and after rehabilitation (Miyai et al., 2003). Similar results were found when both fNIRS and fMRI were utilized to obtain data on brain activity in the motor cortices while six recovered hemiplegic stroke patients performed a hand movement task (Kato, Izumiyama, Koizumi, Takahashi, & Itoyama, 2002). Cortical activation patterns from fNIRS and fMRI yielded parallel findings. A typical activation sequence was shown when patients performed the movement task with their unaffected hand, whereas bilateral and ipsilateral activation was shown when the patients used their affected hand. More specifically, patients exhibited significant increases in activation of the ipsilateral motor cortex via fNIRS and fMRI when the affected hand was used (Kato et al., 2002).

Cerebral activity in the motor cortices of stroke patients prior to and following rehabilitation results in changes of hemodynamic response patterns during a gait performance task. For example, a shift in activation (laterality) from the unaffected to affected hemisphere in the sensory motor region is significantly associated with better gait performance. Furthermore, the surrounding motor regions in an affected hemisphere displays a significant increase in activation, particularly in the premotor cortex, after rehabilitation (Miyai et al., 2003). Similar findings are seen in the sensory motor cortices when stroke patients perform gait (Miyai, Suzuki, Hatakenaka, & Kubota, 2006) and hand movement tasks before and after rehabilitation, suggesting that increases in cortical activity in the motor regions of the brain serves a vital part in stroke rehabilitation (Takeda et al., 2007).

Summary

Research suggests the use of CIMT is tremendously effective in chronic stroke patients' ability to regain and improve the functioning of their impaired limb (e.g., arm), and that such improvements have long-term effects (Grotta et al., 2004; Kunkel et al., 1999; Liepert et al., 1998; Wolf et al., 1989). Animals and human patients who receive CIMT have been shown to generalize the use of their affected arm in other settings (Taub et al., 1994; Taub et al., 2006). Neurological implications of CIMT are demonstrated by the brain's ability to reorganize its use of various networks and structures to facilitate improved motor functioning after therapy (Ward & Cohen, 2004). The above literature review of NIRS studies indicate this device is sensitive in detecting cortical activation and monitoring physiological processes while patients perform various tasks.

This study utilized functional Near-Infrared Spectroscopy (fNIRS) to examine brain activation of the motor cortex in stroke patients before and after receiving CIMT. Because fNIRS allows for movement, it is an ideal method of exploring brain activity in stroke patients while they perform a unimanual and bimanual task. The purpose of this project was to (1) explore hemoglobin activation patterns among stroke patients who underwent two weeks of CIMT and (2) examine if the implementation of CIMT during stroke rehabilitation is associated with change in neural activity.

CHAPTER III

METHODS

This chapter describes the methodology used to investigate the changes in hemoglobin signal in the motor cortices using functional Near Infrared Spectroscopy (fNIRS) imaging in stroke patients who received constraint induced movement therapy (CIMT) for upper extremity hemiparesis. The participants, measures, procedure, and data collection and analyses that were carried out in the study are outlined in this chapter.

Participants

Six participants with a left middle cerebral artery (MCA) stroke who received rehabilitation services at Pate Rehabilitation were enrolled in this study. Pate Rehabilitation is a multidisciplinary treatment facility for individuals who have had stroke, concussion, and brain injury. Treatment services include speech, occupational, and physical therapy. Participants were right-hand dominant and the time of stroke was at least 3 months prior to enrollment in the study. Selection criteria included adults of both genders who were above 18 years old and were able to provide consent. No racial or ethnic groups were excluded; however, only English speakers with no impairment in verbal comprehension, as indicated on the Standardized Mini Mental State Examination (SMMSE), were included in the study to ensure their understanding of verbal instructions.

Individuals were not appropriate for the study if they had a history of multiple strokes or complete physical disability. A patient was excluded from the study if he or she had a pre-existing traumatic brain injury, cerebral palsy, mental retardation/intellectual disability, autism, epilepsy, schizophrenia, pervasive development disorder, or a diagnosis of learning disability.

Procedure

Participants were initially screened via a chart review to determine if they met inclusion criteria. If the patient met the inclusion criteria, he/she completed selected items from the SMMSE to confirm intact verbal comprehension abilities. If a patient was able to complete at least 3 out of 4 screening items, he/she was given the opportunity to enroll in the study. The purpose of the study, study procedures, participant expectations, and the possible use of the patient's de-identifiable data for research purposes as well as the likely publication of the results were explained. Participants were also asked various questions to ensure that they understood their rights (e.g., Do you understand that you can stop at any time? Do you understand that your name will be removed from all data collected here and all forms that you have completed?). If agreeable, they signed informed consent and Health Insurance Portability and Accountability Act (HIPPA) forms. Participants were allowed to discontinue their participation in the study at any time for any reason.

Constraint Induced Movement Therapy (CIMT)

The CIMT regimen was designed for the participants to achieve and maintain functional use of an impaired upper extremity following a stroke. Based on the learned non-use theory, CIMT targets the patient's use of his or her affected limb to improve its function and recovery. Therefore, CIMT is approached using specific behavioral methods such as shaping. Shaping is a technique employed to enhance the movement of an affected limb through multiple attempts and repetition of performing a task that progresses in difficulty level (Taub, 2012).

The CIMT protocol that was used in this study is detailed below and generally followed Taub's (2012) shaping guidelines.

1. The occupational therapist selected the appropriate shaping task that involved movements that demonstrated the participant's most profound deficits, suggested the highest probability for improvement, and was based on their treatment goals and participant preference.
2. The occupational therapist modeled the chosen shaping task and provided a significant amount of encouragement and positive verbal praise no less than 50% of the trials.
3. The difficulty level of the chosen shaping task was slightly higher than what the participant was able to achieve with ease.
4. When the participant's performance on the present difficulty level of the shaping task improved and attained a relative plateau, the subsequent difficulty level of

the task was introduced. The subsequent difficulty level is intended to be achievable to the participant when he/she provides effort.

Note: A relative plateau is shown when the participant does not demonstrate an improvement in their performance following five consecutive trials of the task.

5. If a participant demonstrated extensive difficulty with the movements to execute the shaping task, a simple, less complex task consisting of similar movements was introduced.

The researcher and participant then discussed targeted upper extremity movements to shape that were based on the patient's treatment goals. In addition, the researcher and participant reviewed a behavioral contract to ensure the participant's agreement that he or she would attempt to use their affected upper extremity outside the rehabilitation setting and would practice any assigned daily living activities at home. The behavior contract document was signed by the patient and researcher (Taub et al., 2013). During the study, the CIMT regimen took place over the course of two weeks or ten consecutive business days. If a participant was absent, the regimen continued on the day they returned. Participants wore a mitten on their intact upper extremity during each full day visit at Pate in order to limit functional use to only their affected upper extremity.

As part of the Taub et al.'s (1993) CIMT guidelines, the participant and researcher completed a Motor Activity Log (MAL) at the beginning of each shaping session. The MAL is a list of 30 daily motor activities in which patients rated how much and how well they engaged their affected limb during each activity (Taub et al., 2013;

Uswatte, Taub, Morris, Light, & Thompson, 2006). Following the completion of the MAL, participants completed 10 trials of different shaping tasks that addressed targeted upper extremity movements. Only one parameter for each shaping task was altered at a time to increase the level of difficulty associated with the participant's movement problems such as height or time of upper extremity response. Rest periods were provided to participants during every trial period. Although longer intervals were warranted at times, rest periods between trials lasted one minute (Taub, 2012). Each shaping session took place for 30-45 minutes. In the event a participant was absent during the two week period, he/she rescheduled the missed session to the next available day and continued the planned treatment regimen.

The researcher tracked the participants' performance and progress utilizing a shaping data sheet during each session. The shaping data sheet provided a description of the shaping tasks and tracked the parameters used during the session. The shaping data sheet was used to indicate when a participant's performance reached a plateau (5 consecutive successful attempts of task) and when an alteration in a parameter was warranted. In addition, a home skill assignment worksheet was given at the end of each session. The home skill assignment worksheet consisted of three to four assigned daily living activities the participant was to engage in at home to ensure the practiced use of their affected upper extremity in an alternative setting. The completion of the worksheet was discussed at the beginning of the next treatment session to emphasize the importance of utilizing the affected upper extremity and to facilitate accountability.

Neuroimaging

Participants underwent a neuroimaging session at Pate Rehabilitation before and after receiving the CIMT regimen. The fNIRS machine used to collect neuroimaging data was the Hitachi Optical Topography System ETG 4000 (ETG 4000; Hitachi Medical Corporation, 2006). This fNIRS machine uses hemoglobin's absorption of near infrared light to process the fluctuations of blood volume within the surface of the brain. The optical topographic system calculates differences in oxygenated and deoxygenated hemoglobin concentration within 3 centimeters below the skull at various points concurrently, and recreates a two-dimensional (2D) topographic image on the ETG 4000 monitor. The 2D topographic image illustrates the supply of blood volume during the session from the dorsal view of the skull. The ETG 4000 consists of a monitor, optical topographic system main unit and power supply (see Figure 3), and a 3D probe positioning unit (Hitachi Medical Corporation, 2006).

Figure 3. The Hitachi ETG 4000 system was used in the present study which included a monitor and system main unit (Hitachi Medical Systems Europe, 2017a).

The ETG 4000 provides up to 52 optodes or channels of measurement data points. Each channel is able to collect 10 samples of data per second. The channels of measurement data points consist of laser diodes and receptors. The laser diodes emit two wavelengths of light (695nm and 830 nm) concurrently. The light is received by the adjacent receptors that measure the amount of hemoglobin signal in grams per deciliter (g/dL) (Hitachi Medical Corporation, 2006).

The optode pad consists of sockets that correspond to specific laser diodes and receptors that are labeled numerically. The laser diodes and receptors plug into an optode pad and was placed within a head cap. The fNIRS cap that was used in this study contained two 4 by 4 optode pads. Within each of the two optode pads, there were a total of 16 channels (8 laser diodes and 8 receptors). Each channel was placed 3 centimeters apart from one another (see Figure 4). The two optode pads within the cap were located on the right and left parietal region of the head to cover the motor cortices. This positioning setup was pre-programmed on the ETG 4000 to ensure the laser diodes and receptors are accurately placed on the head when acquiring data. The cap was placed on each participants' head and aligned to the positioning setup programmed on the ETG. The ETG 4000 was pre-selected to filter out additional data that could contribute to cortical activation, such as body movement.

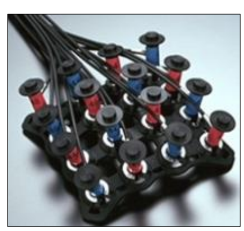


Figure 4. A 4 by 4 optode pad contains 16 channels. Eight laser diodes (red) and eight receptors (blue) are placed 3 centimeters apart from each other (Hitachi Medical Systems Europe, 2017b).

Several steps were taken to select the measurement procedure on the ETG 4000 before the channels began recording hemoglobin signal. First, the method of measurement that was selected is called *stimulation measurement*. This method can analyze a participant's reaction to repeated stimulation and can obtain an average waveform or signal during his or her performance. As a result, stimulation measurement allowed the researchers to monitor and review cortical activation at specific time points during the neuroimaging session.

