ASSESSING NEUROPHYSIOLOGICAL AND BEHAVIOURAL OUTCOMES OF THE PROXIMAL UPPER LIMB MUSCLES IN RESPONSE TO NOVEL MOTOR SKILL ACQUISITION

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Abstract

A single session of motor training with the distal upper limb muscles leads to changes in brain and spinal cord processing. However, the neuroplastic response of the proximal upper limb muscles to novel motor training has not been studied. The development of a proximal motor task which shows neurophysiological changes in response to motor learning will allow for future investigation of the neurophysiological changes associated with common occupational postures and movements, and provide a way to assess the neural consequences of ergonomic modifications on neural plasticity. This thesis found significant changes in neural activity, measured using somatosensory evoked potentials (SEPs) following a single session of motor training session with the proximal upper limb task. Additionally, sex-based differences in motor task performance were seen for the proximal upper-limb task, indicating a male advantage to gross motor tasks, with no sex differences seen when the same task was performed using the thumb.

Key Words

Somatosensory evoked potentials (SEPS), motor training, sensorimotor integration, upper-limb, motor learning

Statement of Originality

I hereby declare that this thesis is, to the best of my knowledge, original, except as acknowledged in the text, and that the material has not been previously submitted either in whole or in part, for a degree at this or any other University.

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To my family, including my dog, through editing my literature review, and listening to me rant about the nervous system, you have all played a huge role in the development of this thesis. Thank you for your continued love and support, you have truly shaped me into the person I am today.

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Abbreviations

APB: Abductor pollicis brevis

BOLD fMRI: Blood oxygen level dependent functional magnetic resonance imaging

CNS: Central nervous system

DCL: Dorsal column lemniscal tract

EEG: Electroencephalogram

FDI: First dorsal interossei

fMRI: Functional magnetic resonance imaging

IFCN: International Federation of Clinical Neurophysiologists

MEPs: Motor evoked potentials

PNS: Peripheral nervous system

S1: Primary somatosensory cortex

SEPs: Somatosensory evoked potentials

TMS: Transcranial magnetic stimulation

Introduction

Within the primary sensory and motor cortices, each anatomical location on the body is represented within a cortical map, which stretch from the longitudinal cerebral fissure through the post-central and pre-central gyri in each hemisphere. These cortical maps are commonly referred to as the sensory and motor homunculi, meaning little man, as the maps provide a layout of the sensory and motor innervation of the entire body (Buonomano & Merzenich, 1998). The representation of each anatomical location is determined not by size, but by the degree of innervation. As displayed in Figure 1, anatomical locations with higher levels of innervation, such as the fingers, tongue, and face will be represented as a larger portion of the homunculi than areas with lower levels of innervation, such as the trunk and limbs.

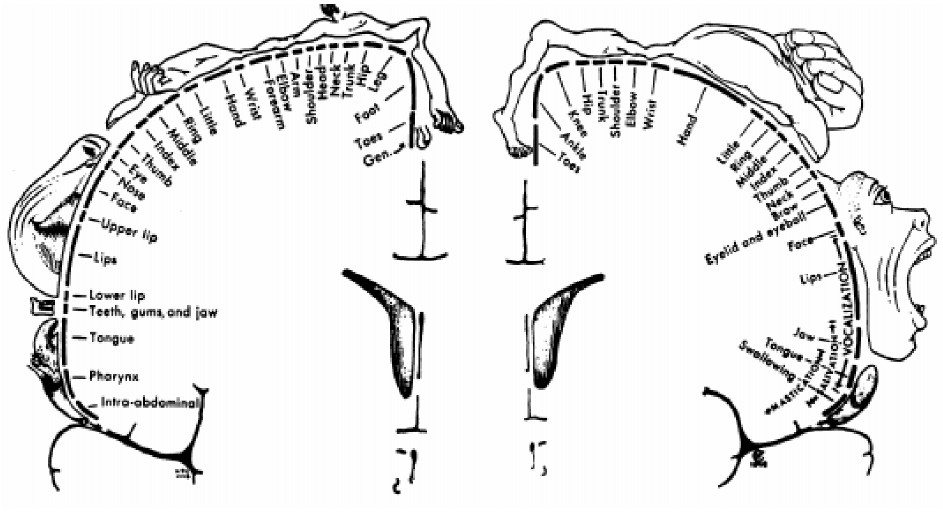

Figure 1. The motor and sensory homunculi, representing the location and amount of cortical area dedicated to specific skeletal muscles. Adapted from (Schott, 1993).

The cortex possesses the ability to preferentially represent the sensory input and motor output sources that are proportionally the most used (Buonomano & Merzenich, 1998). This ability of the cortex to change in response to experience, is referred to as neural plasticity. Neural plasticity allows for the creation and reinforcement of synaptic connections between neurons. Thus, the homunculus is not a fixed entity, but rather, is a dynamic interaction between the cortex and its environment, and is continuously modified by experience (Buonomano & Merzenich, 1998). The ability of the brain to change in response to its environment is an essential component during the process of learning, allowing for the acquisition of new skills. These changes within the brain can be as subtle as increases in neuronal excitability, or as dramatic as the rewiring of the auditory cortex to process visual stimuli (Moucha & Kilgard, 2006).

While neural plasticity is used to reinforce frequently used synapses, it can also create new synaptic connections through motor learning. Motor learning is a change in the body’s ability to respond to a situation, resulting from practice or exposure to a novel situation (Andrew, Haavik, Dancey, Yielder, & Murphy, 2015). Motor learning paradigms are most commonly used to induce neural plasticity through the introduction of a novel motor task, which results in the creation of new synaptic connections. Through the use of novel motor tasks, previous functional magnetic resonance imaging (fMRI) studies have displayed quantifiable evidence for neural plasticity following a period of motor learning (Iacoboni et al., 1999; Ungerleider, 1995). Following a repetitive finger task (opposing the fingers to the thumb in a set sequence), large areas of the cortex were activated during a blood oxygen leveldependant (BOLD) fMRI (Ungerleider, 1995). These changes persisted for several months, which suggests an experience-dependent reorganization of the adult cortex, in response to motor learning (Ungerleider, 1995). However, BOLD fMRI studies track the changes in blood flow throughout the cortex, and while providing an accurate spatial measure of brain plasticity, they provide an indirect measure of brain activity. In contrast, whole head or partial electroencephalogram (EEG) recordings provide a temporally accurate measure of changing activity levels throughout the cortex, in response to motor learning (Andrew, Yielder & Murphy, 2015).

EEG recordings provide a direct measure of cortical and subcortical activity through the placement of electrodes directly onto the scalp, at locations of hypothesized neural generators. While there is currently no set definition regarding neural generators, in practice they are complexes of discrete functional neurons, which assimilate input and distribute output along postulated neural pathways (Andrew, Yielder & Murphy, 2015 (Andrew, Yielder, & Murphy, 2015; Cruccu et al., 2008; Haavik & Murphy, 2013). Following a period of motor learning, the levels of activity at these neural generators change (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Haavik & Murphy, 2013). Through the comparison of pre-test baseline and post-test somatosensory evoked potential (SEP) measurements, a direct measure of cortical and subcortical activity in response to motor learning can be investigated.

Previous studies have successfully used SEPs to assess the motor-learning potential of fine motor tasks. Andrew et al. (2015) displayed significant increases in the N24 and N30 SEP peaks following a novel typing task, in which the participant was required to type sequences of numbers with their thumb. In conjunction with significantly increased cortical and subcortical activity, participants showed a significant improvement in reaction time, inferring that motor learning had occurred. This typing task was then further investigated in the comparative study by Andrew, Yielder and Murphy (2015). This study compared the motor learning outcomes of the typing task, to a newly developed tracing task. The study determined that a pursuit-based tracing task showed improvements accuracy and retention, in conjunction with differential SEP peak changes, when compared to a typing task. Through these studies, it is evident that there is a direct link between SEP peak changes, and motor learning. The 2015 comparative study indicated that a pursuit-based tracing task is the optimal task for inducing motor learning and neural plasticity. This finding provided the basis for the upper-limb motor learning task utilized within this proposed study. However, as current research has focused primarily on motor learning and SEPs with the use of small hand muscles, there is a gap in the literature with respect to whole-arm tasks.

Hypotheses

1. A single training session of a novel proximal upper-limb motor learning task will result in increased measures of in-task accuracy.
2. A novel motor learning task will result in changes in neural processing within the proximal upper-limb muscle groups, as reflected through short-latency median nerve SEP amplitudes.
3. Males and females will display similar levels of task accuracy on a novel motor learning task.

Overview

The following research project is divided into four sections:

1. A literature review, with emphasis on:
    a. Neuroanatomy, the cerebellum, and sensorimotor integration
    b. Motor learning
    c. Somatosensory Evoked Potentials
    d. Upper-limb workplace injuries
    e. Strengths, limitations, and gaps in the research
2. A manuscript for each completed study in the format for submission to The Journal of Neurophysiology
3. A summary of the thesis
4. Appendices, which include all recruitment posters, informed consent forms, and related questionnaires

Chapter One: Literature Review

Introduction to Literature Review

This chapter reviews current literature relevant to the proposed objectives of this thesis. It begins with a section on general neuroanatomy relevant to motor learning. It then provides an overview of sensorimotor integration, and its relevance to performance based tasks. Next, somatosensory evoked potentials (SEPs) are discussed in depth as a method of measuring neural plasticity. The next section discusses motor learning, the role of the cerebellum in motor learning, and movement observation as it relates to motor learning. The following section provides an overview of work-related upper limb injuries, and how these injuries can impact sensorimotor integration. Finally, the overall strengths and limitations of the reviewed research are identified, as are potential gaps in the reviewed body of literature.

Neuroanatomy

The performance of fine and gross motor skills relies on the optimal functioning of the central and peripheral nervous systems (CNS and PNS). The CNS is composed of the cortex, cerebellum, and spinal cord, while the PNS is limited to the cranial and spinal nerves exiting and entering the spinal cord. The nerves within the PNS synapse directly onto the sensory receptors in the skin and muscle, and enter the spinal cord via the dorsal root ganglion. Within the spinal cord, sensory feedback is transmitted to the brain through sensorineural tracts, each of which transmits different types of sensory feedback. Within this research, the targeted sensorineural tract is the dorsal column lemniscal tract (DCL), which transmits sensory feedback from fine touch, vibration, and proprioception. During stimulation of the median nerve, sensory feedback is transmitted from the sensory receptors to the DCL tract, via sensory neurons. This sensory information then travels along the DCL tract to the brain, where it is processed. The processing of the sensory information following peripheral nerve stimulation results in specific peaks of activity, within certain regions of the brain (somatosensory evoked potentials). These peaks provide a direct measure of the level of electrical activity at each neural generator within the brain, which can be recorded using EEG electrodes placed on the scalp. The levels of activity at each of these neuronal generators can be altered through beneficial or maladaptive processes, such as motor learning tasks, neurological disorders, or injuries.

Sensorimotor Integration

Sensorimotor integration refers to the ability of the CNS to receive incoming sensory stimuli, process and integrate this feedback, and formulate appropriate motor outputs. The sensorimotor system is comprised of several different components, including joint position sense, sensation of force, neuromuscular control, proprioception, and kinesthesia (Myers, Wassinger, & Lephart, 2006). A high level of sensorimotor integration is essential for novel skill acquisition, as the sensory system must effectively transmit and process appropriate feedback, allowing for the motor system to correct for in-task errors in performance. Previous research has displayed that when injured or fatigued, skill acquisition and performance can be impaired, due to altered sensorimotor integration (Haavik & Murphy, 2012; Zabihhosseinian, Holmes, & Murphy, 2015). In this sense, although changes in sensorimotor integration are essential for novel skill acquisition, these changes can be maladaptive, due to injuries, fatigue, or repetitive movement patterns. These maladaptive changes in sensorimotor integration could lead to impaired performance and further injury. Further research is needed to assess sensorimotor impairments associated with common workplace postures and movements.

Somatosensory Evoked Potentials

SEPs are a measure of electrical activity along the somatosensory pathway, in response to the stimulation of a peripheral nerve (Yamada, Yeh, & Kimura, 2004). The somatosensory system consists of five sub-systems: mechanoreception, thermoreception, nociception, proprioception, and visceroception (Cruccu et al., 2008). The combination of the afferent input from these systems provides conscious perception of sensory information from the musculoskeletal system, the skin, and the visceral organs (Cruccu et al., 2008). The somatosensory system contains two major pathways, the DCL tract and the spinothalamic tract. While the DCL tract is responsible for the detection of mechanoreception and proprioception, the spinothalamic tract is responsible for thermoreception, nociception, and visceroception (Cruccu et al., 2008). The primary afferent fibres projecting into the dorsal column-lemniscal tract are primarily composed of type Ia, Ib, and II fibres, which are all highly myelinated and of large diameter, giving them extremely fast conduction properties between 33-120m/s (Cruccu et al., 2008). These fibres have the lowest threshold for electrical stimulation, thus providing the optimal target for peripheral stimulation (Cruccu et al., 2008). In contrast, the afferent fibres of the spinothalamic tract are primarily composed of type III and IV fibres, which have an extremely small diameter, and either thinly myelinated or unmyelinated. Due to their small diameter and minimal myelination, these fibres have relatively slower conduction velocities, ranging from 0.5-30 m/s. These properties ensure that the spinothalamic fibres are highly resistant to electrical stimulation, which prevents the activation of the pain receptor fibres during SEPs testing (Cruccu et al., 2008). Standard SEP techniques are primarily used to assess the electrical activity of the dorsal column-lemniscal system, in response to a peripheral motor stimulation

(Cruccu et al., 2008). It has been shown by Gandevia and colleagues (S C Gandevia & Burke, 1988; S.C. Gandevia, Burke, & McKeon, 1984) that muscle afferents are largely responsible for the SEPs evoked in response to stimulation of the median nerve at the wrist.

