EFFECTS OF SHORT-TERM BIMANUAL COORDINATION TRAINING ON MODULATION OF SENSORIMOTOR CORTICAL ACTIVITY AND MOTOR PERFORMANCE

by

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ABSTRACT

Chronic upper extremity hemiparesis is common after stroke (Jørgensen et al., 1995). This chronic impairment has a direct impact on functional independence and the ability to perform daily activities (Lloyd-Jones et al., 2010). Given the high levels of functional losses after stroke, investigation into treatments for chronic impairments should be considered. The purpose of the current study was to examine the effects of short-term bimanual coordination training on the modulation of sensorimotor cortical activity and motor performance. Thirty healthy participants were randomized to one of three training groups: 1) physical practice, 2) observational practice, and 3) no practice (control condition). Movement-related potentials (MRPs) and somatosensory evoked potentials (SEPs) were collected before and after training to examine the effects of training on cortical activity. Motor performance on the bimanual coordination task was also compared between groups. The results showed that: (1) there was no significant difference in MRP or SEP measures between groups, (2) the physical practice group performed significantly better (as indexed by greater accuracy following practice) than the control group on the bimanual coordination task, (3) although the observational practice group did not perform as well as the physical practice group, there was a trend for greater accuracy following observation as compared to the control group. These results suggest that both short-term physical and observational practice of a bimanual coordination task can result in improved motor performance and provide support for the use of observational practice in motor learning.

PREFACE

This thesis contains a research experiment conducted by candidate, Katharine L. Cheung, under the supervision of Dr. Lara Boyd, with guidance from Dr. Jayne Garland, Dr. Nicola Hodges and Dr. Naznin Virji-Babul. The collection, analysis and writing of the experiment were principally the work of the candidate. The supervisory committee provided direction, support and critical feedback on the design of the study. This thesis will be submitted for publication as a multi-authored manuscript in a peer-reviewed journal. Ethical review and approval for this thesis was performed by the University of British Columbia Clinical Research Ethics Board (H12-03367).

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LIST OF ABBREVIATIONS

APB: Abductor pollicis brevis

EEG: Electroencephalography

EMG: Electromyography

ECR: Extensor carpi radialis

fMRI: Functional magnetic resonance imaging

M1: Primary motor cortex

MNS: Mirror neuron system

MRP: Movement-related potential

M-wave: Motor wave

PET: Positron emission tomography

RAP: Reafferent potential

S1: Primary somatosensory cortex

SEP: Somatosensory evoked potential

SMA: Supplementary motor area

TMS: Transcranial magnetic stimulation

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Finally, to my friends, family and partner, I thank you, to the moon and back, for the endless years of encouragement and support. I would not be where I am today without you.

1.0 INTRODUCTION

The overall objective of this thesis is to determine the effects of short-term bimanual coordination training on modulation of sensorimotor cortical activity and motor performance.

1.1 Bimanual Coordination

1.1.1 The Problem

Upper extremity hemiparesis is the dominant functional limitation in as much as 80% of patients with acute stroke (Jørgensen et al., 1995; Nakayama, Jorgensen, Raaschou, & Olsen, 1994). Even after traditional therapeutic interventions are used, 50-95% of these individuals are persistently impaired (Gowland, deBruin, Basmajian, Plews, & Burcea, 1992; Gresham et al., 1975; Mayo et al., 1999). This chronic impairment has a direct impact on functional independence (Lloyd-Jones et al., 2010). Given the high levels of residual impairment and functional loses after stroke, investigation into treatments for chronic impairments, beyond traditional interventions, need to be considered.

1.1.2 An Overview of the Bimanual Approach in Rehabilitation

Amongst a variety of rehabilitation strategies targeted at restoring motor function, bimanual (two-handed) training has gained popularity and shown promise as a means of upper extremity rehabilitation (Cuadrado & Arias, 2001; Luft et al., 2004; Mudie & Matyas, 2000). Re-training bimanual skills is particularly relevant since the majority of daily activities involve the use of both arms. Furthermore, this approach is likely to be highly impactful, especially because bimanual deficits after stroke are believed to be underreported due to the fact that few studies actually measure bilateral functional outcomes (McCombe Waller & Whitall, 2008). Studies that assess bilateral impairments note that after stroke individuals have dis-coordination between limbs, impaired bilateral reaching and impaired bilateral arm swing (McCombe Waller & Whitall, 2004; Peters, 1977; Ustinova, Fung, & Levin, 2006).

1.1.3 An Overview of Bimanual Movements in the Context of Motor Re-Learning

In the context of motor impairment following stroke, evidence from research with animal models suggests that learning novel motor skills is a key component to functional recovery (Nudo, 2003). After unilateral stroke, bilateral movement (thus causing activation of both cerebral hemispheres) may increase motor-related brain activity in the (more) affected hemisphere (Silvestrini, Cupini, Placidi, Diomedi, & Bernardi, 1998; Staines, McIlroy, Graham, & Black, 2001). Furthermore, bilateral movement training has been shown to help restore sensorimotor control in a variety of paradigms (Cuadrado & Arias, 2001; Luft et al., 2004; McCombe Waller & Whitall, 2004; Mudie & Matyas, 2000; Stinear, Barber, Coxon, Fleming, & Byblow, 2008); however, the neurophysiological mechanisms by which this form of training exerts its effects have yet to be fully elucidated.

While a recent meta-analysis of bilateral movement training revealed general positive outcomes associated with training during subacute and chronic phases of stroke recovery (Stewart, Cauraugh, & Summers, 2006), an obstacle to our complete understanding of the extent of bilateral deficits following injury to the motor system is that the majority of published research studies report only unilateral outcome measures, even if they implemented a bimanual training intervention. This is problematic because the control of each arm separately is not equivalent to the control of both together (McCombe Waller & Whitall, 2008) and the underlying principles of single-limb tasks cannot all be generalized to the principles of performance of bilateral coordination tasks (Swinnen, 2002). Indeed, studies of interlimb coordination have helped illustrate that unilateral and bilateral skills have different neuromotor control mechanisms (Kelso, Southard, & Goodman, 1979; Kelso, Putnam, & Goodman, 1983). Furthermore, although it is possible for some initial unilateral practice to transfer to improvements in bilateral coordination in some cases (see Charles, Wolf, Schneider, & Gordon, 2006; Eliasson, Krumlinde-Sundholm, Shaw, & Wang, 2005), task specificity in practice is known to help optimize an individual's ability to learn (Schmidt & Lee, 2005) and thus bilateral recovery may be best accrued with bilateral training. On the whole, in order to understand how and when is best to implement bimanual training interventions, more research, especially controlled trials that measure bilateral outcome measures, needs to be conducted.

1.1.4 Neurophysiological Justification for Bimanual Training

The exact neural mechanisms and anatomical pathways affected by bimanual training interventions in stroke are not yet fully understood, but several possibilities have been postulated. Included in these possibilities are: an interaction in the more affected hemisphere between spared cells of the ipsilesional and crossed corticospinal pathways; a facilitation of ipsilesional pathways from the contralesional hemisphere; and an interaction between the more affected hemisphere and indirect pathways (e.g. reticulospinal or rubrospinal tracts) (Lewis & Byblow, 2004; Mudie & Matyas, 1996).

Multiple techniques and methods have been used to help elucidate the effects of bimanual training on the sensorimotor system. In addition to electroencephalography (EEG) studies, which will be discussed in further detail below, studies using transcranial magnetic stimulation (TMS) have helped substantially in investigating the efficacy of bimanual training. In general, assessing intracortical excitability with TMS allows for investigation into the mechanisms of cortical plasticity (Ziemann, Corwell, & Cohen, 1998), including the effects of practiced movement (Liepert, Classen, Cohen, & Hallett, 1998). In support of bimanual training, a study by Stinear & Byblow (2004) used TMS to examine the effects of a 4-week period of repetitive bimanual coordinated movement training post-stroke on upper limb corticomotor excitability (of the wrist flexor and extensor representation areas of the primary motor cortex (M1)) and motor function. Their findings suggested that the bimanual movement therapy initiated an improvement of motor function associated with a balancing of between-hemisphere corticomotor excitability.

Additional work with TMS has demonstrated that bimanual movements result in a *reduction* of intracortical inhibition in both hemispheres, whereas unimanual movements result in an *increase* of inhibition in the ipsilateral hemisphere (McCombe Waller, Forrester, Villagra, & Whitall, 2008; Stinear & Byblow, 2002). With respect to recovery of motor skills after stroke, a reduction in intracortical inhibition could be beneficial for recovery while an increase in inhibition in the ipsilateral hemisphere during unimanual training (of the non-paretic arm) could be detrimental to recovery (of the paretic arm) because it may reinforce inhibitory processes in the damaged hemisphere (McCombe Waller & Whitall, 2008) (Figure 1). Indeed, several studies have demonstrated the influence of intracortical inhibition from non-lesioned cortices on lesioned cortices during sensorimotor processing (Floel et al., 2004; Murase, Duque, Mazzocchio, & Cohen, 2004; Werhahn, Mortensen, Van Boven, Zeuner, & Cohen, 2002). For example, a study by Murase et al. (2004) examined interhemispheric inhibition between intact and lesioned M1 during voluntary movement of the (moderately) paretic hand in patients with stroke. The authors found an abnormally high interhemispheric inhibitory drive from the intact M1 to the lesioned M1 during paretic hand movement and suggest that this irregularity could potentially negatively affect motor recovery. Furthermore, Floel et al. (2004) helped demonstrate the interhemispheric competition of sensorimotor processing by showing that temporary cutaneous anesthesia of chronic stroke patients' unaffected hands elicited site-specific motor performance improvements in their paretic hands. This is in line with similar findings by Werhahn et al. (2002) who showed that acute deafferentation of the right hand led to enhanced tactile spatial acuity and changes in cortical processing of the left hand. Taken together, these studies help demonstrate interhemispheric competition of sensory and motor processing in the brain. Moreover, this evidence suggests that interventions focused solely on unimanual training may cause inhibition in the affected hemisphere that is detrimental to recovery of the paretic arm. Overall, evidence from TMS research and behavioural studies reported above supports the notion that some forms of bimanual training may be effective in producing positive neural adaptations, whereas unimanual training may produce negative effects.

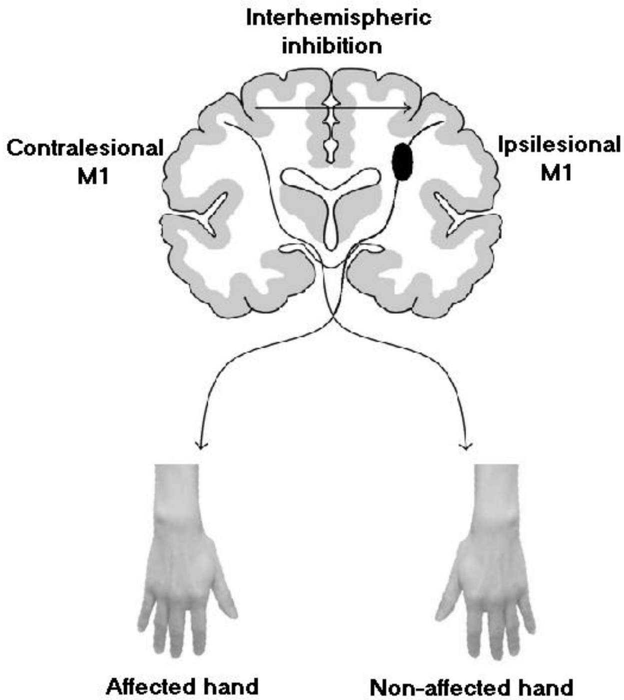

Figure 1. Interhemispheric inhibition between contralesional and ipsilesional M1 (figure adapted from Takeuchi et al. (2012)).

1.2 Training: Physical and Observational Practice

1.2.1 Motor Control and Learning: Physical Practice

After an insult to the brain such as stroke, cooperation between muscles in the proximal and distal upper extremities (a component essential for the execution of skilled hand/wrist movements (Porter & Lemon, 1993)), may be diminished either by reduced neuronal activity (caused by a reduction in ability for neurons to fire) or a reduction in the number of fast corticospinal fibers (fibres that conduct impulses from the brain to the spinal cord) (Turton & Lemon, 1999). These factors may result in inadequate recruitment of specific muscles, causing movement deficits (Gowland et al., 1992). Studies have suggested that it is possible for plasticity within the cortex to enable compensation for these deficits (e.g. Johansen-Berg et al., 2002; Traversa, Cicinelli, Pasqualetti, Filippi, & Rossini, 1998) and thus it is important to consider neuroplasticity in the context of motor learning when implementing rehabilitation strategies.

