Abstract

Comparing Outcomes for Normal Aging and Post Stroke Populations in Interactive Metronome® Therapy

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The purpose of this study was to compare post-stroke and normal aging populations' outcomes on the Interactive Metronome® and functional motor measures after completion of Interactive Metronome® protocols. Data from a previous study with healthy participants was compared with data gathered from post-stroke participants. Percentages of change from pre- to post-test measurement with the Long Form Assessment of the Interactive Metronome® and the Nine Hole Peg Test were compared. Overall, both groups showed improvement on the outcomes, with the healthy participants averaging higher percentages of change. Data analysis did not find statistically significant differences between groups on any measure, indicating that the Interactive Metronome® may equally be effective with a post-stroke population as with the healthy aging population. These results give preliminary evidence that the Interactive Metronome® may be an effective tool in stroke rehabilitation, and add to the body of evidence that incorporating Interactive Metronome® therapy into occupational therapy interventions can lead to successful outcomes.

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CHAPTER 1: Problem Formulation

The Interactive Metronome® (IM®) is an intervention tool that can be used in rehabilitation programs for many diagnoses, including traumatic brain injury, Parkinson's disease, attention deficit hyperactivity disorder, and stroke (Interactive Metronome®, 2007). The basis for its therapeutic effects lies in the fact that accurate timing of neuronal firing in the nervous system is necessary for every process within the brain, whether it is cognitive or motoric. When there is dysfunction in the brain, these processes and their underlying timing can be disrupted, leading to various impairments. Fortunately, the natural plasticity of the brain provides the potential to regain or improve function when new pathways and synapses are established or existing ones are strengthened for increased efficiency. This plasticity is the target of IM® intervention, which employs bilateral coordination and repetitive motion synchronized to a reference tone, with guide sounds and a visual display providing feedback. Theoretically, as timing is improved, the processes it supports increase in accuracy and efficiency, and impairment is reduced (Interactive Metronome®, 2007).

While the IM® is used as an intervention in many fields, it could be an important tool in occupational therapy, as reduced impairment in function supports increased engagement in occupations and participation in life. As clients in occupational therapy identify valued occupations in which they are experiencing difficulty, the IM® can be utilized to improve the performance skills underlying those difficulties, enabling participation. The majority of individuals will seek assistance or therapy when they find that their lives are impacted by a disabling factor, and many of the complaints that come to occupational therapists can be addressed by the use of the IM®. Currently, although anecdotal evidence for the effectiveness and benefits of IM® therapy is available, actual research supporting its use is limited. As the field of occupational therapy seeks to support its profession through a knowledge base with which to engage in evidence-based decision making (EBDM), research with the various populations IM® therapy has been proposed for is crucial. The aim of this research is to investigate outcome performance in the post-stroke population as compared to a normal aging population, in both IM® outcome measures and in measures of motor performance.

CHAPTER 2: Review of the Literature

Stroke Incidence and Etiology

Cerebrovascular accident (CVA), or stroke, is the leading cause of disability and the need for long-term care in the United States (Llinas, 2007). According to the American Heart Association (2010), every 40 seconds in the U.S. someone suffers a stroke. Despite incidence of stroke remaining high, there has been a 33.5% decline in the annual rate of stroke deaths between 1996 and 2006, likely due to advances in acute and emergent care (American Heart Association [AHA], 2010). With more individuals surviving stroke, costs associated with long-term disability have increased, including hospitalization, nursing home care, home health care, and durable medical equipment, so that now the estimated total annual direct and indirect economic burden in the United States is approaching $74 billion (AHA, 2010). Residents who were born and raised in the Stroke Belt, which includes the states of North Carolina, South Carolina, Georgia, Tennessee, Arkansas, Mississippi and Alabama, are at the highest risk for stroke (Glymour, Kosheleva, & Boden-Albala, 2009). Recently, regional studies have indicated the average age of stroke victims has dropped by nearly three years, as increasingly younger individuals suffer strokes (Laino, 2010). It is clear that research validating effective rehabilitation to regain function and maximize independence is needed to not only lessen economic burden, but also to restore interrupted lives.

A stroke is defined as a focused, neurological event that is primarily vascular in nature, and may be further classified as ischemic or hemorrhagic. Stroke that is due to an interruption of blood supply to an area of the brain is known as ischemic stroke and is responsible for 80% of all strokes (Llinas, 2007). This loss of blood supply can be due to artery blockage by emboli that have traveled from another source and become lodged, or due to blockage or stenosis as seen in thrombosis. This blockage results in a hypoperfusion of the blood in the tissues the affected arteries supply. Hemorrhagic stroke occurs when there is disruption of the blood supply due to bleeding into the brain. This is often due to the weakening of vessel walls due to hypertension, vascular malformations, or bleeding disorders. Tissue death is related to increased intracranial pressure from pooling blood and hypoperfusion of tissues downstream from the affected vessel. Lacunar strokes are ischemic in nature but typically involve smaller, deeper vessels. Transient ischemic attacks (TIAs) result from temporary hypoperfusion in the brain, often due to arterial stenosis, in which symptoms usually resolve in less than 24 hours (Llinas, 2007).

Symptoms and deficits resulting from strokes relate to the location of the tissue death and the amount of tissue death or the size of the stroke. The location of the stroke depends on the artery affected and the area of the brain it supplies. Three main arteries that can be affected are the anterior, middle and posterior cerebral arteries. The anterior cerebral arteries (ACA) supply the anterior frontal lobes and the medial portions of both hemispheres. A stroke involving the ACA can present with contralateral hip and leg paresis and sensory loss, loss of urinary control, and decreased cognitive spontaneity (Llinas, 2007). The middle cerebral artery (MCA) is the primary source of circulation for a majority of the cortex, supplying the frontal, parietal, and temporal lobes, and white matter deep within the brain (Llinas, 2007). Depending on the hemisphere and area affected, MCA strokes may present with aphasia, eye gaze deviation, contralateral hemiplegia which is most severe for the face and upper extremity, sensory loss, and contralateral neglect or inattention (Llinas, 2007). The posterior cerebral arteries (PCA) supply the occipital and medial temporal lobes and thalami, and strokes involving these areas may present in contralateral visual field loss, and memory deficits or confusion (Llinas, 2007). Other arteries affected may supply the cerebellum, brainstem, or cranial nerves and result in deficits related to the functions of those areas of the brain.

The tissue of the brain is densely packed with neurons, intricately and extensively connected to one another. Like any other cell, the neuron is dependent on a constant supply of blood for the nutrition necessary to operate its machinery and send signals to other neurons. Without oxygen and other various proteins, ions, and molecules, the neuron eventually dies through a cascade of events involving metabolic failure, excitatory neurotoxins, necrosis, and apoptosis (Llinas, 2007). With neuronal death, signal pathways are interrupted and functional communication not only within but amongst brain regions is disrupted, resulting in the clinical deficits seen. Previously thought to be limited only to prenatal and perinatal development, it is now generally accepted that the generation of new neurons may occur in adulthood (ref needed). However, it is under debate whether neurogenesis is limited to subventricular and hippocampal areas of the brain or occurs elsewhere in the cortex and cerebellum, and further whether these processes might be enhanced and utilized following stroke (Arvidsson, Collin, Kirik, Kokaia, & Lindvall, 2002; Colucci-D'Amato, Bonavita, & di Porzio, 2006; Marti-Fabregas et al., 2010; Rossini & dal Forno, 2004). While some amount of recovery after incidence of stroke occurs spontaneously, typically it does not constitute a full functional recovery (Cheatwood, Emerick, & Kartje, 2008; Cramer & Riley, 2008). Research is needed and ongoing to determine not only what biomedical interventions but also what therapeutic interventions might optimize the amount of recovery after a stroke (Cheatwood et al., 2008; Cramer & Riley, 2008).

Current Practices in Rehabilitation

After a stroke occurs, it is the physician's priority to minimize the extent of damage and prevent further stroke from occurring. Once survivors are stabilized, it is the rehabilitation team’s priority to help recover function. Occupational therapy is a vital part of this team, typically focusing on upper extremity, fine motor, and cognitive function for participation in activities of daily living (ADLs) and other client-valued occupations (Levitt & Aldrich, 2007). Rehabilitation may begin in the acute setting and then continue in a variety of settings (inpatient, outpatient, and home health) for several months. Duration and frequency of rehabilitative therapies is dependent on the severity of stroke deficits, future discharge environment and support, and client progress. For survivors of stroke, it is suggested that the greatest recovery of function occurs in the first three to six months, although improvement may continue more slowly past this timeframe, and there has been functional magnetic resonance imaging (fMRI) evidence of functional improvement related changes even one to nine years post-stroke (Carey, L. et al., 2002; Tombari et al., 2004). In a review of data from positron emission tomography (PET), fMRI, and transcranial magnetic stimulation (TMS) studies, Nelles (2004) concludes that “training-induced” plasticity is possible in not only the acute but also the chronic phase of stroke (p. 242). Murphy and Corbett (2009) suggest that while the mechanisms that support plasticity in the months after stroke do indeed decrease, they do not cease altogether, and therefore the window of recovery is never truly closed. It has also been suggested that the usual course of reducing therapy amount or frequency over time may actually contribute to the phenomenon of “plateau” in stroke, and that it may be similar to the plateau frequently seen in sport training and exercise regimens as neuromuscular adaptation sets in when variability is lacking (Demain, Wiles, Roberts, & McPherson, 2006; Page, Gater, & Bach-y-Rita, 2004). However, unfortunately in today’s managed-care systems, reimbursement for services provided typically hinges on evidence of progress, and if a patient fails to show further improvement following a stroke, reimbursement and services will cease (Page et al., 2004).

The implication of these timeframes and practices is obvious for the practitioner looking for rehabilitative strategies and interventions for a client who is post-stroke. In occupational therapy, the overall goal is to increase function and participation in valued occupations, although interventions may target the underlying client factors and performance skills inhibiting performance (Sabari & Lieberman, 2008). Many different modalities exist in the rehabilitation of underlying deficits after stroke, most of which operate on the basis of neuroplasticity and neuromuscular re-education, however, there is little conclusive evidence to support their use (Patel & Rudd, 2004). A few modalities, such as rhythmic auditory cueing, also target the timing and synchrony within the brain, and show promising results, although again, research is limited (Malcolm, Massie, & Thaut, 2009; Thaut, Kenyon, Hurt, McIntosh, & Hoemburg, 2002; Thaut, McIntosh, & Rice, 1997). It is clear that novel, evidence-based approaches that incorporate motor learning principles are needed, and that practitioners may need more than one approach in their toolbox as they work with a client over time.

The Interactive Metronome®

One such tool that is receiving attention and demonstrates this potential is the Interactive Metronome® (IM®). The IM®, developed in 1992 and later patented by James F. Cassily, is unique from a standard metronome in the "interaction" it provides (Shaffer et al., 2000). Through computer technology and special software, the IM® provides a metronome beat, and precisely measures the listener's motor response activating a trigger on that beat to within 0.5 milliseconds (ms). Guide sounds as well as visual cues are then used as feedback from the motor response, indicating whether the response was "right on" (within 15 ms), mildly early or late (15ms to 100ms), or very early or late (over 100ms). These parameters may be adjusted to enhance training or decrease frustration. The three categories of guide sounds are distinguished by tone as well as spatially; early tones are heard in the left ear's headphone, late tones are heard in the right ear, and "right on" tones are heard in both ears. These guide sounds are used to train the listener to make the appropriate adjustments to his/her motor response. Initially these corrections require conscious effort, but as training progresses they become more automated and timing improves.

The IM® software also provides a variety of exercises or movements that can be used in treatment to help coordinate the body's movements; for example, bilateral movements and movements that involve crossing the body's midline. These exercises can be adapted in many ways, and exercises may be created as needed to match client ability and needs. Scores for average ms away from the beat, and other data regarding the performance such as percentage of "right on" hits and highest number of "right on" hits in a row are presented at the end of each exercise. Keeping track of progress and competing against themselves can be highly motivating for clients using the IM®. The Interactive Metronome® also includes two assessments within its software to evaluate performance and progress: the Short Form Assessment (SFA), consisting of two short clapping tasks, and the Long Form Assessment (LFA), consisting of fourteen short tasks involving both the upper and lower extremities. These assessments have been age-normed for ages 6 through adult, and measure accuracy of performance in milliseconds (ms). Determining whether the IM® is an effective intervention for improving motor performance post-stroke, as well as whether it could be an assessment tool in measuring progress in recovery from stroke were two major questions this study aimed to address.