SEPs have been consistently used to assess the impact of motor learning on neurophysiological processing. Previous research has displayed large changes in SEP amplitudes following motor learning tasks with the fingers and thumbs (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Haavik & Murphy, 2013). However, no research to date has utilized SEPs following motor learning with the entire upper limb. This research aimed to utilize short latency median nerve SEPs to assess the neurophysiological changes associated with motor learning in the proximal upper-limb muscles.

SEP Peak Recording Parameters and Nomenclature

This electrical activity is recorded through the placement of electrodes directly onto the participant's scalp, at the locations of hypothesized neural generators. The electrode sites utilized within this paper were a frontal cephalic site (Rossi site, 6cm forward from the vertex and 2cm contralaterally), and a posterior parietal site (20% of tragus to tragus and 2cm posteriorly), in accordance with international recommendations (Cruccu et al., 2008; Rossi et al., 2003; Yamada et al., 2004). Each electrode is placed on the scalp contralateral to the peripheral stimulation, and measure cerebral potentials by analyzing the electromagnetic properties of the brain. These potentials represent the summation of the synchronous activity of neurons within the same spatial orientation (Cruccu et al., 2008; Yamada et al., 2004). Each potential produces a peak in electrical activity, which is time-dependent upon the peripheral stimulation. Each peak within the recorded waveforms are termed positive (P) or negative (N), depending on their polarity. According to the International Federation for Clinical Neurophysiologists (IFCN), a positive peak is denoted as a downwards deflection on the waveform, while a negative peak is an upwards deflection (Cruccu et al., 2008). This polarity prefix is then followed by the latency of the peak, in milliseconds (ms). As each potential occurs at a different location along the somatosensory pathway, each peak occurs at a different latency, which is the transmission time between the point of stimulation and the chosen neural generator (Cruccu et al., 2008; Fujii et al., 1994; Yamada et al., 2004). For example, the N24 peak would consist of a negative wave-form deflection, occurring 24 ms following the initial stimulation. In terms of latency, SEPs are categorized into Short Latency potentials (8-30ms), Medium Latency potentials (40-100ms), and Long Latency potentials (>100ms). Although short latency potentials produce a smaller amplitude, they are the most stable and resistant to changes in consciousness, which makes them more suitable for diagnostic testing and research (Yamada et al., 2004).

According to the IFCN guidelines, when recording SEP peaks, peripheral stimulations should be generated through a 0.1-0.2 ms, bipolar transcutaneous electrical stimulation, applied to the skin directly overlying the selected peripheral nerve (Cruccu et al., 2008; Nuwer et al., 1999). The peripheral nerve of interest is most commonly the median nerve in the palmar side of the wrist, or the tibial nerve in the shin (Cruccu et al., 2008; Yamada et al., 2004). For the proposed study the median nerve was chosen, as the task involved the use of the upper limb. The cathode electrode should be placed proximally to the anode to reduce the possibility of anodal block. For SEPs involving the median nerve, the anode should be placed 2-3cm proximal to the wrist crease of the chosen limb (slightly toward the ulna to prevent activation of the flexor digitorum tendon), with the cathode placed approximately 2cm proximally (Yamada et al., 2004). Additionally, to minimize the stimulus artifact, a ground electrode should be placed on the stimulated limb, between the point of stimulation and the recording electrodes (Cruccu et al., 2008). The ideal intensity of the stimulus applied to the median nerve is the lowest possible intensity that consistently produces a visible muscle twitch in the abductor pollicis brevis (ABP) muscle, with a stimulation rate between 3-5Hz (Cruccu et al., 2008; Yamada et al., 2004). By further refining this rate to 4.98Hz, it allows for the attenuation of the N30 SEP peak, which allows for the accurate identification and measurement of the N24 SEP peak (Andrew, Yielder, et al., 2015; Fujii et al., 1994; Haavik & Murphy, 2013; Yamada et al., 2004). To reduce noise, and ensure reliability and reproducibility, SEP peaks are averaged over 500-2000 frames (stimulations) (Cruccu et al., 2008; Fujii et al., 1994; Haavik & Murphy, 2013; Yamada et al., 2004). Lastly, the optimal filters for recording SEP peaks are a high-pass filter at less than 3Hz, and a low-pass filter over 2000Hz (Cruccu et al., 2008; Nuwer et al., 1999; Rossini, Cracco, Cracco, & House, 1981; Yamada et al., 2004).

SEP Peak Neural Generators

N9 Peak

The N9 peak is a negative potential recorded approximately 9ms following the peripheral stimulation of the median nerve. Electrodes are placed over the ipsilateral brachial plexus, at Erb's point, within the angle formed by the posterior border of the clavicular head and the lateral border of the sternocleidomastoid muscle, and referenced to the ipsilateral earlobe (Cruccu et al., 2008). This peak represents the arrival of the peripheral nerve volley at the brachial plexus (Cruccu et al., 2008).

N13 Peak

According to IFCN guidelines, the N13 peak can be recorded through the placement of an electrode over the 5th, 6th, or 7th cervical spinous processes, which is referenced to an electrode on the anterior neck at the level of the trachea (Cruccu et al., 2008; Yamada et al., 2004). The N13 SEP peak represents the postsynaptic potential of the interneurons within the midcervical cord and dorsal horn, and is generated at or near the first synaptic relay of the spinothalamic tract (Cruccu et al., 2008; Desmedt & Cheron, 1981).

P14 Peak

The P14 SEP peak is recorded through the placement of an electrode over a contralateral frontal cephalic site (Rossi site, 6cm forward from the vertex and 2cm contralaterally) (Cruccu et al., 2008; Rossi et al., 2003). The P14 peak is generated at or above the level of the foramen magnum, but below the cortex (Cruccu et al., 2008; Desmedt & Cheron, 1981) and is thought to be generated by the arrival of the afferent volley at the medial lemniscus, and the nucleus cuneatus within the medulla oblongata (Desmedt & Cheron, 1981; Tinazzi et al., 2000)

N18 Peak

The N18 peak is best recorded from a frontal cephalic site. Rossi et al., (2003) showed that the optimal location for recording the P14, N18, N24, and N30 peaks is a location 6cm forward from Cz, and 2cm contralaterally to the site of stimulation (Rossi et al., 2003) Recorded from the frontal Rossi site and referenced to the ipsilateral earlobe, the N18 is a subcortical peak arising from the brainstem above the spinal cord, within the lower medulla and midbrain-pontine region (Cruccu et al., 2008; Sonoo, 2000). Current research suggests that the N18 peak originates specifically within lower medulla nuclei, including the accessory inferior olives and dorsal column nuclei (Noël, Ozaki, & Desmedt, 1996; Sonoo, 2000). Due to the location of its neural generators, the N18 peak has the potential to reflect activity changes within the cerebellum.

N20 Peak

According to IFCN guidelines, the N20 peak is recorded 2 cm posterior to the contralateral central scalp site C3/4, referred to as Cc' (Cruccu et al., 2008; Yamada et al., 2004). This peak represents the early cortical processing activity of Brodmann's area 3b, within the primary somatosensory cortex (S1) (Desmedt & Cheron, 1980, 1981; Desmedt & Ozaki, 1991; Noël et al., 1996).

N24 Peak

The N24 SEP peak is recorded at the contralateral Rossi site, representing the neuronal pathway linking the cerebellum and S1 (Restuccia, Marca, Valeriani, Leggio, & Molinari, 2006; Restuccia et al., 2001). However, appearing as a notch in the P22-N30 complex, the N24 peak is difficult to record with slower stimulation rates. Previous work by Haavik-Taylor Taylor and Murphy

(2007) has demonstrated that faster stimulation rates attenuate the N30 peak, allowing for easier differentiation and measurement of the N24 peak. Representing the pathway between the cerebellum and S1, the N24 peak allows for investigation into cerebellar changes following motor learning.

P25 Peak

Recorded from the contralateral parietal site Cc' and referenced to the ipsilateral earlobe, the P25 peak represents a group of neurons within Brodmann's area 1, within the primary somatosensory cortex (Cruccu et al., 2008; Yamada et al., 2004)

N30 Peak

The N30 peak is recorded at a site 6cm forward from the vertex, and 2cm contralaterally, (further referred to as the Rossi site), and is thought to represent a complex cortical and subcortical loop linking the thalamus, basal ganglia, premotor areas, and primary motor cortex, originating from the frontal lobe and posterior wall of the central sulcus (Cebolla & Cheron, 2015; Lelic et al., 2016; Rossini et al., 1981; Tinazzi et al., 2000). Current research therefore suggests that the N30 peak reflects sensorimotor integration within the cortex (Lelic et al., 2016; Rossi et al., 2003).

Motor Learning

Motor learning is a change in an individual's capacity to respond to a situation or stimuli, following a period of learning, whether through practice or novel experience (Ito, 2000; Karni, Meyer, Jezzard, & Adams, 1995). This process of motor learning allows for the faster and more accurate discrimination and performance of motor skills. The process of motor learning contains four primary characteristics: the process (skill acquisition), the practice (skill development), inferred learning (observation of performance and neural measures), and that the learned skill is relatively permanent (Ito, 2000).

During the research conducted within this thesis, the process of motor learning occurred through the completion of a novel, pursuit-based tracing task. Each participant completed four trials as their pre-test measure, twelve trials during the learning phase (practice and skill development), then four more trials as their post-learning measure. The twelve learning trials allowed the participant to practice the newly learned skill, and consolidate it. While motor learning cannot be directly measured, it is inferred through improvements in motor performance. Motor performance can be measured in two ways: performance outcome measures (accuracy, reaction time, measures of error), and through neural measures. This study utilized both performance outcome measures (improvements in accuracy from baseline) and neural measures (SEPs) to assess overall motor performance. These motor performance measures were recorded during the pre- and post-test trials of the tracing task. Finally, following the process of motor learning, the newly learned skill must be relatively permanent.

To assess the permanence of the motor learning, each participant completed a retention test, 24-48 hours after the initial learning period.

Motor learning in the upper limb occurs through a two-way interaction between the neural processes controlling transport of the hand, which allows for adjustment and correction of errors (Van Vliet & Heneghan, 2006). This two-way interaction uses both feedforward and feedback mechanisms. During the initial stage of a motor task, feedforward control is used in preplanning the motor command and executing the initial movement. Evidence shows that the feedforward mechanism works by comparing the target position to an instantaneous predictive estimate of hand position, allowing for the movement to be planned to reach the target. This predictive estimate then allows for modification of the ongoing motor command (Van Vliet & Heneghan, 2006). During the final components of the motor task, the feedback mechanism is used, which relies on vision and proprioception of the hand to adjust for errors. The use of visual and proprioceptive systems is useful during the final phase of the task as the minimum time needed to react to feedback is approximately 100ms (Van Vliet & Heneghan, 2006).

In the presence of enhanced proprioceptive and visual feedback, motor learning performance and retention has been shown to improve (Adams, Gopher, & Lintern, 1975). Adams et al (1975) used a spring-loaded slide rule to assess visual and proprioceptive input on motor learning. During their motor learning task, each participant attempted to move a block to a predetermined distance on the slide rule. By removing the spring, and using a one-way mirror, the participant's proprioceptive and visual feedback was distorted or removed (Adams et al., 1975). This task proved successful in assessing the impact of visual and proprioceptive feedback on motor learning, demonstrating that enhanced proprioceptive and visual feedback resulted in improved motor learning performance (Adams et al., 1975).

The motor learning task utilized within the completed studies builds upon the use of enhanced visual feedback to improve motor learning outcomes. During the pursuit-based tracing task, participants were required to replicate a vertically scrolling sine wave composed of dots, displayed on a touch screen. Error feedback was provided visually on-screen throughout the task. During perfect replication of the sine wave, each dot within the wave was green. As the distance away from the sine wave increased, each dot gradually turned from green to yellow. During the task, the participant is instructed to move their arm only in the horizontal plane, rather than follow the sine wave vertically. Through the use of enhanced visual feedback (sine wave changing colours in response to errors), the participant is able to see their errors in real-time, and develop motor strategies to improve their performance.

The tracing task used within this research has successfully been used in previous motor learning studies to induce cortical and subcortical activity changes (Andrew, Yielder, et al., 2015). Following a ten-minute training session with the thumb, the tracing task produced increased amplitudes of the N13, N20, P25, and N30 SEP peaks, while significantly decreasing the N24 peak. These amplitude changes coincided with an overall increase in task accuracy, which was retained post-intervention (Andrew, Yielder, et al., 2015). The changes in SEP amplitudes following this task indicate changes in the activity levels of neural generators, resulting from induced neural plasticity (Andrew, Yielder, et al., 2015). However, this motor learning task has previously only been used with small hand muscles, such as the first dorsal interosseous (FDI) muscle, or the abductor pollicis brevis (APB) muscle. As muscles capable of fine-motor control, the FDI and APB muscles have a relatively larger representation on the sensory and motor homunculi, allowing for easier stimulation and recording over the sensory and motor cortices. In addition, the FDI and APB muscles act to adduct the first finger, and abduct the thumb, respectively. These movements are seldom used in daily life, providing an optimal target for a novel motor learning task.

The Role of the Cerebellum in Motor Learning

The cerebellum is a structure found beneath the cerebral hemispheres, composed of three main regions: the anterior, middle, and flocculonodular lobes. These lobes are further divided into three functional divisions: the vestibulocerebellum, the spinocerebellum, and the cerebrocerebellum. During the process of motor learning the spinocerebellar and cerebrocerebellar regions are highly active, working to coordinate voluntary movements, regulate posture, plan movements, and process sensory information to correct for errors (Akshoomoff & Courchesne, 1992).

When initially performing a novel, complex movement, the cerebellar adjustment of the onset and termination of the movement is often inaccurate (Akshoomoff & Courchesne, 1992). Following successive trials (motor training), the action becomes more precise, as the cerebellum begins to adjust for any errors in motor performance. When the motor cortex sends a command to the motor system for the performance of a voluntary movement, the spinocerebellum receives an "efference copy" of the intended movement. As the movement proceeds, the proprioceptive input about the actual movement is transmitted to the interpositus nucleus and intermediate cerebellum via the ascending dorsal spinocerebellar tract (Scott, 2004). Simultaneously, the pontine nuclei activate to transmit a strong projection from the M1 about the movement being performed (Scott, 2004). The cerebellum then utilizes any differences between the efference copy and the performed movement to correct for errors as the movement continues. In addition, the cerebellum receives sensory information regarding the velocity and direction of the performed action. The cerebellum uses this information to predict the final displacement of the limb, and determines exactly when to stop the movement to ensure that the limb stops moving at the intended position.