Neurophysiologically, when an individual learns new motor movements, cortical excitability changes can be observed in M1 (Classen, Liepert, Hallett, & Cohen, 1999). These changes in cortical excitability can happen even over the course of a short period of motor practice (i.e. minutes/hours) (Classen, Liepert, Wise, Hallett, & Cohen, 1998; Kleim et al., 2004; Nudo, Milliken, Jenkins, & Merzenich, 1996; Nudo & Milliken, 1996). Changes in the somatotopic representation of the limb areas in M1 can also occur over time (Kleim, Barbay, & Nudo, 1998).

Behaviourally, learning novel motor movements involves repeated practice of the movement, eventually leading to a decrease in the time required or errors made during the performance of the movement (Schmidt & Lee, 2005). In the context of motor learning, "fast learning" is the rapid change often seen early in practice (within session) that does not necessarily translate to sustained improvements in motor skill (Doyon & Benali, 2005). With continued practice (over multiple training sessions), performance improvement commonly plateaus and the rate of change associated with learning decreases (Karni et al., 1998). This is characteristic of the "slow learning" phase of motor learning, which can persist for a long period of time (Doyon & Benali, 2005). Following practice, motor memories may be strengthened by the process of consolidation, which allows for the motor memories to stabilize and be available for recall in the future (Brashers-Krug, Shadmehr, & Bizzi, 1996). From a neurophysiological perspective, rapid changes in the amount and location of neurotransmitters within and between neurons are associated with early "fast learning" (Karni et al., 1998), while structural modifications that create new connections between neurons are associated with "slow learning" (Kleim et al., 2004). As such, rates of change in motor performance associated with learning vary between early and late learning because the alteration of neuronal structure requires more time than does reallocating neurotransmitters (Karni et al., 1998).

Overall, learning and practising new motor skills is important for inducing neuroplastic change and functional recovery after an insult to the nervous system and physical practice is an effective means of rehabilitation after motor system injuries.

1.2.2 Motor Control and Learning: Observational Practice

Physical practice is not the only method of acquiring new motor skills; observational practice has also been shown to facilitate the acquisition of a variety of motor skills (Bandura, 1986; Blandin & Proteau, 2000; Mattar & Gribble, 2005) . From a behavioural perspective, numerous studies have demonstrated this concept. For example, Badets & Blandin (2005) showed that participants could learn absolute and relative timing of movement sequences solely via action observation with no physical practice while Vogt (1995) showed action observers could learn parameters of spatio-temporal control on a task requiring unilateral cyclical flexion-extension movements of the forearm. Furthermore, a study by Hayes et al. (2009) examined learning of a three-segment movement sequence and found that observational practice resulted in similar movement kinematics after one session of training compared to physical practice. Taken together, research has illustrated that observational practice can indeed lead to similar levels of motor proficiency as physical practice (Hayes, Elliott, & Bennett, 2010) and this can happen even after short periods of time. For example, Gatti et al. (2013) showed that participants who trained via observational practice for approximately 7 minutes could learn to perform a novel motor task and likewise Heyes & Foster (2002) showed that after approximately 7 minutes of observational practice participants showed as much sequence learning (as measured by reaction times) as other participants who trained via physical practice.

From a physiological perspective, the notion of physical and observational practice sharing many similarities has been supported by numerous studies. For example, observational learning can be influenced by various experimental manipulations in much the same manner as learning by physical practice, suggesting similar cognitive processes are involved in both physical and observational practice (Adams, 1986). Likewise, studies have identified shared neural networks associated with both action production and action observation, including the premotor cortex and supplementary motor area (SMA), as well as deeper structures (Gallese & Goldman, 1998; Grèzes & Decety, 2001). Moreover, past work has demonstrated that the cortical areas involved in the actual execution of simple finger movements are also activated during observation of identical movements by another individual, but are not activated by the presentation of spatial or symbolic cues (Iacoboni et al., 1999), suggesting there are indeed areas of the brain associated specifically with action observation. The link between physical and observational practice is also supported by data that suggests that when an individual is undergoing observational practice, they are coding the model's actions into a neural representation similar to how one would during motor execution (this neural representation serves as the foundation for the processes subsequently involved in the control of movement) (Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995). On the whole, research to date supports the notion that the processes of observational and physical practice are closely linked (Aziz-Zadeh, Maeda, Zaidel, Mazziotta, & Iacoboni, 2002; Buccino et al., 2004).

The neural mechanism widely believed to be responsible for motor learning associated with observational practice is a system of neurons that fire when an individual performs a specific action as well as when they watch another individual performing the same action (Gatti et al., 2013; Iacoboni et al., 1999; Mattar & Gribble, 2005). In humans, this system of neurons, called the mirror neuron system (MNS), is found in the inferior parietal lobule, the ventrolateral premotor cortex and the caudal portion of the inferior frontal gyrus (Fabbri-Destro & Rizzolatti, 2008). Past work has demonstrated that during observational learning of complex actions (when an individual must master motor sequences not already in their motor repertoire) where an individual is asked to repeat the actions immediately following observation, areas within the MNS are active from the time of observation of the model until the actual execution of the movement (Buccino et al., 2004; Vogt et al., 2007). Furthermore, Stefan et al. (2005) used TMS to demonstrate that observation of another individual performing simple repetitive thumb movements alone could lead directly to the formation of kinematically specific motor memories in M1. The authors' findings support the notion that M1 displays mirror neuron activity in response to observation of movement and support an overall role for the MNS in motor memory formation and potentially motor learning.

While the vast majority of past work has focused on observation of unilateral actions (e.g Buccino et al., 2004; Mattar & Gribble, 2005; Vogt et al., 2007), a recent study was the first to investigate the cortical regions involved in the observation of bimanual actions (Heitger, Macé, Jastorff, Swinnen, & Orban, 2012). Using functional magnetic resonance imaging (fMRI), the authors found that observation of bimanual and unimanual actions activated similar occipito-temporal, parietal and premotor networks, but that bimanual actions resulted in more bilateral activity, particularly in the parietal cortex. Despite this finding, further work is needed to fully understand the action observation network and the neural processing involved in the observation of bimanual actions. On the whole, despite recent work investigating the role of the MNS in unilateral motor learning, and identifying the cortical regions involved in bimanual action observation, the exact neurophysiological mechanisms involved in bimanual motor learning with observational practice have yet to be elucidated.

1.3 Studying the Effects of Bimanual Coordination Training

1.3.1 Movement-Related Potentials

1.3.1.1 General Description of Movement-Related Potentials

The movement-related potential (MRP), first recorded by Kornhuber and Deecke (1964), is an event-related potential used to study temporal aspects of motor learning, specifically movement planning and preparation preceding voluntary movement. Recorded via EEG (generally over the premotor and primary motor cortices and/or the SMA), the MRP is characterized as a low-frequency (0-5 Hz) negative shift visible approximately 1.5-2 seconds before the onset of voluntary movement (Kornhuber & Deecke, 1964; Shibasaki & Hallett, 2006; Taylor, 1978). Since regional cortical EEG negativity is generally associated with increased synaptic activity (whereas regional positivity in EEG is generally associated with decreased activity) (Deecke, 1996), MRPs are thought to represent increased cortical processing (synaptic activity) prior to the production of movement (Wright, Holmes, & Smith, 2011). Depending on the type of impending movement (physical and psychological properties inclusive), the characteristics of the MRP can vary (Birbaumer, Elbert, Canavan, & Rockstroh, 1990). For example, the *amplitude* or *slope* of the MRP may be used as a measure of the cortical energy expenditure required for a particular motor plan to be formed prior to actual movement (Lang, Beisteiner, Lindinger, & Deecke, 1992). Likewise, the MRP *latency* may be interpreted as a measure of the length of time required to prepare a movement plan prior to actual movement (Tarkka & Hallett, 1990). Due to their low frequency and relatively small amplitude (approximately 5-30 μV), MRP waveforms are typically collected by recording multiple trials of the same task and averaging the recordings across trials (Wright et al., 2011). Otherwise, MRP waveforms can be masked by cortical activity in higher frequency bands (Wright et al., 2011).

The MRP is often divided into three components: the early component, the late component and the reafferent potential (RAP) (Figure 2). The early component is thought to principally represent motor preparatory activity from the SMA (Shibasaki & Hallett, 2006). The late component is thought to be generated mainly by activity of the contralateral M1 and the reafferent potential is thought to be generated by activity in the primary somatosensory cortex (S1) (Colebatch, 2007; Shibasaki & Hallett, 2006).

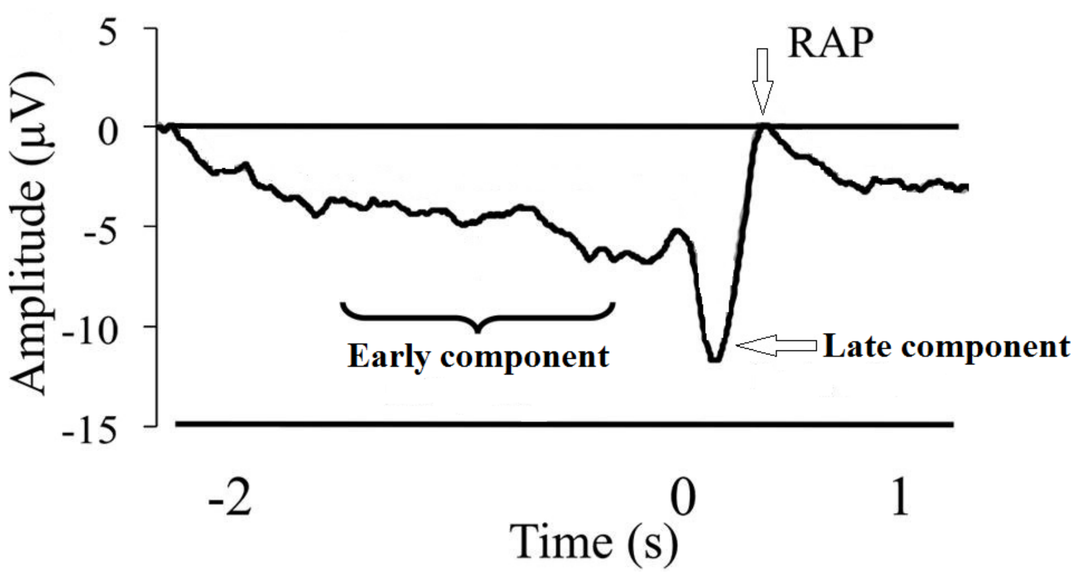

Figure 2. A grand average movement-related potential time-locked to onset of voluntary movement, recorded from electrode site FCZ. The early component, late component and reafferent potential (RAP) are labeled (figure adapted from Smith & Staines (2012)).

1.3.1.2 MRPs and Motor Learning

Many studies have examined changes in MRPs associated with skill learning. For example, Taylor (1978) examined the relationship between MRP amplitude and skill acquisition. In Taylor's study, EEG was recorded while participants performed 45 trials of a 6-button sequence with their right hand and their response time for each trial was measured. Taylor found that MRP amplitude increased at all recorded electrode sites (FZ, CZ, C3" and C4", which sit over frontal and motor cortices) while participant performance was improving (i.e. response time was decreasing) during the acquisition phase of the motor skill. After acquisition of the skill, when the skill became more automatic, and thus both the attentional demands and the amount of feedback required to maintain the level of performance were reduced (and the participant's response time stayed relatively constant), the amplitude of the MRP decreased over the frontal area and ipsilateral M1 (Taylor, 1978). Since MRP amplitude is thought to be indicative of neural effort of motor performance, these findings contributed to the notion that the learning phase of skill acquisition requires more effort than performance of the same skill after one has become competent. Indeed, past work has confirmed that during the skill acquisition phase, increases in motor performance (accuracy and preparation to respond) are associated with an increase in MRP amplitude (Ford, MacPherson, & Kopell, 1973; Loveless & Sanford, 1974; McAdam & Rubin, 1971).

More recently, Smith & Staines (2006) used EEG to study the temporal aspects of neural plasticity associated with short-term bimanual movement training as well as the associated effects on motor performance. The authors showed that cortical adaptations took place even after short-term training (approximately 45 minutes) within a single session. Specifically, the authors found a strong relationship between modulation of the early component of the MRP amplitude and reaction time in a unimanual task following bimanual movement training, such that a decrease in reaction time was associated with an increase in early MRP amplitude. On the whole, the MRP may serve as a useful measurement tool for exploring cortical adaptations involving movement planning and execution associated with motor training, since the size and distribution of the MRP is strongly linked to proficiency of a motor response with learning.