Next, the stimulation measurement parameters were set to follow the study's design. A default time to acquire the data and the desired stimulation sequence and length of repeated trials were selected and saved as the measurement protocol. The parameters also displayed a real-time map of oxygenated and deoxygenated hemoglobin signal for each channel on the ETG 4000 monitor as a 2D topographic image. The data collected from the stimulation measurement method provided the amount of hemoglobin signal that occurred in each channel every 10 Hz.

Overview of the Study Protocol

Prior to enrolling in the study, each participant was screened to determine if they met eligibility criteria. If inclusion criteria were met, consent was obtained. Demographic information was collected from all study participants who underwent pre- and post-treatment evaluations, two weeks of CIMT, and neuroimaging sessions. The expected timeframe each individual actively participated in the study was approximately four weeks. The CIMT regimen was monitored for safety and compliance by an occupational therapist and the researcher. Neuroimaging data was processed in Dr. Carlos Marquez's imaging lab at Pate Rehabilitation with the assistance of Dr. Georgios Alexandrakis and Ms. Jianwei Cao from the University of Texas at Arlington.

Every effort was made to maintain the confidentiality of study records. The data from the study may be published; however, participants will not be identified by name. All participants were assigned an alphanumeric code. Neuroimages were also de-identified by the participants' initials. Documents with identifiable data, such as the consent forms, were kept in a secured storage box in a locked office room at Pate Rehabilitation. Data obtained from the participants during the study were entered into a password-protected database in Microsoft Excel. The researcher and Principal Investigator had access to the data.

Measures

Assessment of Motor Functions

Participants' upper extremity motor functioning was assessed before and after receiving CIMT. Two performance-based assessments were conducted in order to (1) characterize and classify upper extremity impairment and (2) obtain a baseline measure of upper extremity motor function to compare to post-CIMT. The Wolf Motor Function Test (WMFT; Wolf et al., 1989) was administered to characterize upper extremity impairment and provide a better understanding of the severity and functionality of each participant's hemiparesis. A finger tapping task and a selected activity from the Chedoke Arm and Hand Activity Inventory (CAHAI; Barreca et al., 2004) were administered during the neuroimaging sessions to determine if there was an improvement in upper extremity motor functioning that resulted in changes in cortical activity within the motor cortex.

Wolf Motor Function Test (WMFT). The WMFT was designed to evaluate the functionality and severity of stroke patients' motor impairment. It was originally created by Dr. Steven Wolf in 1989 to examine the effectiveness of CIMT in patients with traumatic brain injury and stroke (Morris, Uswatte, Crago, Cook III, & Taub, 2001; Wolf et al., 2001; Wolf et al., 1989). In 2001, Dr. Edward Taub and his colleagues developed a modified version of the WMFT to accommodate higher functioning stroke patients (Kopp et al., 1997 as cited in Morris et al., 2001) which was used in the present study. The modified version consists of 15 functional tasks, two strength-based tasks, and a functional ability scale (FAS). The 15 functional tasks assess the quality of a patient's motor ability. These tasks are timed (120 seconds) and advance from proximal to distal joint movements. The two strength-based tasks measure grip and lift strength (Hodics et al., 2012; Morris et al., 2001; Taub, Morris, & Crago, 2011). Performance on the 15 functional and two strength-based tasks are rated utilizing the FAS to evaluate the motor functioning of an affected upper extremity. The FAS provides six rating options that range from 0 to 5, with 0 indicating the patient did not attempt the task with their affected upper extremity and 5 indicating the displayed movement appears normal. The total FAS score denotes the mean score of the individual items completed by the participant. Higher FAS scores and/or shorter time completion of the timed tasks indicate better performance (Lang, Bland, Bailey, Schaefer, & Birkenmeier, 2013; Taub et al., 2011).

Finger tapping task. From as early as the 19th century, finger tapping tasks (FTTs) are commonly used to measure motor functioning, particularly in functional neuroimaging research (Jobbágy, Harcos, Karoly, & Fazekas, 2005; Witt, Meyerand, & Laird, 2008). The FTT is an objective assessment of upper extremity fine motor skills and is often utilized in neuropsychiatric evaluations for various neurological conditions, such as Parkinson’s disease and stroke. Due to its simplicity, FTTs provide the utilization of accommodations and is typically assessed visually in clinical settings. Although it has been reported the average movement frequency for tapping tasks is 1.73 Hz, there is significant variability across studies investigating the rate of tapping tasks (Criswell, Sterling, Swisher, Evanoff, & Racette, 2010; Jobbágy et al., 2005; Witt et al., 2008).

The right and left hemisphere appear to coordinate more closely than researchers anticipated in patients who experience a unilateral lesion (de Groot-Driessen, van de Sande, & van Heugten, 2006). Research suggests the FTT is correlated with brain activation in the primary sensorimotor cortex, supplementary motor area, basal ganglia, and cerebellum (Witt et al., 2008). Neurorehabilitation has shown to improve stroke patients' performance on finger tapping to normative function. The improvement in finger tapping speed has shown to be linked to functional outcomes on performance-based measures such as the Frenchay Activities Index and Barthel Index. These results indicate finger tapping speed in the ipsilateral hand provides helpful information in the assessment of motor recovery (Carey, Abbott, Egan, Bernhardt, & Donnan, 2005; Haaland, Temkin, Randahl, & Dikmen, 1994).

Chedoke Arm and Hand Activity Inventory (CAHAI). Historically, there was an overall lack of a systematic evaluation of the functional recovery of patients' upper extremity paresis. Researchers and clinicians resorted to utilizing an excessive amount of performance measures; therefore, Barreca and colleagues (2004) developed the CAHAI to highlight the assessment of bilateral features of functional upper extremity tasks specifically in stroke patients. The CAHAI is a functional and clinical measure of an individual's recovering upper extremity and entails five primary objectives: (1) to differentiate between classifications of UE dysfunction; (2) to predict the potential functional recovery of a paralyzed upper extremity; (3) to calculate the extent of functional change in the UE; (4) to regulate the significance of that change to stroke survivors; and (5) to facilitate treatment planning. The development of this measure was based on five theoretical constructs: (1) definition of upper extremity function, (2) important characteristics of normative upper extremity activities, (3) prospective of functional change, (4) relevance to stroke survivors whose upper extremity differ in their recovery of motor functions, and (5) involvement of upper extremity paresis in bilateral functional activities (Barreca et al., 2004).

Originally, the CAHAI consisted of 13 tasks that involved the use of the right and left arm. Shortened versions of the CAHAI, such as the CAHAI-7 and CAHAI-9, are available if a researcher or clinician is faced with time restrictions. Each task is rated on a

7-point likert scale, with 1 indicating the patient needed complete assistance on the task and the impacted limb performed less than 25% of the task, and 7 indicating the patient demonstrated complete independence in performing the task. A greater score on the CAHAI suggests the patient has more functional independence of their upper extremity (Lang et al., 2013).

Due to time restrictions and to prevent over-exhaustion and fatigue, participants in this study were asked to complete one CAHAI task. The CAHAI task was chosen for its overall functionality and applicability to daily living skills. The task required the participant to wring a washcloth, a task that is indicative of various types of motor movements, including gross motor (moving wrist forward and backward), fine motor (grasping the washcloth with fingers), and the coordination of fine and gross motor skills.

Psychometric Properties

In this section, the reliability, validity, and range effects of the WMFT and CAHAI are reviewed.

Reliability. Reliability measures the extent of consistency or stability in an assessment (Gravetter & Forzano, 2012). A reliability coefficient delineates the ratio of variance in an observed score to a true score (Meyers, Gamst, & Guarino, 2013). In theory, reliability coefficients range between a high value of 1.00 to a low value of .00. A reliability coefficient of 1.00 suggests the score is a reliable index of the features being measured and that the score holds no measurement error. A reliability coefficient of .00 suggests the score relays no practical information regarding the features being measured and that measurement error accounts for all of the observed variance. Reliability coefficient values that are .90 or higher are considered outstanding, .80-.89 are very good/good, and .75-.79 are acceptable (Meyers et al., 2013). Inter-rater reliability measures the amount of agreement two observers have after assessing the qualities of a behavior concurrently, whereas internal consistency examines the amount to which the variables in an assessment jointly measure the same construct (Gravetter & Forzano, 2012; Henson, 2001).

Overall, the modified WMFT demonstrates excellent psychometric properties. The internal consistency and inter-rater reliability of the FAS and performance time on the tasks range from .88 to .99, with a majority of the reliability coefficients approximating .95 in several research studies (Duff et al., 2015; Morris et al., 2001; Taub et al., 2011; Whithall, Savin, Harris-Love, & Waller, 2006; Wolf et al., 2001). Test-retest reliability was found to be high for the FAS (.95) and performance time (.90). Test-retest and inter-rater reliability for the individual items on the WMFT were mostly shown to be high (Morris et al., 2001). Research studies report the CAHAI has high internal consistency (.98), test-retest (.98), and inter-rater (.98) reliability (Barreca, Stratford, Lambert, Griffiths, & McBay, 2006; Barreca, Stratford, Lambert, Masters, & Streiner, 2005)

Validity. Validity examines the amount to which an assessment measures the construct or variable it proposes to measure. Internal validity evaluates the extent to which an assessment generates a clear explanation for the association between the measured variables. Concurrent validity indicates whether scores from a new assessment are directly associated to scores from a well-known or conventional assessment of a similar variable. High convergent or predictive validity suggests scores from two different assessments have a strong relationship in the way they measure the same variable. Divergent validity, also called discriminate validity, indicates two different methods have been utilized to evaluate two separate variable with little or no relationship in scores between the variables (Gravetter & Forzano, 2012).

Research supports concurrent validity for the WMFT with the Fugl-Meyer Assessment (FMA) as well as the Action Research Arm Test (ARAT) (Fugl-Meyer, Jaasko, Leyman, Olsson, & Steglind, 1975; Nijland et al., 2010; Wolf et al., 2001). The average time and functional ability of the WMFT and FMA provide strong support for concurrent validity ($r = -.88$) and how researchers use them to rate a patient's affected limb ($r = -.57$). A Spearman correlation coefficient suggested high concurrent validity ($r_s = .86$, $p < .001$) between the WMFT's FAS and the ARAT total score. In addition, the two strength-based measures on the WMFT provide high concurrent validity ($r_s = .70$, $p < .001$) with the ARAT. Furthermore, construct validity for the WMFT is displayed in its ability to effectively differentiate patients' impaired and non-impaired upper extremity, regardless of if they had a stroke (Ali, 2010; Nijland et al., 2010; Whithall et al., 2006; Wolf et al., 2001).

Cross sectional and longitudinal convergent validity between the CAHAI-13 and the shortened versions, CAHAI-9, 8, and 7, have shown to be strong (.99, .99, .99, respectively). The convergent validity coefficient was high for the CAHAI-13 and ARAT (.93) as well as for the CAHAI-13 and Chedoke-McMaster Stroke Assessment (CMSA; .81). In addition, discriminate validity was demonstrated by a low correlation of the CAHAI-13 and ARAT (.47 and .52, respectively) with the CMSA shoulder and pain scale (Barreca, Stratford, Lambert et al., 2006; Barreca, Stratford, Masters, Lambert, & Griffiths, 2006; Barreca et al., 2005; Chedoke Arm and Hand Inventory [CAHAI], n.d.).