Previous research has displayed large decreases in the amplitude of the N24 SEP peak in patients with cerebellar lesions (Restuccia et al., 2006; Restuccia et al., 2001). These results indicate that the N24 peak specifically represents the influence of the cerebellum on neurophysiological changes within the primary somatosensory cortex (Restuccia et al., 2006; Restuccia et al., 2001). Therefore, the measurement of the N24 SEP amplitude provides a way of assessing the impact of changes in the excitability of cerebellar pathways in response to motor learning in the proximal upper limb.

Movement Observation

Within the human brain, specific neurons, termed “mirror neurons”, activate both when performing a movement, and when observing that movement. These mirror neurons form a complex network within the brain, including occipital, temporal, and parietal visual areas, the inferior parietal lobule, the lower part of the precentral gyrus, and the posterior part of the inferior frontal gyrus (Rizzolatti & Craighero, 2004). First discovered in the F5 area of the primate premotor cortex, these mirror neurons primarily activate following an interaction between a biological effector and an external object (Rizzolatti & Craighero, 2004). While the majority of mirror neuron research has focused on the non-human primate cortex, neurophysiological and brain-imaging experiments have indirectly proved the presence of an analogous mirror neuron system in humans (Rizzolatti & Craighero, 2004). During early EEG experiments, it was observed that the desynchronization of the mu rhythm occurs both during active movements, and during movement observation (Gastaut & Bert, 1954). This observation was then further confirmed through the use of EEG recordings, and by using magnetoencephalographic (MEG) recordings (Cochin, Barthelemy, Lejeune, Roux, & Martineau, 1998; Cochin, Barthelemy, Roux, & Martineau, 1999; Hari et al., 1998).

During the previously mentioned Ungerleider (1995) study, participants were asked to perform a repetitive finger task (opposing the fingers to the thumb in a set sequence). Following this task, a BOLD fMRI displayed increased blood flow to areas of the cortex, indicating that motor learning-induced neural plasticity had occurred. This study was then investigated further, with the addition of a movement observation task. Iacoboni et al. (1999) asked participants to observe and then replicate a repetitive finger movement. This observation and imitation task resulted in an increased signal intensity of the left frontal operculum, right anterior parietal region, and the right parietal operculum during an fMRI, indicating an increased activation of these structures following a period of movement observation (Iacoboni et al., 1999). These similar results further reinforce the presence of a mirror-neuron system in humans, and provide evidence for the use of movement observation as a method of motor learning.

Previous movement observation studies have displayed that observing another person undergoing the process of motor learning directly influences the later motor performance of the observer (Mulder, 2007). After watching a video of someone learning to navigate a novel force field, subjects performed significantly better in the same force field, when compared to a control group with no knowledge of the field (Mattar & Gribble, 2005). This indicates that by watching someone else attempt to accurately move within the force field, subjects were able to create a neural representation of the force field's mechanical properties, and then use that representation to improve their motor performance within the same environment (Mattar & Gribble, 2005; Mulder, 2007).

For the purposes of investigating movement-based motor learning, the possibility of learning through movement observation had to be eliminated. During the motor learning task utilized within this thesis, the participant's view of their own arm was occluded, through the use of dual monitors. While the participant traced the sine wave on a touchscreen monitor or small trackpad, their arm was fully occluded from sight, and they could only see their performance on a separate monitor, which provided real-time error feedback. Without the visual feedback of arm position, in-task measures of error provided the only means for performance improvement. This ensured that any motor learning that occurred during the task occurred as a direct result of movement-based motor learning.

Occupational Tasks and Workplace-Related Injuries

The most commonly reported biomechanical factors associated with work-related injuries are repetitive actions, excessive force, and abnormal postures (da Costa & Vieira, 2010). Within modern occupational settings, many tasks primarily require the use of repetitive glenohumeral rotation, such as typing and assembly line production. These repetitive shoulder movements, even in the absence of excessive force and abnormal postures, can put the workers at a higher risk for a number of upper-limb disorders, such as tendinitis, focal hand dystonia, and rotator cuff impingement.

Following a physical assessment of 146 female workers in highly repetitive jobs (garment and automotive trim sewing, electronic assembly, metal parts assembly, supermarket cashiering, and packaging), 56% of the workers studied displayed upper-limb musculoskeletal disorders, which were potentially work-related (Ranney, Wells, & Moore, 1995). 44% of those affected displayed muscle pain and tenderness in the upper limb, 31% displayed tendon injury (9.6% experienced rotator cuff tendinitis), and 21% displayed neurological injury (Ranney et al., 1995). In addition, during a cross-sectional study of over 6000 working-aged adults in the general population, 52% reported pain or dysesthesia in the past week in the upper limb or neck. Allowing for overlap of symptoms, this corresponded to a one-week prevalence of 24.1% for neck pain, and 36.2% for upper-limb pain (Walker-Bone, Palmer, Reading, Coggon, & Cooper, 2004). Following further examination, the most commonly experienced cause of shoulder pain was adhesive capsulitis (8.2% prevalence for males, 10.1% prevalence for females) and rotator cuff tendinitis (4.5% prevalence for males, 6.1% prevalence for females) (Walker-Bone et al., 2004).

The development of a proximal upper-limb muscle motor learning task will allow for the examination of neurophysiological changes associated with common workplace postures and movements, such as glenohumeral rotation, allowing for investigation into the potentially maladaptive neuroplastic changes associated with common work-place tasks.

Summary

The reviewed research has provided conclusive evidence for the ability of motor learning to induce neural plasticity, which can be quantitatively evaluated through the use of SEPs.

However, despite the fact that upper-limb disorders are some of the most common work-related injuries, due to repetitive movements, excessive force, and abnormal postures, no studies have yet utilized SEPs in conjunction with a motor learning protocol to investigate the neuroplastic changes associated with movements used in common workplace tasks, specifically repetitive glenohumeral rotation.

Conclusion

Sensorimotor integration allows for the optimal processing and coordination of sensory input and motor output. However, current research has shown alterations in sensorimotor integration, proprioception, and joint position sense in the presence of pain and fatigue. Within the modern workplace, upper-limb disorders most commonly result from repetitive motions, excessive force, and abnormal postures. Within this study, the measurement of the N13 and N30 SEP peaks allows for the investigation of changes in sensorimotor integration following a period of repetitive glenohumeral rotation. This will allow for an examination of the neurophysiological changes associated with common occupational postures and movements. In addition, the cerebellum is highly active during periods of motor learning, functioning to decipher motor coding, anticipate future movements, and synchronizing sensorimotor integration and muscle activation. Representing the connection between the cerebellum and S1, the N24 peak provides the optimal method to assess the impact of motor learning on cerebellar activity. Little is currently known about the impact of repetitive proximal upper-limb motions on both sensorimotor integration and the cerebellum. With improved knowledge of the neurophysiological changes associated with repetitive shoulder movements, researchers and workplaces will gain a better understanding of the potentially maladaptive neurological processes associated with common tasks.

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Chapter Two: Manuscript 1 - Neurophysiological and behavioural outcomes of the proximal upper limb muscles in response to novel motor skill acquisition

Abstract

Previous studies have shown significant changes in cortical and subcortical activity levels in response to motor training with the distal upper-limb muscles (Andrew, Yielder, et al., 2015; Haavik & Murphy, 2013). However, no studies to date have assessed the neurological processing changes associated with motor training in the proximal upper-limb muscles. The proximal upper limb muscles are a common source of work-related injuries, due to repetitive glenohumeral movements. Testing and development of a proximal motor task would allow for the investigation of the neurophysiological changes associated with common occupational postures and movements. This study sought to assess the impact of a novel motor learning task on neural processing of the proximal upper-limb muscle groups, through short-latency median nerve somatosensory evoked potentials (SEPs). One group of 12 participants completed a novel motor training task, consisting of tracing a sinusoidal waveform varying in amplitude and frequency. Baseline SEP measurements were recorded from each participant, followed by a mental recitation control task. Pre-test SEP measurements were then recorded, followed by the motor training task, and followed by post-test SEP recordings. The participants completed the tracing with their right thumb, using glenohumeral rotation to move their hand. Significant improvements in task accuracy were demonstrated, indicating that motor learning had occurred. Significant changes were also seen in the N11, N13, N20, N24, P25, and the N30 peaks, following the motor training task. Conclusion: Early SEPs appear to be a valid measure of changes in sensorimotor integration in response to novel motor skill acquisition within the proximal upper-limb muscles.

Keywords: somatosensory evoked potentials, SEPS, motor learning

Introduction

Cortical plasticity refers to the ability of the cortex to alter its synaptic connections. These changes can include the pruning of unused synapses, strengthening current connections, or the generation of new synapses (Buonomano & Merzenich, 1998). These cortical changes can be induced through altered afferent input, such as injury, or motor learning. Previously, motor learning research has focused primarily on the use of brain-imaging techniques, such as BOLD fMRI scans and PET scans. However, while providing an accurate spatial representation of cortical plasticity, these techniques are temporally limited, provide an indirect measure of brain activity, and are both expensive and limited in the types of tasks that can be used for routine use in research studies (Pelletier, Sauerwein, Lepore, Saint-Amour, & Lassonde, 2007). Previous motor learning studies have successfully displayed learning-dependent changes in cortical plasticity, through the use of somatosensory evoked potentials (SEPs) (Andrew, Yielder, et al., 2015; Haavik & Murphy, 2013).

SEPS, when used with partial or whole-head electroencephalogram (EEG) recording electrodes, provide a temporally accurate, direct measure of cortical and subcortical activity. In combination with behavioural data through the use of motor learning paradigms, SEPs can provide an insight into the neural activation directly following the process of learning. While multiple studies have used a repetitive typing task to induce motor learning (Andrew, Haavik, et al., 2015; Haavik & Murphy, 2013) the 2015 study by Andrew et al. displayed larger changes in SEP amplitudes following a more complex tracing task, when compared to the traditional typing task. This study indicated that a more intricate, unpredictable task provided the optimal motor learning environment to induce neuroplastic changes (Andrew, Yielder, et al., 2015).

However, while multiple studies have utilized SEPs to quantify cortical plasticity, current research has focused solely on the use of small hand muscles. Within the modern workplace, the upper limb is a common source of work-related injuries, due to repetitive motions, abnormal postures, and excessive force (da Costa & Vieira, 2010). Due to its anatomical structure, the shoulder is at high risk for ergonomic injuries, such as rotator cuff impingement, tendinitis, and adhesive capsulitis. Previous studies of over 6000 adults have reported that 52% of the general working population experienced pain or dysesthesia in the upper limb or neck in the week leading up to the study (Walker-Bone et al., 2004). The development of a whole-arm motor learning task would allow for the investigation of neuroplastic changes associated with work-place injuries. Based upon previously successful motor learning paradigms (Andrew, Yielder, et al., 2015; Dancey, Murphy, Srbely, & Yielder, 2014; Haavik & Murphy, 2013), this study piloted the use of the tracing task utilized by Andrew et al., for use with the proximal upper limb muscles. The aim of this study was to validate the use of the proximal upper-limb tracing task, as a method of inducing cortical plasticity.

Methods

Participants

12 right-handed participants (6 males and 6 females), aged 19-25 (mean age 20.25, ± 1.82 years), recruited from the University of Ontario Institute of Technology participated in this study. All participants consented to two experimental sessions: a motor learning intervention, and a retention test no less than 24 hours and no more than 48 hours later. Each participant was required to complete a pre-screening questionnaire, and was required to have no history of neurological disease.

The primary exclusion criteria for the study was the presence of a known neurological condition, left-handed dominance, and classically trained musicians. The technique used within this study to assess motor learning (SEPS) relies on the full functionality of the nervous system, thus any neurological deficits (demyelination, cerebellar lesions etc.) would interfere with SEPs and thus were excluded. In addition, this study required right-hand dominant subjects. As this study aimed to compare upper-limb motor learning tasks, right-hand dominant subjects were selected to reduce any the influence of potentially confounding factors resulting from differences in motor learning strategies between the two arms (Mutha, Haaland, & Sainburg, 2013). Participants completed the Edinburgh Handedness Inventory to ensure right-hand dominance (Caplan & Mendoza, 2011). Lastly, classically trained musicians have displayed functional and structural changes in the sensorimotor and auditory systems within the brain, which could potentially impact any motor learning resulting from the tracing task (Altenmüller, 2008). For this reason, classically trained musicians were specifically excluded from the study.

The use of SEP peak recordings was chosen to measure cortical and subcortical activity changes during this study due to its successful use in previous, similar studies (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Haavik-Taylor & Murphy, 2007; Haavik & Murphy, 2012; Haavik & Murphy, 2013). Although previous studies have used fine-motor tasks, this study will attempt to validate the use of SEPs to assess whole-arm tasks, and their ability to investigate neuroplastic changes associated with work-related injuries.

This study received ethical approval from the UOIT ethics committee (REB# 07-072 & 07-073). Each participant completed an informed consent form prior to participation in the study, outlining the potential risks and benefits to the study, explaining the procedures to be undertaken, and including a pre-screening questionnaire to eliminate any of the exclusionary criteria.

Stimulation of the median nerve

The stimuli delivered to each participant consisted of 1500 electrical square pulses of 1ms in duration, through the use of an optically isolated Digitimer (DSA-7). The stimulus was delivered through Ag/AgCl ECG conductive adhesive electrodes (MEDITRACE™ 130 by Ludlow Technical Products Canada Ltd., Mansfield, MA) (impedance ≤ 5Ω) placed over the median nerve at the wrist of the right hand, at rates of both 2.47Hz and 4.98Hz. SEPs were recorded at 2.47Hz and 4.98Hz as the faster rate allows for the attenuation of the N30 SEP peak, allowing for accurate measurement of the N24 peak, while the slower rate does not result in SEP peak attenuation, allowing for the accurate measurement of the remaining peaks (Fujii et al., 1994; Haavik & Murphy, 2013). The stimulus intensity was increased for each participant until the first visible muscle contraction of the abductor pollicis brevis muscle, known as motor thresholding.