1.3.2 Somatosensory Evoked Potentials

1.3.2.1 General Description of Somatosensory Evoked Potentials

An evoked potential is electrical activity recorded from the nervous system in response to external stimulation (Yamada, Yeh, & Kimura, 2004). Somatosensory evoked potentials (SEPs), which can be elicited by various stimuli and recorded via EEG, are used as a probe into the somatosensory system. A simple method to elicit SEPs is via electrical stimulation of a peripheral nerve (e.g. the median nerve in the wrist or the tibial nerve in the leg). SEPs can be used in laboratory settings, such as to study cortical adaptations before and after an intervention, and in clinical settings, such as to assess the integrity of a connection between a peripheral nerve and S1. Analysis of the SEP waveform is often divided into different components (short-latency components (<80ms) and long-latency components (>80ms)) that reflect different stages of neural processing as sensory information ascends from distal limbs proximally to be processed in the brain (Bulut, Özmerdivenli, & Bayer, 2003; Tanaka et al., 2008; Yamashiro et al., 2013).

Past work has lead to the anatomical characterization of many specific components of the SEP waveform (n.b. the components are named based on their negative (N) and positive (P) inflections and average latency (in milliseconds) in an average EEG waveform). For example, the N9 component of the SEP is taken to represent conduction of a potential along the peripheral nerve, the N13 component is taken to represent the conduction of a potential in the cervical dorsal horn and the P14-N20 component is taken to represent the conduction of potential in the cervicomedullary junction near the cuneate nucleus (Golding, Ashton, Marsh, & Thompson, 1986; Macefield & Burke, 1991; Urasaki et al., 1988; Urasaki, Wada, Yasukouchi, & Yokota, 1998). Further, the *latency* of the N20-P26 component is taken to represent the arrival of sensory information to S1, while the *magnitude* of the N20-P26 component is taken to represent the size of synaptic input arriving in S1 (Nardone & Schieppati, 1989; Yamada et al., 2004).

Many components of the SEP have also been characterized functionally. For example, the N20 and P26 early components of the SEP (Figure 3) have been used to investigate processes such as the effects of training or attention on the sensory integration response (e.g. Bulut et al., 2003; Elbert, Pantev, Wienbruch, Rockstroh, & Taub, 1995; Hashimoto, 2004). In a study with peripheral nerve stimulation, Murakami et al. (2008) compared racquetball players to non-athletes and showed that stimulation of the median nerve resulted in significantly greater short-latency SEP amplitudes in racquetball players compared to non-athletes, demonstrating that long-term training may induce neuroplastic changes to the neural circuit and excitability of S1. Similar studies have been conducted to examine adaptations to long-latency components of the SEP as well. For example, Yamashiro et al. (2013) studied sensory processing and response time related to P100 and N140 components during hand movements in baseball players versus other athletes (who do not play sports involving fine motor control of the hand). The authors found that peak P100 and P140 latencies, as well as response times, related to hand movements were significantly shorter in the baseball group compared to the other athlete group. The authors suggested that specific athletic training involving the hands such as baseball may induce neuroplastic alterations in the cortical hand representation area of M1, playing an important role in fast sensory processing and initiation of motor responses that can be detected via SEP waveform analysis.

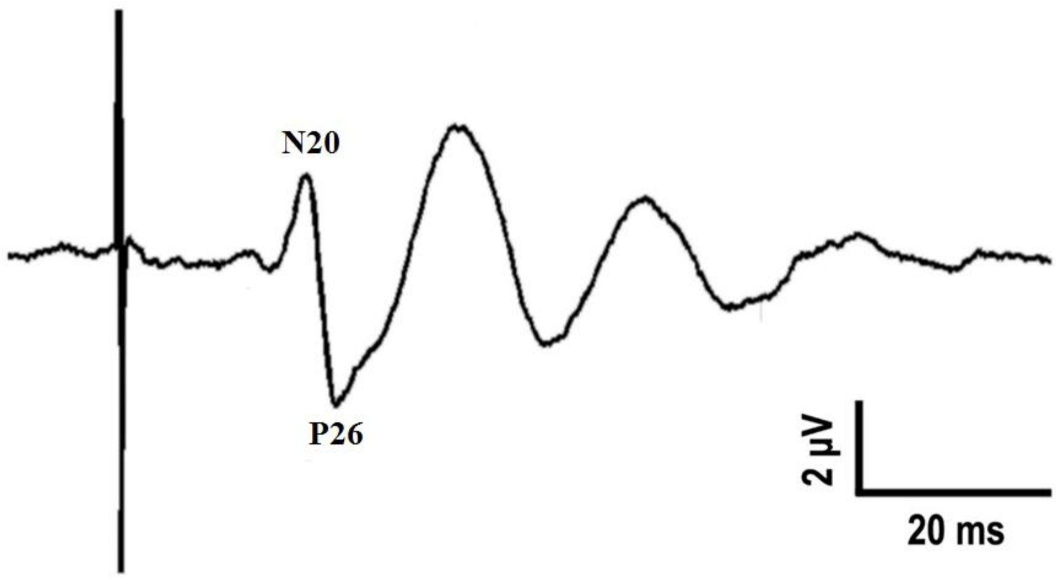

Figure 3. A grand average somatosensory evoked potential recorded over S1. N20 and P26 components are labeled (figure adapted from Muller-Dahlhaus et al. (2010)).

1.3.2.2 The Sensorimotor System, SEPs and Motor Learning

The relationship between S1 and M1 has been studied extensively. For example, physiologically, past work has shown that sensory input reaches motor and pre-motor areas of the brain either after synapsing in S1 (Jones & Friedman, 1982) or by direct parallel pathways from thalamic relays (Mauguière, Desmedt, & Courjon, 1983; Rossini et al., 1989; Traversa et al., 1998). Furthermore, Iriki et al. (1989) showed that tetanic stimulation of the neurons in S1 produced long-term potentiation effects in M1, whereas tetanic stimulation to other parts of the brain which also project to M1 did not.

With respect to motor learning, past work has shown that sensory feedback plays an important role in skilled motor learning (Hwang & Shadmehr, 2005; Pavlides, Miyashita, & Asanuma, 1993; Schmidt & Lee, 2005; Vidoni & Boyd, 2009). Further, it has been shown that afferent input is critical to learning new skills and manipulation of this input can cause organizational changes in M1 (Zanette, Manganotti, Fiaschi, & Tamburin, 2004). Likewise, Ziemann et al. (1998) showed that removing sensory input (via transient forearm deafferentation) can modulate motor cortical plasticity, and that subsequent restoration of this sensory input can reverse this change.

In further support of the link between S1 and M1, Schabrun et al. (2012) recently demonstrated that changes in M1 excitability (as indexed by TMS) mirrored changes in S1 excitability (as indexed by the amplitude of SEP components) following peripheral electrical stimulation, and that the potential mechanisms of S1-M1 excitability co-modulation are cortico-cortical projections between S1 and M1. Overall, since the somatosensory system is as an important component of motor learning (Vidoni, Acerra, Dao, Meehan, & Boyd, 2010), there is a logical basis for examining SEPs in conjunction with cortical activity measures of the motor system, such as MRPs, when examining the influence of training on the brain.

2.0 RATIONALE

The overarching objective of the study described in this thesis was to improve our understanding of how short-term physical and observational practice of a bimanual coordination task may alter cortical excitability and influence motor performance. Since much remains unknown regarding motor skill learning, observational practice and bimanual movement, all which are thought to be important factors in the recovery of motor function after stroke, the current study focused on examining the modulation of sensorimotor system following bimanual coordination training in healthy individuals. In turn, the knowledge gained from the current study will contribute to the body of knowledge related to the development of rehabilitation programs aimed at promoting the reorganization of sensorimotor areas of the brain that have been damaged by an injury such as stroke.

2.1 MRP Justification

While past work using TMS has provided insight into some of the potential changes in cortical excitability associated with observational practice, and studies using fMRI have highlighted potential areas of the brain involved in observational practice, EEG enables exploration of the effects of observational practice on neural activity over any area of the cortex, and with high temporal resolution. As discussed above, past work by Smith & Staines (2006) has demonstrated the effects of short-term bimanual training on cortical adaptations and subsequent motor performance using MRPs recorded via EEG. The current study sought to add to this body of work by investigating the effects of short-term observational training in addition to physical training with a bimanual task. Specifically, the purpose of the current study was to determine if observational training could result in modulation of the motor and sensory cortices, as measured via MRPs and SEPs, and if changes in motor performance would be noted following solely observational training. This would be particularly beneficial for those with severe movement impairments (for example, major hemiparesis following stroke). While long-term training (years) has been associated with less motor cortical effort and less time required to plan and prepare a motor movement, as indexed by a decrease in MRP amplitudes (Hatta, Nishihira, Higashiura, Kim, & Kaneda, 2009; Tarkka & Hallett, 1990), short-term training (minutes) has been shown to result in increased MRP amplitude, indicative of increased motor cortical activity during the planning and preparation stage prior to movement (Ford et al., 1973; Loveless & Sanford, 1974; McAdam & Rubin, 1971; Smith & Staines, 2006; Taylor, 1978).

2.2 SEP Justification

Past work has demonstrated the importance of S1 in the planning and production of movement. As such, examining the effects of a novel bimanual coordination task on S1 modulation, in addition to motor cortical areas, is logical, especially since the sensory and motor cortices share anatomical and functional connections. As discussed above, it is well established that the motor cortex receives specific input from the sensory cortex (Jones, Coulter, & Hendry, 1978; Waters, Favorov, & Asanuma, 1982) and further work has specifically characterized cortico-cortical projections between S1 and M1 in both animal models and humans (Kaneko, Caria, & Asanuma, 1994a; 1994b). In further support, studies using positron emission tomography (PET) have shown activation of both M1 and S1 after repetitive motor task performance (Mima et al., 1999; Weiller et al., 1996). Additionally, Schwenkreis et al. (2001) investigated whether repetitive motor training caused plasticity of S1, similar to what had previously been shown in M1. The authors used EEG source localization of SEPs, specifically focusing on the N20 component of the SEP, and found that one hour of motor training indeed induced neuroplasticity in the contralateral S1. Overall, given the evidence supporting the close association between M1 and S1, it is reasonable to hypothesize that changes in S1 activity may take place during/after bimanual movement training, even following observational practice.

2.3 Behavioural Task Justification

A significant number of previous studies have investigated learning-related changes associated with in- and anti-phase coordination patterns (e.g. Debaere et al., 2001; Jäncke et al., 2000; Toyokura, Muro, Komiya, & Obara, 1999). In- and anti-phase coordination patterns are considered intrinsic to the human motor system and do not require learning to be performed with ease (Kelso & Jeka, 1992; Swinnen, Jardin, Meulenbroek, Dounskaia, & Hofkens-Van Den Brandt, 1997); whereas patterns that deviate from in- and anti-phase coordination often require a considerable amount of practice before an individual can perform the pattern reliably (Lee, Swinnen, & Verschueren, 1995; Swinnen, Lee, Verschueren, Serrien, & Bogaerds, 1997).

In the current study, the selected task involved the acquisition of a novel bimanual coordination pattern. This task involved rhythmic flexion and extension of the wrists in a 90-degree out-of-phase pattern, similar to the task used by Debaere et al. (2004). While the movements required of each limb were not difficult, the spatial-temporal relationship required of the limbs was not intuitive and took practice to be able to be performed reliably (Hodges & Franks, 2001; Debaere, Wenderoth, Sunaert, Van Hecke, & Swinnen, 2004). Furthermore, in the scurrent study underlying movement kinematics (specifically, data of the participants' hand positions over time) were collected during task performance to quantify the behavioural correlates of the task thoroughly, instead of simply using general performance indicators (e.g. reaction times, total number of errors, etc.). Movement kinematics were explicitly collected in order to help eliminate the potential confounds associated with movement kinematics changes over time as a result of learning (Debaere et al., 2004). Additionally, qualitative (visual) feedback was provided throughout each trial of the task to aid in effective learning (Badets & Blandin, 2005).

2.4 Summary of Study Rationale

The study performed in this thesis sought to characterize the cortical activity associated with sensory and motor processes following short-term training of a novel visuomotor bimanual coordination task. Additionally, the current study sought to characterize motor performance throughout the progress of training with this novel task, and to compare motor performance across physical practice and observational practice groups at the end of the training intervention. The current study also involved examining the potential transfer of bimanual training to cortical adaptations during unimanual movement (during the collection of MRPs), similar to studies by Smith & Staines (2006; 2012).

In particular, the specific aims of the study were to:

1) Determine whether short-term bimanual coordination training (two types: physical practice and observational practice) alters motor cortical excitability as measured by MRP slope.

2) Determine whether short-term bimanual coordination training (two types: physical practice and observational practice) alters sensory cortical excitability as measured by SEP amplitude.

3) Compare physical practice to observational practice in terms of motor performance on a bimanual coordination task following training.