Range effects. A floor effect occurs when the grouping of scores toward the low end of an assessment permits little or no leeway to reduce in value, where as a ceiling effect occurs when the scores permit little or no leeway to increase in value (Gravetter & Forzano, 2012). Assessments with floor and/or ceiling effects suggest a basic inconsistency between the assessment procedure and the participants being evaluated. In such cases, the assessment entails tasks that are too challenging (floor effect) or too easy (ceiling effect) (Gravetter & Forzano, 2012).

Floor effects were found on the WMFT for five out of 40 patients in a study prior to receiving movement therapy; however, the floor effects decreased to two out of the five patients post-therapy. Similar effects were found when psychometric properties of other assessments of motor function were evaluated such as the Motor Assessment Scale. These results suggest functional ability is expected to be overestimated in patients with motor dysfunction, irrespective of the type of assessment that is utilized (Thompson-Butel, Lin, Shiner, & McNulty, 2015). Notably, a study conducted by Nijland and colleagues (2010) that investigated the psychometric properties of the WMFT did not find significant floor or ceiling effects. Floor and ceiling effects for the CAHAI have not been published.

Research Questions

This research project utilized functional Near-Infrared Spectroscopy (fNIRS) to examine brain activation of the motor cortex in stroke patients before and after receiving CIMT. The following research questions were addressed:

(1) What are the differences in hemoglobin signal before and after stroke patients receive two weeks of CIMT?

(2) What is the association between upper extremity hemiparesis and hemoglobin activity among patients who experienced a left MCA stroke?

Research Design

Changes in hemoglobin signal in the motor cortices of stroke patients who received CIMT were investigated via fNIRS. A within-subjects quasi-experimental pretest-posttest design was implemented. This design method utilizes one sample of participants who are examined before and after a treatment or intervention. Only a small number of participants are needed for a within-subjects design, particularly when it is challenging to recruit a unique sample of participants (Gravetter & Forzano, 2012). Although it is ideal to include more participants to attain sufficient statistical power, utilizing six individuals generally coincides with sample sizes in the CIMT literature given the nature and specific population targeted in this study. Furthermore, a within-subjects design fundamentally removes the challenges that are typically encountered in other designs due to individual variances, such as a between-subjects design. As a result, the amount of confounding variables and differences between participants within a treatment group decreases because each participant acts as their own baseline or control. This allows researchers to assess differences between participants throughout the treatment groups, which can then be removed from the remaining variance in the data. In doing so, researchers are able to better evaluate the effects of the proposed treatment or intervention (Gravetter & Forzano, 2012).

The potential disadvantage of a within-subjects design is participant attrition. Because this design entails participants undergoing repeated measurement, some who begin the study may leave before it is completed. Although this issue is particularly problematic when a research study prolongs over several months or years in which participants must return for further follow up observations, this research study was designed to take place within four weeks for each individual. Because the participants in this study were already enrolled in a rehabilitation program at Pate that extended over several months, a four-week timeframe was deemed appropriate to control for attrition (Gravetter & Forzano, 2012; Meyers et al., 2013).

Pretest-posttest designs often encounter external variables that may limit internal validity. For within-subjects pretest-posttest designs, time-related factors pose a threat to internal validity. The five different time-related factors include history (occasions that occur outside the study), maturation (psychology or physiological changes patients experienced), instrumentation (changes in the assessment measure), testing effects (participant's experience in previous treatment condition), and statistical regression (inclination of extreme scores regressing toward the mean) (Gravetter & Forzano, 2012). The researcher was able to attempt to decrease threats of instrumentation and testing effects for this study; the finger-tapping and washcloth task were both completed during the neuroimaging sessions pre- and post-CIMT.

Data Collection and Analysis

After consent was obtained, demographic information was collected through chart review, including age, gender, ethnicity, medical and family history, and the treatment services currently received at Pate. Within approximately one week prior to and after starting CIMT, each participant completed the WMFT and a neuroimaging session. The WMFT was administered to classify each participant's motor function and severity of upper extremity hemiparesis. During the neuroimaging session, participants completed a finger tapping and the CAHAI washcloth task to detect significant hemoglobin signal pre- and post-CIMT. While the participants performed the finger tapping and CAHAI tasks, they wore a fNIRS head cap to measure hemoglobin signal across the motor cortices. Participants' performance on the washcloth task was rated using the CAHAI functional rating scale. Participants' demographic information and performance on the WMFT and CAHAI task were entered into an excel database for statistical analyses.

The original fNIRS protocol employed the following procedure: 3 trials of right hand finger tapping, 3 trials of left hand finger tapping, and 4 trials of the CAHAI washcloth task. This protocol was used for the first 3 participants in the study. Further consultation with fNIRS expert Dr. Alexandrakis and Ms. Cao during the course of the study led to an updated protocol for the remaining 3 participants, which consisted of 8 trials of right hand finger tapping, 8 trials of left hand finger tapping, and 4 trials of the CAHAI washcloth task. The updated protocol also consisted of longer rest periods between tasks. With the assistance of Dr. Alexandrakis and Ms. Cao, the fNIRS data was then processed and analyzed.

Lastly, a 3D probe positioning unit as part of the fNIRS machine was utilized to measure the coordinates of the optode channels, also called reference positions, as well as the head position that the optode channels were located on. The reference positions collected by the probe unit were mapped onto a 3D image of the brain via a mapping software. Results from the topographic data were illustrated on the 3D brain image to denote where significant differences in oxygenated and deoxygenated hemoglobin occurred pre- and post-CIMT.

Hemoglobin Dynamics

The raw topographic data extracted from the ETG 4000 was analyzed by the open-source HomER (hemodynamic optically measured evoked response; Huppert, Diamond, Franceschini, & Boas, 2009) software through the MATLAB® (Mathworks, Natick, Massachusetts) computing system. A general linear model (GLM) was utilized to pinpoint image pixels with temporal hemodynamic patterns that were significantly associated with cortical activity. Based on Bonferroni's correction, a threshold value of $p < 0.0001$ was set to locate pixels with significant hemoglobin activation (Cao et al., 2015).

Next, spatial maps of the brain for each participant were generated using the statistical parametric mapping (SPM) software. The SPM software produces activation maps and super-resolution localization of hemoglobin signal on an anatomical MR image of the cerebral cortex. To do so, SPM utilized the head positions obtained from the 3D probe positioning unit to create a spatial map (Tak, 2011). The spatial maps that were generated were used to explore areas of the brain where significant oxygenated and deoxygenated hemoglobin occurred. Because the involvement of multiple types of motor movement facilitates more activation of motor neurons (Knierim, 1997; Pangelinan, Hatfield, & Clark, 2013; Takakura, Nishijo, Ishikawa, & Shojaku, 2015), it was expected the CAHAI washcloth task, which requires both fine and motor movement, would elicit more oxygenated hemoglobin compared to the finger tapping task.

Laterality index and time-to-peak/duration. By analyzing the patients' topographic images to locate the presence of significant cortical activation, the laterality index and the time-to-peak/duration metric was calculated were quantified for each significant pixel, and then averaged across pixels (Cao et al., 2015). The laterality of activation is derived from functional activation patterns and denotes the dominance of one hemisphere in controlling for certain functions. To calculate the laterality index, the following formula was used, where Ncontral refers to the quantity of activation pixels in the contralateral hemisphere and Nipsi refers to the amount of activation pixels in the ipsilateral hemisphere (Cao et al., 2015; Seghier, 2008).

$$L = \frac{N_{contral} - N_{ipsi}}{N_{contral} + N_{ipsi}}$$

The time-to-peak/duration metric analyzes the temporal features of cortical activation patterns. The time-to-peak metric also measures the difference in time from the start of task to the point at which maximum change in hemoglobin occurs. The time in which the amplitude of hemodynamic variation within a pixel surpasses a threshold is referred to as the duration of activation.

Motor Functioning

Utilizing a within-subjects design typically entails the computation of scores and assessing the difference among treatment groups. To determine if an observed difference is statistically significant, a statistical procedure involving a t-test was followed. Employing this statistical procedure evaluates whether mean differences are reliable and if a treatment condition is expected to represent various people. A t-test is utilized exclusively when there is one independent variable (i.e., treatment condition) with two levels (i.e., performance pre- and post-treatment condition) (Gravetter & Forzano, 2012; Meyers et al., 2013).

The present study used a dependent or paired t-test to determine if there was a significant difference ($p < 0.05$) in participants' total score on the WMFT. This statistical procedure provided the researcher an understanding of the characteristics of the sample's upper extremity hemiparesis before and after CIMT. In addition, a paired t-test was conducted on the study sample's performance on the CAHAI washcloth task to investigate changes in functional use of their affected upper extremity. Results of each participant's motor performance on the WMFT and CAHAI washcloth task pre- and post-CIMT was then compared descriptively with their fNIRS data to explore the relationship between upper extremity motor functioning and cortical changes in the brain.

Summary

This chapter describes the methodology utilized to investigate hemoglobin signal in the motor cortices using fNIRS in patients with a left MCA stroke who received CIMT. A within-subjects quasi-experimental pretest-posttest design was implemented. First, the WMFT was administered to participants prior to and after two weeks of CIMT to obtain an understanding of the characteristics and severity of their upper extremity hemiparesis. Then, participants underwent pre- and post-neuroimaging sessions that recorded hemodynamic responses while they performed a finger tapping and functional task from the CAHAI.

Participants' neuroimages were analyzed to determine which pixels illustrated significant hemoglobin signal post-CIMT as compared to baseline. The laterality of activation and time-to-peak metrics were calculated to provide additional information regarding the observed changes in motor performance in tandem with imaging time points. Spatial maps of the brain were generated for each participant to illustrate the specific areas that had significant oxygenated and deoxygenated hemoglobin signal during both neuroimaging sessions. To determine if participants' motor functioning significantly changed after CIMT, a paired t-test was performed on their overall score on the two performance-based measures. Results from the paired t-test were then compared descriptively to the fNIRS results.

The purpose of the study was to (1) examine differences in hemoglobin signal before and after stroke patients received movement therapy and (2) explore the association between upper extremity hemiparesis and cortical activation patterns in the brain during neurorehabilitation. It was hypothesized participants would demonstrate a significant increase in oxygenated hemoglobin signal within the motor cortex of the affected hemisphere during the finger tapping and CAHAI washcloth task post-CIMT. Furthermore, it was hypothesized participants will exhibit significant improvements in motor functioning on both performance-based measures that would reflect neurologically in fNIRS imaging.

CHAPTER IV

RESULTS

The purpose of this study was to utilize functional Near-Infrared Spectroscopy (fNIRS) to investigate brain activity in stroke patients before and after rehabilitation. More specifically, this study examined hemoglobin signal among patients who experienced hemiparesis after a left middle cerebral artery (MCA) stroke and received two weeks of constraint-induced movement therapy (CIMT). Participants' upper extremity motor functioning before and after treatment was also assessed in relation to cortical changes in the brain.

