MOTOR TRAINING AND CERVICAL SPINE MANIPULATION: EFFECTS ON SENSORIMOTOR INTEGRATION

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ABSTRACT

Altered afferent input resulting from neck joint dysfunction has become a growing area of study. Cervical spine manipulation, specifically in individuals with subclinical neck pain (SNCP); induces neurological changes, suggesting it has a positive neuromodulatory effect on brain processing. The effects of manipulation on motor learning in individuals with SCNP have not been investigated until now. Studies in this thesis sought to develop and investigate a novel motor training task to be coupled with cervical spine manipulation to investigate its effects on individual's ability to process new task information. The studies revealed significant changes in neural activity specific to the cerebellum and sensorimotor integration following a complex motor training task as compared to a simple repetitive task, suggesting that those specific regions are involved in processing of more complex motor skill learning tasks. This novel task was then coupled with manipulation which revealed significant activation increases in cortical and decreases in subcortical brain regions following manipulation. Regions specific to sensorimotor integration (SMI) showed increased activation in both the manipulation and passive head movement control groups, corroborating with the results from the first study. The use of a complex motor training task is a useful tool for determining intervention effects on neural processing in individuals with SCNP.

Keywords: somatosensory evoked potentials, cerebellum, sensorimotor integration, subclinical neck pain, cervical spine manipulation, motor training,

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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TABLE OF CONTENTS

LIST OF ABBREVIATIONS USED

ACC	Accuracy
CNS	Central nervous system
DTI	Diffusion tensor imaging
fMRI	Functional magnetic resonance imaging
IFCN	International Federation of Clinical Neurophysiologists
M1	Primary motor area
MEG	Magnetoencephalography
MRI	Magnetic resonance imaging
PC	Purkinje cell
PET	Positron emission tomography
PNS	Peripheral nervous system
rCBF	Regional cerebral blood flow
RSI	Repetitive strain injury
RT	Response Time
SEP	Somatosensory evoked potentials
S1	Primary somatosensory cortex
S2	Secondary somatosensory cortex
SCNP	Subclinical neck pain
SMI	Sensorimotor integration
TMS	Transcranial magnetic stimulation

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION TO THESIS

Neck pain is a common health problem associated with significant disability in the general population (Côté, Cassidy, & Carroll, 1998; Côté, Cassidy, Carroll, & Kristman, 2004; Haldeman, Carroll, & Cassidy, 2010; Hogg-Johnson et al., 2009; Manchikanti, Singh, Datta, Cohen, & Hirsch, 2009). In any given 6-month period, neck pain has a 54% prevalence, 4.6% of which experience significant limitations (Côté et al., 1998). Risk factors of neck pain include increased dependence on technology such as computers, laptops and cell phones as well as poor work station set-up and workplace settings including prolonged sitting, standing and computer use (Carroll et al., 2008; Haldeman et al., 2010; Hogg-Johnson et al., 2009). Neck pain may result in decreased work place performance and limitations in daily activity. It is important to identify parameters that may indicate neck pain becoming chronic or recurrent.

Repetitive strain injuries, occupational overuse syndromes as well as associated neck and back pain may play a role in altering the way the brain processes incoming sensory information and subsequent motor output to muscles, a process known as sensorimotor integration. A primate study has shown (Byl et al., 1997) that a period of repetitive muscular activity results in altered afferent input to the brain and may change the way that the brain processes subsequent sensory information. In addition, altered afferent input may facilitate changes in the cortical representation of the area devoted to processing input from that body part due to the plastic nature of the brain. Recent work suggests that dysfunctional joints may result in altered afferent input to the central nervous system (CNS) and if prolonged, may result in disordered sensorimotor integration (Haavik Taylor & Murphy, 2007a, 2007b; Haavik Taylor & Murphy, 2010a, 2010b; Tinazzi et al., 2000; Tinazzi et al., 1998)

Little is known on the implications of dysfunction joints in humans; however some studies have demonstrated changes in cortical somatosensory evoked potentials following the cessation of a repetitive typing task (Haavik-Taylor & Murphy, 2007; Haavik Taylor & Murphy, 2007a; Murphy, Bossé, & Daligadu, 2008; Murphy, Taylor, Wilson, Oliphant, & Mathers, 2003). Chiropractic care is one of the most common treatments for neck and back pain, however, little is understood about the biological mechanisms for its efficacy. Recently, studies have shown that physical treatments such as chiropractic care may help modulate disordered sensorimotor integration and thus counteract changes in the processing of sensory information by the brain and spinal cord (Haavik Taylor & Murphy, 2006, 2007b; Haavik Taylor & Murphy, 2008; Herzog, Scheele, & Conway, 1999; Murphy, Dawson, & Slack, 1995; Suter, McMorland, Herzog, & Bray, 1999, 2000).

This research aims to help researchers gain a better understanding of how sensorimotor processing is altered due to chiropractic treatment of neck pain as measured by neurophysiological changes as well as behavioural changes in motor training tasks. It will use a technique called somatosensory evoked potentials (SEPs). SEPs are elicited via stimulation of peripheral nerves and recording the resulting activity from scalp recording electrodes. The amplitudes of different SEP peaks are known to reflect processing by different brain structures. This thesis will take a deeper look at how spinal manipulation in people with neck pain affects the way the brain responds to a motor training task. In particular, the study will focus on the role of the cerebellum in sensorimotor integration, something which has received little attention to date. It is hoped that the planned research will help to shift from pain management to a preventative approach and create policies to reflect this paradigm shift.

HYPOTHESES AND OBJECTIVES

Objectives of this Research

1. Differentiate the effects of simple and complex motor learning tasks on sensorimotor integration and neural processing.

2. Investigate the immediate effects of passive head movement and cervical spine manipulation in addressing disordered sensorimotor integration, motor performance and neural processing.

Specific Hypotheses of this Research

1. A more complex motor training task will lead to greater changes in SEP amplitudes, particularly the N18, N24 and N30 SEP peaks, compared to a simple motor training task.

2. A single session of manipulation of dysfunctional cervical joints will lead to alterations in the amplitude of SEP peaks related to cerebellar function (N18 and N24) and sensorimotor integration (N30 and P40) following a complex motor training task.