Plasticity

The basis for the rehabilitative potential of the Interactive Metronome® lies in the plasticity of the human brain and the use of timing, rhythm, and synchronization to improve processes underlying motor behavior. The brain's capability for plasticity is the basis of rehabilitation in stroke, and typically refers to various processes of reorganization, recruitment, and remodeling within the brain. "Hebbian" plasticity refers to the changing of strength of transmitted signals at existing individual synapses through long-term potentiation (LTP) or long-term depression (LTD) processes (Butz, Worgotter, & van Ooyen, 2009). Another type of plasticity, known as structural plasticity, involves processes such as changes in the number of synapses, the formation of dendritic spines, the growth, branching, or retraction of axons and dendrites, and synaptic rewiring (Butz et al., 2009). These two types of plasticity are inter-related: for example, dendritic spines and synapses may be either strengthened and stabilized via LTP, or may be weakened and eventually retracted via LDP (Butz et al., 2009). By these mechanisms, new connections between neurons are formed, and these connections strengthened. Originally, this plasticity was thought to be mainly confined to infancy and early childhood, however recent evidence shows it can occur throughout adulthood, and moreover, is activity- or experience-dependent (Butz et al., 2009; Gynther, Calford, & Sah, 1998; Mora, Segovia, & del Arco, 2007). This refers to the concept that synapses and pathways that are activated or used more (via activity or behaviors) will be strengthened, while synapses and pathways that are not will become weaker.

Plasticity and Aging

Given that the majority of stroke survivors are older adults (AHA, 2010), it is important to consider the effects of aging on plasticity within the brain. Some research suggests that plasticity in the motor cortex is reduced in elderly (ages 60-79) but not in middle-aged (ages 40-59) adults (Fathi et al., 2010). Different areas of the brain may age differently than others, and studies have shown that there may be an overall decline in amount of gray matter in the brain as it ages. However, this is not due to a significant loss of neurons, but is proposed to be rather a decline in the number of dendritic spines and synaptic density (Mora et al., 2007). Expression of neurotrophic factors that may influence plasticity processes, such as nerve growth factor (NGF) or brain-derived neurotrophic factor (BDNF), may also be reduced in aging brains. However, animal studies have shown that many of the factors involved in plasticity, such as dendritic branching and spine density, are responsive to an enriched environment and the physical and mental activity it promotes (Mora et al., 2007). Additionally, recent research has shown that gene expression of important neural growth factors is increased for a period of time following a stroke (Carmichael, 2006; Murphy & Corbett, 2009), and plasticity in the mature brain may actually be at its highest following lesion or injury (Rossini et al., 2007).

Plasticity and the Motor Cortex

Considering that 50% to 80% of stroke survivors are affected by motor deficits (Calautti & Baron, 2003; Kwakkel, Kollen, van der Grond, & Prevo, 2002; Mayo et al., 1999; Nelles, 2004), it is important to specifically consider the properties of the motor cortex within the context of plasticity. The “homunculus” is commonly used to portray the somatotopy or representational mapping of the parts of the body onto the primary motor cortex (Marieb & Hoehn, 2007). However, recent research indicates that this specific corresponding organization may only follow along the major zones of the body, such as arm or leg. Within these body regions, instead of a strictly organized, point-to-point representation, there exist numerous broadly distributed networks that even functionally overlap (Sanes & Donoghue, 2000). Distinct movements may therefore be controlled by differing patterns of activation of a broad network within the cortex for that body region. Within a network, neurons also have vast horizontal connections, enabling them with the capability to participate in the activation patterns for all possible movements (Sanes & Donoghue, 2000). These horizontal connections, may be unmasked by disinhibition or strengthened by activity-dependent processes of LTP. This system of motor control allows for the flexibility we see evidenced by motor skill learning and relearning via the mechanisms of plasticity.

Indeed, a great deal of research has shown evidence that the primary motor cortex undergoes long-lasting reorganization in response to a variety of conditions (Sanes & Donoghue, 2000). Some of the proposed mechanisms of plasticity in motor recovery following stroke include: localized reorganization (“remapping”) in the areas adjacent the lesion in the primary motor cortex, higher activation of non-primary motor areas, recruitment of motor networks in the non-lesioned hemisphere, and normalization of cortical overactivation (Askim, Indredavik, Vangberg, & Haberg, 2009; Cauraugh & Summers, 2005). Interestingly, Wittenberg (2010) in noting that signals from output neurons in the primary motor cortex are passed along the brainstem and spinal cord to lower motor neurons before finally activating muscles, indicates that plastic changes could also be occurring below the level of the motor cortex.

Plasticity and Recovery in Stroke

When considering recovery in stroke, it is suggested that the term “functional recovery” may be more applicable (Murphy & Corbett, 2009). With the neuronal loss and the subsequent disruption of their circuitry, it is highly improbable that post-stroke movement patterns will be exactly the same as pre-stroke movement patterns. It is more likely that improved motor performance represents a combination of compensatory movement patterns as well as recovery of functional neuronal circuitry for that movement. Whether it occurs through new motor learning or true recovery, brain plasticity and reorganization seem to be “the primary observable neuroanatomical phenomenon associated with functional recovery from stroke,” and it is suggested that interventions targeting this plasticity may be the key to optimal recovery (Cheatwood et al., 2008, p. 43).

Plasticity following stroke may make use of the previously mentioned horizontal connections, or “redundant connectivity,” within multiple expansive cortical networks as previously silent neurons are unmasked and neurons from other pathways are recruited to form new pathways to accomplish the neuronal communication and functions lost in a stroke (Gynther et al., 1998; Murphy & Corbett, 2009, p. 862). Current research has shown that the brain’s response to stroke appears to be different from its response to trauma in that a “growth-permissive” environment is created by the upregulation of growth-inducing molecules rather than growth-inhibiting ones, allowing axonal sprouting to take place surrounding the lesion and in other functionally connected areas (Carmichael, 2006, p. 737). Evidence also suggests an overall process of early disinhibition and excessive formation of synapses and connections followed by a period of pruning back and normalization of activity (Butefisch, 2004; Calautti & Baron, 2003; Murphy & Corbett, 2009; Rossini et al., 2007). In the affected hemisphere, cortical areas adjacent to the lesion may experience reorganization as decreased inhibition enhances the formation of new synapses and axonal sprouting. In the penumbra area surrounding the lesion site, neurons suffer reduced oxygenation during stroke but recover when blood flow is restored to the area. As a result, this area is a site of much activity-dependent reorganization and competition for cortical map territory (Murphy & Corbett, 2009). Various studies have found shifts or expansion of cortical areas associated with recovery of function in a body region (Butefisch, 2004; Calautti & Baron, 2003; Carey L. et al., 2006; Rossini et al., 2007).

A study by Bastings, Greenberg, and Good (2002) used transcranial magnetic stimulation (TMS) to map the motor output areas of the cortex in 12 stroke patients and 12 control subjects.

Through the TMS mapping, the authors could identify the relative location and size of the motor areas specifically for the hand, and then compared this data with measures of hand motor function. Stroke patients classified as having intermediate or poor outcomes were found to have significantly smaller map surface areas and weights for the cortical hand area in the affected hemisphere. Map areas in the non-affected hemisphere for these patients showed no significant differences from the control group. For the group of stroke patients with good outcomes, there were no significant differences for either map area or weight compared to the control group; in fact, the cortical hand motor output areas in the stroke hemisphere were often larger than their corresponding motor areas in the non-affected hemisphere (Bastings et al., 2002).

Regarding the unaffected hemisphere, there is general consensus that it is involved in the recovery process, but there is some debate about what role it plays. Some research points to increased activation in the unaffected hemisphere and the recruitment of ipsilateral motor areas as a beneficial and adaptive response in stroke patients with good recovery of motor function (Butefisch, 2004). Other research suggests that the use of these ipsilateral areas and pathways in motor recovery denotes an incomplete recovery in the brain's inability to use normally lateralized activation, and suggest that ipsilateral control is less efficient than ipsilesional (contralateral) control (Calautti & Baron, 2003; Calautti, Leroy, Guincestre, Marie, & Baron, 2001; Carmichael, 2006; Murphy & Corbett, 2009; Serrien, Strens, Cassidy, Thompson, & Brown, 2004).

In a review of neuroimaging studies on plasticity during recovery from stroke, Rossini and colleagues (2007) found overactivation of ipsilesional pre-motor and non-motor areas as well as supplementary motor areas in both hemispheres, suggesting enhanced recruitment of cortex both outside of and within the usual physiological networks for motor control. In looking at longitudinal imaging studies, they found a correlation between higher measures of recovery and balanced activation between hemispheres, noting weak activation of the affected hemisphere in those individuals with poor recovery (Rossini et al., 2007). Nelles (2004) notes that early on in the recovery process, bilateral activation in motor control may be beneficial for motor recovery, but that a shift from contralesional activation to ipsilesional activation (normalization of activation) in control of the affected extremities appears to be associated with better motor recovery (Calautti & Baron, 2003). In their study of 12 patients post-stroke, Askim et al. (2009) also noted that the return of lateralization of motor control was associated with better recovery. They also suggest that the patterns and locations (cerebellar and striatal) of brain activation found early on in recovery are associated with those found in motor learning, such as in unconscious and conscious monitoring of feedback and correction of performance (Askim et al., 2009). Additionally, they found increased activation in locations associated with sensory input integration, such as bilateral thalami and somatosensory association areas, and suggest activity in these areas is associated with better motor recovery (Askim et al., 2009).

A meta-analysis and systematic review done in 2008 found strong evidence that activity-dependent movement training of the upper extremity resulted in cortical plasticity changes in the affected hemisphere after stroke (Richards, Stewart, Woodbury, Senesac, & Caraugh, 2008). From the 13 studies included, they found that these plastic changes, such as enlarged dedicated cortical areas and increased activation within the affected hemisphere, were associated with functional motor improvement. The authors cite this along with other studies as further evidence that increased activation of the affected hemisphere (versus the unaffected hemisphere) in control of the paretic arm is associated with better recovery and functional use of that arm (Richards, Stewart et al., 2008). While the cause and outcome of abnormal activation balance between hemispheres remains unclear, some suggest that it does play a role in spontaneous recovery after a stroke (Cramer & Riley, 2008).

Bilateral Movement

One of the interventions receiving much attention in stroke rehabilitation research is constraint-induced movement therapy (Taub et al., 1993). The basis for this therapy is that by compensating with the unaffected limb to accomplish tasks, patients may hinder recovery of the affected limb, or may fall into the phenomenon of learned dis-use. Constraining the unaffected limb forces the patient to use the affected limb. Many studies show positive functional gains with this therapy, however, there are limitations in that typically only patients with mild to moderate severity of stroke are candidates (Liepert, Bauder, Miltner, Taub, & Weiller, 2000; Stoykov & Corcos, 2009; Stoykov, Lewis, & Corcos, 2009). However, this type of therapy does not focus on the practice of tasks requiring bimanual coordination, which most activities of daily living involve (Tabak & Plummer-D'Amato, 2010). Research now suggests that incorporating the unaffected limb into bilateral therapeutic interventions may provide a facilitative influence for the recovery of the affected limb (Cauraugh & Summers, 2005; Cunningham, Stoykov, & Walter, 2002; Renner, Woldag, Atanasova, & Hummelsheim, 2005). Additionally, this type of therapy would not exclude, and may even especially benefit plasticity processes in patients with moderate to severe strokes (Mudie & Matyas, 2000).