Study Sample

Six patients from Pate Rehabilitation participated in this project. Of the six study participants, four were female and two were male and their age ranged between 39 and 63-years-old. Participants belonged to two ethnic groups: Latino/Hispanic (n=2) and White (n=4). Study participants met all eligibility criteria: right-hand dominant, time of stroke was at least 3 months prior to enrollment, above 18 years old, ability to provide consent, and no prior diagnosis of stroke, learning disability, complete physical impairment, seizures, or brain injuries. Ability to consent was measured through participants' verbal comprehension skills by successfully completing at least 3 of 4 items on the Standardized Mini Mental State Examination.

Patient 1 is a 61-year-old Caucasian female whose CIMT addressed gross motor functions and muscle strength in her right arm/hand. Tasks completed during therapy consisted of grasp and release, extension, and lifting. Patient 2 is a 46-year-old Hispanic female who exhibited muscle spasticity as a result of her stroke. Extension and the ability to grasp were targeted tasks for Patient 2's CIMT regimen. Patient 3 is a 63-year-old Hispanic female whose treatment focused on fine motor skills. Patient 3's therapy consisted of functional daily living tasks she struggled with in the home environment, such as picking up small items and using a plastic knife to cut therapy putty. Patient 4 is a 53-year-old Caucasian male who presented with muscle spasticity and weak gross and fine motor functioning in his right fingers and arm. Patient 4's therapy included tasks that involved extension, grasp and release, and horizontal abduction/adduction. Patient 5 is a 50-year-old Hispanic female who experienced low muscle tone in her right arm and exhibited weakness in fine motor functioning. Her CIMT involved tasks related to grasp, extension, and muscle strength. Behavioral observations noted for Patient 5 involved the need for moderate levels of accommodations during treatment sessions and some resistance to homework assignments. Patient 6 is a 39-year-old Caucasian male whose treatment targeted fine motor functioning through grasp and release tasks to challenge shoulder flexion or abduction/adduction.

Statistical Analyses

Two main components were analyzed in this study: hemoglobin activity (including laterality index and time-to-peak metrics) and motor functioning. All results were analyzed on a case by case basis, with the addition of a group analysis conducted to determine the study sample's overall motor improvement following CIMT.

Hemoglobin dynamics

A total of 20 optode channels (Figure 5) were selected to analyze hemoglobin activity; 10 channels within the left hemisphere and 10 within the right hemisphere. Brain areas corresponding to the selected optode channels consisted of the pre-motor, supplementary, and primary motor cortices. Channels 7, 10, 13, 14, 17, 20, 21, 23, and 24 on the left hemisphere are associated with the pre-motor and supplementary motor cortex and channels 10, 16, 17, 20, and 23 are associated with the primary motor cortex. For the right hemisphere, channels 28, 32, 35, 36, 39, 43, 46, and 47 correlate to the pre-motor and supplementary motor cortex and channels 32, 36, 39, 40, 43, 44, and 47 correlate to the primary motor cortex. Hemoglobin activity obtained by the optode channels while participants completed the finger tapping and washcloth tasks was stored as raw data in the ETG 4000 and processed by Ms. Cao through the MATLAB software.

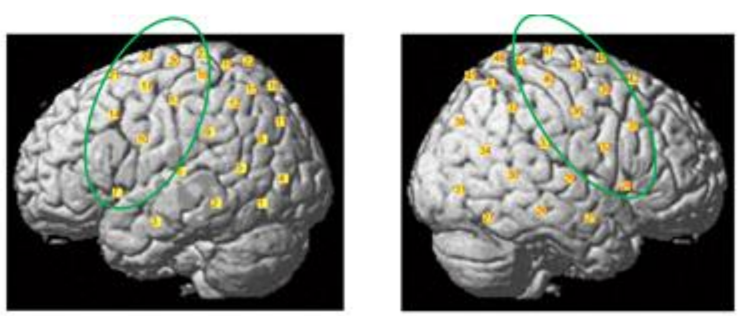


Figure 5. Selected optode channels that correspond to motor-related brain areas within the left and right hemisphere, respectively.

Raw data. The raw data of each participant's hemoglobin activity was collected from the ETG 4000 and processed using the HomER program through MATLAB. The HomER program utilized the general linear model to identify significant activation of hemoglobin while participants completed both tasks. The raw data's signal-to-noise ratio was analyzed to determine if there was sufficient data for the detection of significant brain activity. Due to a limited number of trials for the finger tapping and washcloth task in the original protocol, the raw hemoglobin data for Patients 1 and 2 and pre-CIMT data for Patient 3 were not interpretable and removed from the analyses. An updated protocol was developed to include an increased number of trials and duration to complete each task as well as rest periods. This updated protocol was determined adequate and interpretable for Patients 3 (post-CIMT), 4, 5, and 6.

Statistical Parametric Mapping. An anatomical magnetic resonance (MR) image was generated by the ETG 4000 to show where significant differences in cortical activity occurred pre- and post-CIMT for each participant. The statistical parametric mapping (SPM) software utilized the raw data of hemoglobin activity to map onto the MR image. Areas of the brain image colored in red indicates that a significant amount of oxygenated hemoglobin activity took place, whereas areas colored in blue suggests a significant amount of deoxygenated blood flow occurred in that area. A description of each participants' hemoglobin activity and their MR image is discussed below. The term contralateral refers to the hemisphere opposite to the extremity being utilized whereas ipsilateral refers to the hemisphere on the same side an extremity is completing the activity.

Patient 3. Following treatment, bilateral activation is shown while Patient 3 completed all three tasks. As would be expected, there is significant oxygenated blood flow in the contralateral hemisphere during the left hand finger tapping task (Figure 6.a). Although greater in the contralateral hemisphere, cortical activation is evident bilaterally when Patient 3 completed the right hand finger tapping task, suggesting an early stage of neuronal recovery in the affected hemisphere (Figure 6.b). The activation pattern illustrated during the CAHAI washcloth task (Figure 6.c) suggests the right (unaffected) hemisphere has taken upon most of the workload for carrying out this task. Although there is some oxygenated blood flow in the contralateral hemisphere, Patient 3's unaffected extremity continues to be stronger.

Patient 4. During the left hand finger tapping task (Figure 7.a) prior to CIMT, the presence of some activation appears in the right hemisphere; however, this occurs in the brain region that correlates with arm and shoulder movements. Following treatment, Patient 4 exhibits greater blood supply in both hemispheres, particularly in the right hemisphere, which is localized within the brain regions that control for hand movement. Bilateral activation is shown during the right hand finger tapping task (Figure 7.b) pre- and post-CIMT; however, the activation is greater and more localized in the right hemisphere following treatment.

(6.a)
(6.b)
(6.c)

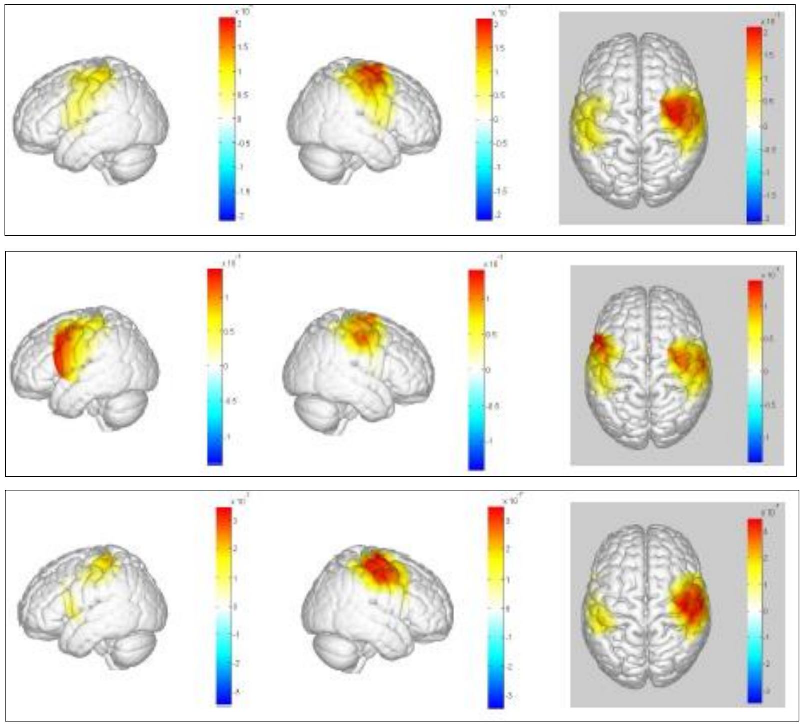
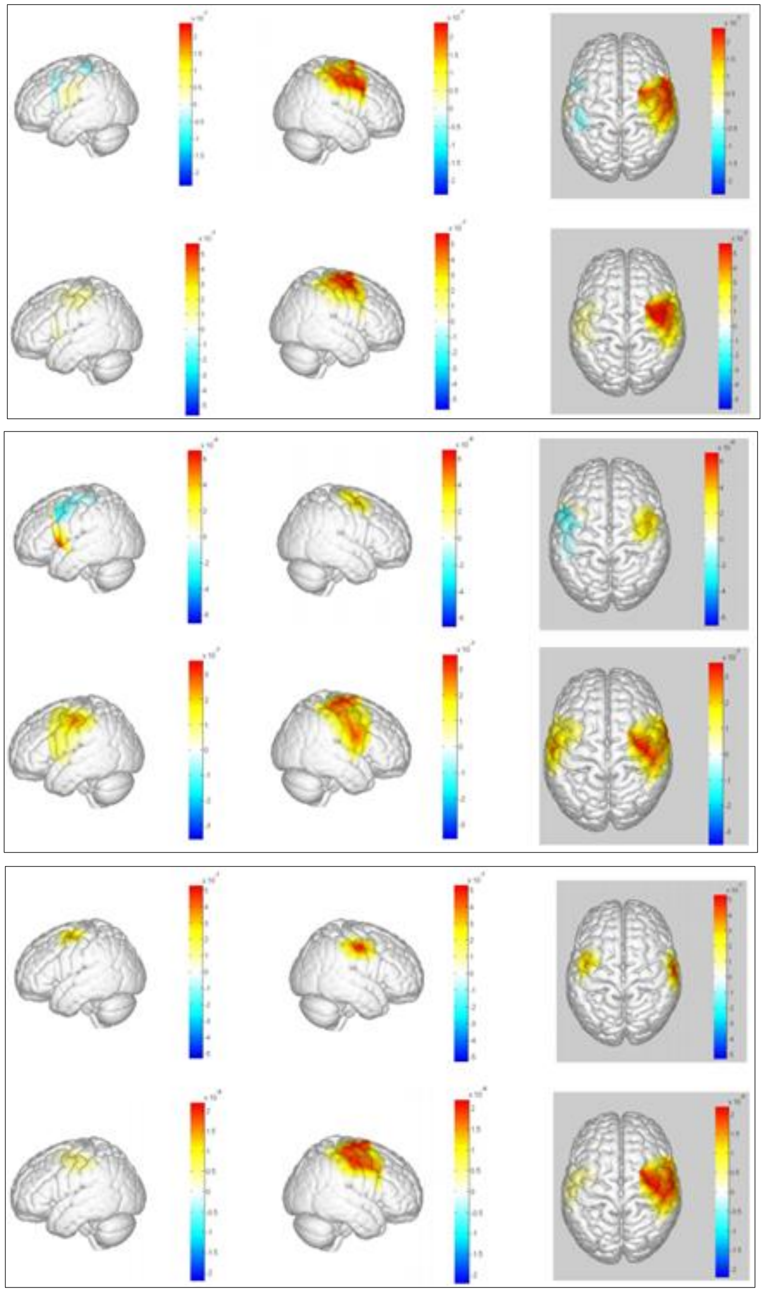


Figure 6. Localization of significant brain activity for Patient 3 after CIMT during the left hand finger tapping (a), right hand finger tapping (b), and CAHAI washcloth task (c).