OVERVIEW

This thesis is divided into four sections:

1. Literature review
2. Proposed research project
3. Manuscripts for each specific study, in the format specified for submission to Experimental Brain Research
4. Appendices that include the advertisement poster, questionnaires and consent forms

SECTION 1: LITERATURE REVIEW

Introduction to Literature Review

This chapter reviews current literature relevant to the proposed objectives of this thesis. It begins with an overview of sensorimotor integrations, focusing on how it changes with motor sequence acquisition. It then provides an overview of the neuroanatomy of the cerebellum and its role in motor learning, followed by a review and synthesis of motor learning theories in relation to motor sequence acquisition. It then provides background on neck pain particular in relation to overuse injuries and disordered sensorimotor integration. Finally, the role of somatosensory evoked potentials (SEPs) as a tool to study changes in neural processing following motor sequence learning in discussed and evidence for the neural generators of various SEP peaks is critically reviewed.

Sensorimotor Integration

Sensorimotor integration (SMI) relates to the ability of the central nervous system (CNS) to integrate sensory signals in the form of afferent information from the environment and formulate appropriate motor outputs from the muscles. Afferent information refers to incoming sensory information moving through neural pathways to higher order centres within the brain and spinal cord. When learning new skills and performing new tasks it is essential to employ effective sensorimotor integration. Impaired sensorimotor integration may be useful in explaining the reoccurring or high level of injury found in workers with jobs consisting of high levels of repetitive activity. The study of sensorimotor integration has increased dramatically in recent years, with emerging evidence of maladaptive plastic changes in sensorimotor integration of various movement disorders such as overuse injuries (Byl et al., 1997; Classen, Liepert, Wise, Hallett, & Cohen, 1998; Haavik Taylor & Murphy, 2007a, 2007b; Kim et al., 2004; Murphy, Taylor, Wilson, Oliphant, et al., 2003). It is important to note that although it appears that changes in sensorimotor integration are essential for normal functioning and learning new skills, undesirable changes may also occur due to the plastic nature of the central nervous system.

The central nervous system is thought to maintain its ability to reorganize itself following altered afferent input (Classen et al., 1998; Haavik Taylor & Murphy, 2007a, 2007b; Murphy et al., 2008; Murphy, Taylor, Wilson, Knight, et al., 2003; Murphy, Taylor, Wilson, Oliphant, et al., 2003; Tinazzi et al., 1997; Tinazzi et al., 1998). The plasticity of the brain refers to its malleable ability; its ability to change due to experience. Plasticity is defined as ‘any experience dependent enduring change in neuronal or network properties either morphological or functional’ (Donoghue, Hess, & Sanes, 1996). This would relate to changes in neuronal activity (increase or decrease) as measured by techniques such as somatosensory evoked potentials (SEPs), which are further discussed in this literature review. It is known that with altered afferent input to the CNS, plastic changes occur in the way the CNS responds to further afferent input. These plastic changes can occur following both increased and decreased afferent input (Byl et al., 1997) and can lead to both inhibition and facilitation of neural input. The study of sensorimotor integration is important in the understanding of both normal physiological function and maladaptive plastic changes in the form of sensorimotor system malfunctions. A greater understanding of these changes may aid in developing appropriate treatment options for patients with movement disorders, overuse injuries such as repetitive strain injury and other musculoskeletal syndromes such as vertebral dysfunction and pain.

The Cerebellum

The cerebellum, found at the base of the brain under the cerebral hemispheres, is a structure that is involved in motor control and learning, cognitive functions, coordination as well as learning to adjust to changes in sensorimotor relationships (Gasbarri, Pompili, Pacitti, & Cicirata, 2003; Ide & Li, 2011; Laforce & Doyon, 2001; Ramnani, 2006; Ramnani et al., 2006; Schmahmann, 1991, 1996, 1997; Wolf, Rapoport, & Schweizer, 2009, pp. 206-207). It is the largest part of the hindbrain and lies posterior to the pons and the medulla oblongata (Snell, 1997, p. 204). It occupies the inferior and posterior aspects of the cranial cavity and has a highly folded surface, like the cerebrum, that increases the surface area of its outer gray matter cortex, allowing for a greater number of neurons. Constituting only 10% of the total volume of the brain, the cerebellum contains approximately 50 billion neurons – roughly half of the total number of neurons in the brain (Kandel, Schwartz, & Jessell, 2000, p. 322 & 832; Millers, 2007; Ramnani, 2006). The cerebellum is divided into three main lobes: anterior, middle (posterior) and the flocculonodular lobe (Kandel et al., 2000, p. 834; Lundy-Ekman, 2007, p. 257; Snell, 1997, p. 204). The three lobes are further subdivided into 10 lobules, designated I to X (Schmahmann, Doyon, Toga, Petrides, & Evans, 2000).

The cerebellum is connected to other parts of the central nervous system by several afferent and efferent fiber tracts, grouped together into three larger bundles called peduncles on each side of the cerebellum. The superior peduncle connects the cerebellum to the midbrain and is often called the brachium conjunctivum. The middle peduncle, also known as the brachium pontis, connects the cerebellum to the pons. Lastly, the inferior peduncle, or restiform body, connects the cerebellum to the medulla oblongata (Lundy-Ekman, 2007, p. 10 & 258).