SEPS recording parameters

SEP recording electrodes (1.8288m Traditional Lead, 10mm disc, 2mm hole gold cup EEG electrodes, Grass Technologies, An Astro-Med, Inc. Subsidiary, Rockland, MA) (≤5Ω impedance) were placed according to the International Federation of Clinical Neurophysiologists (IFCN) recommendations.

The recording electrodes were placed in the same locations on each subject: the ipsilateral Erb's point (brachial plexus), over the C5 spinous process, on the anterior side of the trachea, 2cm posterior to contralateral central C3/4 (which will be further referred to as Cc'), and a final electrode at a frontal site 6cm anterior and 2cm contralateral to Cz, which will be further referred to as the Rossi site (Rossi et al., 2003). Each electrode was referenced to the contralateral earlobe, with the exception of the C5 electrode, which was referenced to the trachea. In addition, a ground electrode (1.8288m Traditional Lead, 10mm disc, 2mm hole gold cup EEG electrode) was placed in the mouth of each participant.

Data collection

Throughout each data collection session participants were seated in a comfortable, upright chair with arm rests, and were instructed to remain as quiet and as still as possible throughout the testing session. During all SEP recordings, the lights in the room were turned off to minimize electrical noise, and participants were asked to keep their eyes open.

The SEP recording was composed of 1500 electrical stimulations (sweeps), which were delivered at the chosen frequency through a Signal® configuration (Cambridge Electronic Design, Cambridge, UK). The SEP signal was amplified (gain 10,000), filtered between 0.2-1000

Hz, and then stored on the laboratory computer. The recording was then averaged over all 1500 sweeps for each stimulation rate.

Motor learning task intervention

Motor Learning Task Development

The task was developed through the use of the Unity ™ (Personal Edition) game development software.

Motor Learning Task Design

The motor learning task used within this study required participants to trace a scrolling sine wave composed of dots, using their right thumb. Participants were instructed to hold their elbow, wrist, and hand rigid, and use glenohumeral internal and external rotation to move their hand across the touchscreen, as displayed in Figure 1 below.

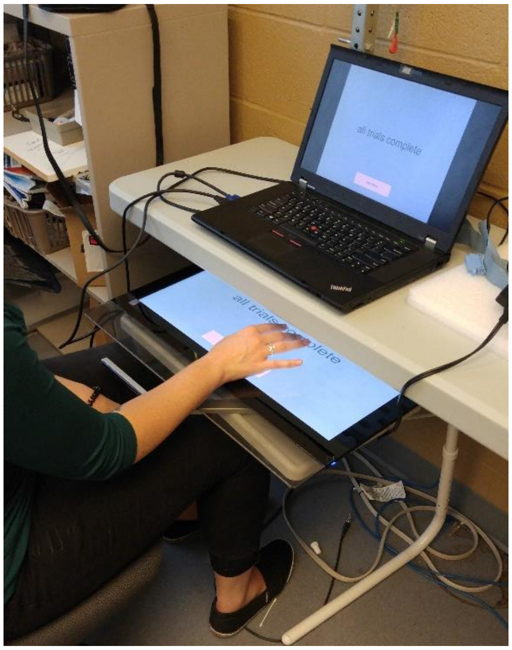

Figure 1. Tracing data collection setup. A laptop is placed on the table displaying the motor training task. Large touchscreen is placed on desk directly below the table ensuring that the table blocks the participants view of their own arm.

Dot colour ranged from green (perfect accuracy, 0% error) to varying shades of yellow (>0% error), as displayed in Figure 2 to allow for in-task error correction. The sinusoidal wave included four patterns of varying amplitude and frequency, to provide high levels of contextual interference. Contextual interference refers to the effect in which interference during task practice leads to superior task performance and retention, thus high levels of contextual interference will result in the optimal learning environment within a motor learning paradigm (Magill & Hall, 1990; Shea & Morgan, 1979). Each trial consisted of 500 dots. For the pre and post tests, each of the four patterns was performed once; for the acquisition and learning phase each version was performed three times for a total of 12 traces. During each trial, accuracy was measured in dot-widths distance from the target trace. One dot-width away from the target trace was equal to 100% error (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Dancey et al., 2014; Holland, Murphy, Passmore, & Yielder, 2015).

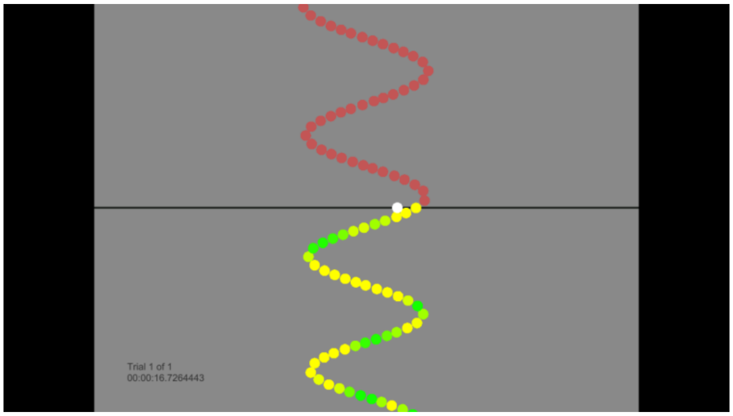

Figure 2. Motor learning task design.

For each of the participants within the study, baseline SEP measurements were recorded before the pre-test trials. This was then followed by a mental recitation task, in which participants mentally recited sequences of numbers on a slide presentation (PowerPoint). This mental recitation task was included to control for the potential effects of attention on SEPs, as the control task required the same level of attentional resources without the involvement of the motor task. Pre-test SEP measurements were then performed, followed by the motor learning task. Behavioural measures of accuracy were recorded during the pre and post-test phases of the task. Lastly, post-test SEP measurements were taken. After a minimum of 24 hours and a maximum of 48 hours, dependent upon participant availability, participants were required to return for a retention test, during which four trials of the tracing task were performed.

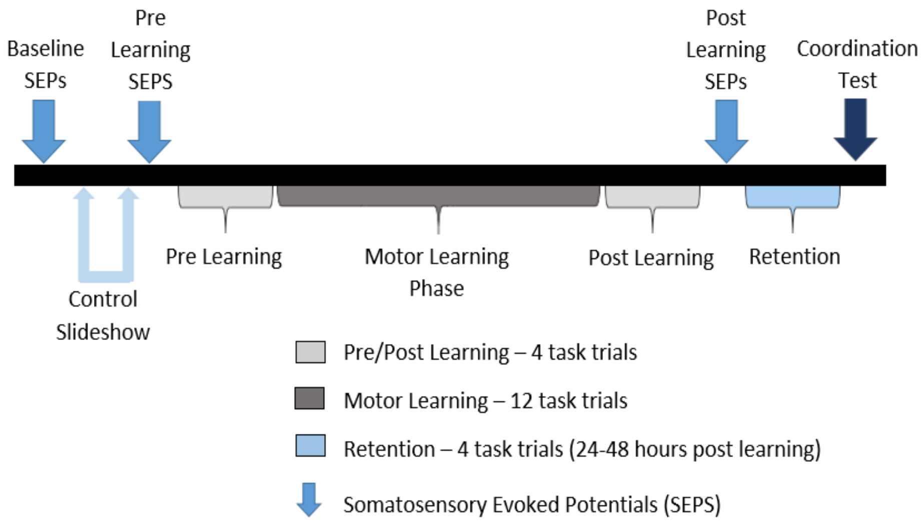

Figure 3. Study design.

Data analysis

Changes in SEP peak amplitude and latency were measured at baseline, following the control intervention and prior to motor learning, and post-learning. Additionally, task accuracy was measured during the first four learning trials, the last four learning trials, and during the retention session. In order to make changes in SEP peak magnitude comparable between subjects, all SEPs data was normalized, and expressed as a proportion of the baseline measurement. A repeated measures ANOVA was performed in SPSS (IBM Software), comparing both post-control and post-learning SEP amplitudes to the initial baseline amplitude. Statistical significance was set at $p<.05$. Additionally, only participants with a stable N9 recording were included in statistical analysis to ensure stable peripheral nerve volleys. As the N9 records the arrival of the peripheral nerve volley to the brachial plexus, trials in which the N9 differs by greater than 10% could indicate alterations in afferent input, possibly due to postural changes. The amplitude of each SEP peak was measured from peak of interest to the preceding or succeeding peak or trough, in accordance with international recommendations (Cruccu et al., 2008; Nuwer et al., 1999). Amplitudes and latencies were measured for the following peaks: N9, N11, N13, P14, N18, N20, N24, P25, N30.

Results

All 12 participants who completed the study were included in the statistical analysis of SEP amplitudes and in the statistical analysis of the task accuracy data. No significant changes in latency were seen for any of the measured peaks. As displayed in Figure 4 below, significant changes in amplitude were seen for the N13, P14, N18, N20, and N24 SEP peaks following motor learning. No significant changes in amplitude were seen following the control task, as displayed in Figure 4.

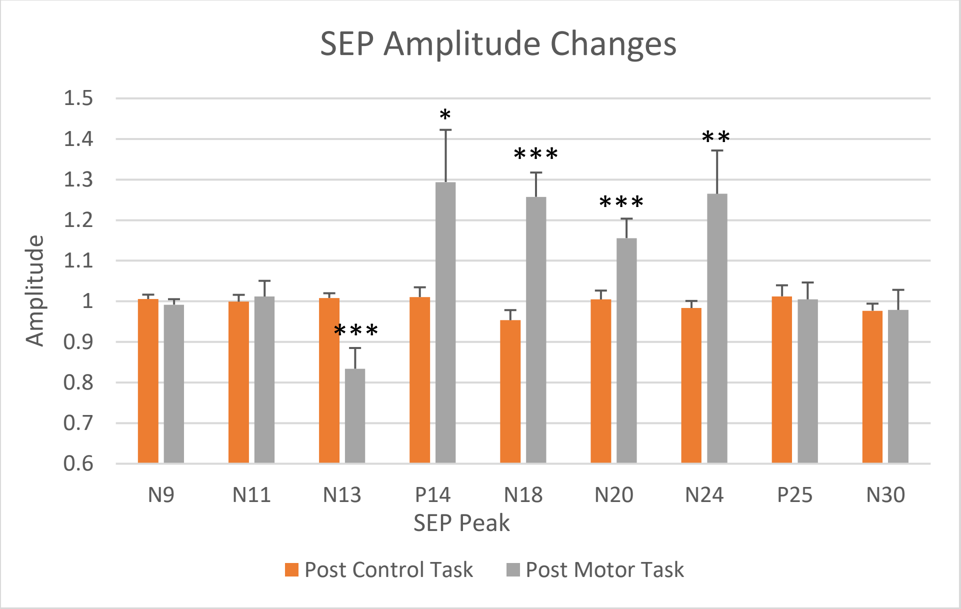

*Figure 4. Normalized mean percent amplitude change following control task and motor training task, +SE. Note the significant change in amplitude for the N13, P14, N18, N20, and N24 peaks. *P<0.05, **P<0.01, ***P<0.001, with respect to baseline. Normalized baseline SEP amplitudes are equal to 1.*

N9 SEP Peak (Erb's point)

The repeated measures ANOVA indicated that there were no significant differences in the N9 SEP peak between baseline, control, and post-intervention amplitudes. This indicates that any succeeding changes in SEP amplitudes resulted from changes in neural processing, rather than altered afferent input.

N13 SEP Peak (C5 spinous process)

The N13 SEP peak showed significant changes following motor training, [F(2,22)=11.66, $p<0.0001$], specifically between baseline and post-intervention SEP measures [F(1,11)=10.56, $p<0.01$]. There was a mean decrease of 16.7% following the motor training task.

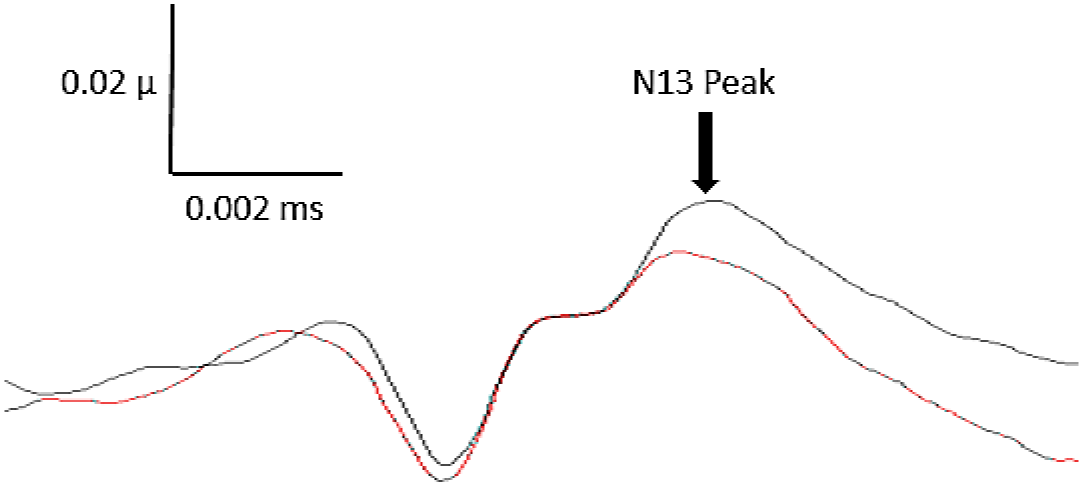

Figure 5. Pre and post tracing intervention SEP peaks for one representative participant. Black trace is the pre-intervention trace, red trace is the post-intervention trace. Note the large decrease in amplitude for the N13 peak.

P14 SEP Peak (Rossi Site)

Significant increases (29.4%) were seen in the P14 SEP peak following motor training [F(2,22)=4.91, $p<0.05$], specifically between baseline and post-intervention [F(1,11)=5.22, $p<0.05$].