It was hypothesized that:

1) The average slope of the MRP will increase following both physical and observational practice of the bimanual coordination task. The MRP slope will not change in the control group. After the training intervention, both physical and observational practice groups will be able to form a more efficient preparatory movement plan prior to movement, and this adaptation will be reflected in the MRP slope.

2) The average SEP reflected in N20-P26 amplitude will increase following both physical and observational practice of the bimanual coordination task. The N20-P26 amplitude will not change in the control group. Physical and observational practice will both result in increased cortical activity of S1 due to the functional and anatomical connections between M1 and S1.

3) On average, the physical and observational practice groups will perform significantly better than the control group on the bimanual coordination task. Specifically, the physical and observational practice groups will maintain a 90-degree out-of-phase bimanual position a greater proportion of the time than the control group.

The study outlined in this thesis was the first study to consider the effects of short-term bimanual coordination training via both physical and observational practice on cortical adaptations (as indexed by MRPs and SEPs) and motor performance. Studying the effects of observational practice has clinical relevance. For example, if an individual with a motor impairment is not physically able to practice a motor task, but is able to obtain some sort of benefit from observational practice alone (e.g. increased excitation or "priming" of motor execution pathways that eventually drives the individual to a point at which they can undergo task-specific repetitive training (Pomeroy et al., 2011)), this would be valuable information to consider when designing their rehabilitation programs. The bimanual coordination aspect of the current study is also important. After stroke, some individuals have unilateral impairments due to a lesion on one hemisphere, but since bilateral control mechanisms are neurophysiologically distinct from unilateral control mechanisms (as discussed above), one might alternatively be able to capitalize on those separate resources to improve motor function.

3.0 METHODS

3.1 Participants

Thirty healthy individuals (M=12, F=18; age=25.03 years, SD=4.14, range [20-34]) participated in this study. Recruitment was predominately from students at the University of British Columbia. Participants were randomized to one of three groups using a computer-based randomization program. In one group, participants physically practiced a bimanual coordination task. In the second group, participants watched a series of videos depicting a learning model performing the same bimanual coordination task. In the third group, participants watched non-motor movement related videos (control group). All participants were right-handed and did not report any history of neurological or motor impairments. All participants provided written informed consent to participate. All experimental procedures were approved by the Clinical Research Ethics Board at the University of British Columbia (Approval # H12-03367).

Inclusion Criteria	**Exclusion Criteria**
Ages 19-35	Psychiatric diagnosis; neurodegenerative disorder; substance abuse; neurological or muscular deficits that affect vision, oculomotor, or manual control
Right-hand dominance	Personal or family history of seizure or epilepsy

Table 1. Study inclusion and exclusion criteria.

3.2 Task

3.2.1 Task Set-Up

Participants were seated in a dimly lit room in front of a colour computer monitor placed horizontally on a table with a 30° angle towards them. The medial aspects of the bilateral forearms were supported with elbows flexed to 90° and shoulders in forward flexion (between approximately 0 and 10°). The wrists were oriented in a neutral position so that flexion and extension of the wrist occurred in the horizontal plane. This position was maintained for all trials. Participants' hands were secured separately in two handles of a custom-built wrist movement device situated directly in front of them with adjustable Velcro straps (see Figure 4). Participants rotated the handles in clockwise and counter clockwise directions. The handles were linked to potentiometers that measured wrist movement during performance of the bimanual coordination task. Participants rested the 5th metacarpal of each hand on the bottom portion of the custom device so that the musculature of the wrists and arms were relaxed prior to movement. Rotation of the handles, in conjunction with a custom program (LabVIEW, National Instruments, Austin, TX, USA; Graeme Kirkpatrick), allowed the participants to control a cursor on a computer monitor that was horizontally positioned on the desk by flexing and extending the wrists in the horizontal plane. Left wrist movement controlled vertical movement of the cursor, such that extension moved the cursor upward and flexion moved it downward. Similarly, right wrist movement controlled horizontal movement of the cursor, such that extension moved the cursor to the right and flexion moved the cursor to the left. The goal of the task was to perform rhythmic left and right wrist flexion and extension with a 90° phase off-set (whereby one hands leads the other by a quarter-cycle). The relative motion pattern (Lissajous figure) resulted in a circle configuration on the monitor. Visual feedback was provided via a 2-second real-time trace on the display monitor. Each trial was metronome paced at 1 Hz by a visual display located directly above the participants' movement workspace boundary. Participants were instructed to move continuously and to produce one complete cycle of flexion/extension per metronome pace. Task performance, captured as x and y coordinates sampled at a rate of 200 Hz, was stored on the computer for subsequent analysis of phase accuracy for each trial performed.

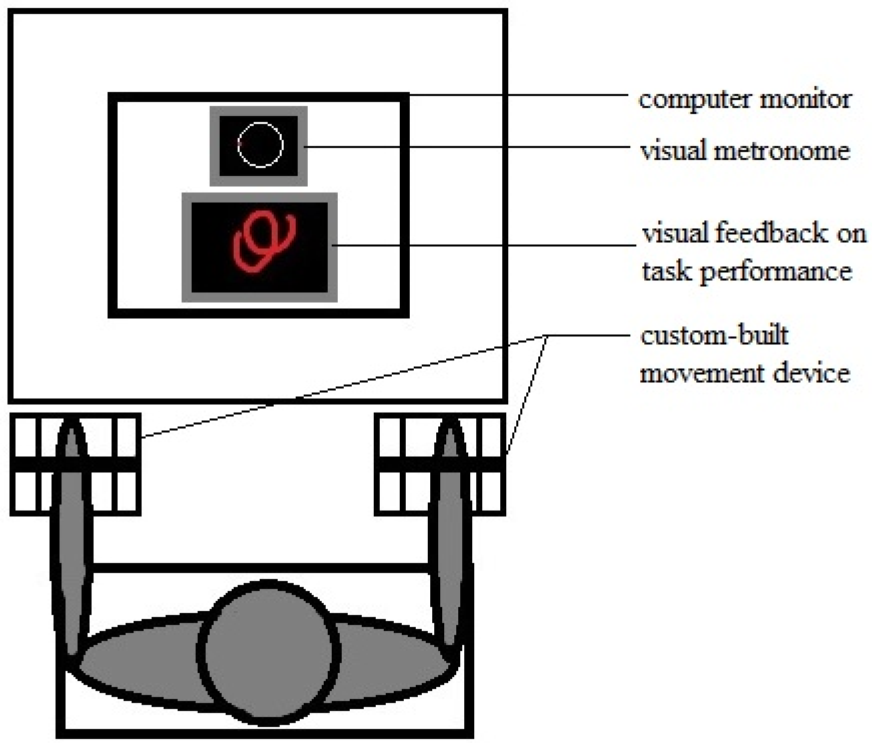

Figure 4. Experimental set-up.

3.2.2 Physical Practice (PP) Group

The participants completed a total of 45 minutes of repeated practice of the 90° phase offset bimanual coordination task using the custom wrist movement device in 3 blocks. Each block consisted of 15 trials and each trial lasted 60 seconds (45 total trials). A training session of 45 minutes was determined based on previous studies that have shown training-related cortical activity modulation in single sessions of 45 minute durations (Smith & Staines, 2006, 2012).

3.2.3 Observational Practice (OP) Group

The participants watched a total of 45 minutes of a naïve actor performing repeated practice of the 90° phase offset bimanual coordination task. The actor was naïve to the task and received the same verbal instructors as the physical practice group, thus the observational practice group observed the learning experience. Observational practice via learning models (that show a process where the model develops a skill) has been shown to be effective for observational learning (McCullagh & Caird, 1990; McCullagh & Meyer, 1997; Pollock & Lee, 1992).

The session was divided in 3 blocks, each block consisting of 15 trials and each trial lasting 60 seconds (45 total trials). The video provided a first-person perspective of the task performance. The participants watched a video of an individual training, rather than watching a live model, in order ensure each observer received the same observational training experience, thereby reducing potential variability in this group. Participants were instructed not to move their wrists throughout the training session and muscle activity of both forearms was recorded via electromyography (EMG) throughout the training session to ensure the participants did not physically practice the task as they were observing. Studies have shown that even short-term training via action observation is sufficient to learn a novel task (Gatti et al., 2013; Heyes & Foster, 2002). The observational practice group trained for the same duration as the physical practice group to control for training dosage.

3.2.4 Control Group

The participants in the control group performed neither physical nor observational practice. Participants watched a total of 45 minutes of video depicting ocean life (Planet Earth, Ocean Series, BBC Natural History Unit) instead of the bimanual coordination task performed by humans. The ocean life video (containing no human movement) was selected because these images were not likely to elicit significant activity in sensory or motor areas. Participants were instructed not to move their wrists throughout the control training session.

3.3 EEG

3.3.1 EMG and EEG Recording Procedures

Scalp electroencephalographs were recorded using the International 10-20 System (Jasper, 1958) and a 64-channel electrode cap (NeuroPrax; NeuroConn, Ilmenau, Germany). The channels were recorded to view cued MRPs and SEPs; however, not all electrode positions were included in quantitative analysis. A subset of electrode sites was used for MRP analysis (C4, FCZ, CZ electrodes over SMA and contralateral M1) and a separate electrode site (CP4 electrode over contralateral S1) was used for SEP analysis (Figure 5). All EEG channels were referenced to an electrode placed on the right mastoid process. Vertical eye movements were monitored with bipolar recordings above and below the right eye. EEG signals were recorded with a notch filter (50 Hz) at a sampling rate of 2000 Hz (NeuroPrax; NeuroConn, Ilmenau, Germany). Electrode impedance was maintained below 5KΩ at all EEG sites. All post-processing of the EEG data was performed using NeuroPrax (NeuroConn, Ilmenau, Germany) and EEGLAB MATLAB toolboxes (The MathWorks, Inc.). EMG was recorded from the left extensor carpi radialis (ECR) muscle using bipolar electrodes placed longitudinally over the muscle belly for MRP collection, and from both left and right ECR during observational practice. EMG was also collected from the left abductor pollicis brevis (APB) muscle using bipolar electrodes placed over the muscle belly for SEP collection. EMG signals were sampled at 2000 Hz, pre-amplified (1000x) and band-pass filtered at 10-1000 Hz using Powerlab amplification and EMG systems (AD instruments, Colorado Springs, CO, USA). Data were recorded in a 450 ms sweep from 100 ms before to 350 ms after stimulus delivery.

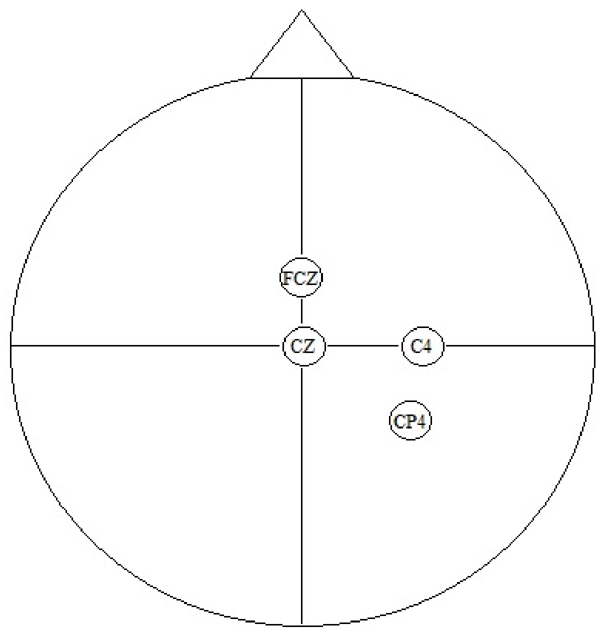

Figure 5. EEG cap set-up with electrodes of interest. (C4, FCZ and CZ for MRP collection and CP4 for SEP collection)

3.3.2 Event-Related Potentials: the Cued MRP

Two sets of MRPs were collected for each participant- one set before training and one set after training (See Figure 6 for outline of experimental methodology). For each set, participants performed 120 repetitions of a visually-cued left wrist extension. Participants performed a quick extension while secured in the left handle of the custom wrist movement device. The device was used to maintain movement kinematics between trials and did not control a cursor on the computer monitor during MRP collection. The participants were asked to fixate on an “X” located in the center of the computer monitor display while performing the movements. A custom program written in LabVIEW (LabVIEW 8.5; National Instruments, Austin, TX, USA; Mohammad Amanian) presented a visual target (a 1.5 cm red dot) below the “X” that cued the subject to move. The visual target appeared randomly between 3-6 seconds apart. Random cue intervals were chosen so that the subjects were not able to accommodate or anticipate the presentation of the cue and move prior to the appearance of the cue. The participants were asked to abstain from blinking throughout the performance of the trials to prevent the imposition of artifact into the data collection. EEG was recorded from 3 electrodes (C4, FCZ, CZ) plus a reference electrode. MRPs were obtained by averaging individual artifact-free epochs time-locked to the onset of the cue for movement (the presentation of the red dot). Prior to averaging, individual EEG epochs were inspected for contamination from eye movements or other artifacts. The temporal window of analysis was from 1900 ms before to 600 ms after stimulus onset (presentation of the visual cue). The period of 1900-1700 ms before stimulus onset was used as a baseline.