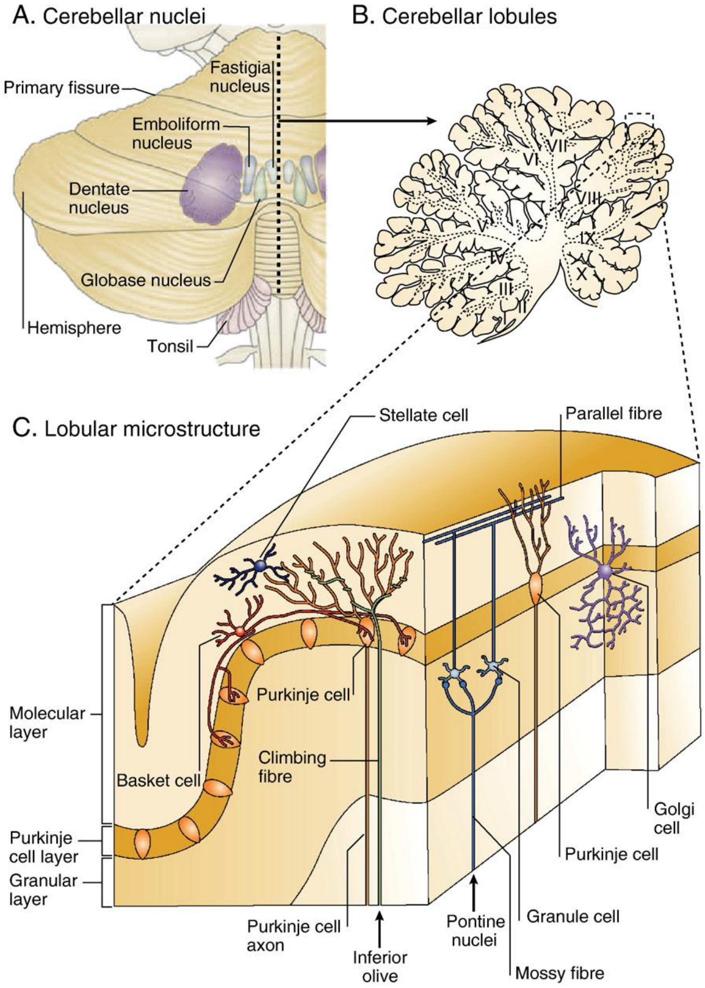

Figure 1: Cerebellar anatomy.
a) Posterior view of the human cerebellum. b) Drawing of midsagittal cross-section through the human cerebellum. c) The microstructural organization of the cerebellar cortex. (Figure reproduced from Ramnani, 2006, Figure 1: Anatomical architecture of the cerebellum).

The cerebellum, much like the cerebrum, consists of both grey and white matter. The cerebellar cortex consists of grey matter organized into three layers (Fig. 1). The outer layer, the molecular layer, consists of two types of inhibitory interneurons: stellate cells and basket cells. The middle layer of the cortex, the purkinje cell layer, consists of inhibitory interneurons called purkinje cells (PC). The dendrites of PCs are extended into the molecular layer and are the sole output neurons of the cerebellum, making them essential to cerebellar-cortical information processing (Apps & Garwicz, 2005). The inner layer, the granular layer, derives its name from the densely packed inhibitory golgi cells and excitatory granular cells. It is in this layer that the granular cells bifurcate to become parallel fibers (Afifi & Bergman, 2005, p. 203; Apps & Garwicz, 2005; Kandel et al., 2000, p. 835; Lundy-Ekman, 2007, pp. 257-258; Millers, 2007; Snell, 1997, pp. 204-206). There are deposits of grey matter, intracerebellar nuclei, in four masses embedded in the white matter of the cerebellum. These four masses are called the dentate, emboliform, globose and fastigial nuclei (Kandel et al., 2000, p. 835; Lundy-Ekman, 2007, pp. 257-258; Snell, 1997, pp. 204-206).

Cerebellar white matter is comprised of three fiber types: intrinsic, efferent and afferent (Snell, 1997, pp. 206-207). Intrinsic cerebellar fibers do not leave the cerebellum as they connect regions within the cerebellum, while afferent and efferent fibers are the input and output regions. Originating in deep cerebellar nuclei (Fig. 2a), cerebellar efferents arrive at specific cortical areas by disynaptic pathways via the thalamus which may explain how the cerebellum modulates motor control and cognitive functions (Molinari, Filippini, & Leggio, 2002). The greater part of white matter is the afferent fibers, composed of excitatory interneurons called mossy and climbing fibers, which enter the cerebellum through the inferior and middle cerebellar peduncles and proceed to the cerebellar cortex.

The cerebellum receives information from the cerebral cortex through two primary pathways: the inferior olivary complex, terminating as climbing fibers in the cerebellar cortex and various precerebellar nuclei, terminating in the cerebellar cortex as mossy fibers (Apps & Garwicz, 2005; Gasbarri et al., 2003; Kandel et al., 2000, pp. 835-837; Manzoni, 2007; Moulton, Schmahmann, Becerra, & Borsook, 2010; Snell, 1997, pp. 210-211). Climbing fibers directly target PC afferents, while mossy fibers excite PCs indirectly by synapsing onto granule cells which form the granule cell-parallel fiber-purkinje cell pathway (Apps & Garwicz, 2005). Both climbing and mossy fibers also project to cerebellar nuclei and subsequently brainstem nuclei and thalamus, relaying information to the cerebral cortex (Moulton et al., 2010). Each cerebellar climbing fiber can contact anywhere from 1-10 purkinje neurons by wrapping around PC dendrites, often making multiple synapses with a single PC. Single mossy fibers may stimulate thousands of PCs through granular cells which project to the molecular layer and contact PCs in the form of parallel fibers. Thus, purkinje neurons receive input from up to one million parallel fibers, which receive input from many mossy fibers, and a single climbing fiber (Afifi & Bergman, 2005, p. 204; Apps & Garwicz, 2005; Manzoni, 2007; Ramnani, 2006; Snell, 1997, pp. 201-211). Despite the difference in projections of climbing and mossy fibers, it is hypothesized that both inferior olivary complex and pontine projections converge on a single mechanism, and when one of the afferent inputs is disrupted, both projections become functionally deactivated (Gasbarri et al., 2003). These findings also corroborate the suggestion that the cerebellum plays a crucial role in motor behaviour and spatial memory (Gasbarri et al., 2003).