These findings suggest prior to CIMT, the motor neurons in the right hemisphere were compensating for the stroke-affected areas in the left hemisphere and appear to be in the process of becoming restored. Figure 7.c illustrates Patient 4's performance on the CAHAI washcloth task pre- and post-CIMT. Cortical activation is primarily seen in the right hemisphere, with some oxygenated blood flow occurring in the left hemisphere. Following treatment, oxygenated blood is shown covering a greater surface area in the right hemisphere. This suggests that while completing a bimanual task, Patient 4 may rely more on and use his unaffected extremity.



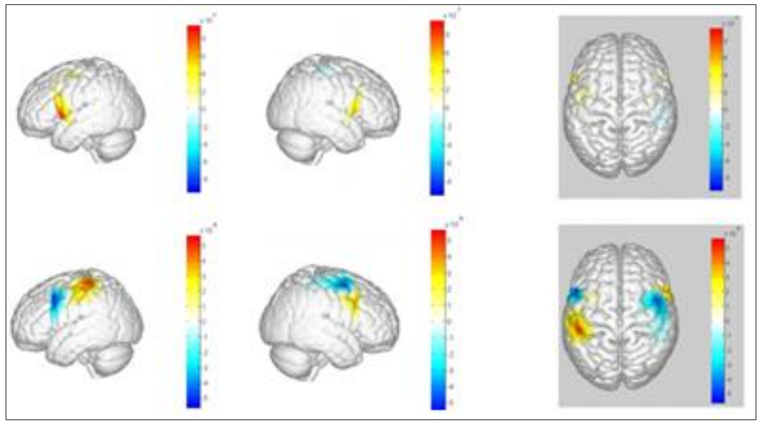
(7.a)

(7.b)

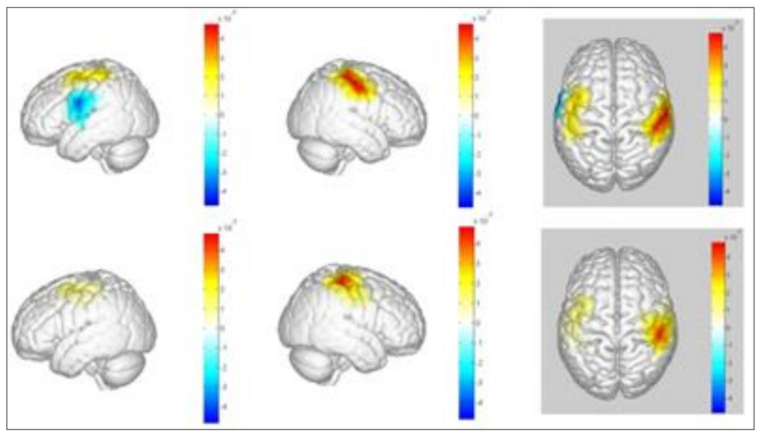
(7.c)

Figure 7. Localization of significant brain activity for Patient 4 before (top) and after (bottom) CIMT during the left hand finger tapping (a), right hand finger tapping (b), and CAHAI washcloth task (c).

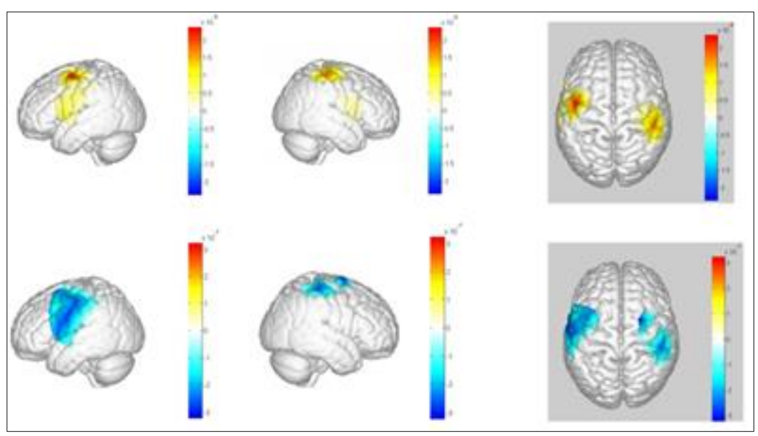
Patient 5. The left hand finger tapping task (Figure 8.a) elicited little activation pre-CIMT and a very scattered activation pattern after treatment, both of which were bilateral. Following treatment, an increase in oxygenated blood flow is evident in the left hemisphere; however, this activity occurred within the sensory cortex. There is also significant deoxygenated blood flow surrounding the motor area that controls for shoulder movement in the right hemisphere. The right hand finger tapping task (Figure 8.b) showed activation primarily in the right hemisphere both pre- and post-CIMT. The similarity in cortical activity seen before and after treatment may be explained by Patient 5's overall limited use of her affected extremity prior to treatment and compliance concerns during the treatment regimen. Patient 5's performance on the CAHAI washcloth task (Figure 8.c) pre-treatment correlates with bilateral activation patterns located in areas that would typically be seen when completing similar tasks. After treatment, however, Patient 5's brain activity appears to be exceptionally unilateral.



(8.a)



(8.b)

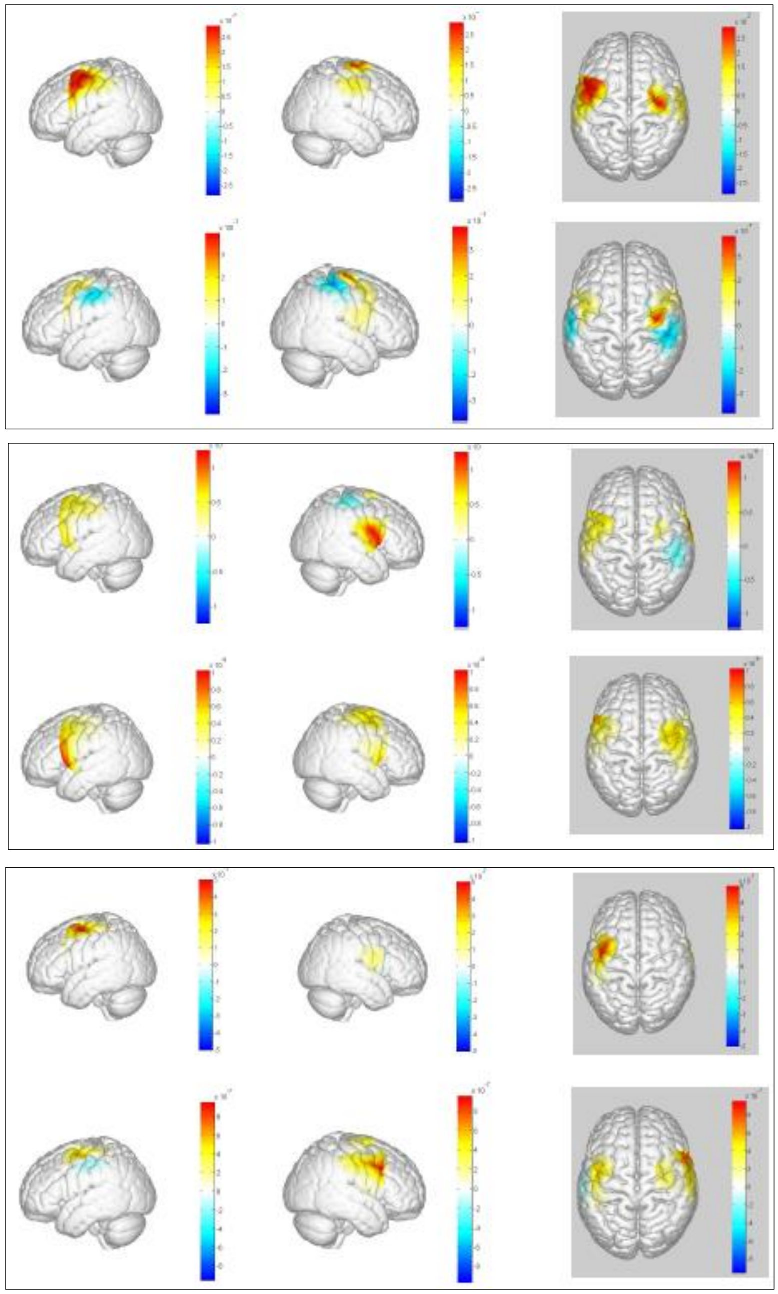


(8.c)

Figure 8. Localization of significant brain activity for Patient 5 before (top) and after (bottom) CIMT during the left hand finger tapping (a), right hand finger tapping (b), and CAHAI washcloth task (c).

Patient 6. Similar to Patient 5's performance on the left hand finger tapping task, Patient 6 displayed bilateral activation with an overall decrease in oxygenated blood flow post-treatment (Figure 9.a). Significant oxygenated and deoxygenated blood flow is seen bilaterally during the right hand finger tapping task (Figure 9.b) prior to treatment. During this task before therapy, oxygenated hemoglobin is localized in the right hemisphere, along with some activity occurring in the left hemisphere. After CIMT, some significant oxygenated hemoglobin shifted to the left hemisphere, with an absence of deoxygenated blood flow on either side. During the CAHAI washcloth task (Figure 9.c), cortical activity appears to be present solely unilaterally (left hemisphere) before treatment. Following treatment, the activation pattern occurs bilaterally, with a shift in oxygenated blood flow from the left to the right hemisphere.

Laterality index. Table 1 shows each participant's laterality index pre- and post-CIMT for the finger tapping and washcloth tasks. Laterality index values of zero indicate the occurrence of bilateral activation during the task. A positive value suggests there is activation in the contralateral hemisphere of the extremity whereas negative values signify the activation of the ipsilateral hemisphere.



(9.a)

(9.b)

(9.c)

Figure 9. Localization of significant brain activity for Patient 6 before (top) and after (bottom) CIMT during the left hand finger tapping (a), right hand finger tapping (b), and CAHAI washcloth task (c).

Table 1.

Patients' Laterality Index for Each Task Pre- and Post-CIMT

	Right Finger Tapping		Left Finger Tapping		Washcloth	
Patient	Pre-CIMT	Post-CIMT	Pre-CIMT	Post-CIMT	Pre-CIMT	Post-CIMT
3	--	0	--	.02308	--	0.25
4	.04286	-0.0667	0.0667	0	0	0.3333
5	0.3333	0	0.3333	-0.2	0	-0.3333
6	0	0.0769	-0.1429	0.2727	-0.2	0.2

Note. Values with "--" indicates an insufficient amount of hemoglobin data to calculate the laterality index.