The theory behind bilateral therapy lies in the view of the upper extremities as a "centrally linked coordinative unit" wherein their use together in a coordinative fashion is related to activation of a widely distributed neural network (Cauraugh & Summers, 2005, p. 311; Swinnen & Wenderoth, 2004). When performing tasks requiring the coordination of two hands, there is a propensity of the limbs to synchronize, both spatially and temporally (Swinnen &

Wenderoth, 2004), also known as the symmetry constraint (Cunningham, et al., 2002; Stoykov & Corcos, 2009). This synchronization between homologous muscle groups is proposed to operate via trans-corpus callosum communication and perhaps the facilitation of one hemisphere by the other (Swinnen & Wenderoth, 2004). Indeed, research has shown synchronization between hemispheres during the organization of bilateral movements and learning of bilateral skills (Andres et al., 1999; Serrien & Brown, 2002). In healthy adults this synchronization is typically "led" by the dominant hand or hemisphere; in a person with stroke, the hope is that the intact hemisphere will entrain the movement of the paretic limb and lesioned hemisphere to the unaffected movement (Cauraugh & Summers, 2005). While some research has supported this (Cunningham, et al., 2002), other studies have found the unaffected arm slowing velocity to match the affected limb (McCombe-Waller, Harris-Love, Liu, & Whitall, 2006).

Another potential facet in the basis of bilateral movement is the "cross transfer" or "cross education" effect (Tabak & Plummer-D'Amato, 2010, p. 15). This is the phenomenon of increased muscle strength in an untrained extremity after resistance training in the contralateral extremity. While the underlying mechanisms are not well understood, the reduced inhibition between hemispheres and increased cortical excitability found during bilateral movements may be responsible (Tabak & Plummer-D'Amato, 2010). Studies have shown increases in electromyography (EMG) recordings for paretic limbs when movements are done bilaterally versus unilaterally, even in densely hemiplegic extremities, as well as in both acute and chronic stroke survivors (Cauraugh & Kim, 2003; Mudie & Matyas, 2001).

According to a review by Stoykov and Corcos (2009), the recruitment and facilitation of ipsilateral corticospinal pathways (uncrossed fibers), activation of the contralesional hemisphere, and the normalization of balance of activation and inhibition between hemispheres are among the mechanisms suspected to underlie improvements in function after bilateral training. As limbs are moved symmetrically, the motor control areas in the bilateral hemispheres are activated and the intracortical inhibition that normally serves to eliminate associated mirror movements is reduced (Cauraugh & Summers, 2005; Stinear & Byblow, 2002). Often in stroke, the unaffected hemisphere demonstrates conditions of over-excitability and over-activation; however, whether this is due to compensatory mechanisms of recovery in the brain or to disruption in the balance of activation between hemispheres remains unclear (Cauraugh & Summers, 2005). If one hemisphere is significantly damaged, as in stroke, that hemisphere may be less able to inhibit the intact hemisphere, leading to the condition of over-excitation, a byproduct of which would then be increased inhibition back to the lesioned hemisphere (Cauraugh & Summers, 2005). This increased inhibition of the lesioned hemisphere may interfere with recovery processes. It is suggested that bilateral movement may help to reduce abnormal inhibitory effects of the intact hemisphere on the lesioned hemisphere, hence facilitating its role in motor control and recovery (Cauraugh & Summers, 2005; Stinear & Byblow, 2002). Comparing bilateral sequential movements to bilateral simultaneous movements post-stroke, researchers found that in simultaneous movement, greater coupling of movement time and velocity were present, and suggest mutual disinhibition between hemispheres may improve activation for the affected limb (McCombe-Waller, et al., 2006).

Another aspect of normalizing hemispheric interaction and bilateral coordination is the role of sensory integration between the hemispheres. As the brain uses afferent sensory feedback to guide and refine movements, especially in coordination, having reduced or normalized inhibition into the lesioned hemisphere may help potentially weak or incomplete incoming sensory information be integrated and used more effectively in plastic reorganization (Cauraugh

& Summers, 2005). Stinear and Byblow (2002) found that passive movement of a limb during bilateral symmetrical training provided sufficient afferent information to decrease inhibition.

Evidence for bilateral movement in stroke rehabilitation appears to have been accumulating significantly in recent years. A study done by Whitall, Waller, Silver, and Macko (2000) investigated the use of bilateral arm training with rhythmic auditory cueing (BATRAC). Patients with chronic upper extremity hemiparesis used a bilateral arm trainer to complete either active or partially assisted movements to the beat of a metronome set at the patient's preferred tempo. The subjects were assessed pre- and post-test on several measures, including: the Fugl-Meyer Upper Extremity Motor Performance Test, the Wolf Motor Function Test, the University of Maryland Arm Questionnaire, and dynamometer and goniometer measurement of the upper extremity. After six weeks of training, results showed significant improvement in measures of sensorimotor function, speed of performance, daily use of paretic extremity, and some increases in strength and range of motion, which were sustained at two months' follow-up (Whitall et al., 2000). In a randomized control trial comparing BATRAC with dose-matched therapeutic exercises, Luft et al. (2004) found significant increases in upper extremity function in patients with chronic stroke as measured by the Fugl-Meyer Motor Performance Test, although not significantly different from increases in the control group. However, they also found changes in patterns of activation using fMRI suggesting reorganization in both hemispheres but particularly in the contralesional hemisphere and cerebellum after BATRAC therapy (Luft et al., 2004). McCombe-Waller and Whitall (2004) found that bilateral arm training using BATRAC also improved fine motor control for 2 out of 4 subjects with mild chronic stroke, and suggest a generalizable effect on centralized motor control.

Another type of bilateral movement training, active-passive bilateral therapy (APBT) has also been found to influence both functional movement and cortical changes post-stroke (Stinear & Byblow, 2004). APBT uses a mechanical device in which both hands are attached to platforms which are linked so that movement generated by the unaffected hand is transferred and moves the affected hand in a symmetrical, synchronous fashion. It is suggested that this method sends bilateral synchronous somatosensory information to the brain, functionally coupling the limbs as a unit, and promoting the reduced inhibition between the hemispheres needed to allow mirror movements (Stinear, Barber, Coxon, Fleming, & Byblow, 2008). A pilot study in 2004 found that five out of nine patients made upper limb motor improvements as measured by the Fugl-Meyer, as well as had decreases in TMS cortical map volume in the unaffected hemisphere, suggesting decreased excitability, reduced inhibition on the affected hemisphere, and more balanced activation between hemispheres (Stinear & Byblow, 2004). More recently, researchers examined the effects of APBT as a preparatory adjunct to motor practice on those with chronic stroke. They found that compared to the control group, which had the same motor practice intervention but no APBT, the APBT group had significantly more improvement of upper extremity motor function, increased excitability in the lesioned hemisphere, and increased inhibition both transcallosal (coming from the lesioned hemisphere to the non-lesioned hemisphere) and intracortically within the non-lesioned hemisphere (Stinear et al., 2008). The authors suggest that the use of APBT and its repetitive, synchronous, symmetrical coupling of movement may assist the lesioned hemisphere to more normally inhibit the non-lesioned hemisphere and promote more balanced activation between the hemispheres. This reduced inhibition and increased excitability may enhance activity-dependent plasticity within the lesioned hemisphere, in effect, “priming” the brain for functional, plastic changes associated with motor practice and learning (Stinear et al., 2008, p. 1387).

Other studies have shown improved kinematic quality of paretic limb movement during synchronized bilateral movement, including accuracy, control of speed, and smoothness of the movement path (Cunningham et al., 2002; McCombe-Waller, Liu, & Whitall, 2008; Mudie & Matyas, 2000; Rose & Winstein, 2004). These improvements also appear to translate into improved performance of functional activities as measured by assessments such as the Fugl-Meyer and the Wolf Motor Function tests (McCombe-Waller et al., 2008; Stinear & Byblow, 2004; Whitall et al., 2000). McCombe-Waller et al. (2008) also found improvement in unaffected limb movement kinematics following bilateral (BATRAC) training, which may be an important aspect considering that some research suggests that the ipsilateral limb may experience subtle deficits after stroke (Desrosiers, Bourbonnais, Bravo, Roy, & Guay, 1996).

Stoykov and Corcos (2009) suggest that some form of bilateral movement training or bilateral priming may be beneficial for individuals post-stroke, whether they are severely impaired, with little to no active movement distally or whether they are more mildly affected. This is in contrast to a study in 2008 that only found motor performance improvements after a modified BATRAC protocol in subjects with severe stroke (Richards, Senesac, Davis, Woodbury, & Nadeau, 2008). A systematic review and meta-analysis done by Stewart, Cauraugh, and Summers (2006) found an overall large cumulative effect size (0.582 – 0.732), considering 11 studies, indicating that bilateral movement is an effective rehabilitation approach in the treatment of stroke motor deficits, whether used alone or in conjunction with techniques such as auditory cueing or electrical stimulation. However, a Cochrane review of bilateral movement training including only randomized controlled trials (RCTs) concluded that due to inadequate evidence of high quality, they could not say bilateral training was any more or less effective than other usual therapies in post-stroke rehabilitation (Coupar, Pollock, van Wijck, Morris, & Langhorne, 2010). In their review of bilateral movement training research, Tabak and Plummer-D'Amato (2010) suggest that bilateral movements in therapy should be complex, requiring multi-joint use and movement through multiple planes. They also note that a metronome may be useful for maintaining rate of movement and that passive movement of a hemiplegic extremity simultaneously with the unaffected extremity may still offer benefits (Tabak & Plummer-D'Amato, 2010).

Timing and Auditory Cueing

Many of the studies investigating bilateral benefits in stroke rehabilitation also use auditory cueing (Luft et al., 2004; McCombe-Waller et al., 2008; McCombe-Waller & Whitall, 2004; Stoykov et al., 2009; Thaut et al., 2002; Whitall et al., 2000). It has been suggested that these auditory cues, when offered in a rhythmic fashion, offer additional sensory information which can promote temporal organization and stability of central motor control, as well as help focus attention and promote accuracy of movement repetition (Malcolm et al., 2009; Thaut et al., 2002; Whitall et al., 2000). This theory is employed in the mastery of high level, complex movement patterns, as found in music and sport performance (Thaut et al., 2002). Research shows that auditory signals serve to increase excitability at the spinal level in preparation for movement and when in rhythm, act as anticipatory perceptual traces that help couple motor output to the auditory input, possibly through feed-forward mechanisms (Chen, Penhume, & Zatorre, 2009; Fujioka, Trainor, Large, & Ross, 2009; Malcolm et al., 2009; Rossignol & Melvill-Jones, 1976, as cited in Thaut et al., 2002).

In a study comparing metronome-cued movement training and non-cued movement training with stroke survivors, Thaut and colleagues (2002) found that auditory rhythm decreased spasticity and reduced variability in the timing and trajectory of reaching, as detected by kinematic analysis. Previously, Thaut, McIntosh, and Rice (1997) found the use of auditory rhythm improved gait velocity, stride length, and the consistency and synchronicity of EMG-measured motor neuron activity in stroke patients. More recently, Malcolm and colleagues (2009) found that rhythmic auditory stimulation (RAS) during motor training significantly improved arm reaching kinematics, which was reflected in significant gains in the functional Wolf Motor Function and Fugl-Meyer assessments. When internal mechanisms for controlling movement parameters become damaged as in stroke, using an external source of cues may help re-establish optimal movement patterns during motor re-learning, and temporal cues may help the motor system to “scale smoother time parameters of position change across the entire movement interval” (Thaut et al., 2002; Thaut, Kenyon, Schauer, & McIntosh, 1999, p. 105). Since the auditory system is better suited for perception and processing of temporal information (Aschersleben, 2002), using an auditory source of cues, such as a metronome, may be more beneficial than a visual cueing source. Additionally, as auditory rhythm is perceived and processed bilaterally, it is relevant and beneficial whether a patient has had a right- or left-hemispheric stroke (Thaut, McIntosh et al., 1997).

Evidence has also been found for cortical effects in response to movements synchronized to auditory cues from a metronome, particularly increased cortical excitability and decreased intracortical inhibition (Classen, Liepert, Wise, Hallett, & Cohen, 1998; Ackerley, Stinear, & Byblow, 2007). Using TMS, Ackerley et al. (2007) found evidence of increased cortical excitability and use-dependent plasticity in healthy subjects, and suggest that training in auditory synchronization may be beneficial for enhancing these processes following stroke. Interestingly, they also note that the external source of cueing may be crucial for use-dependent plasticity rather than simply self-paced (Ackerley et al., 2007).