Cerebellar activity can be measured through neuroimaging techniques; magnetic resonance imaging (MRI), positron emission tomography (Schmahmann et al., 2000), magnetoencephalography (MEG) and diffusion tensor imaging (DIT), as well as other non-invasive neurophysiological methods such as transcranial magnetic stimulation (TMS) and SEPs (Parsons et al., 1997; Ramnani et al., 2006; Restuccia et al., 2001; Stoodley & Schmahmann, 2009; Tesche & Karhu, 1997). The cerebellum is known to be essential in the integration of somatosensory input and vestibular input in order to control postural stability (Manzoni, 2005) and appears to provide optimal input-output needed for proper control of motor activity (Manzoni, 2005, 2007) by providing an integrative role in combining learned movements together to produce well-executed motor skilled behaviours (Laforce & Doyon, 2001). There is evidence to suggest that the cerebellum is involved in skill acquisition as well as short and long-term repetition priming (see Automaticity and Skill Acquisition) (Poldrack & Gabrieli, 2001). The cerebellum also plays an important role in cortical processing such as verbal and spatial skills, deciphering motor coding, movement anticipation, timing of motor commands, sensorimotor synchronization, learning of motor behaviour, learning from movement errors and cognitive control (Bloedel, 2004; Criscimagna-Hemminger, Bastian, & Shadmehr, 2010; Gasbarri et al., 2003; Ide & Li, 2011; Laforce & Doyon, 2001; Manzoni, 2007; Molinari et al., 2002; Ramnani, 2006; Xu, Lui, Ashe, & Bushara, 2006). Sensorimotor synchronization refers to the synchronization between timed sensory stimuli and motor responses, and there is evidence suggesting a connection between the cerebellum, timing and coordination of sensory feedback as well as motor responses (Molinari, Leggio, & Thaut, 2007). Additionally, neuroimaging evidence suggests cerebellar role in working memory, explicit and implicit learning and memory (Desmond & Fiez, 1998; Kawashima et al., 2000) as well as language (Desmond & Fiez, 1998).

Input is received from sensory systems and from others parts of the brain and spinal cord. This incoming information is then integrated in the cerebellum and utilized for fine-tuning motor activity, thus, damage to the cerebellum results in disorders in fine movement, posture and motor learning (Fine, Ionita, & Lohr, 2002). Topographic organization through magnetic resonance imaging have been compared between humans and macaque brains (Ramnani et al., 2006). As expected, fibres from the cortical motor system in macaques occupied the largest proportion of the cerebral peduncle compared to a small portion of fibres from the prefrontal cortex. Contrarily, human brains demonstrated a larger contribution from the prefrontal cortex than from the cortical motor areas suggesting that human cerebellums play a more important role in processing abstract information from the prefrontal cortex than macaques (Ramnani, 2006; Ramnani et al., 2006). This finding provides insight to the different neural connections within human cerebellums and may be useful in further understanding its role in neural processing.

Understanding the role of the cerebellum in processing of different forms of cortical information requires an understanding of its connections with the cerebral cortex. Together with cortico-ponto-cerebellar projections, the cerebral cortex forms a closed loop system where the cerebellum modulates activity through return projections to the cerebral cortex via the thalamus (Manto & Bastian, 2007; Schmahmann & Pandyat, 1997; Thach, 1972). A proposed mechanism by which the cerebellum contributes to motor control is that it houses copies of motor commands to predict sensory effects of movements thereby reducing dependence on time-delayed sensory signals (Manto & Bastian, 2007). In this theory, the efference copy is brought to the cerebellum via cortico-ponto-cerebellar tracts and an expected sensory outcome would be generated by the cerebellum and relayed to the cerebral cortex via excitatory pathways to the thalamus and via inhibitory pathways to the inferior olive. The thalamus would then compare the input received from the sensory state of the limb with that of the predicted sensory state and send signal error feedback to the cerebellum in order to better train it in making accurate predictions of future state of the motor system based on the received sensory input (Ebner & Pasalar, 2008; Manto & Bastian, 2007).

Damage to the cerebellum not only results in motor deficits such as tremors (Manto, 2005) but also deficits in learning complex sequences and spatial tasks (Gasbarri et al., 2003; Leggio et al., 2008). The most common sign of cerebellar disorder or disease is termed ataxia which describes irregularity in voluntary movement typically present in early and in the later stages of extensive cerebellar lesions (Holmes, 1939). Since cerebellar lesions result in uncoordinated movements despite massive inputs from every sensory system (Holmes, 1939), it has been hypothesized that the cerebellum plays a major role in sensory acquisition and discrimination without cortical processing of sensory input (Restuccia et al., 2001). Cerebellar lesion studies have demonstrated decreased cortical excitability of the contralateral motor cortex as well as significant reduction in specific SEP peak amplitudes contralateral to the damaged cerebellum (Di Lazzaro, Molinari, et al., 1994; Di Lazzaro, Restuccia, et al., 1994). These findings were confirmed through a SEP study coupled with dipolar source analysis of traces through brain electrical source analysis (Restuccia et al., 2001). In this study, cortical SEPs were recorded following median nerve stimulation in five patients with unilateral cerebellar damage. The amplitude of the frontal N24 peak was significantly smaller in subjects after stimulation of the symptomatic side, indicating that those specific peaks represented cerebellar-induced neurophysiological changes in the somatosensory cortex (Restuccia et al., 2001).

Memory

Once information has entered the system, it is processed, and a response is generated. This information is then ‘stored’ for future use, and the persistence of this stored information is termed *memory* (Schmidt & Lee, 2011). When a new environmental stimulus acts on the body, it is transferred into a neurological impulse, travels up towards the brain and eventually contacts memory, where an aspect of the stimulus has been memorized and stored for later retrieval (Schmidt & Lee, 2011).

Memory Systems

Sensory Memory

Short-term sensory store has the capacity to store massive amounts of information that can be retained for a brief period of time (Schmidt & Lee, 2011). This storage of information is seemingly limitless, however experiences a very rapid decay (Schmidt & Lee, 2011; Shiffrin & Schneider, 1977; Sperling, 1960). When information is presented to an individual, short-term sensory storage accepts the information without much encoding or filtering. When individuals are prompted to recall items they have just been exposed to, their ability to recall is strongest within tens of milliseconds (ms) following presentation and rapidly decays as early as 150 ms following presentation with a maximum storage duration of less than 1 s (Sperling, 1960).

Short-Term Memory

Short-term memory allows for storage and recall of information longer than sensory memory. Large amounts of information can be activated at any given moment, however, only a limited amount of information will persist for a period of time ranging from 1 s to 60 s (Shiffrin & Schneider, 1977). Unlike sensory memory, short-term memory has a limited capacity for the total number of items stored. Previous work by George A. Miller demonstrated that the store of short-term memory was 7±2 items (Miller, 1956) while modern estimates of short-term memory capacity are lower, between 4-5 items (Cowan, 2000; Sperling, 1960). The term ‘item’ is ambiguous since it may mean a single object and/or number or a group of objects and/or numbers. By separating items into larger collections, termed information *chunking*, individuals may increase memory capacity (Miller, 1956).