3.3.3 Event-Related Potentials: the SEP

Two sets of SEPs were collected for each participant- one set before training and one set after training. Bipolar bar electrodes were used for stimulation of the median nerve. The bar electrode was placed on the left wrist, lateral to the flexor tendon just above the median nerve. Simulation was performed by a constant voltage stimulator that delivered square wave pulse (pulse duration 0.5ms) at random varying inter-stimulus intervals between 500 and 1000ms to ensure the delivery of stimulation was not predictable (thus preventing the participants from accommodating to the stimulation) (Grass SD9 Stimulator with SIU-V Isolation Unit, West Warwick, RI, USA). The voltage output of the stimulator was adjusted individually and varied between 10 and 100 V between participants at the intensity of their APB motor threshold (the voltage required to evoke a just-visible twitch of the thumb). The motor response to the stimulation was monitored throughout each trial by recording EMG via the electrodes placed over the APB muscle. Using EMG, the amplitude of the motor wave (M-wave) (the resultant muscle activity caused by the efferent nerve stimulation) was monitored to certify that it stayed constant. This ensured that a constant number of muscle fibres were stimulated during each trial (so that any potential changes in the SEP trace across sets could be assumed to be the result of the training intervention). EEG was recorded from electrode CP4 and a reference electrode throughout each trial. A total of 200 stimulations were delivered to each participant's left median nerve for each set and an average trace was produced in an analysis program. The temporal window of analysis was from 100 ms before to 300 ms after stimulus onset. The period of 100 – 0 ms before stimulus onset was used as a baseline. The participants were instructed to close their eyes, remain still and relax as much as possible during each trial.

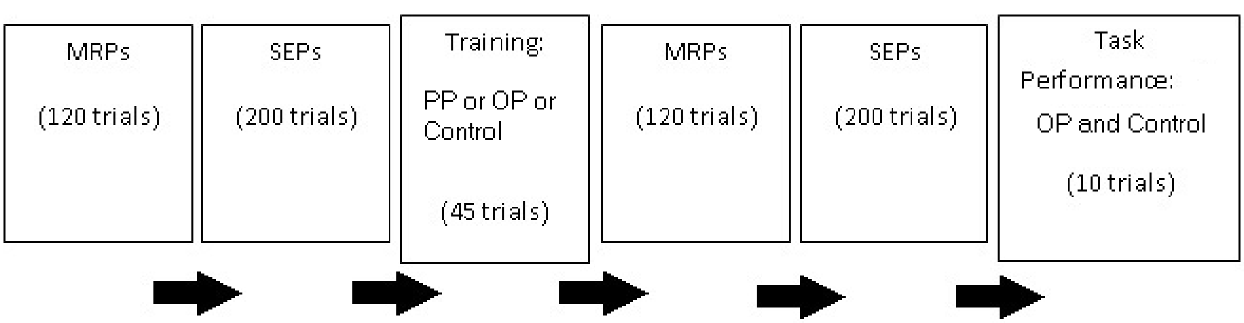

Figure 6. Experimental methodology.

3.4 Data Analysis

3.4.1 MRP Processing

After each MRP set was processed using EEGLAB, MRP components were analyzed using a custom-made MATLAB program (The MathWorks, Inc; Kristopher De Asis). The program calculated the slope latency and value of the MRP as well as the latency and minimum/maximum values of the reafferent potential (Figure 7A/B). Specifically, for each data set, a running standard deviation was first determined (Figure 7A). The running standard deviation should rise to some constant value, stay around that value for a period of time, then begin to rise again. The constant value was found by dividing the running standard deviation into 50 equally spaced test points and determining the mean of a test range (a specified number of points beginning at each of the 50 test points). The constant value was taken to be the value of the first test range that differed by less than a specified percentage of the mean of the previous test range. Next, the region of which the data started to slope downwards was determined (the slope onset was taken to be the point at which the running standard deviation begins to rise again after settling at the constant value; the slope offset was taken to be the time of the visual cue (0ms)). Next, a least-squares linear fit was calculated on the data within the sloped region (Figure 7B). Finally, the maximum and minimum values of the RAP were taken from moving averages calculated following the slope offset.

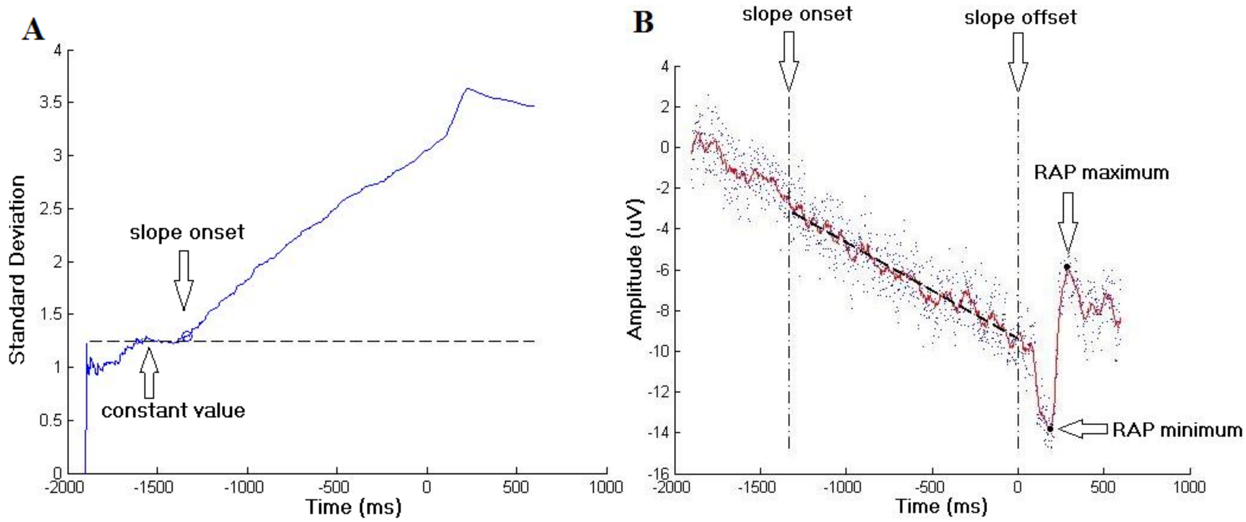

Figure 7 (A/B): MATLAB program for calculating the MRP slope latency and amplitude and the RAP latency and minimum/maximum values. Sample data of averaged post-training trials from participant 13 shown.

3.4.2 Behavioural Data Processing

Performance on the bimanual coordination task was analyzed using a custom-made MATLAB program (The MathWorks, Inc; Kristopher De Asis). The program performed sinusoidal regression analysis, calculated the quantity of data containing waves with phase differences of $90^{\circ} \pm 10^{\circ}$ and then specified the percentage of data that contained waves that fit within this phase difference. Specifically, for each trial, the program divided the data into 12 equally spaced blocks of data and performed a sinusoidal regression analysis, which returned the phase difference. For the sinusoidal regression, the program determined the mean value of the wave data and found all points where the data crossed over this mean value. It then found the average distance between these points and the value of extreme between these points and averaged the magnitude of all the extreme points to determine the wave's amplitude. Then, the program used the above values as the amplitude, frequency and mean of the fit wave and selected a phase shift that minimized the squared error between the fit wave and the data set. After the regression analysis, the program counted how many blocks of data contained a wave that had a phase difference of 90° (for this study, a tolerance of ±10° beyond 90° was selected). Finally, the program determined what percentage of these blocks contained a wave that was 90° (±10°) out of phase. The percentage was used as the measure of behavioural performance for each trial.

3.4.3 Statistical Methods

Hypothesis 1: The average slope of the MRP will increase following both physical and observational practice of the bimanual coordination task. The MRP slope will not change in the control group. After the training intervention, both physical and observational practice groups will be able to form a more efficient preparatory movement plan prior to movement, and this adaptation will be reflected in the MRP slope.

To test Hypothesis 1, separate 2 [time: pre, post] by 3 [group: physical practice (PP), observational practice (OP), Control] repeated measures analysis of variance (ANOVA) were conducted for each electrode site of interest (C4, FCZ, CZ). It was hypothesized that the amplitude of the MRP would be significantly greater after training compared to before training for the PP and OP groups but not for the Control group for each electrode site.

Hypothesis 2: The average SEP reflected in N20-P26 amplitude will increase following both physical and observational practice of the bimanual coordination task. The N20-P26 amplitude will not change in the control group. Physical and observational practice will

both result in increased cortical activity of S1 due to the functional and anatomical connections between M1 and S1.

To test Hypothesis 2, a 2 [time: pre, post] by 3 [group: PP, OP, Control] repeated measures ANOVA was conducted for the electrode site of interest (CP4). It was hypothesized that N20-P26 amplitude would be greater post-training in the physical practice and observational practice groups but not the control group.

Hypothesis 3: On average, the physical and observational practice groups will perform significantly better than the control group on the bimanual coordination task. Specifically, the physical and observational practice groups will maintain a 90-degree out-of-phase bimanual position a greater proportion of the time than the control group.

To test Hypothesis 3, first an independent samples t-test was performed to determine if there was a significant difference between the initial performance of the physical practice group and the control group. It was hypothesized that there would not be a statistically significant difference between the groups. Second, a paired samples t-test was run to determine if there was a significant difference between the average of the first 10 trials and the average of the last 10 trials of bimanual task performance in the physical practice group. It was hypothesized that the average performance in the last 10 trials would be significantly better than the first 10 trials in the physical practice group (i.e. in the last 10 trials, the percentage of time participants were $90^\circ \pm 10^\circ$ out-of-phase would be significantly greater than in the first 10 trials on average). Third, a one-way ANOVA was run to determine if there was a significant difference between the three groups (specifically, between the performance of the last 10 trials of the PP group, the 10 trials the OP group performed after training, and the 10 trials the Control group performed after training). Tukey's HSD test was performed post hoc to determine which groups differed significantly. It was hypothesized that PP and OP group performances would not be significantly different, but that both would be significantly better than Control group performance.

4.0 RESULTS

Aim 1: To determine whether short-term bimanual coordination training (two types: physical practice and observational practice) alters motor cortical excitability as measured by MRP slope.

Cued left-wrist extension elicited measurable MRP slopes in all participants in all groups at all electrode sites (for example, see Figure 8), except one participant at electrodes C4 and CZ.

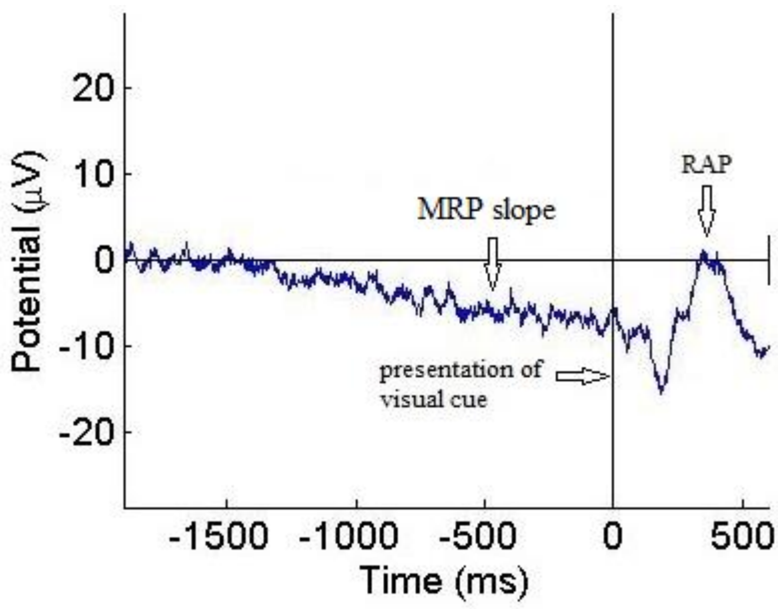

Figure 8. A movement-related potential recorded from electrode site C4 from a representative participant. At 0 ms, a visual cue for movement was presented. The MRP slope and reafferent potential (RAP) are labeled.

Electrode C4: A 2 [time: pre, post] by 3 [group: PP, OP, Control] repeated measures ANOVA was conducted (dependent variable: C4 slope). There was no significant interaction effect of time*group (F(2, 26)=2.144, p=0.137) and no significant main effects of time (F(1,26)=1.000, p=0.327) or group (F(2,26)=0.435, p=0.652). It should be noted that one participant was excluded from the analysis due to excessive artifacts in their dataset at electrode C4.