Timing can be said to be at the core of “Hebbian” plasticity, as it is said of neurons “those that fire together, wire together” (Murphy & Corbett, 2009, p. 865). This firing together requires concurrent activation within tens of milliseconds, and when repeated, the neurons become wired together with a strengthened synapse, as part of a functional circuit (Kwag & Paulson, 2009). Within the last twenty years, research has begun to indicate that rather than information between neurons being coded into rate of firing, it is coded by very precise timing of firing (Baker, Kilner, Pinches, & Lemon, 1999; Hummel & Gerloff, 2005). The synchronization of firing between cells can produce different frequency oscillatory rhythms, such as the “mu” rhythm in the 20-30 Hz range found in the sensorimotor cortex, and various frequency ranges are associated with different functions (Baker et al, 1999; Houweling, van Dijk, Beek, & Daffertshofer, 2010). By definition, rhythm is the distribution of time, as demarcated by events, such as the firing of a neuron or an auditory tone, and is at the center of both cognitive and motor learning and performance (Thaut et al., 2009). More and more, it is being shown that rhythm and the synchronization of rhythm is how the brain communicates, integrates, and activates. It is proposed that these rhythmic oscillations may play a key role in communication and integration of neuronal information, allowing distant neurons or regions to function as a cohesive unit or distributed network (Baker et al., 1999; Pollok, Gross, Muller, Aschersleben, & Schnitzler, 2005). Furthermore, the rhythms emerging from various brain regions are interactive and “show complex phase-relationships” (Salenius & Hari, 2003, p. 678).

Evidence for these central level mechanisms of rhythm and timing in motor control comes from many studies. In Parkinson's disease, symptoms of tremor and bradykinesia represent dysfunction in motor system's rhythmic oscillatory activity (Salenius & Hari, 2003). Research has shown that oscillatory activity emerging from different regions can synchronize, such as the mu rhythms that couple together during bilateral skill learning, and that the communication of rhythms occurs via resonating oscillatory mechanisms, with particular frequencies responsible for rhythmic motor synchronization and bilateral coordination (Andres et al., 1999; Thaut, Demartin, & Sanes, 2008; Pollok et al., 2005; Pollok, Butz, Gross, & Schnitzler, 2007). Synchronization between cerebellar hemispheres, or intercerebellar coupling, also appears during simultaneous bilateral tasks, and may serve to integrate the timing signals between hands, reducing variability in a phenomenon known as "bimanual advantage" (Pollok et al., 2007). In the motor cortex, synaptic plastic processes such as LTP may alter or increase the synchrony between neurons, improving the efficiency of motor neuron recruitment, and strong cortico-spinal synchronization is associated with improved motor performance (Houweling, et al., 2010; Schieber, 2002).

The timing and temporal nature of movements is more than just synchronization to a beat and the brain's propensity towards rhythm is reflected in many types of movement. Even in unsynchronized bilateral movements, limbs tend towards simple ratios and whole integer multiples of frequency to each other (Swinnen & Wenderoth, 2004). In stroke, simple rhythmic movement such as arm swinging during walking may be impaired, even on the nonparetic side, as centralized neural networks that process both efferent and afferent signals (such as proprioception and position in space) are disrupted (Ustinova, Fung, & Levin, 2006). In more complex, goal directed actions, timing is perhaps even more critical, as a goal is translated into precisely timed activation of multiple muscles (Baker et al., 1999). When two hands work together to tie a shoe or open and pour a liquid into a glass, exact timing is necessary to ensure the different sequential movements carried out by each hand are timed relative to each other and that they coincide at crucial, precise moments and locations (Weiss, Jeannerod, Paulignan, & Freund, 2000). This timing of movements for learned tasks is reflected in the precise spatial and temporal patterns of activation within the responsible motor networks. As a motor task is learned, coincidental activation of the various muscles involved becomes represented in the motor cortex not individually but as a coherent unit to that task (Nudo, 2006). In recovery from stroke, it appears that the reorganization of activation for coordinated movement requires both spatial and temporal pattern adaptation as new circuits and alternate networks are strengthened by plastic processes (Murphy & Corbett, 2009).

Accurate synchronization of movements, either between limbs in arm swinging or goal-directed actions, or to an auditory cue or rhythm is achieved at a central level by error correction. The research of Repp (2001) suggests two processes of error correction in timing: phase correction and period correction. Phase correction compares the internal asynchrony between an auditory stimulus and a motor action, such as a tap, whereas period correction is used to adjust to systematic changes in sequential stimuli. It is thought that phase correction is a “bottom-up” process, reliant on stimulus perception and operating independently of awareness, while period correction is more of a “top-down” process that can be influenced by expectations and learning (Repp, 2001, p. 310). Repp and Keller (2004) liken period correction and phase correction to “action planning and on-line control,” respectively (p. 517). That phase correction occurs without conscious awareness of asynchrony suggests that motor control requires and uses even more precise temporal frameworks and information than does the auditory perceptual system

(Repp, 2000, as cited in Aschersleben, 2002). Interestingly, timing perception has been shown to be sensitive to training and fine tuning, and this training can generalize to motor tasks not targeted in training (Meegan, Aslin, & Jacobs, 2000; Buonomano & Karmarkar, 2002).

Motor Learning and Feedback

The processes of plasticity, such as synaptic formation, LTP, and LTD, underlie motor learning (Sanes, 2003), and motor learning plays a role in both true recovery and compensation in functional recovery from stroke (Krakauer, 2006). Motor learning may be classified as the learning and mastery of "new spatiotemporal muscle-activation patterns" or as the adaptation of already learned spatiotemporal muscle-activation patterns; both are dependent on sensorimotor information (Sanes & Donoghue, 2000, p. 400). According to Krakauer (2006), motor skill learning can be thought of as the "practice-dependent reduction of kinematic and dynamic performance errors" (p. 85). Practice can be as simple as repeating a movement, however, adding variability into the demands of the movement context can increase generalization of the movement to other situations (Krakauer, 2006). Considering the activity- or experience-dependent processes of plasticity, the repetition of movements is central to motor learning (Halder et al., 2005). Via fMRI and TMS, studies have shown alteration of motor activation patterns within the primary motor cortex after as little as 5-10 minutes of simple movement repetitions, as well as within and across sessions (Classen et al., 1998; Sanes & Donoghue, 2000). Many motor skills and functional movements, however, often require the combination of simpler movements into specific sequences. The repetitions needed for lasting changes to primary motor cortex representations for sequential movements may be much higher (Sanes & Donoghue, 2000). Research on motor learning and plasticity after brain lesion in animal models typically use amounts in the hundreds of movement repetitions per day, while one recent study found that the average number of movements per session of either inpatient or outpatient rehabilitation was 32 repetitions (Lang et al, 2009). While the minimum amount needed for plastic and functional change in post-stroke humans is unknown, this certainly suggests the need for rehabilitation techniques that allow increased amounts of movement repetition. A typical hour-long session of the Interactive Metronome® can provide over 1000 repetitions of upper extremity movement.

Considering that some survivors of stroke may have hemiplegia, it is important to consider active versus passive movement repetition in motor rehabilitation. Lewis and Byblow (2004) found that repetitive proprioceptive stimulation via passive movement of the wrist increased cortical motor excitability in some, but not all, of their small sample of subjects post-stroke. Evidence exists that repetitive proprioceptive stimulation can increase activation and bring about plastic changes in sensorimotor areas in healthy adults, and is likely due to the modulatory effects of afferent sensory information on motor control networks and their output (Carel et al., 2000). Another study found that repetitive pairing motor stimulation with somatosensory afferent stimulation induced plasticity in healthy adults as well, with results suggesting that this was possible even without voluntary contraction, via cutaneous mechanoreceptors (Stefan, Kunesch, Cohen, Benecke, & Classen, 2000). Calautti and Baron (2003) found in their review that both active and passive movement in intensive stroke rehabilitation resulted in activation within the lesioned hemisphere and were associated with functional motor improvement.

Another concept in motor learning is the schedule of practice. It is now generally accepted that distributed practice, in which shorter practice periods are divided by longer rest periods, is more effective than massed practice, in which there are single or longer blocks of practice periods with no or very short rest periods (Krakauer, 2006). It has been speculated that the so-called “plateau” six months after stroke may in fact be more related to effects of massed practice, lack of variability, and behavioral compensation rather than the closing of a neurobiological window, which stresses the importance of incorporating principles of motor learning into stroke rehabilitation (Demain et al., 2006; Krakauer, 2006).

Wittenberg (2010) points out that in addition to the significant role of experience (activity), the role of error during learning is also important in stroke recovery. Repetition and practice provide a motor system the experience required for learning, and through the system’s interpretation and incorporation of feedback from that practice, actions are refined for increased efficiency and accuracy to meet desired goals (Gilmore & Spaulding, 2001). Just as phase and period correction improve timing and synchronization, detection of error through feedback plays a necessary and critical role in motor learning (Gilmore & Spaulding, 2001; Quaney, He, Timberlake, Dodd, & Carr, 2010).

Two basic categories of feedback exist: extrinsic and intrinsic. Extrinsic feedback refers to information that comes from sources outside the body that guide performance, such as visual or auditory information from environmental targets, auditory cues, or verbal coaching. Intrinsic feedback refers to primarily internal sensory information received as a result of a performance that also informs subsequent performance, such as proprioceptive, kinesthetic, or cutaneous information. In stroke survivors, the mechanisms responsible for processing intrinsic feedback information may be impaired, thus inhibiting motor learning and limiting plasticity (Gilmore & Spaulding, 2001). According to Majsak (1996), using extrinsic feedback in the absence or lack of proper intrinsic feedback can be a key component in rehabilitation for motor control, although some suggest that internalization of extrinsic mechanisms into intrinsic mechanisms is required for permanent rather than temporary changes (as cited in Gilmore & Spaulding, 2001). Within extrinsic feedback there are two forms, known as knowledge of results and knowledge of performance. According to Schmidt (1991), knowledge of results is information on how well the outcome of an action relates to the goal within the context of the environment, while knowledge of performance is information on the action or quality of movement itself (as cited in Gilmore & Spaulding, 2001).

The Interactive Metronome® incorporates these principles of repetition and feedback into its motor learning and timing strategies. The metronome beat provides a source with which to coordinate movements, encouraging repetition of identical movements and synchronizing the firing along neural pathways. The clinician is trained during certification to use demonstration and verbal cues to coach the client on movement strategies, representing extrinsic feedback in the form of knowledge of performance. The visual display of milliseconds off-beat and the guide sounds, which indicate whether a client is going too fast or too slow, provide more immediate sources of extrinsic feedback in the form of knowledge of results. By learning what the different guide sounds indicate, the client using Interactive Metronome® essentially internalizes this form of feedback. As this internalization occurs, the internal rhythm and timing of a client improves, which forms the basis for improvement in movement quality, motor planning, sequencing, and other higher-level adaptive behavior (Koomar et al., 2001).

As mentioned previously, the basis for the rehabilitative potential of Interactive Metronome® intervention lies in its use of timing, rhythm, and principles of motor learning. The IM®'s use of these principles has already proven effective for enhancing motor performance in at least one study with the healthy young adult population. Libkuman, Otani, and Steger (2002) investigated the use of Interactive Metronome® therapy to improve accuracy in golf swing.

These researchers found that accuracy of golf swing improved significantly after completion of IM® treatment as compared to a control group. What allows for the coordination of muscles working in cooperation, as well as the fluidity, or quality, of a movement, is the synchronization of activation of neuronal pathways. Quality of movement can be considered to be comprised of accuracy, control, speed, and smoothness, and is inter-related with socio-cultural and even psychological factors through not just function but communication and expression as well (Skjaerven, Kristoffersen, & Gard, 2008). When areas and pathways within the brain experience damage, even minor, the finely-tuned timing and synchronization essential for motor planning and quality of movement execution can be disrupted. However, using rhythm and the brain's natural plasticity, improvement in timing and reduction in impairment can be made.