N18 SEP Peak (Rossi Site)

Following the motor training session, there were significant increases (25.7%) in the N18 SEP peak, [F(2,22)=19.04, $p<0.0001$], specifically significant between baseline and post-intervention [F(1,11)=18.47, $p=0.001$].

N20 SEP Peak (Cc')

The N20 SEP peak showed significant increases (15.6%) following motor training [F(2,22)=8.89, $p=0.001$], specifically between baseline and post intervention [F(1,11)=10.56, $p<0.01$].

N24 SEP Peak (Rossi Site)

One participant was excluded from analysis of the N24 SEP peak, due to large changes in the N9 amplitude. Following the motor training session, the N24 peak displayed significant mean increases of 26.5% [F(2,20)=6.62, p<0.01], specifically between baseline and post test [F(1,10)=6.14, p<0.05].

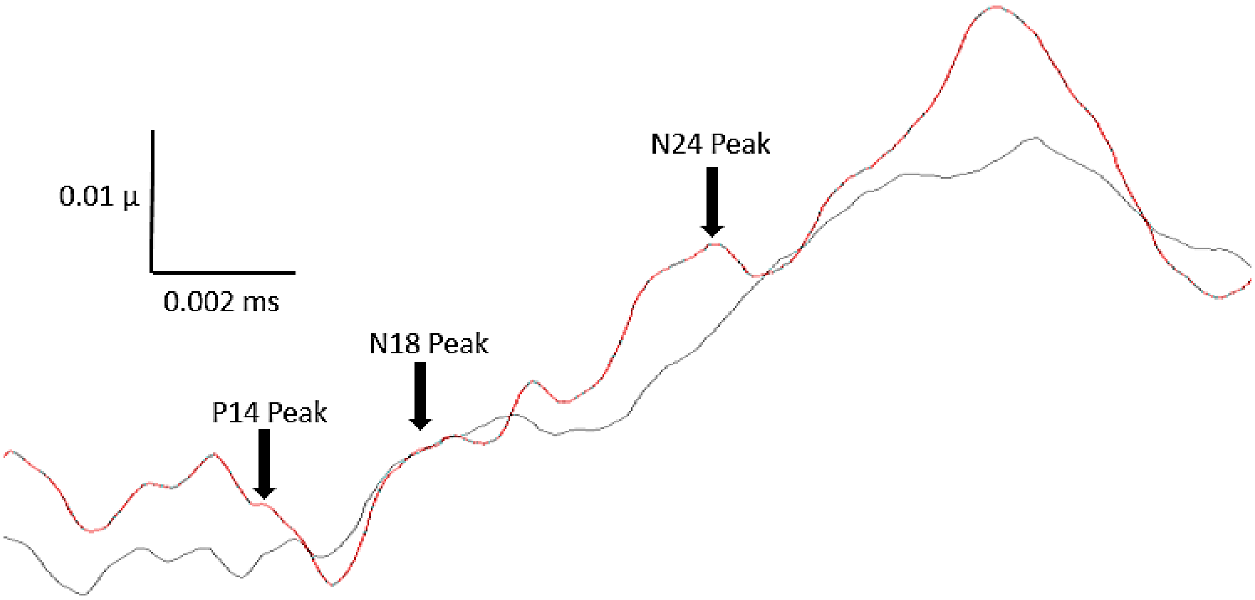

Figure 6. Pre and post tracing intervention SEP peaks for one representative participant. Collected at 2.5Hz. Black trace is the pre-intervention trace, red trace is the post-intervention trace. Note the large increases in amplitude for the P14, N18, and N24 peaks.

Behavioural Data

For the task accuracy behavioural data, significant improvements in performance were seen [F(2,22)=42.15, p<0.0001], specifically from baseline to post-learning [F(1,11)=37.40, p<0.0001], with a normalized mean decrease in error of 36.7%. These improvements in performance were then retained up to 48 hours later, with significant improvements in performance from baseline to retention [F(1,11)=58.68, p<0.0001].

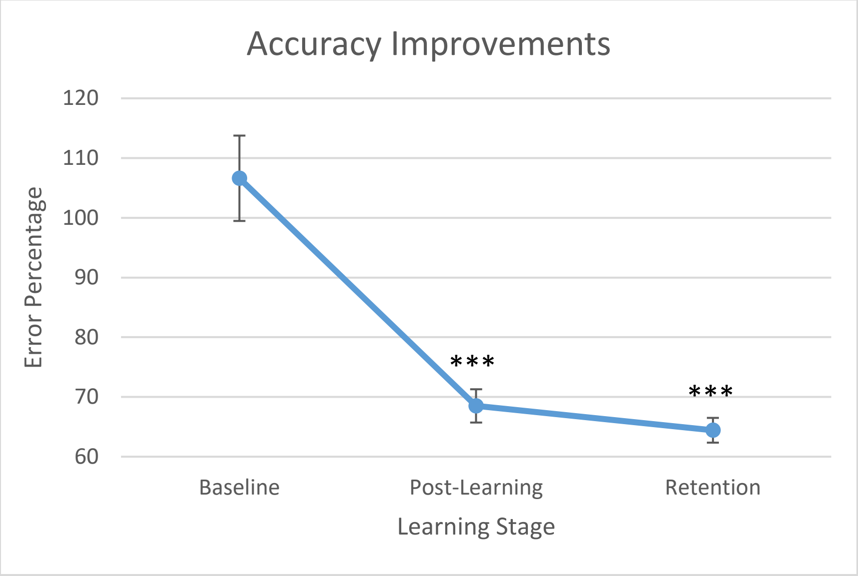

*Figure 7. Improvements in tracing accuracy ± SE. ***=p<0.0001 relative to baseline.*

An interesting point to note, was that although there were low subject numbers within this study, male participants performed better at baseline than their female counterparts, with an average baseline error of 96.3% for males as compared to 119.0% for females, as displayed in Table 1. In addition, relative to baseline, females improved by 37.9% following acquisition, and 44.6% at retention. In contrast, males improved by 30.7% following acquisition, and 35.6% at retention. Based upon the twelve participants within this study, it appears that males performed better at the task at baseline. Large improvements in female performance relative to baseline could reflect a potential power law effect, in that relatively larger performance improvements are seen following worse baseline performance (Newell, & Rosenbloom, 1981).

Table 1. Male and female task accuracy, measured in percentage of error. One dot-width from the target trace was considered 100% error.

Male				Female		
Subject	Baseline	Post-Acquisition	Retention	Baseline	Post-Acquisition	Retention
1	68.8661	58.72983	51.16654	137.8772	81.17576	73.31994
2	110.6765	58.32788	66.6714	104.7306	63.0678	59.78723
3	79.86393	65.30706	57.8178	104.5374	76.47577	59.75464
4	84.14271	79.15275	60.69566	129.0672	71.69248	76.87239
5	141.4211	64.12401	71.40415	138.2799	81.49873	67.54073
6	92.73502	74.87156	64.12928	99.33672	69.1496	58.09508
Average	96.28424	66.75218	61.98081	118.9715	73.84336	65.895

Discussion

Behavioural Measures

A control task was included within this study to ensure that any neurological processing changes resulted directly from the motor learning task. Following the control task, no significant changes were seen in any SEP amplitudes. Following the acquisition and learning phase of the motor learning task, the in-task measures of accuracy revealed that overall, there was a significant 36.7% decrease in error, as displayed in Figure 5 below. In addition, these improvements in task performance were retained between 24 to 48 hours following acquisition.

Male and female participants were counterbalanced in this study based on normative Pegboard data, which suggests sex-based differences in fine motor control (Desrosiers, Hebert, Bravo, & Dutil, 1995). However, additional studies have suggested that these sex-based differences in fine motor control disappear when finger size is used as a covariate (Peters, Servos, & Day, 1990). Future research should look to assess sex-based differences in motor control using a motor learning task where finger size will not affect task performance.

Significant, relatively permanent improvements in task accuracy within this study have successfully demonstrated motor learning within the proximal upper-limb muscles, following a period of motor training. In addition, this work has expanded on previous research that displayed large changes in SEP amplitudes following the same motor learning task, using thenar adduction and abduction (Andrew, Yielder, et al., 2015). While previous studies had used SEPs to show neurological processing changes associated with motor learning in the distal hand muscles, this study was the first of its kind to measure SEPs in conjunction with a proximal upper-limb motor learning task.

However, future studies using this task should look to assess participant perception of task difficulty. Based upon the action-specific perception theory participants will view their environment in relation to their ability to perform within that environment (Witt, 2011). For example, participants who are performing well on the tracing task could perceive the trace to be moving slower, or perceive the amplitude and frequency to be smaller. Based upon this hypothesis, how well the participant performs on the task will impact their perception of task difficulty, which could lead to further errors for participants who display worse baseline task performance, as they become stressed about task performance.

N13 SEP Peak

The spinal N13 SEP peak reflects the activity of interneurons within the midcervical cord and dorsal horn, and is currently thought to reflect changes in sensorimotor integration at the level of the spinal cord (Andrew, Yielder, et al., 2015; Cruccu et al., 2008; Desmedt & Cheron, 1981). Previous motor learning studies have displayed significant increases in the N13 SEP peak following a period of motor learning with the thumb, indicating greater neural processing at the level of the spinal cord, and potentially reflecting the fact that the thenar muscles have their afferent input directly conveyed by the median nerve (Andrew, Yielder, et al., 2015). However, significant decreases in the spinal N13 SEP peak within the present study suggest differing neural activations within the spinal cord for the proximal upper-limb muscles. Decreases to the N13 amplitude for the proximal upper limb muscles could reflect the fact that the sensory feedback from the shoulder muscles is conveyed primarily by the axillary nerve, rather than the median nerve. It could also reflect differences in descending inhibition to the motor neuron pools required to control the shoulder tracing task vs the thumb tracing task. In the thumb task, the thumb is the prime mover whereas in the shoulder tracing task, the thumb has to be held rigid as the shoulder internal and external rotator muscles become the prime movers.

P14 SEP Peak

The P14 SEP peak is generated at or above the level of the foramen magnum, but below the cortex (Cruccu et al., 2008; Desmedt & Cheron, 1981) and is thought to be generated by the arrival of the afferent volley at the medial lemniscus, and the nucleus cuneatus within the medulla oblongata (Desmedt & Cheron, 1981; Tinazzi et al., 2000). The increase in the P14 in this study compared to the absence of changes when completing motor learning tasks with the thumb or first finger could be due to higher levels of proprioceptive input processed during the proximal upper-limb task, which required multi-joint control of the entire upper limb, rather than just the thumb muscle.

N18 SEP Peak

Previous work has demonstrated large decreases in the N18 peak following a simple repetitive motor learning task (Andrew, Haavik, et al., 2015; Haavik & Murphy, 2013). Several studies have suggested that the N18 peak reflects inhibitory activity at the level of the medulla and dorsal column nuclei, potentially displaying a level of afferent processing within the brainstem (Haavik & Murphy, 2013; Noël et al., 1996; Rossi et al., 2003). Therefore, a decrease in the amplitude of the N18 peak following motor learning may suggest a reduction in inhibitory activity, potentially at the level of the cuneate nucleus or the inferior olives (Desmedt & Cheron, 1981; Noël et al., 1996; Sonoo, 2000; Sonoo, Sakuta, Shimpo, Genba, & Mannen, 1991). However, the present study using the proximal upper-limb muscles displayed large increases in the N18 peak following motor learning. This could reflect the increased inhibition needed to control the thenar and rotator cuff muscles during whole-arm motor learning tasks.

N20 SEP Peak

This increased need for processing of incoming stimuli is further demonstrated through large increases in the amplitude of the N20 peak. Representing the early cortical processing activity of Brodmann's area 3b, within the primary somatosensory cortex, the N20 peak displays the role of the somatosensory cortex in motor learning (Desmedt & Cheron, 1980, 1981; Desmedt & Ozaki, 1991; Noël et al., 1996). Large increases in the amplitude of the N20 peak following motor training with the proximal upper limb indicate an increased activation of the somatosensory cortex following motor learning, in accordance with previous research (Andrew, Yielder, et al., 2015; Haavik & Murphy, 2013).

N24 SEP Peak

Previous research using patients with unilateral cerebellar lesions has displayed alterations to the amplitude of the N24 peak, suggesting that the N24 peak represents activity within a neuronal pathway linking the cerebellum and the primary somatosensory cortex (Cruccu et al., 2008; Restuccia et al., 2006; Restuccia et al., 2001; Rossi et al., 2003; Rossini et al., 1981). The large increases in the N24 peak seen with the proximal upper limb further supports previous research suggesting the role of the cerebellum in early motor learning (Akshoomoff & Courchesne, 1992; Haavik & Murphy, 2013; Ito, 2000). The increase in the N24 could also indicate an increase in cerebellar inhibition to the thenar muscles, due to the fact that the shoulder muscles were the prime mover for this complex motor learning task, requiring multi-joint control of the upper limb.

N30 SEP Peak

These differences in sensorimotor integration between distal and proximal muscles are further demonstrated through a lack of changes in the N30 SEP peak for the shoulder tracing task. The N30 peak is a complex loop with multiple neural generators, linking the premotor and motor areas, the thalamus, and the basal ganglia, which reflects changes in sensorimotor integration within the cortex (Cebolla & Cheron, 2015; Lelic et al., 2016; Rossini et al., 1981; Tinazzi et al., 2000). Previous research has shown changes in the N30 SEP peak following complex motor learning tasks performed with the thumb muscle (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Dancey et al., 2014). The lack of change for the proximal shoulder muscles may reflect that processing was not significantly altered in muscles that were not the prime mover for the task. Interestingly, previous work found increased N30 amplitudes in the median nerve

N30 when the radial nerve was transiently deafferented with anesthetic block. The authors suggested that this was due to unmasking of latent cortico-cortical and/or thalamo-cortical connections. In the current study, the proximal shoulder muscles involved in the task used primarily internal and external shoulder rotation, innervated from the C5-6 spinal level through the axillary nerve (deltoid and teres minor), suprascapular nerve (infraspinatus) and lower subscapular (teres minor). As a complex sensorimotor integration peak with more than one neural generator, there may have been increased processing in some neural generators with decreased processing in others, which our single site N30 recording was unable to capture. Future work using whole head EEG and source localization software would be able to tease this apart.