Patient 3. Although the pre-CIMT laterality index for Patient 3 is unknown, she demonstrated healthier post-CIMT laterality values compared to Patients 4 and 5. Patient 3's imaging data also coincides with the interpretation made from the laterality index values of all the three tasks. For the right finger tapping task, it appears cortical activation was originally localized in one hemisphere prior to CIMT. Significant oxygenated blood flow is shown to occur bilaterally following treatment as shown in Patient 3's imaging data and laterality index value. These findings may suggest a shift in activation from the right hemisphere to the left due to the intense motor use of Patient 3's affected extremity and the initial stages of neuronal repair. Laterality index values for Patient 3's left hand finger tapping and washcloth tasks are positive (contralateral activation), which is expected when utilizing the unaffected extremity, and correspond to her imaging results.

Patient 4. Per his imaging, Patient 4 exhibits significant deoxygenated blood flow in the left hemisphere during the right finger tapping task prior to receiving CIMT. His laterality index indicates a shift in cortical activity from the left (pre-CIMT) to right (post-CIMT) hemisphere, suggesting Patient 4's use of his affected extremity resulted in lower cerebral blood flow and may have led to increased involvement of the right hemisphere to carry out motor-related tasks. For the left finger tapping task, the laterality index suggests bilateral activation occurred post-CIMT. Patient 4's imaging illustrated some significant deoxygenated blood flow prior to treatment; however, oxygenated blood flow is shown to replace this pattern post-CIMT. His performance may represent an improvement in Patient 4's ability to carry out basic fine motor tasks with his unaffected extremity. Patient 4's laterality index value for the washcloth coincides with his imaging results and indicates bilateral activity pre-CIMT and a more localized cortical activation pattern in the contralateral hemisphere post-CIMT.

Patient 5. The laterality index value for the right hand finger tapping task indicates the cortical activation pattern was concentrated in the contralateral hemisphere pre-CIMT. Patient 5's neuroimaging suggests this pattern encompassed significant deoxygenated blood flow; however, as indicated by the laterality index post-CIMT, this appears to have been diffused and an increase in oxygenated hemoglobin is presented bilaterally. Patient 5's imaging accurately illustrates the laterality index for the left hand finger tapping task. Prior to treatment, Patient 5's focal activation pattern of deoxygenated hemoglobin appears in the contralateral hemisphere. Following treatment, significant oxygenated hemoglobin blood flow is present in the ipsilateral hemisphere. For the CAHAI washcloth task, Patient 5's neuroimaging correlates with the laterality index values that represents bilateral activation of oxygenated hemoglobin pre-CIMT, but values that suggest ipsilateral activity post-CIMT.

Patient 6. For all three tasks, a shift from bilateral or ipsilateral hemisphere activation to the contralateral hemisphere is demonstrated in both the laterality index values and Patient 6's neuroimaging. These findings suggest CIMT may have facilitated the reorganization of cortical activation patterns to what would normally be expected in healthy participants.

Time-to-peak/duration. The time-to-peak/duration metric during the finger tapping and washcloth tasks for each participant is shown in Table 2. Lower metric values indicate longer activation duration, whereas higher values (values considered closest to 1.0) imply faster activation patterns. Pre-CIMT metric values that increase post-CIMT suggests a normalization of temporal activation patterns, which typically have a time-to-peak/duration value of approximately 1.

Table 2.

Patients' Time-to-Peak/Duration Metric Values for Each Task Pre- and Post-CIMT

	Right Finger Tapping		Left Finger Tapping		Washcloth	
Patient	Pre-CIMT	Post-CIMT	Pre-CIMT	Post-CIMT	Pre-CIMT	Post-CIMT
3	--	0.4615	--	0.4568	--	0.7821
4	0.4004	0.6603	0.4720	0.2187	0.7758	0.6415
5	0.5548	0.8872	0.4939	0.5305	0.6902	1.0019
6	0.5077	0.6471	0.5975	0.6945	0.6111	0.5210

Note. Values with "--" indicates an insufficient amount of hemoglobin data to calculate the laterality index.

Patient 3. Metric values for the finger tapping tasks post-CIMT suggest longer activation patterns while Patient 3 completed these tasks. Behavioral observations noted during the finger tapping tasks included fatigue and prompting, which may have affected her performance. The metric value for the washcloth task is relatively high, suggesting a change toward a normal activation pattern.

Patient 4. An increase in the time-to-peak/duration pattern was shown in Patient 4's performance of the right hand finger tapping task pre- to post-CIMT. Patient 4 displayed a decrease in the time-to-peak/duration metric post-CIMT for the left hand finger tapping task. Although not significant, a slight decrease was shown for the washcloth task, indicating some consistency in activation during this task.

Patient 5. Higher activation patterns for all three tasks are shown post-CIMT, with the greatest increase during the washcloth task. Patient 5's performance during the washcloth task post-CIMT is a value of 1.0, which reflects a normalized pattern of temporal activation.

Patient 6. The finger tapping tasks elicited a slight increase in the time-to-peak/duration metric, but not significant enough to suggest a change toward normalization. The activation pattern for the washcloth task slightly decreased, but was also not significant enough to indicate a discrepancy pre- and post-CIMT. These results indicate Patient 6's performance had consistent neurological effects before and after therapy.

Motor functioning

Group analysis. A paired t-test was conducted on the study sample's performance on the WMFT and the CAHAI washcloth task. As a group, patients significantly improved in their performance score on both measures following two weeks of CIMT (Table 3). Patients' overall performance score on the WMFT after CIMT (*M* = 41.67, *SD* = 18.1) was significantly higher than before they started treatment (*M* = 32.67, *SD* = 17.6), *t*(5) = -5.255, *p* < .05. Similarly, patients' performance score on the CAHAI washcloth task was significantly higher following treatment (*M* = 4.5, *SD* = 1.5) than prior to receiving therapy (*M* = 2.33, *SD* = 1.4); *t*(5) = -13, *p* < .01.

Table 3.

Paired Samples Test Statistics

	Pre-CIMT		Post-CIMT		t	df	Sig (2-tailed)
	M	SD	M	SD			
WMFT	32.67	17.626	41.67	18.074	-5.255	5	.003
CAHAI washcloth task	2.33	1.506	4.50	1.378	13.000	5	.000

Individual performance. Behavioral observations and quality of motor movements while participants completed the WMFT and CAHAI washcloth task are described in this section. The WMFT Data Collection Form uses a 6-point likert scale (Appendix A) to rate participants' functional performance of their affected upper extremity on 15 different functional tasks, with a performance score of 80 suggesting all tasks were performed normally. The CAHAI washcloth task uses the following 7-point likert scale to score a patient's motor performance:

1. Total assist (weak U/L < 25%)
2. Maximal assist (weak U/L = 25-49%)
3. Moderate assist (weak U/L = 50-74%)
4. Minimal assist (weak U/L > 75%)
5. Supervision

6. Modified independence (device)

7. Complete independence (timely, safely)

Patient 1. Prior to receiving treatment, Patient 1 scored a 35 on the WMFT and a 44 post-CIMT. Patient 1 demonstrated an improvement in completing tasks that required her to extend her arm, but continued to struggle with activities that involved lifting. Patient 1's pre-treatment CAHAI score was a 2. During the task, Patient 1 required support in holding one end of the washcloth in order for her to twist it. Following CIMT, Patient 1's performance on the CAHAI washcloth task was scored a 4. Behavioral observations noted during this task was her ability to hold the cloth more independently and her execution of more fluid twisting motions.

Patient 2. Patient 2's performance on the WMFT was limited by her inability to complete tasks that required functional grasp. She received a score of 20 pre-CIMT and a 22 post-CIMT. Patient 2 demonstrated an improvement in her ability to extend her elbow following treatment. Notably, she performed more than half of the WMFT tasks faster and exhibited more fluid movements and less compensatory shoulder hiking post-treatment. The small difference in Patient 2's WMFT scores is likely due to the amount of spasticity experienced in her affected upper extremity that prevented her completing several tasks, which resulted in low scores. Patient 2's performance on the CAHAI washcloth task prior to receiving treatment was categorized as a 2. She was able to grasp the washcloth but needed assistance with maintaining the grasp. Patient 2's score on the CAHAI post-CIMT was a 4; although the motor quality in her performance remained the same, she required less assistance.

Patient 3. Before receiving CIMT, Patient 3's WMFT score was a 65. Although she exhibited difficulty with tasks that involved fine motor skills, her score post-CIMT improved to a 72. It appeared the degree and severity of Patient 3's motor impairment was relatively lower than the rest of the study sample. She demonstrated the ability to complete all tasks, including those that required fine motor grasp, and her overall completion time on the WMFT after receiving treatment was faster. Patient 3's CAHAI score pre-CIMT was a 5; her motor performance while completing the task was slightly shaky and was observed a number of times attempting to complete the task too quickly, which affected the twisting motion of her wrists. After receiving CIMT, Patient 3's performance on the CAHAI washcloth task was observed to be normal and she received a score of 7. She demonstrated fluid motor movements and exhibited good coordination and grasp.

Patient 4. Patient 4's performance on the WMFT earned him a score of 25 prior to receiving CIMT. Tasks that required grasp and lifting objects were difficult for Patient 4 and hindered his ability to complete certain items in a timely manner. Following CIMT, Patient 4 improved in his ability to lift items and the time to complete tasks; however, he continued to struggle with the ability to grasp due to spasticity in his fingers, which earned a score of 37. He required significant support in completing the CAHAI task before treatment, and received a performance score of 1. Although Patient 4 was able to hold the washcloth with his affected extremity, he was unable to maintain grasp or twist the washcloth. After completing the CIMT regiment, Patient 4's score on the CAHAI was a 3. Although he continued to have difficulty with carrying out the twisting motions, he required less assistance with completing the task.

Patient 5. Prior to receiving CIMT, Patient 5's WMFT score was a 16. She had difficulty with grasping, extending her elbow, and fine motor movements, and was unable to complete tasks that required lifting. After CIMT, Patient 5's WMFT was a 26. Although the fluidity of her motor actions was poor, she was able to attempt and complete tasks involving grasp and improved in her time completion of the WMFT. Patient 5 required support to complete the CAHAI washcloth task before the treatment regimen, earning her a score of 1. She was able to squeeze the washcloth with her right hand but needed assistance with maintaining its placement in her hand. After CIMT, Patient 5 needed little support in adjusting the placement of the washcloth in her affected hand while she completed the task. Her ability to carry out the wringing of the washcloth by twisting her wrists back and forth also improved.

Patient 6. Before the CIMT regimen, Patient 6's score on the WMFT was a 35. The ability to extend his elbow and his fine motor grasp were particularly difficult for him. After two weeks of CIMT, Patient 6's WMFT score increased to a 49. Although Patient 6 continued to struggle to complete fine motor tasks, his performance greatly improved on tasks that involved grip, grasp, and the extension of his upper extremity. Patient 6's CAHAI score pre-CIMT was 3, and he required a moderate level of support to complete the task. After CIMT, Patient 6's performance of the CAHAI washcloth task improved to the extent that he no longer required support and earned a score of 5.