Timing, motor planning, sequencing, and quality of movement all impact the ability to do more complex behaviors and skills, which enable engagement in occupation. As clients experience difficulty in valued occupations, the Interactive Metronome® could be utilized to improve the performance skills underlying those difficulties. As Koomar and colleagues (2001) note, the Interactive Metronome® is more of a "bottom-up" approach in a field that is increasingly "top-down," at least in theory, yet often these approaches can be used in a cooperative, complimentary fashion (p. 163). Given the necessity of demonstrating progress in therapy in order to continue rehabilitation, and given the sporadic and somewhat unpredictable nature of stroke recovery, any tool that could be used to additionally target the brain's plasticity warrants investigation. With the lack of conclusive evidence supporting interventions in stroke rehabilitation, it is also crucial to conduct research supporting interventions towards the goal of evidenced-based occupational therapy practice.

CHAPTER 3: Purpose of the Study

The purpose of this study was to further expand the evidence base of the Interactive Metronome® as an intervention tool for the field of occupational therapy, as well as to potentially provide support for the use and direct reimbursement of the IM® as a rehabilitative intervention and assessment tool in the post-stroke population. First, this study examined whether there were significant differences between the normal aging population and post-stroke survivors' response to IM® intervention, as measured by outcome performance with the Long Form Assessment. Secondly, it examined if there were significant differences between the two groups following IM® intervention as measured by a functional outcome measure, the Nine-Hole Peg Test (Kellor, Frost, Silberberg, Iversen, & Cummings, 1971). Lastly, the relationship between the IM® outcome performance measure, the Long Form Assessment, and the functional outcome measure, Nine-Hole Peg Test, was analyzed.

CHAPTER 4: Methods

Design

This exploratory study compared outcomes of healthy adult individuals to post-stroke survivors following intervention with the Interactive Metronome®. Existing data from a previously conducted study, here after referred to as "Healthy IM® Participants" (HIP), was compared to data collected from the current study involving individuals post stroke, here after referred to as "Post-Stroke IM® Participants" (PSIP). The initial HIP study was conducted by the East Carolina University Department of Occupational Therapy during the 2006 – 2007 academic year and established successful outcome measurements using the IM® as an intervention. It also validated and established protocols for subsequent IM® studies, including the current PSIP study. Participants from both the HIP and the PSIP studies were assessed with the Long Form Assessment (LFA) of the IM® and the Nine-Hole Peg Test (NHPT) before receiving six sessions of IM® treatment protocol. The treatment protocols were intended to reflect the intervention time frames and number of interventions allowed by Medicare funding. After completing the series of sessions, each participant was again asked to complete the LFA and NHPT as post-intervention outcomes measurement.

Participants

The HIP study included 12 healthy aging adults, however, only eight participants had usable data. These participants were drawn from the general northeastern North Carolina area via convenience sampling and were included based on the following selection criteria: (a) ability to speak English and follow verbal directions, (b) motor ability to do fine motor tasks, (c) ability to initiate and sustain repetitive movements, (d) no previous conditions that would affect motor and cognitive performance in the IM®, (e) tolerance to wear headphones, and (f) willingness to complete IM® protocol series. The study excluded anyone who had visual and/or hearing impairments severe enough to interfere with IM® therapy. Of the group of eight participants whose data was used for this study, five were females and three were males, and ages ranged from 55 to 68 years, with an average age of 58.9 years (see Table 1).

The PSIP study was completed during the 2008-2009 academic year and consisted of 25 participants who were also drawn from the general northeastern North Carolina area via convenience sampling. The following selection criteria were used: (a) identified as a post-stroke survivor, (b) the ability to respond to verbal command, and (c) ability to minimally perform a "clapping motion" as visually verified by the investigator. Out of the 25 PSIP participants, only 12 had NHPT data for both hands, and for the purposes of comparison with the HIP NHPT data, a group of eight participants was drawn out of these twelve. Purposive quota sampling was used to generate the group of eight participants to match the HIP participants as closely as possible on the variable of gender and age. The PSIP group of eight therefore also included five females and three males, with an age range of 52 to 76 years, and an average age of 60.4 years (see Table 1).

Table 1

Demographic Configuration of Participant Groups

Group	Gender	Age Range	Average Age
HIP	5 females, 3 males	55 – 68 years	58.9 years
PSIP	5 females, 3 males	52 – 76 years	60.4 years

Instrumentation

Both the HIP and the PSIP studies' functional outcome data was gathered using the Nine-Hole Peg Test. The Nine-Hole Peg Test (NHPT) is a widely used test of manual dexterity and has been shown to be sensitive to increases or decreases of function for clients with higher levels of upper extremity function (Grice et al., 2003; Jacob-Lloyd, Dunn, Brain, & Lamb, 2005; Kellor et al., 1971). It has also been indicated for assessing the impact of sensory loss and ataxic symptoms on function (Murphy & Roberts-Warrior, 2003). The NHPT consists of placing pegs one by one in three rows of three holes, spaced 15 millimeters (mm) apart, and then removing them individually while being timed (Kellor et al., 1971). It is recommended that the average of three trials be used for more valid results (Grice et al., 2003). Inter-rater reliability for the NHPT has been shown to be high, ranging from $r = 0.75$ to $r = 0.99$, while test-retest reliability has been shown to be moderate to high at $r = 0.44$ to $r = 0.90$ (Grice et al., 2003; Mathiowetz, Weber, Kashman, & Volland, 1985; Murphy & Roberts-Warrior, 2003). The NHPT has also been shown to have acceptable to good validity (Mathiowetz et al., 1985, Murphy & Roberts-Warrior, 2003).

The Long Form assessment (LFA) is an assessment developed by the IM® to provide a measure of overall change and progress of the individual using the IM® as an intervention (see Appendix B). The LFA eliminates visual clues which are available during the intervention time frames and collects data from shorter bursts of repetitive activities that then provide an aggregate percentage of change for the individual to track their progress. The fourteen tasks assessed target the upper and lower extremities in isolation and in bilateral coordination, at a set tempo of 54 beats per minute. For post-stroke participants, standardized adaptations were used as needed according to the side of the body affected by hemiplegia or hemiparesis severe enough to interfere with completion of the tasks as intended on the LFA (see Appendix C). Scores are presented as the average number of ms performance was off the metronome beat during the task. The expected change ratio for the LFA is between 12% and 25% of improvement over any given initial baseline score, and the LFA is age-normed for its default parameter settings (Interactive Metronome®, 2007). The IM® Pro 8.0® software and hardware devices are installed on a Windows XP operating system and provide a precise auditory metronome beat delivered through headphones with optional visual cues provided via the computer screen. Data from a participant's performance was recorded into their coded file as per Institutional Review Board and HIPAA requirements. The foot and hand triggers as well as the headphones used are part of the IM® system package, with the exception of a separate pressure switch used for a dual switch as designed by the protocols established in prior pilot testing.

IM® Intervention Protocols

IM® intervention for both the HIP and PSIP studies consisted of eight sessions over a one-month time frame: two evaluation sessions and six intervention sessions (see Appendix D). Participants completed the LFA and NHPT at the beginning and again after 6 intervention sessions with the IM®. The Short Form assessment (SFA), also included in the IM® software, was given at the beginning of each session to track performance more closely. Each session included both bilateral tasks and unilateral tasks with both of the right and left upper extremities, as well as a task crossing midline and a task involving the unaffected lower extremity. Participants had brief breaks between tasks, and took longer rest breaks as individually needed, although sessions did not typically extend beyond an hour in time. Each session consisted of either 1,350 or 1,450 movement repetitions, with the entire treatment protocol comprising 8,400 movement repetitions. Participants in both HIP and PSIP studies received two $25.00 gas cards, one at the initial evaluation session and the second after completion of post-intervention evaluation, as compensation for time and travel.

Procedure and Data Analysis

The studies from which the HIP and PSIP data were obtained are part of a larger study, approved by East Carolina University and Medical Center Institutional Review Board (UMCIRB), which is evaluating the IM® for its overall ability to improve the motor and general functional skills of individuals affected post-stroke. Due to the existing nature of the data, exemption from IRB review was approved and obtained from the UMCIRB prior to commencing this study. As mentioned previously, before gathering data, a group of eight PSIP participants was formed based on the age and gender characteristics of the eight participants from the previous HIP study. Demographic data and data from outcome measures (NHPT and LFA) for these 16 participants were checked for accuracy and entered into Microsoft Excel and PASW Statistics 17.0. Descriptive statistical analysis (distribution and central tendency) was done to describe the groups on the demographic variable of age, as well as for the outcome measure variables of NHPT and LFA. To analyze the NHPT data, the three trials at pre- and post-test were averaged for each hand giving a right and left hand millisecond (ms) score. The percentage of change from pre- to post-test ms score was then calculated for each hand and a cumulative percentage of improvement was calculated from the sum of the right and left hand percentages of change for each participant. In analysis of the LFA data, two variables were considered; the calculation of these variables is included in the LFA scoring report computed by the IM® software. The “Super Right On” percentage (SRO%) is defined as the percentage of hits in which the participant activated the trigger within 15 ms of the beat (Interactive Metronome®, 2007). The adjusted ms average is the average number of ms away from the beat the trigger is activated during 12 of the 14 tasks of the LFA (Interactive Metronome®, 2007). Excluded are the diagonal bilateral tasks: left foot and right hand, and right foot and left hand. For both the SRO% and adjusted ms average variables, a percentage of change from pre- to post-test was calculated.

In addition, visual and graphical analysis was conducted for the percentages of change of the SRO% and adjusted ms average of the LFA and the cumulative percentage of change of the NHPT. Correlational analysis was done to determine the degree of relationship between the outcome measure variables (NHPT and LFA), using Pearson's product-moment correlation as both were at the ratio level of measurement (time in seconds). Tests of significance were then conducted as pre- and post-test NHPT and LFA scores were analyzed for the amount of change and a between-groups comparison. To analyze for amount of change in outcome measures within groups, a paired t-test was used. The t-test is used to compare only two means at a time when both means are at the interval level or above of measurement (Currier, 1990). Comparing one outcome measure at a time between groups suggested an independent t-test to determine whether the means of the HIP group and the PSIP group are statistically and significantly different. Ordinarily, use of parametric statistical analyses, such as the t-test, requires a sample size of 30, however, throughout the literature, examples where this stipulation is relaxed are common (Currier, 1990).

CHAPTER 5: Results

Descriptive Statistics

Overall, both the HIP and PSIP groups showed a positive mean percentage of improvement in all outcome measures. With regards to the IM$^{®}$ outcome measures, every participant in the PSIP group except one showed a positive percentage of improvement in adjusted ms average on the LFA, with a group mean of 30.4% improvement. In the HIP group, there was a positive percentage of improvement in LFA adjusted ms average for every participant, and a group mean of 53.7% improvement. Every participant in the PSIP group showed a positive percentage of improvement in SRO%, with a mean of 41.1% improvement. All but one participant in the HIP group showed a positive percentage of improvement in SRO%, with a mean of 56.9% improvement (see Table 2). For the NHPT outcome measure, in the PSIP group, all but one participant showed a positive cumulative percentage of improvement, with a mean of 16.4% improvement. Regarding the NHPT outcome measure in the HIP group, all participants showed a positive cumulative percentage of improvement, with a mean of 26.5% (see Table 3).