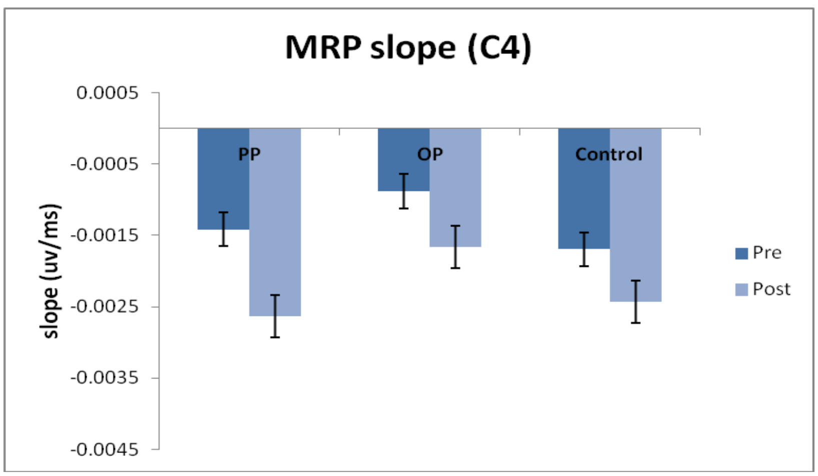

Figure 9. MRP slope pre- and post-training between physical practice (PP), observational practice (OP) and control groups ± SE at electrode C4.

Electrode CZ: A 2 [time: pre, post] by 3 [group: PP, OP, Control] repeated measures ANOVA was conducted (dependent variable: CZ slope). There was no significant interaction effect of time*group (F(2, 26)=0.234, p=0.793) and no significant main effects of time (F(1,26)=0.117, p=0.735) or group (F(2,26)=0.312, p=0.734). It should be noted that one participant was excluded from the analysis due to excessive artifacts in their data set at electrode CZ.

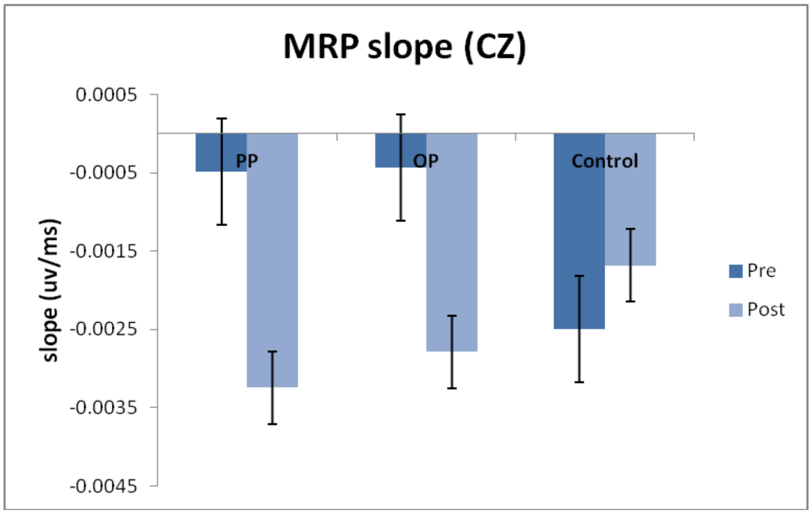

Figure 10. MRP slope pre- and post-training between physical practice (PP), observational practice (OP) and control groups ± SE at electrode CZ.

Electrode FCZ: A 2 [time: pre, post] by 3 [group: PP, OP, Control] repeated measures ANOVA was conducted (dependent variable: FCZ slope). There was no significant interaction effect of time*group ($F(2, 27)=0.290$, $p=0.750$) and no significant main effects of time ($F(1,27)=0.138$, $p=0.713$) or group ($F(2,27)=1.596$, $p=0.221$).

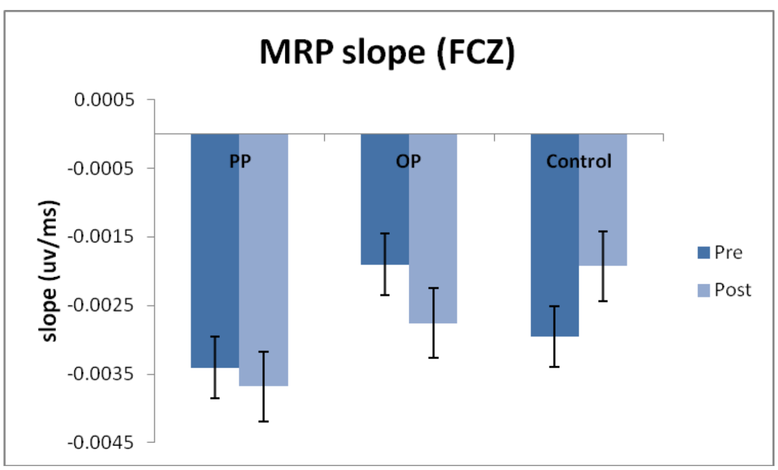

Figure 11. MRP slope pre- and post-training between physical practice (PP), observational practice (OP) and control groups ± SE at electrode FCZ.

Aim 2: Determine whether short-term bimanual coordination training (two types: physical practice and observational practice) alters sensory cortical excitability as measured by SEP amplitude.

Electrical stimulation elicited the N20 and P26 components in all participants in all groups (for example, see Figure 12). The peak-to-peak amplitudes of N20-P26 were measured relative to the pre-stimulus baseline.

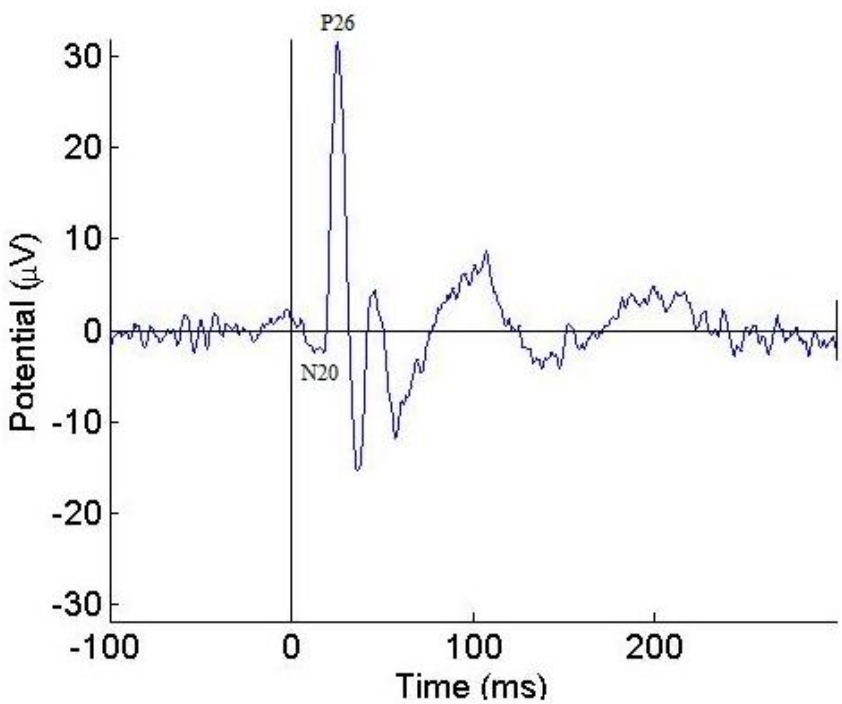

Figure 12. A somatosensory evoked potential recorded from channel CP4 from a representative participant. N20 and P26 components are labeled.

A 2 [time: pre, post] by 3 [group: PP, OP, Control] repeated measures ANOVA to compare N20-P26 SEP amplitudes was performed. There was no significant interaction effect of time*group ($F(2, 27)=0.072$, $p=0.931$), no significant main effect of time ($F(1, 27)=0.234$, $p=0.633$) and no significant main effect of group ($F(2,27)=0.021$, $p=0.979$).

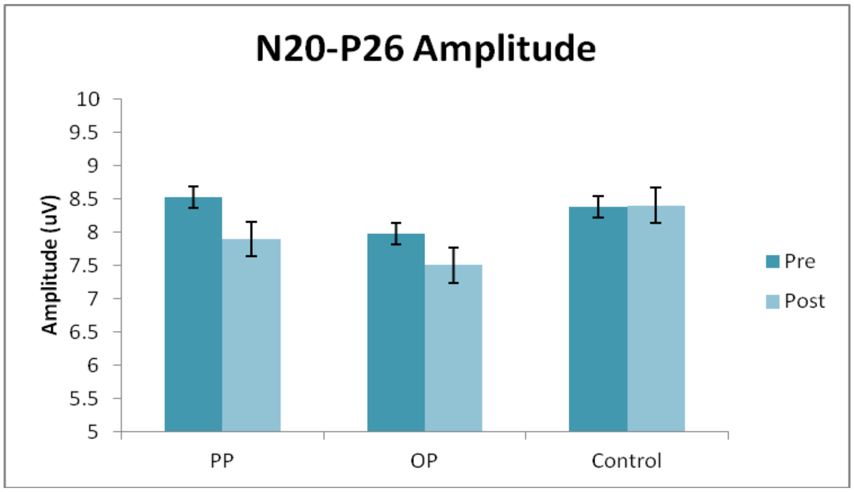

Figure 13. N20-P26 SEP amplitude pre- and post-training between physical practice (PP), observational practice (OP) and control groups ± SE at electrode CP4.

Aim 3: Compare physical practice to observational practice in terms of motor performance on a bimanual coordination task following training.

An independent samples t-test was run to determine if there was a significant difference between initial task performance in the physical practice group and the control group. There was no significant difference in initial task performance between the groups ($t=0.919$, $p=0.370$) and the assumption of Homogeneity of Variances was not violated (Levene Statistic= 1.866, $p=0.189$).

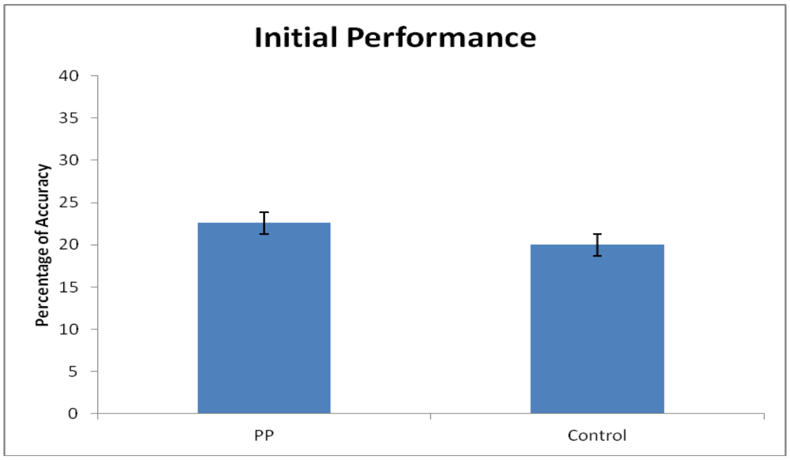

Figure 14. Bimanual training task performance. Mean initial performance of control group versus physical practice group ± SE for percentage of task trial participant's hands were 90° ± 10° out-of-phase.

A paired samples t-test was run to determine if there was a significant difference between the average of the first 10 trials (early) and the average of the last 10 trials (late) of bimanual task performance in the physical practice group. There was a significant difference between early-late performance ($t=-3.728$, $p=0.005$), with the mean for the late trials being significantly higher.

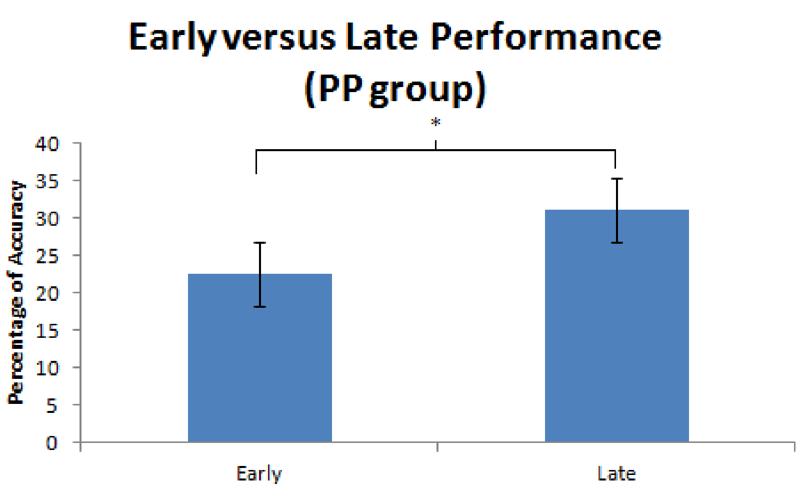

Figure 15. Bimanual training task performance. Physical Practice group means ± SE for percentage of task trial participant's hands were 90° ± 10° out-of-phase from early and late trials. *Indicates P < 0.05.