Summary

In summary, stroke patients who underwent two weeks of constraint-induced movement therapy (CIMT) demonstrated positive changes at both the neurological and physical level. All patients exhibited significant differences in their hemodynamic responses after receiving CIMT and overall demonstrated greater involvement of their left hemisphere during motor tasks after therapy. A shift in cortical activity from the right hemisphere to the left hemisphere was a finding seen across several patients post-treatment. Changes in motor functioning of the affected upper extremity were measured by patients' completion of the Wolf Motor Function Test (WMFT) and the Chedoke Arm and Hand Activity Inventory (CAHAI) washcloth task. As a group, study participants significantly enhanced their performance score on both measures after therapy. Specific tasks on the WMFT that patients commonly improved their score on were those related to extension of the arm and lifting. In addition, the time patient's took to complete WMFT tasks were generally faster following treatment. Patients who experienced spasticity in their upper extremity demonstrated more difficulty, and as a result lower performance scores on the WMFT and CAHAI washcloth task.

CHAPTER V

DISCUSSION

The current study employed functional Near-Infrared Spectroscopy (fNIRS) to examine brain activity in the motor cortex of stroke patients before and after they received constraint-induced movement therapy (CIMT). Participants were administered the Wolf Motor Function Test (WMFT) to assess the functionality of their affected upper extremity and severity of motor impairment. Hemoglobin metrics, including time-to-peak/duration and the laterality index, were measured for each participant while they completed a finger tapping task and a functional motor activity from the Chedoke Arm and Hand Activity Inventory (CAHAI). Hemoglobin signal during each task was brain mapped to illustrate significant cortical activation patterns pre- and post-therapy. Upper extremity motor functioning on the WMFT and CAHAI washcloth task was measured to determine if and to what degree patients improved in their performance. Patients' motor performance was then qualitatively described in relation their neuroimaging results.

Purpose of the Study

This study examined differences in hemoglobin signal of participants with a left middle cerebral artery (MCA) stroke prior to and after receiving two weeks of CIMT. Neuroimaging research suggests CIMT facilitates neuronal plasticity and functional reorganization of cortical activity and initiates new activation in areas of the brain related to motor movement (Puh, 2012; Ro et al., 2006; Wang et al., 2012). Improvements in motor function after adult patients received CIMT have been found to correlate with increased brain activity in the motor cortices of the uninjured hemisphere via fMRI (Schaechter et al., 2002). In addition, the brain's ability to utilize unaffected neural networks to assist in motor recovery during CIMT may explain why this rehabilitation technique can influence cortical restructuring (Ward & Cohen, 2004). The use of fNIRS with hemiplegic stroke patients following various rehabilitation techniques has sparked a relatively recent interest in the field, and has led to several cross-sectional and longitudinal research projects (Lin et al., 2008). fNIRS allows researchers to map the activity of localized brain areas and provides patients mobility while hemoglobin signal is obtained (Ferrari & Quaresima, 2012), making this neuroimaging tool an ideal method for exploring brain activity in stroke patients while they perform a unimanual and bimanual task. This new imaging technology provides researchers a vast amount of information about the brain and has yet to be used with patients who experienced a left MCA stroke who receive CIMT. For the current study, it was hypothesized participants will demonstrate a significant increase in oxygenated hemoglobin signal within the motor cortex of the affected hemisphere following CIMT.

The second purpose of this study was to investigate the association between upper extremity hemiparesis and hemoglobin signal. As demonstrated in children with cerebral palsy who received CIMT (Cao et al., 2015), movement therapy initiates the rewiring of the brain to facilitate the activation of areas compromised by neurological insult. The current study utilized psychometrically sound functional performance assessments to explore therapy outcomes that were qualitatively described in to cortical changes in the brain. As a result, it was hypothesized improvements in motor functioning on both performance-based measures are expected to be reflected neurologically via neuronal recovery and plasticity (activation of new or unused brain areas) of the motor cortex, particularly in the injured hemisphere.

The present study provides further support of the role of neurorehabilitation on the brain’s ability to reorganize and recover following injury. Additional insight is gained into how neurorehabilitation facilitates the recovery of motor movement in relation to neural plasticity. The results of this study verify previous research on the use of CIMT as an effective method of treatment to improve motor abilities in an impaired limb. This study also confirms fNIRS, a relatively new neuroimaging technology, is a unique tool of collecting data on brain activity while patients complete motor tasks.

Summary of Results

Six patients at the Pate Rehabilitation facility enrolled in and completed this study. All participants were diagnosed with a left MCA stroke with resulting paresis of the right upper extremity. The ages of study participants ranged between 39 and 63 years and all were right handed. Patients had no previous diagnosis of traumatic brain injury, cerebral palsy, mental retardation/intellectual disability, autism, epilepsy, schizophrenia, pervasive development disorder, or learning disability. Prior to and at the end of receiving CIMT, patients completed a motor performance-based measure and neuroimaging session. During the neuroimaging session, participants completed a finger tapping task for both the right and left hand as well as the CAHAI washcloth task while the fNIRS machine collected data on brain activity. One hour of CIMT was provided to each participant during their treatment day at Pate for a total of 10 consecutive business days.

Patient 1's treatment regimen addressed her gross motor functioning and muscle strength in her right arm/hand. Patient 2 primarily experienced muscle spasticity as a result of her stroke whereas Patient 3 experienced some difficulty with fine motor skills. Similar to Patient 2, Patient 4 exhibited muscle spasticity and weak gross and fine motor functioning in his right fingers and arm. Patient 5 presented with low muscle tone in her right arm and fingers and displayed some resistance during her treatment sessions and required accommodations to facilitate her motivation to complete CIMT tasks. Patient 6's CIMT addressed fine motor functioning and tasks that challenged his shoulder flexion or abduction/adduction.

The statistical analyses conducted for this project were completed in two parts to address the study's research questions. First, brain activity collected from the fNIRS machine was analyzed to determine significant differences before and after CIMT. Next, participants' motor functioning on two performance measures was analyzed in relation to their hemoglobin activity.

Hemodynamic Responses

Hemoglobin data of participants' brain activity during the completion of the finger tapping and CAHAI washcloth task pre- and post-CIMT were collected from an fNIRS machine, the Hitachi ETG 4000. The data were then processed through an interface software called Hemodynamic optically measured Evoked Response (HomER). Magnetic resonance images of the brain for each participant were generated from the Hitachi ETG 4000 to illustrate the location of significant differences in oxygenated and de-oxygenated hemoglobin activity before and after therapy. To further investigate the cortical activation patterns of the significant differences in hemoglobin activity, the time-to-peak/duration and laterality index metrics were collected. The time-to-peak/duration metric analyzed the temporal features of the activation patterns and the laterality index metric analyzed the dominance of one hemisphere in controlling for certain functions. The data for the first 2 patients and pre-CIMT data for Patient 3 were not interpretable and removed from the analyses due to the time interval of tasks, resulting in insufficient hemoglobin signal that was obtained during these neuroimaging sessions.

Patient 3. Bilateral hemoglobin activity was observed during all three tasks post-CIMT. Although stronger cortical activity occurred in the unaffected hemisphere, the high time-to-peak/duration values suggest Patient 3's activation pattern post-CIMT may reflect a shift toward a profile that would be typically seen in a healthy subject.

Patient 4. The presence of significant deoxygenated hemoglobin in the affected hemisphere prior to receiving CIMT during both finger tapping tasks indicate this activity was neurologically taxing for Patient 4. After therapy, significant oxygenated hemoglobin is shown in the injured hemisphere, suggesting an early process of neuronal recovery in the affected motor areas. A shift from minimal bilateral oxygenated hemoglobin to significant localized activation patterns in unaffected hemisphere during the CAHAI washcloth task indicates Patient 4 displays an over-reliance on uninjured motor areas to complete a bimanual activity.

Patient 5. Prior to therapy, Patient 5 demonstrated significant bilateral activity during a unimanual task. Following therapy, Patient 5's activation patterns were scattered. She demonstrated an increase in bilateral activity during both finger tapping tasks. Notably, significant de-oxygenated hemoglobin appeared in both hemispheres during the left hand finger tapping task. Although her left extremity was not affected by her stroke, research has shown a decline in performance of an unaffected limb can be a result of intense treatment of an affected extremity (Cao et al., 2015). During the CAHAI washcloth task, Patient 5 displayed a shift from oxygenated (pre-CIMT) to deoxygenated (post-CIMT) hemoglobin signal. Given Patient 5's behavioral profile and approach to treatment, her imaging results suggest the introduction of CIMT may have facilitated the brain's attempt to reorganize and stimulate injured and unused motor neurons in the affected hemisphere.

Patient 6. During the left hand finger tapping task, bilateral activation with an overall decrease in oxygenated blood flow post-treatment may be explained by the nature of CIMT's emphasis on motor functioning of the affected arm/hand. A shift from localized oxygenated hemoglobin signal in the affected hemisphere pre-CIMT to bilateral activation and slight deoxygenation in the injured hemisphere post-CIMT may suggest a transfer or stabilization in the rewiring of motor neurons that would mirror a healthy subject.

Motor Functioning

A paired t-test of the sample's performance score on the WMFT and CAHAI washcloth task was conducted to determine if there was an improvement in upper extremity motor functioning after CIMT. As a group, there was a significant increase in the study sample's overall score on the WMFT and CAHAI washcloth task following therapy. An overview of the qualitative information regarding each participants' upper extremity motor functioning as well as their performance in relation to their fNIRS data is described below.

Although Patient 1 continued to struggle with activities on the WMFT that involved lifting, she demonstrated an improvement in her completion of tasks that required her to extend her arm. Prior to receiving CIMT, Patient 1 required support from the examiner to carry out the twisting motions of the CAHAI washcloth; however, she was able to hold the cloth with less support and executed more fluid twisting motions post-CIMT. Patient 2's performance on the WMFT was limited by the amount of spasticity experienced in her affected upper extremity that prevented her completing several tasks, particularly with functional grasp, which resulted in low scores. She exhibited an improvement in her ability to extend her elbow following treatment and completed more than half of the WMFT tasks faster post-therapy. In addition, Patient 2 exhibited more fluid movements and less compensatory shoulder hiking post-treatment.

Although the motor quality in her performance of the CAHAI washcloth task remained the same post-treatment, she required less assistance afterward.

Patient 3 demonstrated the ability to complete all tasks on the WMFT at a faster pace following CIMT. During the CAHAI washcloth task, Patient 3 displayed full independence in completing the activity, including fluid motor movements and good coordination and grasp. Given Patient 3 exhibited less motor impairment and relatively stronger performance on the WMFT prior to receiving CIMT, her improved performance score may explain the increased cortical activity in both hemispheres while she completed a bimanual task after therapy. These results suggest qualitatively there appears to be a strengthening of neuronal connections in brain areas related to motor planning and control that may have led to an increase in time completion of related tasks on the WMFT. It appears CIMT may have facilitated a neurological and physical recovery pattern for Patient 3 that reflects healthy individuals.