Table 2

Interactive Metronome® Long Form Assessment (LFA) Results

Group	ID	Pre Adj ms	Post Adj MS	% Improvement Adj ms	Pre SRO%	Post SRO%	% Improvement SRO%
PSIP							
	AWB0702	62.1	32.2	48.1%	19.3	31.6	38.9%
	BJW1029	145.5	69.8	52.0%	9.3	18.9	50.8%
	LCH0920	70.9	47.9	32.4%	15.9	23.2	31.5%
	EMP1113	72.8	102.5	-40.8%	15.0	19.1	21.5%
	GVW0827	30.4	24.8	18.4%	35.6	40.8	12.7%
	JWW1007	173.8	70.9	59.2%	3.5	24.4	85.7%
	RBR1110	101.6	82.1	19.2%	13.6	25.2	46.0%
	SOF0910	101.4	45.8	54.8%	13.2	22.8	42.1%
	AVERAGES			30.4%			41.1%
HIP							
	DEG1111	82.3	19.2	76.7%	8.8	48.5	81.9%
	EXG3333	162.3	68.1	58.0%	12.3	30.9	60.2%
	XMB2222	184.3	46.4	74.8%	6.3	23.9	73.6%
	PGW2222	22.8	15.8	30.7%	43.2	55.7	22.4%
	MJW0826	125.7	69.9	44.4%	7.9	20.9	62.2%
	CJC1104	469.6	100.5	78.6%	1.1	6.8	83.8%
	MPC0713	117.5	58.5	50.2%	1.6	21.3	92.5%
	MCS0617	151.4	126.9	16.2%	7.9	6.5	-21.5%
	AVERAGES			53.7%			56.9%

Table 3

Nine Hole Peg Test (NHPT) Results

Group	ID	Right Pre	Right Post	Right % Improvement	Left Pre	Left Post	Left % Improvement	Cumulative % Improvement
PSIP								
	AWB0702	20.95	20.63	1.53%	23.12	21.86	5.45%	6.98%
	BJW1029	31.28	29.60	5.37%	117.63	77.16	34.40%	39.78%
	LCH0920	19.43	18.43	5.15%	24.51	25.24	-2.98%	2.17%
	EMP1113	23.62	22.10	6.44%	32.73	31.65	3.30%	9.73%
	GVW0827	16.87	15.90	5.75%	106.12	71.12	32.98%	38.73%
	JWW1007	36.43	37.12	-1.89%	49.74	50.40	-1.33%	-3.22%
	RBR1110	86.03	85.65	0.44%	22.63	18.36	18.87%	19.31%
	SOF0910	74.61	63.49	14.90%	25.58	24.78	3.13%	18.03%
	AVERAGE			4.71%			11.73%	16.44%
HIP								
	DEG1111	15.17	14.25	6.06%	15.58	14.90	4.36%	10.43%
	EXG3333	16.87	16.00	5.16%	20.49	15.34	25.13%	30.29%
	XMB2222	14.19	13.94	1.76%	15.75	14.02	10.98%	12.75%
	PGW2222	17.77	14.39	19.02%	17.43	15.64	10.27%	29.29%
	MJW0826	19.20	17.14	10.73%	18.49	17.60	4.81%	15.54%
	CJC1104	21.06	17.92	14.91%	24.07	20.64	14.25%	29.16%
	MPC0713	19.41	13.80	28.90%	19.45	13.85	28.79%	57.69%
	MCS0617	20.32	17.26	15.06%	21.23	18.80	11.45%	26.51%
	AVERAGE			12.70%			13.76%	26.46%

Correlational Analysis

Pearson's *r* was used to explore correlation between the LFA adjusted ms average percentage of improvement and the NHPT cumulative percentage of improvement, as well as the LFA SRO% percentage of improvement and the NHPT cumulative percentage of improvement, in both the PSIP and HIP groups. The NHPT cumulative percentage of improvement and percentage of improvement in adjusted ms were weakly negatively correlated in both the PSIP and the HIP groups (*r* = -0.011 and *r* = -0.271, respectively). The NHPT cumulative percentage of improvement and SRO% percentage of improvement were weakly negatively correlated in the PSIP group (*r* = -0.398) and weakly positively correlated (*r* = 0.102) in the HIP group.

These low correlations may be seen represented especially in individual cases. See Figures A and B. For example, in the stroke group, one participant had a negative percentage of improvement (performance declined from pre- to post-test) in the LFA adjusted ms outcome, yet still showed a positive percentage of improvement in both LFA SRO% and the cumulative NHPT. Another participant in the stroke group showed the highest percentages of improvement in both LFA SRO% and adjusted ms average, yet showed a slightly negative percentage of improvement in cumulative NHPT performance. Within the control group, one participant showed a large negative percentage of improvement in the LFA SRO%, yet showed positive percentages of improvement in both the LFA adjusted ms average and the cumulative NHPT.

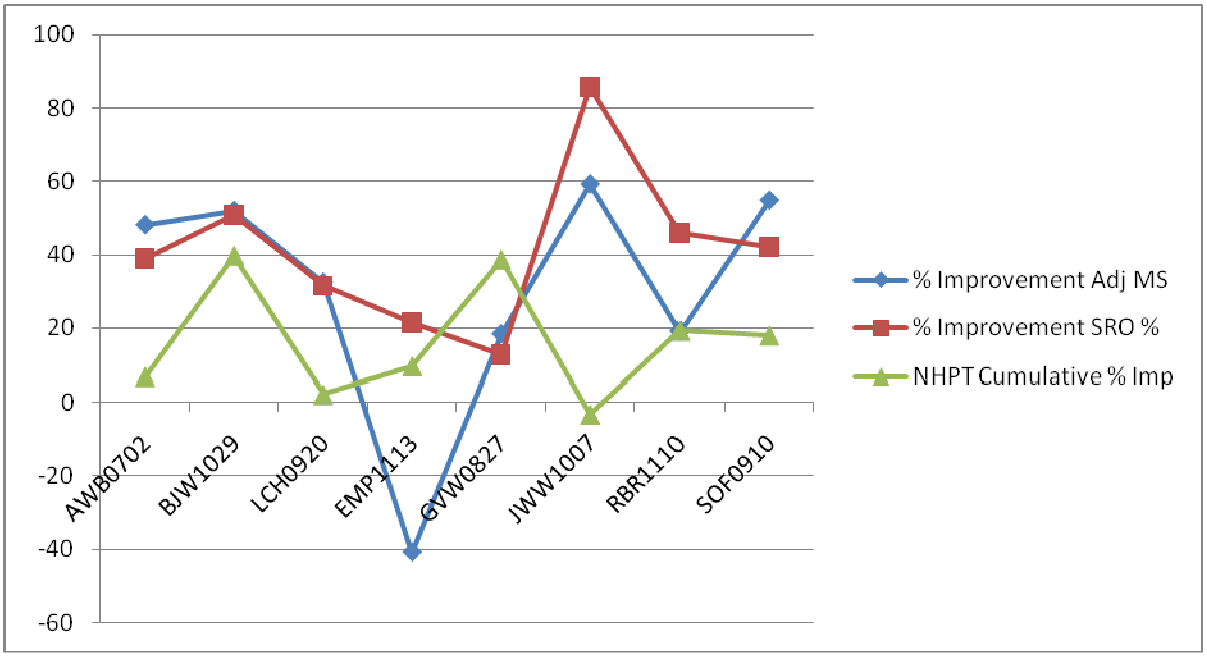

Figure A. Comparison of LFA and NHPT outcome results per participant, PSIP group.

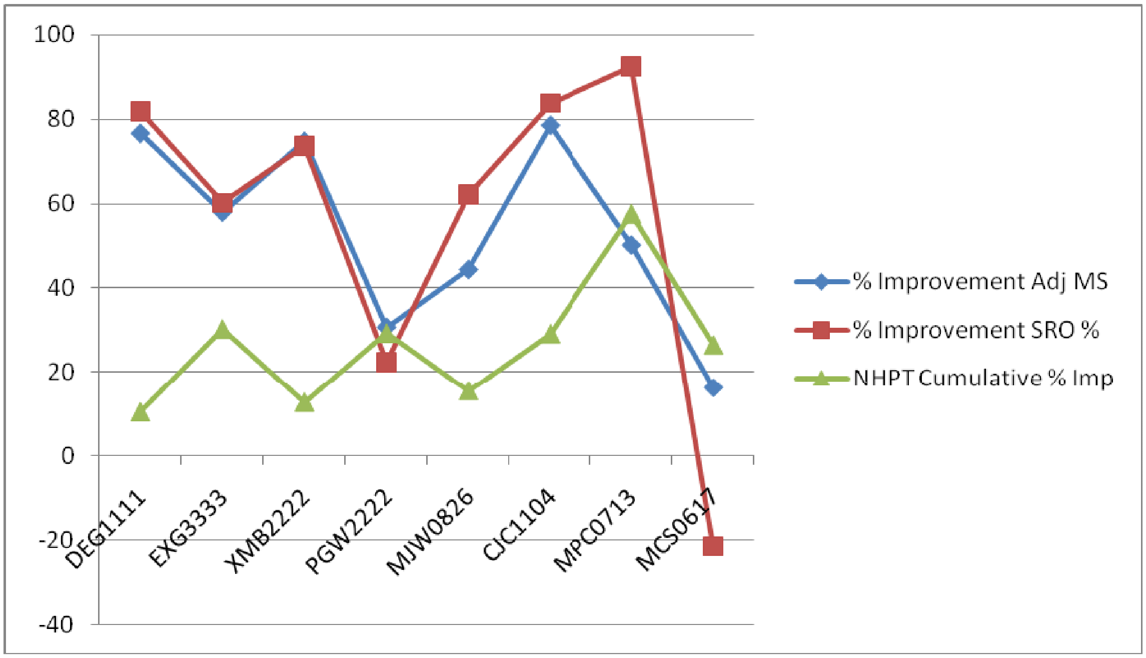

Figure B. Comparison of LFA and NHPT outcome results per participant, HIP group.

Tests of Significance

An independent t-test was used to compare outcome measures between groups. A p-value of 0.05 or less was used to indicate a statistically significant difference between groups. For the LFA adjusted ms average, there was no significant difference (p = 0.124) in percentages of improvement between groups. There was also no significant difference found (p = 0.335) between the groups in percentage of improvement in LFA SRO%. For the NHPT cumulative percentage of improvement, again there was no significant difference (p = 0.216) between the PSIP group and HIP group.

CHAPTER 6: Discussion

Overall, the results showed positive outcomes after intervention with the IM® for both the PSIP and HIP groups. With regard to the IM® outcome measures, 15% was pre-established in collaboration with university statisticians as a "clinically meaningful" percentage of improvement prior to the study. The HIP group greatly exceeded this figure, with results of 53.7% and 56.9%, for the LFA adjusted ms average and SRO%, respectively. In a post-stroke population, recent research with upper extremity measures suggests that percentages of change from 16% to 30% are clinically meaningful to patients (Lang, Edwards, Birkenmeier, & Dromerick, 2008). The PSIP group exceeded both definitions of clinically meaningful change, with results of 30.4% and 41.1% for the LFA adjusted ms average and SRO%, respectively. This, combined with the finding of no significant differences between groups, indicate that IM® therapy may be just as effective as an agent of change in a post-stroke population as in a normal aging population. This is especially significant considering the deficits both motoric and cognitive that post-stroke patients must overcome.

To consider clinically meaningful change with the NHPT outcome measure, it is important to consult the established norms. Mathiowetz et al. (1985) established norms for healthy adults using a constructed wooden version of the test. Since a 2003 normative study with a commercially available version, similar to the one used in this study, found no significant statistical differences in norms, the original normative data is considered here (Grice et al., 2003; Mathiowetz et al., 1985). Considering males and females together in the age range (ages 55-68) of the HIP group, normed scores range from 17.8 seconds (s) to 20.7 s for the right hand and 19.4 s to 22.9 s for the left hand (Mathiowetz et al., 1985). The HIP subjects in this study had an average of 18.00 s at pre-test and 15.59 s at post-test for the right hand and 19.06 s at pre-test and 16.35 s at post-test for the left hand. These HIP group scores fell within or slightly below average norms to start and improved to well below average times following IM® intervention. Considering the age ranges of the PSIP group (ages 52-76), normed scores were slightly different, ranging from 18.0 s to 22.9 s for the right hand, and 20.1 s to 26.4 s for the left hand (Mathiowetz et al., 1985). The PSIP subjects had an average of 38.65 s at pre-test and 36.62 s at post-test for the right hand and 50.26 s at pre-test and 40.07 s at post-test for the left hand. While the averages for the PSIP subjects clearly improved following IM® intervention, they were still well above normal average times both at pre-test and post-test.

This, combined with the lack of correlation between either of the IM® outcome measures and the functional measure of the NHPT, prompt several considerations. First, it is likely with such a small sample that individual differences and external influences to performance may have greater effects of hiding any true correlations. Secondly, it may be possible that the IM® benefits the timing and performance of larger, more proximal muscles (gross motor movement) moreso than fine motor dexterity, denoting more task-specific benefits in a post-stroke population. There may also be other aspects of the IM® intervention, such as rate or pace of cues, that, if adjusted, may maximize the therapeutic benefits. Lastly, it could also be possible that the duration of treatment was not long enough for a post-stroke population to see functional gains.