Strengths

There are currently no proximal upper-limb motor learning tasks that have been shown to induce changes in SEP peaks. This study was the first of its kind to pilot a whole-arm motor learning task that lead to changes in SEP peak amplitudes.

Limitations

While the use of partial EEG has proved sufficient for recording SEP changes in small hand muscles, the results of this study indicate the need for whole head EEG recordings to assess whole-arm tasks. Certain SEP peaks, such as the frontal N30 peak have multiple neural generators. Using a larger number of electrodes would allow for the source localization of these peaks, allowing for a greater discrimination of discrete neural activations.

In addition, this study collected data for the N18 peak from the frontal contralateral site (Rossi site), as previously done by a number of papers (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Cruccu et al., 2008; Haavik-Taylor & Murphy, 2007; Haavik & Murphy, 2013; Lelic et al., 2016). However, additional studies have shown that recording the N18 peak from an ipsilateral electrode results in decreased contamination of the N18 peak by the succeeding N20 and N24 peaks (Sonoo, Genba-Shimizu, Mannen, & Shimizu, 1997; Sonoo et al., 1991). Future research should consider collection of the N18 peak from an ipsilateral electrode to ensure greater reliability.

While this study occluded the participant's view of their hand to assess movement-based motor learning and to control for the effects of movement observation, future research should assess task performance with the hand in full view, to further study the generalizability of the task to workplace settings.

Lastly, future research would benefit from an additional later retention date, to assess the permanence of any neurological changes or performance improvements. In this study, retention was assessed a minimum of 24 hours and a maximum of 48 hours following acquisition, dependent upon participant availability. The use of a 24-48 hour retention period was selected based upon previous research that indicates that 24 hours is a sufficient period of consolidation to allow for the investigation of short-term retention effects of motor learning paradigms (Brashers-Krug, Shadmehr, & Bizzi, 1996; Joiner & Smith, 2008). An additional later retention date would further support these results that indicate that a single session of motor training is sufficient to induce relatively permanent motor learning.

Conclusion

In conclusion, the results of this study indicate that short latency median nerve SEPs have the capability to reflect changes in cortical and subcortical activity levels in response to novel motor skill acquisition using the proximal upper-limb muscles. This suggests that SEPs can be used as a neural marker of changes in sensorimotor integration following motor acquisition and learning with the entire upper limb.

In contrast to previous studies completed using the thumb as the prime mover, this study displayed opposing direction of amplitude changes in both the N13 and N24 peaks (Andrew, Yielder & Murphy, 2015; Andrew et al., 2014). Significant decreases in the spinal N13 SEP peak within the present study suggest differing neural activations within the spinal cord for the proximal upper-limb muscles. In addition, large increases in the N24 peak seen with the proximal upper-limb further supports previous research suggesting the role of the cerebellum in early motor learning, potentially indicating in increase in cerebellar inhibition during motor learning with the proximal upper-limb. (Akshoomoff & Courchesne, 1992; Haavik & Murphy, 2013; Ito, 2000).

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Study 1 Conclusions and Study 2 Rationale

The results of study 1 within this thesis indicate the need for a direct comparison of task-based performance between the proximal and distal upper limb muscles. Preliminary accuracy data collected within study 1 indicates a significant decrease in error on the proximal upper limb task, compared to previous studies using the distal tracing task (Andrew, Haavik, et al., 2015; Dancey et al., 2014). In addition, the results of study 1 indicate a potential sex-based difference in task performance, with males outperforming females on the proximal tracing task.

The second study within this thesis will attempt to investigate the differences in task performance between the proximal and distal upper limb muscles, and any potential sex-based performance differences within each of the motor learning tasks.

Chapter Three: Manuscript 2 – Differences in motor task performance between the proximal and distal upper limb muscles

Abstract

Study 1 within this thesis demonstrated large improvements in task accuracy following a single motor training session with the proximal upper limb. However, when compared to previous studies utilizing the same motor learning task with the thumb, the proximal tracing group appeared to display significantly better performance. In addition, preliminary research using the proximal upper limb revealed sex-based differences in task performance, with males outperforming females on the proximal tracing task. The first aim within this study was to assess potential differences in task performance between the proximal and distal upper limb. The second aim of this study was to assess any sex-based differences in motor performance on both the distal and proximal tracing tasks. 44 right handed participants were recruited from the University of Ontario Institute of Technology. 24 participants completed a novel motor training task using their shoulder as the prime mover, and the remaining 20 participants completed the same task using their thumb. Significant differences in baseline accuracy (204.9% error ± 50.5% SD vs 98.9% error ± 22.1% SD ($p<0.0001$)) and rates of learning were seen between the proximal and distal tasks. No significant sex-based performance differences were seen within the distal tracing group. However, males performed significantly better vs females at baseline on the proximal task, indicating a potential male advantage to gross motor tasks.

Key words: upper limb, motor learning, task accuracy, motor performance

Introduction

Within the field of motor learning, the majority of studies completed by our research group have focused primarily on fine motor skills, using the distal hand muscles (Andrew, Haavik, et al., 2015; Andrew, Yielder, et al., 2015; Dancey et al., 2014; Haavik & Murphy, 2013; Holland et al., 2015). Recent research (Study 1 of this thesis) has displayed large improvements in task accuracy on a novel motor training task performed using the glenohumeral joint. Interestingly, both skill acquisition and retention appeared to be greater than improvements reported in previous studies using the same motor learning task with the distal upper limb muscles (Andrew, Haavik, et al., 2015; Dancey et al., 2014). Thus, the first hypothesis of this study was to determine if the proximal muscles are indeed better at learning this novel motor task.

In addition to hypothesized differences between the proximal and distal upper limb muscles, previous research in the field of motor development and motor control has shown large sex-based differences in task performance. These differences are present in a range of tasks, such as neurocognitive testing batteries, mental rotation of 2D and 3D objects, and general motor skill development within adolescence (Gur et al., 2012; Thomas & French, 1985).

During early stages of motor development, parents and teachers tend to encourage gross motor skill development in boys, such as through sport participation and rougher play, while emphasizing fine motor skills for girls, which often leads to males outperforming females on gross motor tasks In addition, publishing separate normative data for boys and girls in elementary school may lead to different perceptions of ability from teachers and coaches, which acts to further reinforce differences in expectations and leading people to believe that these performance differences are naturally evolving biological factors (Akbari et al., 2009; Barnett, Morgan, van Beurden, & Beard, 2008; Goodway, Robinson, & Crowe, 2010; Thomas & French, 1985; Williams et al., 2008).

Before puberty, the ratio of muscle to fat is similar for males and females. However, following puberty in males, increased levels of testosterone lead to an increase in muscle growth and a decrease in body fat, which gives them an innate advantage in tasks requiring size or power. Previous studies using neurocognitive testing batteries have shown large sex-based differences, with females outperforming males on attention, word and face memory, reasoning speed and all social cognition tests, and males outperforming females in spatial processing, and sensorimotor and motor speed (Gur et al., 2012).

These environmental and biological factors appear to provide males with an advantage during gross motor skill tasks, due to increased practice opportunities during childhood, leading to more refined motor control of the upper limb, and increased muscle mass. These results suggest that males are likely to outperform females on the proximal motor learning task, due to increased spatial processing, and sensorimotor speed, and an increased control over the proximal upper limb muscles. In contrast, females tend to perform better on fine motor tasks. Normative Purdue Pegboard data indicates that females will out-perform males on fine-motor manual dexterity tasks (Desrosiers et al., 1995; Gardner & Broman, 1979; Hamm & Curtis, 1980; Ruff & Parker, 1993). However, when thumb and finger size is used as a covariate, all sex-based performance differences disappear, as there is a negative correlation between finger size and performance (Peters et al., 1990).

Male and female motor task performance should be assessed with a task in which finger size is not correlated with task performance. In addition, performance should be assessed using both the proximal and distal upper limb muscles, to allow for an investigation into the differences in task performance between the proximal and distal upper limb muscles. Thus, the second aim of this study was to assess sex-based differences in both fine motor and gross motor skills, using a pursuit-based motor training task.

The first hypothesis for this study, is that all participants will perform better at the proximal muscle tracing task, compared to the distal tracing task. The second hypothesis for this study is that due to more refined control of the proximal upper limb muscles, males will outperform females on the proximal task.

Methods

Participants

44 right-handed participants (22 males and 22 females) were recruited from the University of Ontario Institute of Technology. Handedness was assessed using the Edinburgh Handedness Inventory to eliminate any left-handed or ambidextrous participants, due to hypothesized differences in control strategies between the limbs (Caplan & Mendoza, 2011; Mutha et al., 2013). Each participant consented to participate in two data collection sessions: one motor training session and one retention session, the latter of which was completed a minimum of 24 hours and no later than 48 hours after training. University aged participants (average age 21.38 ±3.44 years) were used to eliminate any age-related changes in motor control (Voelcker-Rehage, 2008).

Participants were divided into two groups, with equal numbers of males and females in each group. One group completed the motor learning task using their right thumb (using their abductor pollicis brevis muscle) and the second group completed the task using their right thumb, but with the thumb held rigid and the shoulder rotator muscles used to move their hand, as displayed in Fig. 1 below. Separate groups were used to prevent possible transfer of the task ability between the two conditions. Data for the distal tracing (thumb) group was adapted from previous research (Andrew, Yielder, et al., 2015).

This study received ethical approval from the UOIT ethics committee (REB# 07-072 & 07-073). Each participant completed an informed consent form prior to participation in the study, outlining the potential risks and benefits to the study, explaining the procedures to be undertaken, and including a pre-screening questionnaire to eliminate any of the exclusionary criteria.

Motor learning task intervention

Motor learning task development

The motor learning task was developed using Unity ™ (Personal Edition) game development software.

Motor learning task design

The motor learning task was adapted from previous work (Andrew, Yielder, et al., 2015; Dancey et al., 2014; Holland et al., 2015). The task itself consists of a vertically scrolling sine wave, composed of 500 coloured dots. The participant is instructed to trace the sine wave, with their movements limited to a horizontal axis. The sinusoidal wave included four patterns of varying amplitude and frequency, which were randomized to increase task difficulty, with the "easiest" of the 4 patterns able to be completed by all participants and the most difficult pattern sufficiently challenging to enable continued improvement (Andrew, Yielder, et al., 2015; Dancey et al., 2014; Holland et al., 2015). For the baseline task performance, participants completed each of the four patterns once, for a total of four traces. For the learning and acquisition phase, each pattern was completed three times, for a total of twelve trials. For the final post-acquisition phase, each pattern was completed once. An additional four traces were completed 24-48 hours following the training session to assess task retention. Accuracy was measured in terms of error percentage. One dot-width away from the target trace was considered 100% error, while two dot-widths from the trace was 200% error. Accuracy was measured at baseline and post-acquisition, through averaging the dot by dot error percentage on each of the four trials within that section.

Data collection

Throughout each collection session, participants were seated upright in a comfortable, straight-backed chair. The motor training task was displayed on a laptop placed on a table directly in front of the participant, approximately 24 inches forward from their centre of mass, to replicate an average workspace. For the distal tracing group, the trace was completed on a 4 inch Lenovo trackpad placed on the table. Participants within the distal tracing group were instructed to complete the task using their right thumb, limiting their movements to adduction and abduction of the thumb. For the proximal tracing group, a 23 inch touchscreen (Acer T232HL, Acer Inc.) was placed on a desk directly below the table, as displayed in Figure 6. The table acted to block the participant's view of their own arm, while allowing the participant to complete the motor training task on the touchscreen. Each participant was instructed to watch the motor training task on the laptop, while completing the task using the touchscreen. Participants in the proximal tracing group were instructed to complete the task using their right thumb, using glenohumeral rotation to move their hand across the screen. They were instructed to hold their elbow, wrist, and hand rigid throughout the entire task. The task was completed with an angle of approximately 45 degrees at the shoulder, and 135 degrees at the elbow, as displayed in Figure 6 below.

Figure 6. Proximal tracing data collection setup. A laptop is placed on the table displaying the motor training task. Large touchscreen is placed on desk directly below the table ensuring that the table blocks the participants view of their own arm. For the thumb tracing group, setup was the same, however the trace was completed on a small 4-inch trackpad.

Data analysis

Task accuracy was measured in terms of error percentage. One dot-width away from the target trace was considered 100% error, while two dot-widths from the trace was considered 200% error. Baseline task accuracy was measured by averaging the total error percentage for the four pre-test trials, while post-test accuracy was measured by averaging the four trials following the learning and acquisition phase of the task. Finally, retention was measured as the average error percentage for the four retention trials.

Data was not normalized to baseline, as the normalization process would remove possible differences at baseline between the two tasks, which was one of the goals of the study. A two group ANOVA was run through SPSS (IBM software) to assess baseline differences in task accuracy between the proximal and distal tracing tasks. A repeated measures ANOVA was run for the entire data set with body part used as a factor, to assess differences in learning progression between the distal and proximal upper limb. Separate repeated measures ANOVAs were then run for the proximal and distal tasks to determine the impact of biological sex on the outcome measures. Statistical significance was set at $p<.05$.

Results

All 44 participants were included in the final data analysis. At baseline, there was a significant difference between the overall thumb (204.9% ± 50.5% SD) and shoulder (98.9% ± 22.1% SD) accuracy (F[1,42]=86.24, $p<0.0001$), with participants performing significantly better on the shoulder task at baseline. Both groups improved significantly from baseline (F[2,39]=76.95, $p<0.0001$). In addition, there was a significant interactive effect of accuracy by group (shoulder vs thumb), with the shoulder group significantly outperforming the thumb group at every stage of task performance (F[2,39]=11.58, $p<0.0001$).