A chunk of information typically consists of a “collection of concepts that have strong associations to one another and much weaker associations to other chunks concurrently in use” (Cowan, 2000). A well-worn example of information chunking involves an individual trying to remember a string of 12 letters, “fbicbsibmirs”. There are letter triads within this sequence (FBI, CBS, IBM, and IRS), that if known and recognized by individuals, can be used to assist in recall (Cowan, 2000). Information chunking is also evident in everyday practices such as telephone numbers. A far more effective way of remembering telephone numbers is observed by chunking numbers into an area code, a three-digit chunk and a four-digit chunk, rather than attempting to remember a string of 10 digits.

Long-Term Memory

Unlike short-term memory, which is limited to a certain number of information chunks, long-term memory is essentially limitless (Miller, 1956). Long-term memory contains learned sequences of information processing, initiated by various internal and external inputs, but are executed automatically with few demands on the capacity of short-term memory (Shiffrin & Schneider, 1977). Long-term memory is thought to consist of levels which include sequences of encoded information executed automatically. An automatic process refers to a process in which sequences of information become active in response to specific input without active control or attention by the individual and utilizes permanent associative connections within long-term memory. These processes are the result of significant training, and once learned, are difficult to suppress or alter (Shiffrin & Schneider, 1977). Early notions regarded information chunks as existing in short-term memory only. However, assumptions have been made to argue that chunks of information can be formed with the aid of long-term memory, and larger chunks of information are present in long-term memory stores (Cowan, 2000). When new chunks of information are formed, there is no limit to the size or number of stimulus elements that comprise each chunk except when these new chunks are formed by new associations (Cowan, 2000). Similarly, the capacity of long-term memory, although seemingly limitless, is challenged by the presentation of large numbers of items for a brief period of time. This limits the time available for item rehearsal or recoding (Cowan, 2000).

Information stored in long-term memory can be retrieved by both automatic and controlled processing. Controlled processing is demanding of attention, serial in nature, dependent on load and while easily established, it is also just as easily altered or reversed

(Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977). Automatic processing is found within long-term memory, demanding of attention when targets are presented, parallel in nature, unaffected by load and very difficult to alter, reverse or suppress (Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977). While information in short-term memory can easily be forgotten, the forgetting of information in long-term memory is more clearly defined as retrieval failure (Shiffrin & Schneider, 1977).

Long-term memory is divided into two major categories: explicit and implicit memory. Explicit, or declarative, memory develops within the 1st postnatal year. It is known to play a major role in mediating conscious recollection of prior events (Desmond & Fiez, 1998; Schacter, 1987). This type of memory is voluntary and deliberate with a limited capacity and capable of partial retrieval with decay effects of concrete information (Rovee-Collier, 1997; Schacter, 1987). It has been suggested that although explicit memory is dependent on medial temporal lobe structures and unimpaired in patients with cerebellar damage, the cerebellum may still be involved in normally invoked explicit memory circuitry (Desmond & Fiez, 1998). Implicit, or procedural, learning and memory are systems that are functional very early in life which process information automatically, without conscious awareness (Rovee-Collier, 1997; Schacter, 1987). This type of memory is involuntary and automatic with unlimited capacity for abstract information storage (Rovee-Collier, 1997; Schacter, 1987). This form of learning and memory is independent of hippocampal structure activation and includes motor skill learning and priming. With the large amounts of evidence demonstrating the effects of cerebellar damage on motor behaviour, the cerebellum is suspected to played a role in motor learning (Desmond & Fiez, 1998).

Motor Skill Learning and Control

Cerebellar Contributions to Motor Learning

Motor skill learning tasks are useful to investigate neurophysiological function. More specifically, they can be used to determine possible cerebellar contributions to motor skill learning. A review article on cerebellar activity during learning found that sequence learning, used in conjunction with neuroimaging techniques, not only demonstrated learning by a decreased reaction time from stimulus to onset of response but also decreases in superior cerebellar and deep nuclear region activation (Desmond & Fiez, 1998). The olivo-cerebellar system has been shown to play a role in timing, further explaining its role in motor control as well as nonmotor cognitive functions (Harrington, Lee, Boyd, Rapcsak, & Knight, 2004; Ivry, Keele, & Diener, 1988; Xu et al., 2006).

A cognitive associative learning paradigm investigated the effect of cerebellar disease on learning (Timmann et al., 2002). The task involved participants beginning each trial by pressing the central home button on a specialized keyboard. A filled circle, an arrow or a colour pair were presented on the screen followed by a growing lateral black circle to the left or right of the stimulus. Participants were required to hit the target button on the appropriate side of the home button with their index finger. The simple motor condition required participants to press the answer button once while the difficult motor condition required it to be pressed three times. Performance was measured by measuring at reaction times. Cerebellar patients demonstrated a learning deficit compared to normal controls. This deficit was independent of motor demands, thus no real difference was found between the simple and complex motor conditions indicating that the cerebellum contributes to motor-independent processes (Timmann et al., 2002).

Other motor sequence learning tasks requiring subjects to perform a sequence of motor responses using one or more fingers have demonstrated cerebellar activation changes following learning tasks. One such study looked at the effect of simple repetitive motor tasks on regional cerebral blood flow (rCBF) changes using PET (Friston, Frith, Passingham, Liddle, & Frackowiak, 1992). The task consisted of participants using their right hands to perform brisk, sequential finger to thumb oppositions with each digit (2 to 5) in order to a metronome at three per 2 sec and was paired with a rest state. Scanning was performed 6 times (each pair scanned 3 times). Subjects were familiarized with the task prior to scanning, but were not allowed to practice. Activations were observed in the left sensorimotor cortex (Brodmann’s Area 1-4) and bilateral activation of the cerebellar cortex as well as premotor cortex, lateral thalamus and deep cerebellar nuclei (Friston et al., 1992). Results demonstrated that there were CBF increases during performance of the simple repetitive motor task and these adaptations were a consequence of practice in the cerebellum but not in the sensorimotor cortex (Friston et al., 1992). This study was limited in that no measures of performance were taken and the PET camera had a field of view limited to 10.5 cm. Thus, only the upper part of the cerebellum could be scanned.