Sample Size

In a small sample size, effects from uncontrolled variables are more likely to skew results (Cramer, 2010). This is reflected visually in the results graphs and in correlation statistics, in the healthy aging group and even moreso in the post-stroke group. Due to the uniqueness of a stroke survivor's lesion, genetic, biological, and psychological makeup, comorbidities, medications, and other situational and environmental influences, there is very likely no intervention that will work for every individual. Even when individuals present with “nearly identical early clinical pictures,” it is customary to find a broad range of outcomes at long-term follow-up (Rossini et al., 2007, p. 241), which further challenges interpretation of results in a small sample. In this study, it would have been helpful to have gathered demographic data from PSIP participants as to time since stroke, location of the lesion as determined by diagnostic imaging, and severity of stroke as determined by accepted measures. In stroke rehabilitation research, this information is typically gathered in attempts to create a more homogenous sample, or to determine if an intervention may be more beneficial for a type or level of severity of stroke. If researchers are successful in selecting a homogenous group of stroke survivors without significant comorbidities, and only moderate to mild impairment, results may not generalize to the common clinical picture that may include severely impaired stroke survivors with multiple comorbidities. McCombe-Waller and Whitall (2008) suggest that with such heterogeneity it may be fruitless to attempt to find a single “best” intervention in stroke, and research should instead focus on which intervention or therapy is appropriate for a given clinical picture (p. 30). While the larger post-stroke study included both participants who were greater than six months to years since stroke (chronic stroke) as well as those with subacute stroke, this information was not tracked per participant, and was therefore unavailable to consider for the PSIP participant data used in this study.

Choice of Outcome Measure

The outcome measure used in the original studies from which the present data was gathered needed to be sensitive enough to capture motor improvements following IM® intervention in a typically aging population. However, it is possible the Nine Hole Peg Test (NHPT) was not the best outcome measure to capture improvements gained after intervention with the IM® in the post-stroke population. It has been suggested that the “failure of many recent clinical stroke trials to demonstrate motor recovery may relate more to the choice of outcome measures than to the lack of efficacy of the intervention” (Cirstea & Levin, 2007, p. 409; Duncan, Lai, & Keighley, 2000; Jacob-Lloyd et al., 2005). While some studies of repetitive, bilateral movement therapy have noted benefits for areas of motor performance other than what is trained (McCombe-Waller & Whitall, 2004; Stoykov, et al., 2009), it has been suggested that training effects during rehabilitation following stroke are largely task-specific (Krakauer, 2006). The movements targeted and practiced during the IM® intervention protocol were largely gross motor movements, and so an outcome measure that assesses gross motor function may have better shown the effects of IM® training.

Many studies in stroke rehabilitation literature use the Fugl-Meyer (FM) test as an outcome measure for upper extremity impairment (Cirstea & Levin, 2007; Lin, Chang, Wu, & Chen, 2009; Luft et al., 2004; Malcolm et al., 2009; McCombe-Waller et al., 2006; McCombe-Waller et al., 2008; McCombe-Waller & Whitall, 2004; Richards, Senesac et al., 2008; Stinear & Byblow, 2004; Whitall et al., 2000). The FM test evaluates proximal as well as distal voluntary arm movements, while the NHPT only assesses distal movement as it relates to dexterity. Only one study found during literature search conducted for the present investigation used the NHPT as an outcome measure, and did so in addition to other measures assessing upper limb function (Askim et al., 2009). Research completed in 2005 found that only 50% of participants post-stroke were able to complete the NHPT, even at greater than six months from onset, and concluded the NHPT was not appropriate for the general stroke population where there may be a wide range of severity of impairment (Jacob-Lloyd et al., 2005). For a homogenous sample of mild stroke impairment, in which there is functional use of the upper extremity, the NHPT may be more useful than other measures in sensitivity and avoidance of a ceiling effect (Murphy & Roberts-Warrior, 2003). However, in a heterogeneous sample that may include both severe and mild stroke impairment, a different measure or perhaps even more than one outcome measure may be necessary to capture gains made both proximally and distally following an intervention such as the IM®.

Literature on stroke rehabilitation as well as timing suggests that perhaps kinematic analysis of movement may be useful in giving a clearer picture of change following intervention (Caimmi et al., 2008; Lin et al., 2009; McCombe-Waller et al., 2008; Thaut et al., 2002; Wagner, Rhodes, & Patten, 2008). Taking into account the "how" a goal is accomplished (movement quality), not just the "if" the movement goal is accomplished, is important considering the view of compensation versus true recovery (Calautti & Baron, 2003; Cirstea & Levin, 2007). Conversely, Malcolm et al. (2009), suggest that kinematic analysis alone as an outcome measure also fails to give a complete picture of functional recovery. McCombe-Waller and Whitall (2008) proposed that traditional standardized measures do not "adequately measure changes in control that can be facilitated after training," and that they may not be "sensitive to changes in bilateral versus unilateral control" (p. 756). Considering this, incorporating an outcome measure which assesses aspects of bilateral coordination and functional task performance, such as the Upper Extremity Performance Test for the Elderly (TEMPA), may also have better captured benefits of IM® therapy for the post-stroke population (Hardin, 2002; McCombe-Waller & Whitall, 2008).

Preferred Pace versus IM® Default Pace

The evidence for the benefits of rhythmic auditory cues in movement training is significant, however, many studies involving stroke survivors use auditory cueing that is set to a participant’s preferred pace (Luft et al., 2004; Malcolm et al., 2009; McCombe-Waller et al., 2008; McCombe-Waller & Whitall, 2004; Richards, Senesac et al., 2008; Thaut et al., 2002). In the studies considered in the current investigation, the default setting within the Interactive Metronome® was used for a consistent pace of 54 beats per minute. It is possible that by adjusting this setting to each participant’s preferred tempo, the efficacy of IM® therapy could have been maximized, in particular for the post-stroke population.

Intensity and Duration of Training Schedule

As some research indicates that the processes of plasticity may be reduced in aging brains (Fathi et al., 2010; Mora et al., 2007), it is important to consider other more alterable factors, such as frequency, intensity, and novelty of interventions in order to optimize recovery (Oliviero, 2010). A recent study comparing constraint-induced movement therapy and bilateral movement training of equal intensity found that both significantly improved motor function in people with stroke, and concluded that the “attentional focusing and intensive practice shared by both interventions may be the active component” (Hayner, Gibson, & Giles, 2010). Another study used a training schedule of a total of eighteen-to-twenty 45-60 minute sessions varying from two-to-five times per week in frequency and concluded that “intensive” practice can induce cortical reorganization and functional improvement in chronic stroke (Carey J. et al., 2002, p.780). Studies investigating bilateral arm training with rhythmic auditory cueing (BATRAC) have typically used a training schedule of one hour sessions, three times per week for six weeks, equaling 18 sessions (Luft et al., 2004; McCombe-Waller et al., 2008). Lin et al. (2009) used a training schedule of two hours, five days a week for three weeks with bilateral arm training (BAT), providing a total of 15 sessions and 30 hours of therapy. Yet another study of auditory cued bilateral movement training used a training schedule of one hour sessions, three times per week for eight weeks, yielding 24 therapy sessions (Stoykov et al., 2009). The training schedule for the studies considered in the present investigation was a total of eight hour-long IM® sessions, generally spread over four weeks, which was designed to reflect treatment timeframes typically reimbursed by Medicare. While within-session frequency of movement was quite high (1,350 to 1,450 repetitions), it is possible that a longer duration of sessions over time may be required to see results in the post-stroke population more similar to those found in the healthy aging population.

CHAPTER 7: Limitations

Possible limitations of the study include the small size of the sample due to availability of existing participant data. With a small sample size there is also a decreased likelihood that the sample is representative of the general population, and so results cannot be generalized. Additionally, it is important to consider the limitations of the studies from which the current investigation's data was derived. While all participants in those studies used the same equipment in the same setting, variance in training sessions may still occur. All trainers administering the IM® sessions were IM® certified, however, individual differences may still exist. Participants may have differed on their level of motivation or effort they put forth during training sessions, and this may have affected the benefits of training and even the processes of activation and plasticity within the brain (Calautti & Baron, 2003). This may have impacted the benefits of the treatment despite the trainers' efforts to maximize participant motivation through encouragement and sharing knowledge of progress. Any normal age-related decreased functioning in sensory perception that could have impacted efficacy of treatment should have been controlled for in the purposive quota sampling group selection process.

CHAPTER 8: Directions for Future Research

Recently, neuroimaging has been able to provide insight into the cortical changes and reorganization that may be associated with recovery from stroke. It may also be a powerful tool in addition to standardized assessment in determining the effects of interventions and which interventions may be most effective for type, severity, and chronicity of stroke (Seitz, 2010). This suggests the use of TMS or fMRI to study the effect of IM® therapy on cortical activation and reorganization in individuals post-stroke. Additionally, as mentioned previously, including kinematic analysis in evaluation of IM® therapy effects on motor control and movement quality may provide a more complete picture than standardized assessments alone. Determining if functional gains made were retained at a three or six month follow-up would also be a further step in elucidating the effectiveness of IM® as an intervention tool for survivors of stroke.

Some research suggests that when auditory cues are based in musical context, motor responses are better synchronized and less variable than when derived solely from a metronome (Thaut, Rathburn, & Miller, 1997). Using a rhythm embedded in music may also be more motivating to clients, which may also beneficially impact the effectiveness of a therapeutic program for patients post-stroke (Jeong & Kim, 2007). Future research might compare the effectiveness of IM® therapy that employs music selections with rhythms that match a client's preferred pace with traditional IM® therapy.

Other future research may target whether IM® therapy may be enhanced by including task-oriented training to protocols for clients post-stroke. Cirstea and Levin (2007) suggest that in stroke rehabilitation, "interventions should specifically address the individual's impairments, be sufficiently difficult to challenge the motor system, and should incorporate strategies to enhance transfer of performance gains from the training situation to everyday life" (p. 399).

Trombly and Wu (1999) used motion analysis to determine that movement in goal-directed and object-oriented tasks such as reaching for a preferred food or reaching to pick up a telephone was better organized in terms of speed, smoothness, and force than just rote exercise movement in patients post-stroke. It is possible that combining the benefits of rhythmic cueing with the benefits of goal- and object-oriented tasks in bilateral situations might offer the maximal therapeutic benefits from IM®. Examples of "tasks" used in movement training in the literature include opening and closing jars and clothespins, and grasping various objects such as a spoon, reaching for objects, and throwing a ball (Hubbard, Parsons, Neilson, & Carey, 2009). Coming from the perspective of occupation as means, Hubbard and colleagues suggest that task-specific training involve "ordinary, everyday activities which as intrinsically and/or extrinsically meaningful to the patient or client" (2009, p. 181). The benefit of IM® in this situation may be its adaptability to be used within the contexts of, or incorporating the objects of, everyday life.

Alternatively, the potential use of the IM® as a "priming" preparatory activity before more task-related training warrants investigation as well. The 2008 study by Stinear and associates found that 10-15 minutes of rhythmic active-passive bilateral therapy (APBT) prior to motor practice increased excitability in the lesioned motor cortex and reduced inhibition coming from the contralesional hemisphere, thus normalizing the balance of activation in participants with chronic stroke. The group that received the APBT priming also showed sustained improvement in upper extremity motor function that the control group, which received only the motor practice, did not (Stinear et al., 2008). The IM® incorporates the same principles of repetitive, rhythmic, bilateral motion as the APBT as well as the added benefit of auditory cues that also may serve to enhance corticospinal excitability.