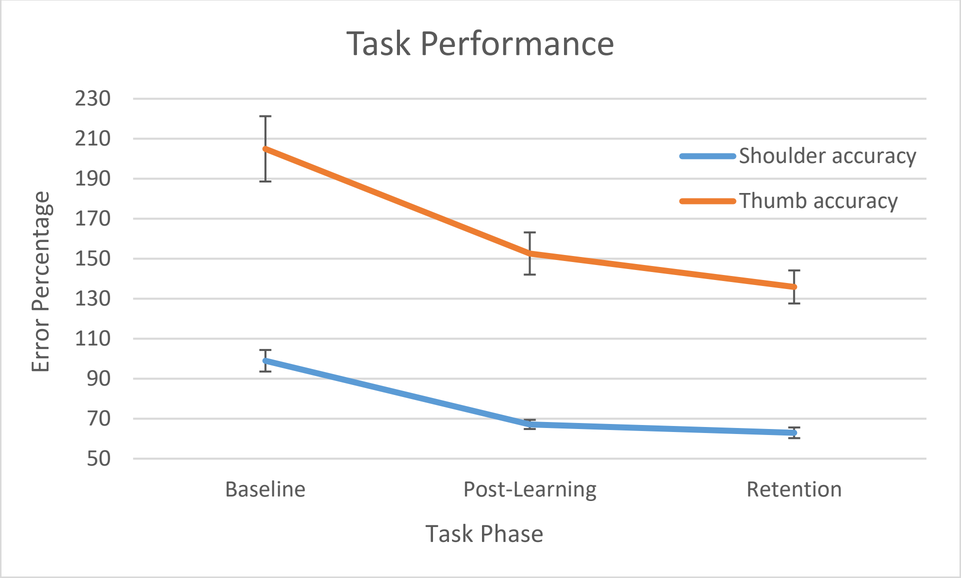

Figure 7. Task accuracy of both the proximal and distal motor task groups.

Distal Tracing

At baseline of the distal tracing task, there was no statistical difference between male and female performance (205.6% ± 56.8% SD vs 204.3% ± 46.5% SD error). Relative to baseline, males improved by 24.4% ± 34.9% SD following acquisition, and 33.4% ± 24.2% SD at retention, vs females who improved by 26.7% ± 31.8% SD following acquisition and 34.0% ± 25.1% SD at retention. Both males and females improved significantly post-acquisition (F[1,18]= 38.97, p<0.0001) and retained these changes up to 48 hours later. However, there were no significant interactive effects of sex on accuracy within the distal tracing group.

Proximal Tracing

Both males and females improved significantly relative to baseline both following acquisition (F[1,20]=64.96, p<0.0001), and at retention (F[1,20]=121.18, p<0.0001). During the proximal tracing task, males performed significantly better than females at baseline, with 87.1% error ± 21.5% SD vs 110.8% error ± 15.9% SD for females (F[1,22]=9.39, p<0.01). Both groups improved significantly relative to baseline (F[2,19]=60.98, p<0.0001), with males improving by 27.7% and females improving by 36.7% on average. Following acquisition, sex-based differences in accuracy were approaching significance (p=0.068), with males displaying 63.0% ± 9.2% SD error vs 71.2% ± 6.7% SD error. At retention, males performed significantly better than females on the proximal tracing task (F[1,20]=6.47, p<0.05), with 59.1% ± 7.4 % SD error vs 69.7% ± 10.2% SD error.

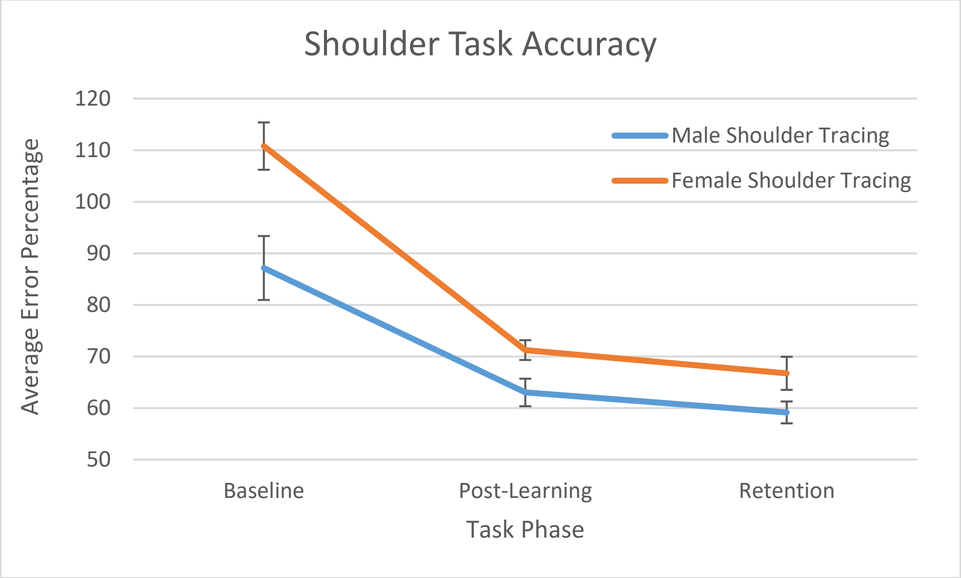

Figure 8. Male and female task accuracy within the proximal motor task.

Discussion

Large improvements in task accuracy that were retained up to 48 hours later were seen in both the distal and proximal tracing tasks, indicating that motor learning had occurred. There was a significant interaction effect present between accuracy and body part used. The proximal tracing group was more accurate than the thumb tracing group at every stage of learning. The first study within this thesis revealed large increases in cerebellar inhibition following motor learning with the proximal upper limb muscles, potentially reflecting the fact that the proximal task requires increased control of the entire upper limb. Since the proximal task requires multi joint control of the entire upper limb, proprioceptive feedback will be received from the thumb, wrist, elbow and shoulder, compared to feedback solely from the thumb in the distal task. This increase in sensory feedback could allow for a higher degree of error correction, due to an increased need for cerebellar inhibition, resulting in overall improvements in task performance. In contrast, previous research has displayed large decreases in cerebellar activity following the same motor learning task with the thumb (Andrew, Yielder, et al., 2015). The authors indicated that with slow learning patterns, the need for cerebellar input decreases (Andrew, Yielder, et al., 2015). However, this decreased cerebellar input, while allowing for learning to occur, could potentially account for the higher levels of error seen within the distal tracing task.

Future research should look to assess the potential transfer of the task between the proximal and distal upper limb muscles. Separate groups were utilized within this study to prevent potential transfer of the task skills, however the transfer of task-based skills between the proximal and distal upper limb could provide an interesting method of motor learning within a rehabilitation setting. While populations with decreased fine motor control may be unable to complete the distal motor task, they could still benefit from the motor learning aspects of the proximal task.

In accordance with previous research, it appears that males and females are equal in performance on the distal tracing task, when a task is used where finger size does not correlate with task performance (Peters et al., 1990). However, the baseline results of the proximal tracing group within this study indicate that males may have an advantage at novel motor training tasks performed using the shoulder, as they performed significantly better than females on the proximal tracing task. This male advantage may be due in part to use-dependent plasticity, as males are more likely to participate in sports, due to increased social pressures (Barnett et al., 2008; Goodway et al., 2010). Throughout childhood and adolescence, males are encouraged to develop their gross motor skills, through sport participation and rough play. Increased opportunities to practice their gross motor skills will encourage structural and functional neuroplastic changes associated with these motions. This use-dependent neuroplasticity could result in improved motor control of the proximal upper limb muscles, leading to improved task performance. An interesting point to address within future research would be the inclusion of highly athletic females, to assess whether the level of sport participation can account for sex-based differences within the proximal upper limb task. Within the present study, sport participation was not screened or balanced for, which could potentially explain some of the male and female performance differences.

Strengths

This study aimed to determine if there are differences in upper limb motor performance between the distal and proximal upper limb muscles, through utilizing the same motor learning task in separate experiments with both the thumb and the shoulder acting as the prime movers. This study was the first of its kind to use the selected motor learning task for comparison of accuracy measures between the shoulder and thumb. In addition, this study used a task in which finger size was not correlated with task performance, which has previously impacted the results of common motor tasks, such as the Purdue Pegboard (Peters et al., 1990), and revealed sex differences in the performance of the shoulder tracing task.

Limitations

Future research should look to assess female task performance in the context of different phases of their menstrual cycle. Previous research has shown improvements in coordination and fine motor skills during the midluteal phase, as compared to the menstrual phase (Hampson & Kimura, 1988) thus female task performance should be interpreted with caution, as the authors of this study did not assess any cycle-based differences in performance.

An additional limitation to this study was the use of a small trackpad for the distal tracing group, and a larger touchscreen for the proximal muscle group. This method was selected to allow for an increase in the scale of the task for use with the shoulder, however future research should look to assess differences between the proximal and distal upper limb muscles using an identical task.

A related limitation to this study, is that the thumb has a narrower anatomical range of motion than the shoulder. This could have caused a greater number of errors within the distal tracing group, as the participants might have reached an anatomical end-range as the traces increased in amplitude. Future studies comparing motor performance between the thumb and shoulder could look to assess anatomical end-ranges at baseline to screen for potentially limited ranges of motion.

Conclusion

In conclusion, the results of this study indicate that the distal tracing task appears to provide a measure of fine motor coordination which is not confounded by the effect of finger size on task performance. In addition, significant improvements in task accuracy following a single training session with the shoulder indicates that the task is capable of assessing motor learning with the proximal upper limb muscles.

The results of this study support both our first and second hypotheses; Firstly, that participants were significantly more accurate on the proximal motor task than the distal task, and secondly, that males significantly outperformed females on the proximal motor task.

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Thesis Summary

Previous motor learning research within our research group has focused primarily on the distal upper limb muscles. However, within modern occupational settings, up to 56% of the working population report shoulder disorders, including tendonitis, rotator cuff impingements, and frozen shoulder syndrome. No studies to date have utilized a motor learning task in conjunction with somatosensory evoked potentials (SEPs) to assess the neuroplasticity of the proximal upper limb muscles. Study 1 within this thesis demonstrated the ability of SEPs to assess the neuroplasticity of the proximal upper limb following a motor learning task. Significant improvements in task accuracy were seen following a single training session with the proximal upper limb, in conjunction with large changes in SEP amplitudes. This suggests that short latency SEPs can be used as a neural marker of changes in sensorimotor integration following motor acquisition and learning with the entire upper limb.

Study 2 built upon the first study within this thesis, to assess potential differences in task performance between the proximal and distal upper limb. In addition, study 2 aimed to assess any sex-based differences in motor performance on both the proximal and distal motor training task. Within this study, significant differences in task accuracy were seen between the distal and upper limb groups, with the proximal upper limb displaying higher levels of task accuracy at every stage of learning. In addition, males significantly outperformed females at baseline on the proximal upper limb task, indicating a potential male advantage to novel gross motor tasks.

The studies within this thesis aimed to develop and pilot the use of a motor learning task for use with the proximal upper limb. Future research should look to utilize the proximal motor learning task in populations with work-related injuries, to assess the potential neuroplastic changes associated with these conditions. A deeper understanding of the neural changes associated with common workplace injuries could allow for improved diagnosis, treatment, and rehabilitation. In addition, the proximal task will provide a measure of an individual’s capability to learn or perform novel tasks while injured, potentially allowing for an on-site assessment of functional capability.

Appendices

Appendix 1: Participant Recruitment and Extra Credit Invitation Form

Greetings,
We would like to inform you of an opportunity to gain extra credit in this course (either HLSC 1812-U Socio-Cultural perspective on health for 1st year Kinesiology students, HLSC 3481U Exercise Physiology for 2nd year kinesiology students, HLSC 3410U Human Motor Control & Learning for 3rd year kinesiology students, or HLSC 4472 Clinical Biomechanics and Ergo for 4th year kinesiology students). Participation is totally voluntary and will have no negative consequences for how you are evaluated in your course with respect to the criteria listed on the course outline.

You have the option of **earning up to 2% extra credit** by participating in research studies related to kinesiology. You get **1% extra credit** for each type of experiment you participate in up to a maximum of **2% per eligible course.** If you are enrolled in more than one eligible course you can earn extra credit for both, BUT it must be for different experiments.
In order to be fair to participants who volunteer but are unable to participate for reasons beyond their control (i.e. failure to meet inclusion criteria or experimental slots already filled) an alternative option will be made available which is that you will be allowed to complete up to two short essays worth 1% each. Each assignment will take a similar amount of time to prepare as the research experiment participation (e.g. 2 hours per essay). For those offered this option you will prepare the assignment(s) in your own time and it is due by the last day of classes in the winter semester (e.g. April 8, 2017).
If you are interested in this opportunity, please email: Sinead O'brien sinead.obrien@uoit.net and Ryan Gilley (ryan.gilley@uoit.net) with the subject header "**Extra credit research participation**" by **Wednesday, March 9, 2017**. Ryan or Sinead will determine if there are available time slots and if not, they will e-mail you the alternative assignment.
The assignment will be submitted via email to Sinead O'Brien sinead.obrien@uoit.net or to Ryan Gilley ryan.gilley@uoit.net Your course instructors will not know if you have participated until after the final exam has been marked. At this time, the research students involved will send your instructors a list of students who have earned either a 1% of 2% extra credit grade. In order for the essay to "count" it must be capable of achieving a passing grade. According to the UOIT calendar, a passing grade reflects basic skill and ability to use analytical or critical thinking to solve basic problems; basic understanding of the subject matter; adequate communication of the concepts discussed and acceptable use of references.
If you would like to know whether you have adequately the inclusion criteria to participate, you may contact Ryan or Sinead.
Who can participate? Males and Females aged **18 and 40.**

We need: Healthy right-handed participants with no current neck pain flareups, or neurological conditions (to act as a comparison group). The benefit of participating is that you will **learn more about how the brain activates muscles**.