A subsequent study performed six PET measurements of rCBF comparing three different experimental conditions, each measured twice (Jenkins, Brooks, Nixon, Frackowiak, & Passingham, 1994). The baseline condition was rest, and was compared to two other conditions. The first was an active condition in which participants learned a new sequence of keypresses comprised of eight moves, performed using digits 2-5 on their right hand on an external keypad with four keys. The second condition involved performing a sequence learned 90 minutes prior to the scan. The sequences were learned by trial and error through different pacing tones (highpitched tone for correct, low-pitch tone for incorrect) sounding every 3 sec. When comparing the prelearned sequences to the resting state, there were significant increases in activation found in the bilateral cerebellar hemispheres and bilateral ventral thalamus as well as the deep cerebellar nuclei. When comparing the new sequences with resting state, there was significant activation in the bilateral cerebellar hemispheres as well as within the cerebellar nuclei (Jenkins et al., 1994). The activation of the cerebellum, although present in both learning conditions, was greatest during new learning. These results indicate that the cerebellum plays a role in the automaticity of motor tasks.

Simple versus Choice Reaction Time

The first attempts to measure thought processes, in the form of reaction times, was made by Dutch physician F.C. Donders (Donders, 1969). Donders' Subtractive Method used three reaction time (RT) methods, differing in systematic ways, to support his idea of the existence of a series of separate, nonoverlapping information-processing stages between a stimulus and a response. RT refers to the chief measure of an individual's behaviour; the interval between stimulus presentation and beginning of response (Schmidt & Lee, 2011). Donders' methods consisted of a single-unanticipated stimulus requiring a single response, known as simple-RT; a more complicated task with 2 stimuli and a response only if one of the stimuli was presented, known as go/no-go task; and finally more than one stimulus requiring a stimulus-dependent response, known as choice-RT. Donders' utilized the difference in RT between the tasks to determine the average length of time it takes for stimulus identification and response selection. Reaction time is slowed by introducing choice, adding uncertainty for the performer by creating an increased number of possible alternatives (Donders, 1969).

Automaticity and Skill Acquisition

Motor learning refers to a change or acquisition of a motor skill with practice or an increase in the repertoire of motor behaviour such as a new behaviour being maintained over a period of time following a motor learning task (Manto & Bastian, 2007). Some would argue that this change in motor behaviour is dependent on attention, referred to as the automaticity theory of attention related to movement (Grant & Logan, 1993; Logan, 1985, 1988, 1990, 1992). An example is this would be a skilled typist accurately typing from a text while holding a conversation. This demonstrates the automaticity of copy typing; the typist can attend to another task at the same time (Shaffer, 1975).

Automatization is interpreted as acquisition of a specific knowledge base through separate instances of exposure to the task and is an accepted product of learning (Logan, 1988, 1990). Numerous daily tasks that are performed quickly and effortlessly with minimal conscious awareness are referred to as automatic (Logan, 1988). Processing is considered automatic if it relies wholly on memory and retrieval of stored information, a consequence of previous exposure and practice, which increases the amount and speed of retrieval (Grant & Logan, 1993; Logan, 1988, 1990, 1992). This phenomenon is an important contribution to skill acquisition as skills are thought to consist of a collection of automatic processes (Logan, 1985). From this perspective, the rate of automatization may limit the rate of skill acquisition. An example of this would be the idea of performing a relatively short, simple and repetitive task. The participant would be presented with a context where their response would be learned very quickly, then becoming automated and performed effortlessly, no longer requiring conscious attention. The consistency and repetitive nature of a task allows the knowledge to be easily encoded and later retrieved so to be useful in future performance (Hauptmann & Karni, 2002; Logan, 1995). There is a positive relationship between the number of repetitions or exposures and the amount and length of knowledge retention, indicating that the experience of exposure acts as a training session which increases performance resulting in skill learning (Guadagnoli & Lee, 2004; Hauptmann & Karni, 2002).

Repetition Priming

Repetition priming refers to the benefit gained by previous exposure of a specific task or stimulus (Grant & Logan, 1993; Logan, 1990; Richardson-Klavehn & Bjork, 1988; Soldan, Habeck, Gazes, & Stern, 2010). More specifically, it is the facilitation in processing of a stimulus due to recent or previous encounter with the same stimulus (Schacter, 1987). This benefit is in the form of information processing; storing sensory and motor information to be extracted at a later time, resulting in faster response times during subsequent presentations of the same stimulus. Specifically, repetition priming refers to this observed difference in response time and is a temporary effect reflecting implicit memory as a consequence of previous stimulus exposure (Grant & Logan, 1993; Hauptmann & Karni, 2002; Logan, 1990).

Although automaticity and repetition priming are two subtopics within the study of memory (Hauptmann & Karni, 2002; Logan, 1990), they possess a major characterizing difference. Repetition priming is theoretically viewed as the first step on the way to automaticity (Logan, 1990). While automaticity looks at the effects of hundreds of exposures of a stimulus or task on subsequent performance, repetition priming is concerned with the effects of a single or very few exposures (Hauptmann & Karni, 2002; Logan, 1990). However, it has been suggested that skill learning and repetition priming rely on common underlying mechanisms (Logan, 1990). Previous fMRI work has demonstrated that specific neural regions exhibited both skill-related changes in activation and repetition priming effects (Poldrack & Gabrieli, 2001). The two phenomena can be explained through a theory developed by Gordon D. Logan from the University of Illinois called *the instance theory of automatization* (Logan, 1990)

Instance Theory of Automaticity

Automatic processing is a subtopic in the study of attention (Logan, 1985, 1988, 1990). Regardless of stage of performance, whether novice or expert, attention plays a key role in performance, but it is also a limitation to learning (Logan, 1990). The theory of automaticity gets around the limitations of attention by stating that automatic processing demands little attention, making it effortless and requiring little conscious thought (Logan, 1988, 1990, 1992). For example, an individual new to a task will require attention to be focused on the steps of the sequence executed to produce the desired outcome or solution. On the other hand, the attention of expert or automatic performers will be focused on solutions provided by memory through previous repeated exposures (Logan, 1992). A better examination of this is provided in the instance theory of automaticity (Logan, 1988). This theory stipulates that in order to retrieve a solution, individuals must attend to a stimulus associated with it, and this retrieval is dependent on how an individual originally attended to the stimulus (Logan, 1988). This theory relates automaticity to memorial aspects of attention, making it a memory phenomenon (Logan, 1988). According to the instance theory, automaticity is a continuum. Thus, regardless of degree of automaticity, the same qualitative effects should be observed (Logan, 1988, 1992). As individuals are exposed to more sessions, the degree of effect may change, but the qualitative effects remain the same. Accordingly, if a positive effect was observed after one session, a positive effect should also be observed following several sessions, however, the degree of positivity may vary. Additionally, the introduction of a different task will interfere with retrieval

(Logan, 1990). Complex tasks are an example of retrieval interference. In a complex test, an environment is created where automaticity is virtually impossible to develop. By always presenting an unpredictable key press sequence in a random order, the participant is forced to use more attentional resources, and thus the response and reaction times will be longer and movement response will not be automated. However, learning outcomes may differ.