A one-way ANOVA was run to determine if there was a significant difference in performance between the three group conditions after the training interventions. There was a significant difference between groups (F(2,27)=7.635, p=0.002). Since there was a significant difference between groups and the assumption of Homogeneity of Variances was not violated (Levene Statistic= 2.713, p=0.084), Tukey's HSD test was performed post-hoc. The mean difference between the physical practice group and the control group was significant (mean difference (I-J)= 11.08333, p=0.002). There was a trend for a significant mean difference between the observational practice group and the control group (I-J=6.3333, p=0.085). There was no significant difference in performance between the physical practice group and observational practice group (I-J=4.75000, p=0.235).

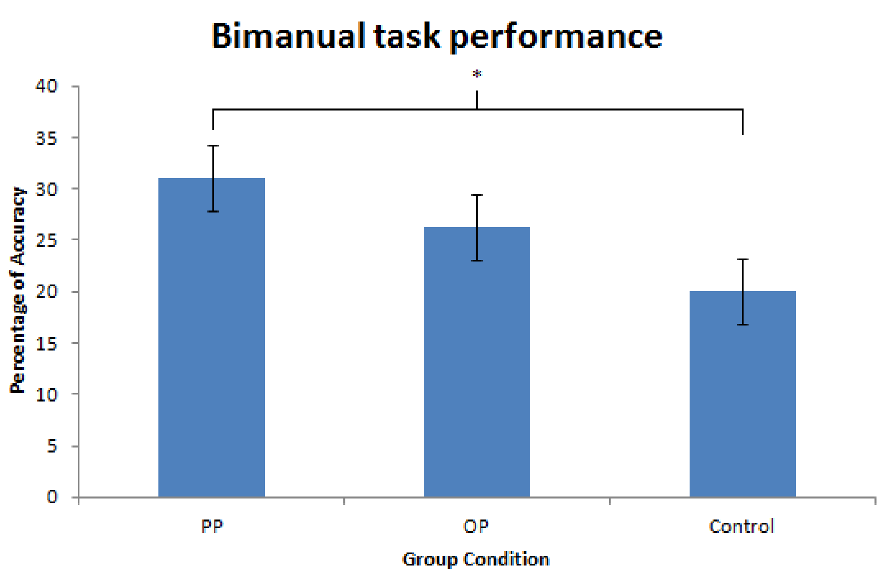

Figure 16. Bimanual coordination task performance. Physical Practice (PP), Observational practice (OP) and Control group means ± SE for percentage of task trial participant's hands were $90^{\circ} \pm 10^{\circ}$ out-of-phase. * Indicates $P < 0.05$.

5.0 DISCUSSION

5.1 Discussion of Results

5.1.1 General Discussion of Findings

Neurophysiologically, the main aims of the study presented in this thesis were to determine whether the slope of the movement-related potential changed following short-term bimanual training, and furthermore, to examine how the effects of physical practice compared to observational practice. A second aim was to determine if the amplitude of the N20-P26 component of the SEP changed following either of the forms of short-term bimanual training. The results showed that neither MRP slope nor N20-P26 amplitude changed after training, regardless of training type.

Behaviourally, the aim of the current study was to determine how different types of training influenced bimanual motor performance. The results showed that physical practice as a means of training resulted in the best performance. Specifically, it was found that physical and observational practice did not result in significantly different bimanual motor performance, but that physical practice resulted in significantly better motor performance than no practice. There was also a trend for a significant difference between the observational practice group and the control group, with the observational practice group demonstrating better motor performance.

It is important to note that although MRP slope and SEP amplitude were not found to differ significantly between groups after training, this does not mean that physical or observational practice of the bimanual coordination task did not or cannot necessarily result in cortical adaptations after training. Rather, it is important to carefully consider the limitations in the experimental methodology. Importantly, the results help demonstrate the benefit of examining both behavioural and physiological measures following an intervention, since no difference between groups was detected via EEG measures after the bimanual training interventions but there was a significant difference between groups that was detectable at the behavioural level.

5.1.2 Movement-Related Potentials

As demonstrated in a study by Smith & Staines (2006), it is possible that bimanual training may not always provide a unimanual benefit post-training (as indexed by MRP modulations); especially in participants who do not have motor impairments and whose unimanual performance may already be optimized. In support of this notion, a study by Renner et al. (2005) showed that simultaneous activation of both hands, as compared to one hand, resulted in no change in motor cortical excitability (as measured by TMS) in non-affected subjects whereas in stroke-affected subjects, this simultaneous activation caused additional facilitation in their affected hemisphere compared to the activation caused by movement of their affected hand alone. This helps demonstrate that overall, it is possible that the potential benefits of bimanual coordination training in a stroke population are not relevant or apparent (at least as indexed by MRPs) in healthy populations. In the current study, only participants without neurological impairments were examined and thus the potential benefits of the bimanual coordination training may not have been present (or fully evident). Moreover, it is possible that any cortical adaptations that may occur after training in healthy participants may be very small, and therefore that this study was underpowered to detect these changes with the sample size used (n=10 per group).

Furthermore, it should be noted that due to the level of noise in the EEG recordings that could not be eliminated during testing sessions, it was not possible to differentiate between early and late components of the MRP in post-collection processing. This limitation led to the development of a program that averaged the whole MRP slope for each trial (as described above), instead of dividing the slope separately into early and late components, and thus the intricacies of the MRP slope components could not be examined individually (this method was based on similar approaches used in past work (e.g. Oishi, Mochizuki, Du, & Takasu, 1995; Suzuki et al., 2010; Yoshida et al., 1999)). It is possible that differences after training may have existed but were not identifiable with the analysis performed here.

5.1.3 Somatosensory Evoked Potentials

In the study presented in this thesis, no significant difference in the N20-P26 amplitude of SEPs between groups was found. Although training is likely to increase S1 excitability throughout the duration of practice due to the interdependence between sensory and motor cortices, it is possible that this increase in excitability did not last beyond the duration of training, such that when SEPs were measured post-training, any cortical modulations had dissipated. In the current study, SEPs were measured approximately 10-15 minutes after training (since MRPs were collected immediately following practice as the primary outcome measure) and it is possible that the short-term effects of training were no longer present or measurable at the time of collection. The time between training and SEP collection, and the order of collection of MRPs and SEPs, should be considered in future experimental designs. Additionally, while past work has clearly demonstrated that long-term training can influence long-latency SEP components, and tasks with different attentional demands can influence short-latency SEP components (Yamaguchi & Knight, 1990), there is some evidence to support the findings of the current study. For example, Thomas & Mitchell (1996) examined P9, P11, P13/14, N20 and P26 components of SEPs elicited by median nerve stimulation of groups of gymnasts, runners and sedentary individuals and found that none of these groups differed significantly from each other in the SEP measures that were examined. It is plausible, therefore, that even long-term athletic training may not influence early sensory processes (and therefore no difference in short-latency components of the SEPs may exist), despite the fact that motor training results in an overall increase in S1 activity.

5.1.4 Behavioural Data

The current study found that both physical and observational practice resulted in improved motor performance. The finding that observational practice alone can improve motor performance on a bimanual coordination task is supported by past work and the potential mechanisms by which observational practice influences motor performance are interesting to consider. Neurophysiologically, previous work has shown that action observation produces excitation of motor pathways in the same temporal-spatial pattern as actual execution of the action (Cowles et al., 2013; Grafton & Hamilton, 2007) and that the mirror neuron system is responsible for this similarity in excitation pattern (Buccino et al., 2004). Furthermore, research has shown that the same neurons are active in the SMA and hippocampus during both action observation and execution of hand movements (Mukamel, Ekstrom, Kaplan, Iacoboni, & Fried, 2010) and that there is increased activity in muscles that would be used to perform an action during observation of that action (Maeda, Kleiner-Fisman, & Pascual-Leone, 2002). Moreover, like motor memory consolidation after physical practice, the memory representation of a skill learned via observational practice also undergoes the process of motor memory consolidation (Trempe, Sabourin, Rohbanfard, & Proteau, 2011). Taken together, past work has helped characterize some of the neural processes involved in observational practice and has provided insight into how observational practice alone may lead to motor performance improvements such as those illustrated in the study described here.

Despite past work that has shown similarities between physical and observational practice, much remains to be investigated with respect to their overall effects, since past work has also revealed differences between these training modalities. For example, studies have demonstrated differences in performance between physical and observational practice when different feedback schedules are presented (Badets & Blandin, 2010) as well as differences in physical performance benefits and perceptual discrimination measures following physical versus observational practice on a bimanual task (Maslovat, Hodges, Krigolson, & Handy, 2010).

While the current study focused solely on short-term effects of short-term bimanual training and motor performance was not found to differ between physical and observational practice groups, it is interesting to consider the effects that longer-term training via physical practice and observational practice may have on performance, especially since consolidation of an observed motor skill has been shown to lead to different behavioural outcomes than consolidation of motor skills that have been physically practiced (Trempe et al., 2011). It is also interesting to consider that given both physical and observational practice of the bimanual task were effective in improving motor performance, it is possible that combining these two methods of practice may also be effective in improving motor performance (or that combining them may result in even greater benefit).

A study by Ertelt et al. (2007) combined action observation of daily actions with concomitant physical practice of the observed actions as a means of therapy for stroke patients with moderate chronic upper extremity hemiparesis. The training intervention involved 18 90-minute sessions over 4 weeks. The authors found a significant improvement in motor function in the intervention group compared to both the intervention group's pre-treatment baseline as well as a control group. At 8-weeks post-training, the observed motor improvement was still present. Additionally, the authors used fMRI to investigate reorganization of the motor system after training. Specifically, the authors compared neural activations between the intervention and control groups pre- and post-training and found that the intervention group had a significantly greater increase in activity in the bilateral ventral premotor cortex, bilateral superior temporal gyrus, SMA and contralateral supramarginal gyrus. Overall, their findings suggested that action observation in conjunction with physical training was associated with an increase in motor function via reactivation of motor areas containing the mirror neuron system. This finding was supported by an earlier study by Shea et al. (2000) that found that a combination of observational and physical practice allowed for unique learning opportunities beyond either physical or observational practice alone. On the whole, the finding in the current study that observational practice alone improved motor performance on a bimanual task is supported by past work and provides further evidence that observational practice may be an effective substitute (or addition) to physical practice in training paradigms.

5.2 Methodological Considerations

5.2.1 Equipment

One limitation of using EEG to capture primary outcome measures in the current study was the variability in the data due to external sources of noise. The collection room was not electrically or noise isolated during the data collection sessions, which could have influenced the quality of EEG data collected.

5.2.2 Movement-Related Potentials

Since MRPs have a low frequency and small amplitude, they must be averaged over many trials (normally around 80 trials) in order to obtain a reading. Participants were asked to be as still as possible throughout each trial while moving their wrist, but movement artifact was detected in some subjects in several trials. Additionally, a visual fixation point was provided to the participant in attempt to reduce blink artifacts, but some trials had to be excluded in virtually all participants due to blinks being detected in the trial. This reduction in trials could influence the quality of the data examined.

5.2.3 Observational Practice Group

The participants in the observational practice group watched three 15-minute video clips totaling 45 minutes. The participants were instructed to pay close attention to the videos the entire time and were told that they would have a chance to perform the task at the end of the study duration (following the EEG measurements), with the hope that this would make the information appear more relevant to them. The participants were given a momentary break between each trial and a longer break as desired in between each block, but the possibility remains that the participant was not paying attention to the task at hand the whole time. Therefore, it is possible that the effects of observational practice on cortical modulations and motor performance were underestimated during this study. Future studies could incorporate longer breaks in between trials or have an eye tracking/mind-wandering system set-up in order to track how well each participant is focusing on the action observation task in order to be able to control for attentional differences.

5.2.4 Control Group

The participants in the control group performed all the same measurements as the physical and observational practice groups in the current study with the exception that they watched a video containing no human motor movement instead of undergoing physical or observational practice of the bimanual task. Due to time constraints and feasibility, only one control condition was used for this study. While the condition controlled well for the observational practice group, it may not have been the ideal control condition for the physical practice group. A potential addition to increase the robustness of this study would be to add a second control condition where the participants physically practiced a novel unimanual task so that cortical activity modulations after the bimanual and unimanual task performances could be compared between groups. In this study, unimanual training was not examined, as any potential effects bimanual training could confer by itself was the primary interest, regardless of the potential for unimanual practice to produce similar effects within the constraints of this experiment.