Experiments we are recruiting for:

1) Somatosensory evoked potentials (SEPs): As part of this research we will collect some information about the electrical signals from your neck and arm muscles or from the parts of your brain that control these muscles. To do this we will use a special stimulator over a nerve at your wrist and measure the way that your brain responds to this stimulation and how this changes when you perform motor training with your hand or arm. Each experiment takes about three hours.
Types of participates needed: Healthy Controls
Number of sessions: One

2) Effect of Cutaneous pain on response to motor training: This investigates how cutaneous pain, created by capsaicin cream (e.g. the ingredient in chili peppers) affects the way your brain responds to motor training. We will collect some information about the electrical signals from your neck and arm muscles or from the parts of your brain that control these muscles. To do this we will use a special stimulator over a nerve at your wrist and measure the way that your brain responds to this stimulation and how this changes when you perform motor training with your hand or arm. Each experiment takes about three hours.
Types of participates needed: Healthy Controls
Number of sessions: One

3) **Effect of altered neck input on shoulder proprioception**: this investigate how neck extensor muscle fatigue will alter the accuracy of the shoulder joint position sense. Participants perform repositioning tasks of a previously presented shoulder angle during non-fatigued and following fatigue conditions. An active shoulder range of motion (ROM) is determined for the shoulder internal-external rotation and flexion- extension. To do this experiment we will measure EMG activity of some muscles and the 3D investigator motion capture system will record upper body joint position. This experiment will take about 2.5 hours.
Types of participates needed: Healthy Controls
Number of sessions: One

If you are interested in this opportunity or have questions about it, please email Sinead O'brien sinead.obrien@uoit.net or Ryan Gilley (ryan.gilley@uoit.net) with the subject header **"Extra credit research participation" by Wednesday, March 9, 2017.** Ryan or Sinead will determine if there are available time slots and if not, they will e-mail you the alternative assignment.

Appendix 2: Informed Consent form

Professor Bernadette Murphy
University of Ontario Institute of Technology
Faculty of Health Sciences
2000 Simcoe St. North
Oshawa, Ontario
CANADA L0B 1J0
Email: Bernadette.Murphy@uoit.ca
Phone: (905) 721-8668 Fax: (905) 721-3179

Title: ***Validating a motor learning task using Somatosensory Evoked Potentials (SEPs) – January 2017.* This study has received ethical approval from the UOIT ethics committee (REB# 07-072 & 07-073)**

This study is being conducted by Dr. Bernadette Murphy and Dr. Paul Yielder, in conjunction with MHSc candidate Sinead O'Brien and fourth year practicum research students from the Faculty of Health Sciences at the University of Ontario Institute of Technology (UOIT), in Oshawa, Ontario, Canada.

Rationale for Research: Research has found that neck pain is a significant burden and affects 30 to 50% of people every year. Research is also showing that neck pain affects the way that people move and their awareness of head and upper arm positioning.

The research we are doing is showing how the brain responds to neck pain. We want to show how neck pain affects movement, as well as the ability to properly respond to outside sources of stimuli.

The other reason we are completing this research is because chronic conditions have become increasingly a problem. Our hope is that this research will show responses of healthy participants. This will provide important clues to how the brain functions normally which is important to know how the brain may be re-wired because of neck pain. This will help us to know why neck pain is a chronic problem and how interventions may work to prevent or reverse the cycle of chronic pain for normal function and improved health outcomes.

Information for participants: To complete this research, we will perform a dominant-hand coordination test, involving placing as many pegs as possible in a pegboard in 30 seconds. We will then perform Pre-Test SEPs measurement on each subject. Each subject will then be asked to mentally recite numbers displayed on a laptop screen, followed by a secondary SEPS measurement. Each participant will then be asked to trace a scrolling sine wave with their dominant hand, followed by a final Post-Test SEPs measurement.

We are seeking people with no known neurological conditions who are between 18 and 50 years of age. To participate in this study you must complete an eligibility checklist in conjunction with one of the researchers to ensure you are eligible to participate. You will also be given a chance to review the details of the study and ask any questions you may have.

Each evaluation session will take approximately 2-3 hours and you will be given a chance to ask questions. We will provide you with a bonus 1% in one of your classes, selected from a pre-determined list of classes.

Your participation in this study is entirely voluntary (your choice), and you are free to decline taking part in this study. You may also withdraw from the study at any time without giving a reason. This will in no way affect your academic progress. Questions about your rights as a volunteer can be made to the Compliance Officer at 905 721 8668 ext. 3693 or compliance@uoit.ca .

Measurement sessions: Should you agree to participate, we will need you to attend one measurement session, which will last 2-3 hours. In addition, each participant will need to complete a retention session within 24-48 hours, which will take approximately 15 minutes.

Measurement procedures:

At the beginning of each measurement session, we will ask you to perform a simple coordination test, involving placing as many pegs as possible on a pegboard with your dominant hand.

During each evaluation session we will collect some information about how your brain processes electrical signals from your hand and arm muscles. To do this it will be necessary to place some electrodes on your skin over your nerves at the wrist or elbow, and over your neck, shoulder and scalp. You may experience some mild discomfort as your skin is prepared for the electrodes by gently shaving and then wiping the area with alcohol. The electrodes over your neck, shoulder and scalp are only recording electrodes and do not pierce the skin and do not run current through your body. Only the electrodes on your arm will be stimulating electrodes. These stimulating electrodes will be used to stimulate some of your hand and/or forearm muscles by passing mild electrical current through them. This creates a mild tingling sensation on the skin over the nerve. This is not painful but may feel quite strange to you. It will also make some of your hand and/or forearm muscles twitch which is not painful either, but can also feel strange.

We will also ask you to complete a task that involves tracing or replicating an image displayed on a computer screen. We will ask that you complete this activity as accurately and quickly as possible, and once you are finished, if you would like we can give you a progress report on your performance.

Risks and benefits

The benefits of participating in this study is that you will learn more about research techniques at UOIT and the somatosensory systems in the CNS.

The surface EMG techniques have low risks such as the person getting a skin irritation from the alcohol swab or electrode gel. These are uncommon and not serious. You may also experience mild discomfort as your skin is prepared for the electrodes by shaving the skin with a razor, or lightly abrading with special tape, and then wiping the area with alcohol. If irritation persists, we recommend that students go to campus health services (and contact the researcher). The electrical stimulation is not painful but you will experience a light twitch of the muscles in your hand as the nerves at the wrist send electrical signals to make these muscles contract.

If the information you provide is reported or published it is done in a way that does not identify you as its source. The data will be stored in a locked area at UOIT for seven years from the completion of the study after which it will be destroyed. You are free to withdraw from the data collection at any time up until the completion of your last data gathering session. Once you have completed the chiropractic care, your data cannot be withdrawn. Taking part in this study is voluntary and your decision to take part in this study (or not) will in no way influence your academic progress or relationship with your chiropractor and/or teacher.

Thank you very much for your time and help in making this study possible. If you have any queries or wish to know more please contact Dr Bernadette Murphy, a Professor at the University of Ontario Institute of Technology, Faculty of Health Sciences, 2000 Simcoe St North, Oshawa, Ontario, L1H 7K4

Phone (905) 721-8668 ext 2778 Fax (905) 721-3179

For any queries regarding this study, please contact the UOIT Research and Ethics Committee Compliance Officer (compliance@uoit.ca and 905-721-8668 ext 3693).

The data from this research will be submitted to scientific conferences and peer reviewed journals. At the completion of the study, you will be sent a summary of the research findings and any place where the data has been published. All published data will be coded so that your data is not identifiable.

Please read the following before signing the consent form and remember to keep a copy for your own records.

- I understand that taking part in this study is voluntary (my choice) and that I am free to withdraw from the study at any time without giving a reason and that this will in no way affect my academic progress, irrespective of whether or not payment is involved.
- This consent form will be kept in a locked area at UOIT, Oshawa, Ontario for a period of seven years before being destroyed.
- The data collected in this study will be coded so that it is confidential from the consent form and stored in a locked area at UOIT, Oshawa, Ontario for a period of seven years before being destroyed.

I, ………………………………………………………. agree to take part in this research.

- I understand that taking part in this study is voluntary (my choice) and that I am free to withdraw from the study at any time without giving a reason and that this will in no way affect my future chiropractic care and/or academic progress, irrespective of whether or not payment is involved.
- I have read and I understand the information sheet dated January 2016 for volunteers taking part in the study designed to investigate the comparison between motor learning tasks. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.
- I will be attending one session where measurements will be taken of the electrical activity in my brain following electrical stimulation of the muscles in my hand/forearm
- I have completed an eligibility checklist to ensure I am eligible to participant in this research.
- I have completed a TMS safety checklist.
- I understand that I can withdraw any data I supply up to the completion of my last measurement session.
- I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.
- I have had time to consider whether to take part.
- I know who to contact if I have any side effects to the study.
- I know who to contact if I have any questions about the chiropractic care portion of the study.

I give consent for the data from this study to be used in future researc ☐ ☐
as long as there is no way that I can be identified in this research. YES NO
(tick one)

I would like to receive a short report about the outcomes of this ☐ ☐

study (tick one) YES NO

Signed …………………………………… Date …………..

I am a varsity athlete (Yes/no)

If yes, which sport? ____

I am a classically trained musician (Yes/no)

Contact numbers of main researchers:

Dr Bernadette Murphy, Phone: + 905 721-8668 ext 2778

RESEARCHER TO COMPLETE

Project explained by: ______________________________________

Project role: ____

Signature: ____ Date: ________________

Appendix 3: TMS Safety Checklist

TMS safety checklist:

The following questions are to ensure it is safe for you to have TMS applied. If you answer yes to any of the questions below, we may need to exclude you from TMS experiments.

QUESTION	ANSWER	
1. Do you suffer from epilepsy, or have you ever had an epileptic seizure?	Yes	No
2. Does anyone in your family suffer from epilepsy?	Yes	No
3. Do you have any metal implant(s) in any part of your body or head? (Excluding tooth fillings)	Yes	No
4. Do you have an implanted medication pump?	Yes	No
5. Do you wear a pacemaker?	Yes	No
6. Do you suffer any form of heart disease?	Yes	No
7. Do you suffer from reoccurring headaches**?	Yes	No
8. Have you ever had a skull fracture or serious head injury?	Yes	No
9. Have you ever had any head surgery?	Yes	No
10. Are you pregnant?	Yes	No
11. Do you take any medication or use recreational drugs (including marijuana)*?	Yes	No
12. Do you suffer from any known neurological or medical conditions?	Yes	No

Comments ____

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Name ______________________________

Signature ______________________________

Date ______________________________

*Note if taking medication or using recreational drugs please read through the medication list on the next page to see if you use contraindicated drugs or medications. You do not need to tell the researcher which medications or drugs you use, unless you wish to. However, all researchers have signed confidentiality agreements and this information will not recorded in writing, if you do wish to discuss this issue.

**Dr. Murphy will meet with participants who answer yes to this question to seek further information.

Medications contraindicated with magnetic stimulation:

1) Tricyclic antidepressants

Name	Brand
amitriptyline (& butriptyline)	Elavil, Endep, Tryptanol, Trepiline
desipramine	Norpramin, Pertofrane
dothiepin hydrochloride	Prothiaden, Thaden
imipramine (& dibenzepin)	Tofranil
iprindole	-
nortriptyline	Pamelor
opipramol	Opipramol-neuraxpharm, Insidon
protriptyline	Vivactil
trimipramine	Surmontil
amoxapine	Asendin, Asendis, Defanyl, Demolox, Moxadil
doxepin	Adapin, Sinequan
clomipramine	Anafranil

2) Neuroleptic or Antipsychotic drugs

A) Typical antipsychotics

Phenothiazines:	Thioxanthenes:
o Chlorpromazine (Thorazine)	o Chlorprothixene
o Fluphenazine (Prolixin)	o Flupenthixol (Depixol and Fluanxol)

o Perphenazine (Trilafon)	o Thiothixene (Navane)
o Prochlorperazine (Compazine)	o Zuclopenthixol (Clopixol and Acuphase)
o Thioridazine (Mellaril)	Butyrophenones:
o Trifluoperazine (Stelazine)	o Haloperidol (Haldol)
o Mesoridazine	o Droperidol
o Promazine	o Pimozide (Orap)
o Triflupromazine (Vesprin)	o Melperone
Levomepromazine (Nozinan)	

B) Atypical antipsychotics

Clozapine (Clozaril)	Quetiapine (Seroquel)
Olanzapine (Zyprexa)	Ziprasidone (Geodon)
Paliperidone (Invega)	Amisulpride (Solian)
Risperidone (Risperdal)	

C) Dopamine partial agonists: Aripiprazole (Abilify)

D) Others

Symbyax - A combination of olanzapine and fluoxetine used in the treatment of bipolar depression.

Tetrabenazine (Nitoman in Canada and Xenazine in New Zealand and some parts of Europe

Cannabidiol One of the main psychoactive components of cannabis.

Regular Cannabis use more often than once per week and/or cannabis use in the past 4 days.

Regular use of other recreational drugs, or single episode within the past three weeks.

Appendix 4: Edinburgh Handedness Inventory

Edinburgh Handedness Inventory

Please indicate your preferences in the use of hands in the following activities *by putting a check in the appropriate column*. Where the preference is so strong that you would never try to use the other hand, unless absolutely forced to, *put 2 checks*. If in any case you are really indifferent, *put a check in both columns*.

Some of the activities listed below require the use of both hands. In these cases, the part of the task, or object, for which hand preference is wanted is indicated in parentheses.

Please try and answer all of the questions, and only leave a blank if you have no experience at all with the object or task.

Task	Left		Right	
1. Writing				
2. Drawing				
3. Throwing				
4. Scissors				
5. Toothbrush				
6. Knife (without fork)				
7. Spoon				
8. Broom (upper hand)				
9. Striking Match (match)				
10. Opening box (lid)				
Total (count checks in both columns)				

Difference	Cumulative TOTAL	Result

Scoring:

Add up the number of checks in the “Left” and “Right” columns and enter in the “TOTAL” row for each column. Add the left total and the right total and enter in the “Cumulative TOTAL” cell. Subtract the left total from the right total and enter in the “Difference” cell. Divide the “Difference” cell by the “Cumulative TOTAL” cell (round to 2 digits if necessary) and multiply by 100; enter the result in the “Result” cell.

Interpretation (based on Result):

below -40 = left-handed

between -40 and +40 = ambidextrous

above +40 = right-handed