Prior to therapy, Patient 4 exhibited difficulty with tasks that required grasping and lifting objects on the WMFT, which hindered his capacity to complete certain activities in a timely fashion. Although he improved in the ability to lift items and time to complete tasks, he continued to struggle with tasks that involved grasping due to spasticity in his fingers. Although Patient 4 required less support from the examiner while completing the CAHAI washcloth task post-treatment, the extent of muscle spasticity in his affected extremity may have led to the over-reliance of motor neurons in his uninjured hemisphere to complete the bimanual task.

On the WMFT, Patient 5 was able to complete tasks that she had difficulty with prior to CIMT more quickly after therapy, despite poor fluidity of her upper extremity motor functioning. For the CAHAI washcloth task, she improved in wrist extension and needed little support post-therapy. Patient 5's initial resistance to completing the CIMT protocol may explain why upper extremity tasks were neurologically taxing on motor areas of the brain. In addition, her neuroimaging results and motor performance may not accurately represent her true capabilities due to compliance concerns related to treatment.

Patient 6's performance on the WMFT greatly improved on activities related to grasp, grip, and elbow extension following his CIMT regimen. Although he continued to struggle to complete fine motor tasks, he no longer required assistance with completing the CAHAI washcloth task. Patient 6's presentation of his motor skills after therapy suggest CIMT may have facilitated functional use of his upper extremity, which is reflected in the cortical reorganization and hemoglobin activation patterns that are typically seen in healthy participants.

Implications for the Field of Neurorehabilitation and Pediatric Psychology

Emerging research in the field of neurorehabilitation has focused on brain injuries and the foundational mechanisms in recovery and neural plasticity. Innovative neuroimaging technology promotes research on more efficient rehabilitation procedures and has led to the assessment of various interventions (Pajaro-Blázquez & Pons, 2014). Therapies that facilitate cortical activation as well as behavior modification, such as CIMT, appear to take on an adaptive function in an affected brain. As a result, noninjured brain areas are reorganized and clinical progression is seen after rehab (Cecatto & Chadi, 2007).

fNIRS is a distinct neuroimaging device in that it is noninvasive and portable. It enables participants to move, making it an efficient tool when analyzing brain activity during unimanual and bimanual tasks. Utilizing fNIRS enabled the current study to map cortical plasticity related to motor functioning before and after therapy that would not be otherwise determined by solely examining changes in clinical scores (Cao et al., 2015). Although introduced 20 years ago, fNIRS is gaining wide use as the field of neurorehabilitation progresses and the demand for alternative non-invasive procedures rise.

Pediatric Psychology

Research suggests the recovery of motor functions depends on the amount of injury to the corticospinal tract (Ward & Cohen, 2004). Traditional views of how the brain recovers, susceptibility to the loss of previously acquired skills, and the development of new skills has been challenged by the plasticity-vulnerability debate. The plasticity perspective proposes that the brain of a younger child is less functionally dedicated to specific skills than the brains of older children or adults. As a result, skills and abilities that are believed to be affected by injured brain regions may be more readily reorganized or transferred to a different region (Anderson et al., 2010). The early vulnerability perspective poses that the brains of younger children may be exceptionally vulnerable to injury and trauma. Furthermore, children who sustain injury in infancy and early childhood are the most at-risk for developing deficits compared to adolescents (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Anderson et al., 2010; Luciana, 2003). The inclusion of adults in the present study provides a unique perspective of how neurological recovery is present in adulthood and the sequela of motor recovery in life-span development.

In addition to stroke, school-aged children suffer from a number of conditions that result in neurological insult and affect brain areas related to motor functioning, including spina bifida, brain tumors, traumatic brain injury, acute disseminated encephalomyelitis, and a lack of oxygen at birth. CIMT is a well-established rehabilitation method for both children and adults (see Chapter 3 for a review of CIMT used in adults) and can be implemented with students who present with a variety of motor programming difficulties, such as apraxia, or difficulties with writing, and receive occupational therapy services. Pediatric research employing fNIRS and CIMT for children diagnosed with cerebral palsy suggests fNIRS helps explain the neurological and physical changes seen as a result of CIMT (e.g., Cao et al., 2015; Sterling, Taub, Davis, Rickards, Gauthier, Griffin, & Uswatte; Taub, Ramey, DeLuca, & Echlos, 2004). Because fNIRS is non-invasive, its use in children can be viewed as a preferred method of collecting imaging data. Although a specific certification or degree is not required for administering CIMT, training to administer this therapy is accessible to professionals from any discipline. Furthermore, occupational and physical therapists are typically familiar with movement therapy given their educational background.

Limitations

There are some limitations that should be noted for the current study, such as the sample size, missing data and resulting changes in the fNIRS protocol, unknown activation patterns for the CAHAI washcloth task, and the interplay of receiving multidisciplinary rehabilitation services when targeting outcomes of a specific treatment. Each limitation is reviewed in the following paragraphs and should be taken into consideration when interpreting the results.

Sample Size

Due to the specificity in criteria and availability of participants eligible during the year of the implementation for this study, the resulting sample size was lower than expected and relatively small compared to similar research studies. A literature review of the number of people who partake in studies related to neuroimaging and rehabilitation/ movement therapy indicated the most frequent sample size to be approximately 10 participants. The study's small sample size limits the results in its generalizability of patients with a left MCA stroke as well as the researcher's ability to conduct more comprehensive statistical analyses that could investigate the impact of other variables, such as gender, on the results.

Missing Data and Change in Protocol

Another limitation to this study includes missing fNIRS data for Patients 1 and 2, and pre-CIMT data for Patient 3. Because the original neuroimaging protocol entailed shortened time intervals between tasks and a limited number of task trials, the fNIRS machine was unable to collect sufficient hemoglobin signal to map significant differences or collect data on time-to-peak/duration and the laterality index. To address missing data, further consultation with fNIRS experts Dr. Alexandrakis and Ms. Cao at the University of Texas at Austin led to an updated protocol per their recommendations. Although Patient 3 participated in the updated protocol post-CIMT, the interpretation and conclusions drawn from her fNIRS data is restricted.

Activation Pattern Comparison for the CAHAI

Although cortical activation patterns of the finger tapping task are well established in both healthy and clinical populations, this is the first study to obtain imaging data for the CAHAI washcloth task. While a general interpretation of changes in the activation patterns for the CAHAI washcloth task pre- to post-CIMT can be made, a comparison of the results to other stroke patients or healthy subjects cannot be made.

Multidisciplinary Rehabilitation

The degree to which CIMT solely improved participants' motor functioning and facilitated neuronal recovery is difficult to conclude because participants received multidisciplinary treatment at the rehabilitation center, such as occupational, physical, and speech therapy. Although the developer of CIMT intended it to be the primary modality of treatment administered as six-hour sessions, it continues to be empirically supported and effective when administered in shorter sessions (e.g., three hours; Grotta et al., 2004). Although the current study employed CIMT for one-hour every business day for two weeks, the inclusion of additional rehabilitation services may have over-represented the magnitude of the results and facilitated a greater extent of improvement, both neurologically and physically, compared to patients who receive CIMT as their primary treatment.

Recommendations for Future Research

The current study employed a relatively new neuroimaging technique, fNIRS, to investigate brain activity in stroke patients following a modified version of CIMT; thus, it is essential for the outcomes of this project be replicated to establish further validity and reliability in the utilization of these methods in neurorehabilitation. Future studies should narrow a specific age range of participants to address the brain's plasticity and recovery at various stages of development. The interplay of brain diseases in adults, such as dementia and Alzheimer's, and one's risk for developing such neurological conditions may impact neuronal recovery.

Research suggests the use of CIMT has long-term improvements in stroke patient's motor functioning (Grotta et al., 2004; Kunkel et al., 1999; Liepert et al., 1998; Wolf et al., 1989). Therefore, additional research using fNIRS is needed to investigate the retention or long-term physical and neurological impact of CIMT and predict functional outcomes. In addition, the current study recruited patients who were right-hand dominant with a left hemisphere stroke. Given that brain plasticity and the recovery of certain skills may differ depending on the hemisphere and location of insult, hand-dominance plays a crucial role in the effects of movement therapy on the functional use of an extremity. A replication of this project with patients who are left-hand dominant would provide information regarding the differentiation in recovery patterns and its impact on functional performance.

An important factor that determines the outcome of neural recovery is the condition of the brain prior to injury. Because the brain mediates all learning, the rate at which a person is able to relearn or acquire new information is affected by the severity of injury. Thus, it is expected that patients with more severe brain injury would possess a slower acquisition of learning, therefore requiring longer periods of rehabilitation or treatment (Gordon & Hibbard, 2005). Additional research that investigated the extent to which fNIRS data and CIMT recovery outcomes differ among stroke patients with varying degrees of severity would benefit the field of neurorehabilitation. Lastly, it is recommended a large sample size should be recruited, which would enable future researchers to conduct statistical analyses and investigate the implications of variables such as gender differences in hemodynamic activation patterns as past research suggests (Okada et al., 1994). Utilizing a control group will also allow future researchers to compare and contrast results to patients with stroke and brain injury.

Summary

In the current study, functional Near-Infrared Spectroscopy (fNIRS) was used to map neural plasticity in adult stroke patients to help explain alterations in motor function following constraint-induced movement therapy (CIMT). Changes in upper extremity motor performance were examined by the Wolf Motor Function Test (WMFT) and Chedoke Arm and Hand Activity Inventory (CAHAI) washcloth task while fNIRS collected hemoglobin data and cortical activation patterns. Although every patient posed his or her own unique pattern of neuronal recovery, the findings confirm and further support the empirical use of CIMT as a valuable rehabilitation treatment to not only enhance the functionality of an impaired limb, but also facilitate the brain's ability to recover from insult and the process of neural plasticity in adult stroke patients.

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APPENDIX A

Wolf Motor Function Test Data Collection Form

WOLF MOTOR FUNCTION TEST
DATA COLLECTION FORM

Subject's Name: ______________________________________ Date: ____________________

Test (check one): Pre-treatment _____ Post-treatment _____ Follow-up ____

Arm tested (check one): More-affected ______ Less-affected _____

Task	Time	Functional Ability	Comment
1. Forearm to table (side)		0 1 2 3 4 5	
2. Forearm to box (side)		0 1 2 3 4 5	
3. Extend elbow (side)		0 1 2 3 4 5	
4. Extend elbow (weight)		0 1 2 3 4 5	
5. Hand to table (front)		0 1 2 3 4 5	
6. Hand to box (front)		0 1 2 3 4 5	
7. Weight to box	______________________________lbs.		
8. Reach and retrieve		0 1 2 3 4 5	
9. Lift can		0 1 2 3 4 5	
10. Lift pencil		0 1 2 3 4 5	
11. Lift paper clip		0 1 2 3 4 5	
12. Stack checkers		0 1 2 3 4 5	
13. Flip cards		0 1 2 3 4 5	
14. Grip strength	______________________________kgs.		
15. Turn key in lock		0 1 2 3 4 5	
16. Fold towel		0 1 2 3 4 5	
17. Lift basket		0 1 2 3 4 5	