The instance theory is composed of three main assumptions: *obligatory encoding, obligatory retrieval* and *instance representation* (Logan, 1988). The first assumption, obligatory encoding, states that attending to a stimulus or event results in it being encoded into memory. This encoding may not be perfect, but it will be encoded based on the conditions of attention during exposure regardless of whether the individual intends to encode it or not. Second, obligatory retrieval, asserts that attention to a stimulus or event is sufficient to retrieve all that has been associated with it in the past. Regardless of whether it is successful or not, retrieval from memory occurs. These two assumptions are intrinsically linked with attention. The same attention that is required to encode events into memory is also required to retrieve those events from memory. The third assumption states that each exposure to a stimulus, event or object is encoded, stored and retrieved separately. These three assumptions together implying a learning mechanism where information is encoded, resulting in increased memory for familiar stimuli, and is made available for future problems through retrieval (Logan, 1992). Additionally, the instance theory suggests that there is an increase in separate episodic instances from repeated experiences which results in a transition from algorithmic processing to memory-based processing (Logan, 1988, 1990). Thus more exposure to a single event will result in stronger memory because each individual experience creates a separate trace that may be retrieved. Thus, as the same items are presented to an individual, they should be more easily retrieved, as demonstrated by decreased reaction time (Logan, 1988, 1992).

A number of studies have examined the way that competing stimuli interfere with learning (Craig, 1985; Verillo, 1985). Neck pain may play a similar role to tactile perturbations that may cause interference with learning. Altered afferent input due to recurrent neck pain and associated neck joint dysfunction has been suggested by Haavik and Murphy (Haavik & Murphy, 2012) to lead to altered afferent processing of incoming sensory information from the upper limb, leading to disordered sensorimotor integration, with the potential to interfere with motor sequence acquisition. Haavik and Murphy have published several studies which suggest that treatment of neck joint dysfunction through spinal manipulation may improve afferent processing and motor control (Haavik-Taylor & Murphy, 2007; Haavik & Murphy, 2012; Haavik Taylor & Murphy, 2006; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2010a, 2010b).

Epidemiology of Neck Pain

Spinal pain is pain that arises from various structures of the spine and has a lifetime prevalence of 54% to 80% (Manchikanti et al., 2009). Neck pain, a form of spinal pain, is a common health problem associated with significant disability in the general population (Côté et al., 1998; Manchikanti et al., 2009). During any 6-month period, 54% of adults suffer from neck pain and 4.6% experience significant limitations due to neck pain (Côté et al., 1998). Currently, 36% of men and women report upper limb pain in any given week (Walker Bone, Palmer, Reading, Coggon, & Cooper, 2004). While the annual prevalence of neck pain varies greatly depending on the definitions used, one study reports prevalence rates ranging between 4.8% to 79.5% (Hoy, Protani, De, & Buchbinder, 2010) while the majority estimate range between 30% and 50% (Côté et al., 1998; Côté et al., 2004; Haldeman et al., 2010; Hogg-Johnson et al., 2009; Manchikanti et al., 2009). A recent population-based cohort study of 1100 randomly selected Saskatchewan adults reported that only 36.6% of individuals reporting prevalent neck pain experienced resolution of their pain. The study also reported that 37.3% of subjects experienced persistent neck pain, 9.9% reported an aggravation of their condition and 22.8% of subjects experienced recurrent neck pain (Côté et al., 2004). These numbers may be a result of lack of successful treatment and understanding of how pain modulates neural processing.

Analysis of risk factors suggests that neck pain is multifactorial. These risk factors can be divided into two categories: modifiable and nonmodifiable.

Nonmodifiable Risk Factors

Evidence regarding age as a risk factor is almost unanimous. In terms of prevalence, studies demonstrate that there is increased incidence of neck pain during mid-life as compared to early and later life and incidence decreases with age following the middle years (Côté et al., 2004; Haldeman et al., 2010; Hogg-Johnson et al., 2009). There is consistent evidence to suggest that younger age is indicative of better recovery from neck pain in a general population, while there is a decrease in positive outcome and less improvement in function disability with increasing age (Carroll et al., 2008; Côté et al., 2004; Hogg-Johnson et al., 2009). In addition, older individuals are less likely to experience complete resolution of neck pain as well as experience more persistent pain in a general population of individuals that experience neck pain (Côté et al., 2004). Gender is another risk factor reported in various studies (Carroll et al., 2008; Côté et al., 2004; Haldeman et al., 2010; Hogg-Johnson et al., 2009). Females are more likely to experience an episode of and persistent neck pain and are less likely to experience complete resolution of their pain (Côté et al., 2004; Haldeman et al., 2010).

Modifiable Risk Factors

There is significant evident to suggest that there are psychological factors important in neck pain prevalence and outcome (Carroll et al., 2008; Haldeman et al., 2010; Hogg-Johnson et al., 2009). Better psychological health and greater social support predict a better outcome in general population samples with initial neck pain whereas individuals reporting poor psychological health (passive coping such as worrying, fear and avoidance) predict poorer outcomes (Carroll et al., 2008; Hogg-Johnson et al., 2009). Two recent review articles reported that cigarette smoking and exposure to second-hand tobacco smoke are risk factors for neck pain (Haldeman et al., 2010; Hogg-Johnson et al., 2009). In addition, alcohol consumption, time spent in automobiles and wearing of high-heels are also neck pain risk factors (Hogg-Johnson et al., 2009).