CHAPTER 9: Conclusion

Many studies suggest it may be beneficial to include both unilateral and bilateral forms of movement training in intervention planning (Lin et al., 2009; McCombe-Waller et al., 2008; McCombe-Waller & Whitall, 2008; Rose & Winstein, 2004; Stoykov et al., 2009). Many of these same studies also suggest the benefits of auditory cueing and the principles of motor learning and feedback in cortical activation, reorganization, and recovery in survivors of stroke. The IM® is a modality that incorporates all of these aspects. The results of this study indicate that the IM® may be just as effective an agent of change with post-stroke adults as it is with healthy aging adults. It further suggests the IM® may be a valid tool in dealing with the complex challenges in recovery from stroke, and may offer not only novelty with which to combat recovery plateau but also a sensitive measure of the slower progress often seen in chronic stroke. Additionally, this research adds to the body of evidence supporting the use of the IM® in occupational therapy, which assists therapists in using evidence-based decision making when selecting interventions for clients and may aid in the validation of its use to third party payers.

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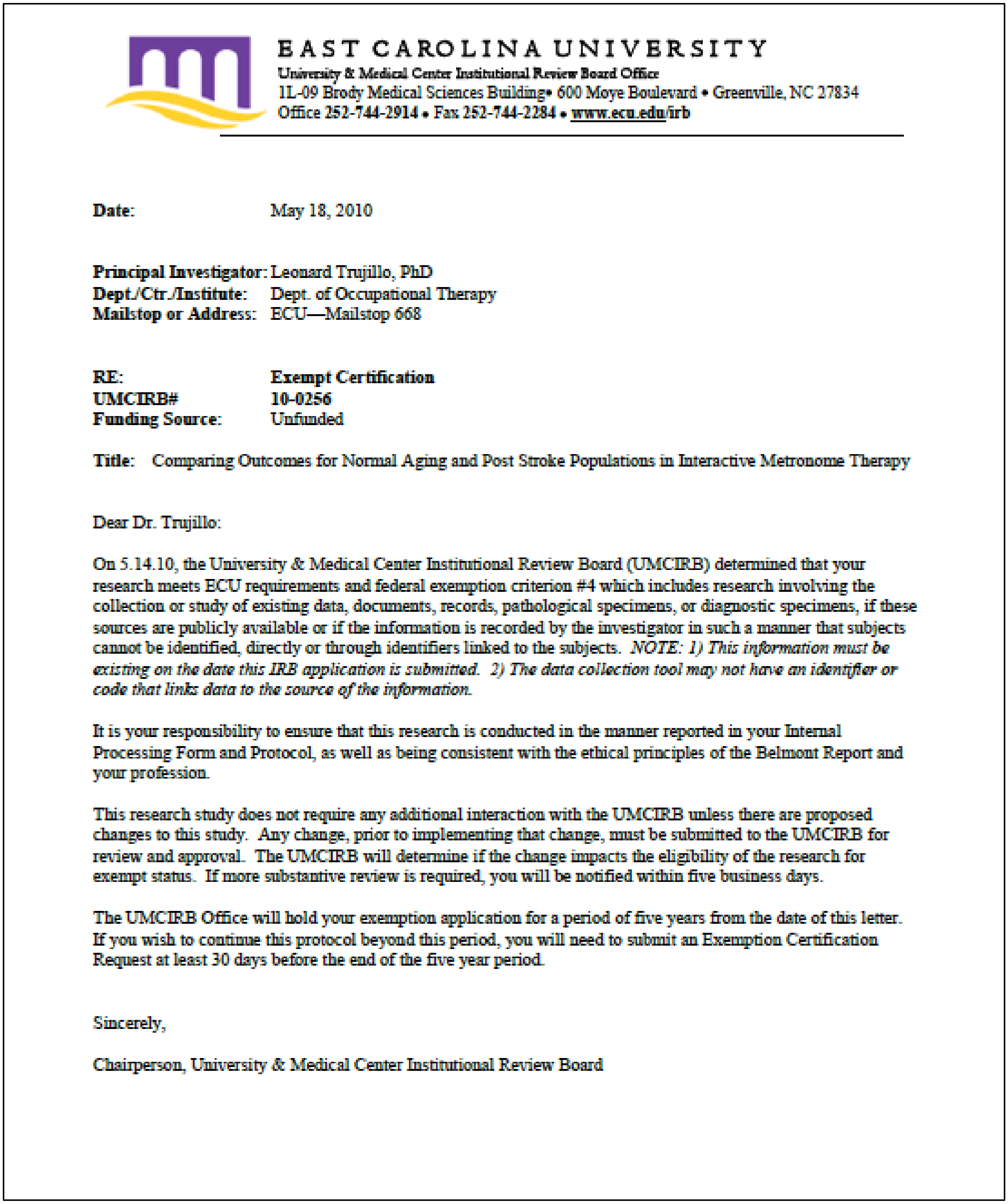
Appendix A



EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board Office
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Office 252-744-2914 • Fax 252-744-2284 • www.ecu.edu/irb

Date: May 18, 2010

Principal Investigator: Leonard Trujillo, PhD
Dept./Ctr./Institute: Dept. of Occupational Therapy
Mailstop or Address: ECU—Mailstop 668

RE: **Exempt Certification**
UMCIRB# **10-0256**
Funding Source: Unfunded

Title: Comparing Outcomes for Normal Aging and Post Stroke Populations in Interactive Metronome Therapy

Dear Dr. Trujillo:

On 5.14.10, the University & Medical Center Institutional Review Board (UMCIRB) determined that your research meets ECU requirements and federal exemption criterion #4 which includes research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. *NOTE: 1) This information must be existing on the date this IRB application is submitted. 2) The data collection tool may not have an identifier or code that links data to the source of the information.*

It is your responsibility to ensure that this research is conducted in the manner reported in your Internal Processing Form and Protocol, as well as being consistent with the ethical principles of the Belmont Report and your profession.

This research study does not require any additional interaction with the UMCIRB unless there are proposed changes to this study. Any change, prior to implementing that change, must be submitted to the UMCIRB for review and approval. The UMCIRB will determine if the change impacts the eligibility of the research for exempt status. If more substantive review is required, you will be notified within five business days.

The UMCIRB Office will hold your exemption application for a period of five years from the date of this letter. If you wish to continue this protocol beyond this period, you will need to submit an Exemption Certification Request at least 30 days before the end of the five year period.

Sincerely,

Chairperson, University & Medical Center Institutional Review Board

Appendix B

IM® Long Form Assessment (LFA)

LFA Task 1: Both Hands
Patient claps both hands in a rhythmic manner in sync with the reference (metronome) tone.

LFA Task 2: Right Hand
Patient hits the right hand on the right leg in a rhythmic manner in sync with the reference tone.

LFA Task 3: Left Hand
Patient hits the left hand on the left leg in a rhythmic manner in sync with the reference tone.

LFA Task 4: Both Toes
Patient taps each toe on the foot trigger in sync with the reference tone, alternating between tapping the left toe and tapping the right toe.

LFA Task 5: Right Toe
Patient taps right toe on the foot trigger in sync with the reference tone.

LFA Task 6: Left Toe
Patient taps left toe on the foot trigger in sync with the reference tone.

LFA Task 7: Both Heels
Patient taps each heel on the foot trigger in sync with the reference tone, alternating between tapping the left heel then tapping the right heel.

LFA Task 8: Right Heel
Patient taps right heel on the foot trigger in sync with the reference tone.

LFA Task 9: Left Heel
Patient taps left heel on the foot trigger in sync with the reference tone.

LFA Task 10: Right Hand, Left Toe
Patient alternates between hitting right hand on right leg and tapping left toe on foot trigger in sync with the reference tone.

LFA Task 11: Left Hand, Right Toe
Patient alternates between hitting left hand on left leg and tapping right toe on foot trigger in sync with the reference tone.

LFA Task 12: Balance on Right Foot, Tap Left Toe
Patient balances on right foot with left foot held in the air. Patient taps left foot on foot trigger to the reference tone beat.

LFA Task 13: Balance on Left Foot, Tap Right Toe
Patient balances on left foot with right foot held in the air. Patient taps right foot on foot trigger to the reference tone beat.

LFA Task 14: Both Hand with Guide Sounds
Patient claps both hands in a rhythmical manner in sync with the reference tone. Upon hitting the trigger, the patient will hear a guide sound that reflects how far clap was from the actual reference tone.

Appendix C

IM® Long Form Assessment Adaptations

Task Number	Original Task	Left Hemiplegia Adaptations	Right Hemiplegia Adaptations
1	Both Hands	Sit, place trigger in R hand and place L hand in center of body, clap.	Sit, place trigger in L hand and place R hand in center of body, clap.
2	Right Hand	Perform sitting.	Sit, place trigger in R hand and use L hand to assist R.
3	Left Hand	Place trigger in L hand and use R hand to assist L.	Perform sitting.
4	Both Toes	Sit, tap R toe, place trigger on L leg and use R hand to assist L hand, alternate.	Sit, tap L toe, place trigger on R leg and use L hand to assist R hand, alternate.
5	Right Toe	Sit and tap R toe.	Sit, place trigger on R leg and use L hand to assist R hand.
6	Left Toe	Sit, place trigger on L leg and use R hand to assist L hand.	Sit and tap L toe.
7	Both Heels	Sit, tap R heel, place trigger on L leg, use R hand to assist L hand.	Sit, tap L heel, place trigger on R leg, use L hand to assist R hand.
8	Right Heel	Sit and tap R heel.	Sit, place trigger on R leg, use L hand to assist R hand.
9	Left Heel	Sit, place trigger on L leg, use R hand to assist L hand.	Sit and tap L heel.
10	Right Hand/ Left Toe	Sit, place trigger on R leg and trigger on table on L, use R hand to alternate between triggers.	Sit, place trigger on R leg and trigger on table on L, use L hand to alternate between triggers.
11	Left Hand/ Right Toe	Sit, place trigger on L leg and trigger on table on R, use R hand to alternate between triggers.	Sit, place trigger on L leg and trigger on table on R, use L hand to alternate between triggers.
12	Balance Right Foot/ Tap Left Toe	Sit, place trigger on L leg and use R hand to assist L hand.	Stand and try, if unsuccessful, sit and tap L toe.
13	Balance Left Foot/ Tap Right Toe	Stand and try, if unsuccessful, sit and tap R toe.	Sit, place trigger on R leg and use L hand to assist R hand.
14	Both Hands with Guide Sounds	Sit, place trigger in R hand and place L hand in center of body, clap.	Sit, place trigger in L hand and place R hand in center of body, clap.

Appendix D

IM$^{®}$ SESSION PROTOCOL

Session 1	**Session 2**	**Session 3**	**Session 4**	**Session 5**	**Session 6**	**Session 7**	**Session 8**
Long Form Assessment	Short Form Assessment	Short Form Assessment	Short Form Assessment	Short Form Assessment	Short Form Assessment	Short Form Assessment	Short Form Assessment
Nine Hole Peg Test	Both Hands (350 reps)	Both Hands (300 reps)	Both Hands (350 reps)	Both Hands (300 reps)	Both Hands (350 reps)	Both Hands (300 reps)	Nine Hole Peg Test
Complete Gas Card Form	Right Hand (150 reps)	Right Hand (200 reps)	Right Hand (150 reps)	Right Hand (200 reps)	Right Hand (150 reps)	Right Hand (200 reps)	Complete Gas Card Form
	Left Hand (150 reps)	Left Hand (200 reps)	Left Hand (150 reps)	Left Hand (200 reps)	Left Hand (150 reps)	Left Hand (200 reps)	
	Assist Both Hands (200 reps)	Diagonal Hand-Thigh (200 reps)	Assist Both Hands (200 reps)	Diagonal Hand-Thigh (200 reps)	Assist Both Hands (200 reps)	Diagonal Hand-Thigh (200 reps)	
	Diagonal Hand-Thigh (150 reps)	Assist Both Hands (250 reps)	Diagonal Hand-Thigh (150 reps)	Assist Both Hands (250 reps)	Diagonal Hand-Thigh (150 reps)	Assist Both Hands (250 reps)	
	Non-Affected Toe (150 reps)	Non-Affected Heel (150 reps)	Non-Affected Toe (150 reps)	Non-Affected Heel (150 reps)	Non-Affected Toe (150 reps)	Non-Affected Heel (150 reps)	
	Both Hands (200 reps)	Both Hands (150 reps)	Both Hands (200 reps)	Both Hands (150 reps)	Both Hands (200 reps)	Both Hands (150 reps)	