5.2.5 Fatigue Effects

As is consistent with training protocols lasting 45 minutes, physical and mental fatigue may result over time. This could have influenced the EEG measures used in the current study (for example, muscular fatigue of the thumb has been associated with altered median nerve SEPs (Montain & Tharion, 2010) and with altered MRPs (Johnston et al., 2001)). This could also influence overall motor performance however examination of the behavioural data showed that the new motor skill was acquired well in the practice groups, with participants improving over time.

5.3 Significance

This is the first study to examine the effects of short-term bimanual coordination training via *both* physical and observational practice on the modulation of sensorimotor cortical activity and motor performance. Although there have been studies investigating cortical activity modulations after short-term physical practice of a bimanual coordination task (as discussed above), studies have not yet compared physical practice to observational practice of a novel bimanual task in a controlled trial. The major finding of this study was that short-term physical practice resulted in significantly better performance on a bimanual coordination task than the control condition (no practice), with participants acquiring the task well over time. The performance of the observational practice group was not significantly different than the physical practice group, and there was a trend ($p=0.085$) for the observational practice group performing significantly better than the control group. This suggests that neurologically healthy participants could potentially improve their performance on a novel bimanual coordination task from observational practice alone.

5.4 Future Studies

Bimanual activities are ubiquitous in daily life and developing appropriate rehabilitation programs using an optimal combination of physical practice (when possible) and observational practice (in addition to, or instead of, physical practice) is a worthwhile endeavour. On the whole, future work should investigate whether there is a positive additive effect of physical practice and observational practice on cortical activity adaptations and motor performance, and if so, should seek to determine the optimal combination of physical and observational practice for optimizing training benefits in different patient populations. In relation to the study presented here, a future study comparing cortical adaptations and motor performance following physical and observational training in individuals with stroke versus neurologically healthy individuals could be conducted. Additionally, it would be interesting to manipulate the parameters of the bimanual task (e.g. alter the frequency or quality of visual feedback, provide verbal cues/auditory information, yoke the observational group to the physical practice group, etc.) and compare motor performance and cortical activity modulations with these new parameters.

In addition to the potential studies above, it would be an interesting to couple investigations of MRPs and SEPs with other techniques such as sensory evoked fields (in the time domain) or brain rhythm analysis (in time and frequency domains) to explore complementary aspects of whole brain activity with high spatial and temporal resolution before, during and after observational practice of a bimanual coordination task (see Rossi et al. (2002) for technique). This would allow for a more complete view of what is occurring in the brain with training. Overall, these future studies could potentially help optimize advantageous cortical adaptations, motor performance and functional recovery in an impactful way.

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APPENDICES

A. Consent Form

THE UNIVERSITY OF BRITISH COLUMBIA

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Title of Study: Effects of Bimanual Coordination Training on Cortical Network Activity and Motor Performance

Consent Form for Healthy Individuals

Principal Investigator: Lara Boyd, PT, PhD. Department of Physical Therapy, Brain Behaviour Laboratory, Faculty of Medicine, UBC (604) 822-7197

Co-Investigator: Nicola Hodges, PhD, School of Kinesiology, Faculty of Education, UBC (604) 822-5895; Katharine Cheung, BScH. Department of Physical Therapy, Brain Behaviour Laboratory, Faculty of Medicine, UBC (604) 827- 3369

Team Members: Michael Borich, Angela Auriat, Marjan Zakeri, Katie Wadden, Cameron Mang, Paul Jones, Sonia Brodie, Katlyn Brown, Tamara Koren

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Invitation to Participate: You are being invited to participate in a research study to determine how bimanual coordination training (how your two hands work together to perform specific tasks) influences cortical network activity (patterns of activity on the surface of your brain) and motor performance.

Participation is Voluntary: You do not have to participate in this research study. It is important that before you make a decision to participate, you read the rest of this form. Please read the following form carefully and ask questions if anything is not clear. This consent form will tell you about the study, why the research is being done, what will happen during the study and the possible risks, benefits, and discomforts.

If you wish to participate, you will be asked to sign this form. If you do decide that you would like to participate, you are still free to withdraw from the study at any time and without giving any reasons for your decision. If you do not wish to participate, you do not have to provide any reason for the decision nor will you lose the benefit of any medical care to which you are entitled or presently receiving.

Please take time to read the following information carefully and to discuss it with your family, friends and doctor before you decide.

Purpose

The purpose of this study is to examine how bimanual coordination training affects brain activation patterns and motor performance. It will also examine how observation of bimanual coordination training, without physical performance of this training, affects brain activation patterns and motor performance. These efforts should help lead to the development of new rehabilitation approaches that can help restore motor function after brain injury such as stroke.

Who Can Participate in this Study?

You have been identified because you are a healthy adult and you are between the ages of 19 and 35 and have the ability to understand English. If you agree to take part in the study, Dr. Boyd or her associates will determine if you have any condition that will prevent you from being in the study. Screening should take no more than 5 minutes.

Who Should Not Participate in this Study? You should not participate in this study if you have a history of seizure, epilepsy, neurodegenerative disorder, head trauma, or a psychiatric diagnosis. If you are younger than 19 or older than 35 you should not participate in this study.

What does the study involve?

If you are eligible and decide to participate in this study, you will come to the Brain Behaviour Lab for one visit. The visit will be expected to last 2.5-3 hours. You will be randomly assigned to one of three experimental groups according to a random number generator where you will have an equal chance of being placed into any of the three groups. Each group will conduct different training activities. One group will physcially perform the bimanual coordination training task. This task involves sitting in front of a computer and moving your wrists in various positions in a moving device to control a computer program. One group will participate in the observation of the bimanual coordination training task. In the observation group you will watch a video of someone else learning how to do to the task, but you will not do the task yourself. The final group will neither physically train nor observe the bimanual coordination training task. In the control group you will watch a non-motor learning related video. On the day of the study you will be asked to come to the Brain Behavior Lab (T142a Koerner Pavilion, University of British Columbia) and undergo assessments of motor and somatosensory function. This means we will look at how efficiently your muscles and brain work together, and how information is sent to, and processed, in the brain. The assessments will be performed before and immediately after the training paradigm.

On the day of the study you will be asked to come to the Brain Behaviour Lab where one of the research staff will meet you to explain the study. Next, in order to pick up a signal from your brain (by a process called electroencephalography (EEG)), we will put a cap over your scalp and insert a conductive gel into wells of the cap. EEG is non-invasive and painless. Prior to the bimanual coordination training, we will perform some tests that will help to index the effect of training. These include a sensory test and two movement tests. In total, these three tests will take about 30 minutes to complete.

During the training task you will be seated in a chair at a desk, facing a computer monitor. The training will take approximately 60 minutes. After the training is completed you will then perform the same three tests that you performed before the training. Again, these three tests will take about 30 minutes.

Future studies: We would like to know if you are interested in learning about future studies. If Dr. Boyd thinks you might qualify for another study by her or her colleagues, she will contact you directly by mail or telephone and ask if you are interested. If you choose not to take part in future studies you should tell her. There will be no impact on you if you choose not to take part. You are not giving permission to do any future studies in this consent form.

Are you willing to be contacted in the future about participation in other studies?
_____ YES _____ NO

What Are Possible Harms and Side-Effects of Participation
The risks are not greater than the risks in everyday life. These procedures will be conducted according to published safety standards by Dr. Boyd. Dr. Boyd or her associates have discussed this research with you and have described them as follows:

Somatosensory-Evoked Potential (SEP): Collection of SEPs involves application of electrodes to measure muscle activity of the thumb (Electromyography (EMG)) as well as electrodes applied to the scalp to measure brain activity (Electroencephalography (EEG)). All EEG and EMG electrodes are surface electrodes and do not actually contact the skin. A conductive gel provides the contact between the skin and the recording electrodes. In rare instances it is possible that your skin may be sensitive to the conductive gels or rubbing alcohol used for surface recordings. In such cases a skin rash is possible. The very brief electrical stimulation to activate nerves in your wrist can cause a mild tingling sensation. You may stop the procedures for any reason at any time by informing the researcher of any discomfort. This will be effective immediately.

Movement-Related Potential (MRP): Collection of MRPs also involves application of electrodes to measure muscle activity of the thumb as well as electrodes to measure brain activity applied to the scalp. All EEG and EMG electrodes are surface electrodes and do not actually contact the skin. A conductive gel provides the contact between the skin and the recording electrodes. In rare instances it is possible that your skin may be sensitive to the conductive gels or rubbing alcohol used for surface recordings. In such cases a skin rash is possible. You may stop the procedures for any reason at any time by informing the researcher of any discomfort. This will be effective immediately.

Bimanual Coordination Task: There are no known risks associated with performing this short-duration computer-based task. This task may be difficult at times and if you begin to feel discouraged please tell the researcher. You may experience some minor irritation where the Velcro straps are placed around your hands. If at any point you feel uncomfortable you can tell the researchers and they will give you and break or stop the testing.

There may be other risks that have not yet been identified, and unexpected side effects that have not been previously observed may occur.

What are the Benefits to You of Participating in the Study

There is no direct benefit to you for participating in this study. It is hoped that additional information gained in this research study may be useful in the treatment and rehabilitation of patients with brain damage. You will be informed if any significant new findings develop during the course of the study that may affect your willingness to participate in this study.

In the Event of an Injury

In the event you experience a serious side effect during this study during normal business hours, you should immediately contact Dr. Boyd at (604) 827-3369. If it is after 5:00 p.m., a holiday or weekend, you should report to an emergency room. Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else, and you do not relsease the study doctors or participating institutions from their legal and professional responsibilities. In case of a serious medical event resulting from this study, please report to an emergency room and inform them that you are participating in a research study and Lara Boyd (Principal Investigator) can be contacted for further information at (604) 822-8225.

Confidentiality

Your confidentiality will be respected. However, research records and health or other source records identifying you may be inspected in the presence of the Investigator or his or her designate by representatives of Health Canada and the UBC Research Ethics Board for the purpose of monitoring the research. No information or records that disclose your identity will be published without your consent, now will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a subject in this study. Only this number will be used on any research-related information collected about you during the course of this study, so that your identity [i.e. your name or any other information that could identify you] as a subject in this study will be kept confidential. Information that contains your identity will remain only with the Principal Investigator (Dr. Boyd) and/or members of her research team who are listed on this consent form. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected and also give you the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor.

Questions

You have read the information in this form. Dr. Boyd or her associates have answered your question(s) to your satisfaction. You know if you have any more questions after signing this you may contact Dr. Boyd or one of her associates at (604) 827-3369. If you have any concerns or complaints about your rights as a research subject and/or your experiences while participating in this study, contact the Research Subject Information Line in the University of British Columbia Office of Research Services by e-mail at RSIL@ors.ubc.ca or by phone at (604) 822-8598 (Toll Free: 1-877-822-8598).

You have a right to change your mind about allowing the research team to have access to your health information. You do not have to provide any reason for your withdrawal if you do not wish to do so. If you want to cancel permission to use your health information, you should either verbally indicate your withdrawal or send a request to Dr. Boyd. The mailing address is Lara Boyd, PT, PhD, University of British Columbia, 212 - 2177 Wesbrook Mall, Vancouver, BC, V6T 1Z3, (604) 827-3369. If you cancel permission to use your health information, you will be withdrawn from the study. The research team will stop collecting any additional information about you. The research team may use and share information that was gathered before they received your cancellation.

Effects of Bimanual Coordination Training on Cortical Network Activity and Motor Performance

Consent

I acknowledge that Dr. Boyd and/or her associates have given me information about this research study and have explained what will be done and how long it will take. Dr. Boyd and/or her associates have explained any inconvenience, discomfort or risks that may be experienced during this study. I freely and voluntarily consent to participate in this research study. I have read and understand the information in this form and have had an opportunity to ask questions and have them answered. **I will be given a signed and dated copy of the consent form to keep for my records.**

My signature on this consent form means:
-I have read and understood the subject information and consent form.
-I have had the opportunty to ask questions and have had satisfactory responses to my questions.
-I understand that my participation in this study is voluntary and that I am completely free to refuse to participate or to withdraw from this study at any time without changing in any way the quality of care that I receive.
-I authorize access to my health record as described in this consent form.
-I understand that I am not waiving any of my legal rights as a result of signing this consent form.

____
Type/Print Subject's Name

__________________________________ ________________
Signature of Subject Date

____
Type/Print Name of Witness

__________________________________ ________________
Signature of Witness Date

____
Type/Print Name of Person Obtaining Consent

__________________________________ ________________
Signature of Person Obtaining Consent Date

____
Type/Print Name of Principal Investigator

__________________________________ ________________
Signature of Principal Investigator Date