The modifiable risk factors that are of most importance to this thesis pertain to workplace physical demands, computer use and desk set-up. A recent review article found that workplace factors such as repetitive activity, precision work and work positions requiring prolonged standing, sitting or computer use are all significant risk factors for neck pain (Haldeman et al., 2010). Additionally, poor work station set-up is linked to increased incidence of neck pain. This includes working with the cervical spine in flexion for prolonged periods; mouse positioned too far requiring shoulder flexion of more than 25 degrees; computer screens positioned too low resulting in head and neck flexion of more than 3 degrees; keyboard placement too close to desktop edge as well as using chairs without armrests (Haldeman et al., 2010). In developed and industrialized countries, there is a higher prevalence of chronic low back pain, 60-85%, and neck pain, 67% (Côté et al., 2004; Lalanne, Lafond, & Descarreaux, 2009; Murphy, Marshall, &

Taylor, 2010). This may be a result of technological advancements readily available and widely used by these populations such as laptops, computers and cellular phones.

These modifiable risk factors provide solid evidence that motor sequence acquisition tasks occurring during technology use are also likely to coincide with risk factors known to lead to neck pain. With the rapidly expanding use of technology, it becomes fundamental to understand how neck pain associated with repetition and incorrect postures may interfere with correct motor sequence acquisition, creating the potential for the development of maladaptive neuroplastic changes.

Spinal Manipulation and Neck Pain

Spinal manipulation is one of the most common treatments for neck pain. Manipulation is a form of treatment provided by chiropractors, medical doctors, physiotherapists and osteopaths which involves high velocity/low amplitude thrusts to specific spinal segments (Murphy, Taylor, & Marshall, 2010). Despite being one of the most common treatments for back and neck pain, little is understood about the biological mechanisms for the efficacy of manipulation. Research in this area has shown a link between impaired neuromuscular and proprioceptive function and back and neck pain patients, potentially explaining how these disorders become and/or remain chronic (Falla, Bilenkij, & Jull, 2004; Michaelson et al., 2003). There is increasing evidence suggesting that spinal dysfunction may affect central neural processing, potentially leading to maladaptive central plastic changes (Haavik-Taylor & Murphy, 2007; Haavik & Murphy, 2012; Haavik Taylor & Murphy, 2006; Haavik Taylor & Murphy, 2008). Evidence is emerging (Haavik & Murphy, 2012; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2010a, 2010b; Herzog et al., 1999; Murphy et al., 1995; Suter et al., 1999, 2000) that spinal manipulation may aid in the potential issues that arise with spinal dysfunction, having a positive neuromodulatory effect, thus contributing to more than simply pain management.

A proposed mechanism for how chiropractic care is hypothesized to aid in neck pain is that with spinal dysfunction, there is altered afferent input towards the central nervous system. This input in turn affects processing and filtering, resulting in altered sensorimotor integration, motor control and finally altered function leading to pain and disability (Haavik & Murphy, 2012). With spinal manipulation, afferent input is normalized, resulting in appropriate somatosensory processing, sensorimotor integration, motor control and eventually normalized function (Haavik & Murphy, 2011, 2012; Haavik Taylor & Murphy, 2006, 2007a, 2007b; Haavik

Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2009; Haavik Taylor & Murphy, 2010a, 2010b). There is also evidence to suggest that patients consulting chiropractors alone (who provide mainly manipulation based care) for neck pain suffer with fewer comorbidities and are less limited in activities than those consulting medical doctors (Côté, Cassidy, & Carroll, 2001). However, further research is needed in order to demonstrate a link between spinal manipulation, pain management and functional abilities and performance.

Possible Role of Chiropractic Care in Addressing Neuromuscular Function

A proposed mechanism explaining how chiropractic care normalizes function is that with a dysfunctional neck or spine, there would be distortion in the afferent feedback. Furthermore, it is proposed that spinal dysfunction can result in an imbalance of afferent input to the central nervous system leading to maladaptive plastic changes (Haavik-Taylor & Murphy, 2007; Haavik & Murphy, 2012). This is an important issue since individuals with chronic neck pain are integrating information on a distorted map, leading to altered SMI of input. Distorted map refers to the changes in physiology at the level of the neck (in chronic neck pain individuals) that alters how incoming information is processed and integrated. Through appropriate chiropractic care and rehabilitation, this distortion in afferent input is normalized. Previous work (Haavik-Taylor & Murphy, 2007; Haavik Taylor & Murphy, 2006; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2010a, 2010b) involving both SEPs and TMS (transcranial magnetic stimulation) techniques indicate that cervical spine manipulation alters cortical integration and SMI. These findings elucidate to the mechanisms responsible for the effective pain management, relief and return to previous functional abilities following spinal manipulation.

The cerebellum, which has been known to be responsible for integrating the incoming signals from the joints of the neck and spine (Manzoni, 2005, 2007) is a candidate for the role of integration of SMI. By demonstrating how chiropractic care alters signal integration and the role that the cerebellum plays in this process, a better understanding of the physiological and neurological benefits of chiropractic adjustments will be made.

The literature demonstrates a growing body of evidence for the role of spinal manipulation in improving SMI. One way of measuring changes in sensory processing is through the use of somatosensory evoked potentials (SEPs) (see following section). Early SEPs (i.e. those with latency less than 100 milliseconds) provide a window into early neural processing of incoming afferent information. They have the potential to provide a tool by which changes in neural processing following motor sequence acquisition can be investigated and how treatments for neck pain and stiffness such as manipulation may influence neural processing. The following section reviews the evidence for the neural generators of early SEP peaks.

Somatosensory Evoked Potentials

A somatosensory evoked potential (SEP) is the response measured following controlled peripheral nerve stimulation. SEPs is a non-invasive technique where potentials are recorded from the surface of the skin and over the scalp close to the location of the hypothesized neural generators (Mauguiere et al., 1999). Electrical activity following peripheral stimulation that is measured over the scalp reflects cerebral action potentials and are best recorded contralateral to the site of stimulation (Dawson, 1947). The application of SEPs may be used in order to detect afferent information travelling along the primary sensory pathways towards the cortex and higher order cognitive processing. A unique feature of SEPs is that they bypass peripheral sensory receptors and directly stimulate nerves of interest, resulting in a more synchronized afferent volley than those elicited by natural stimuli (Mauguiere et al., 1999).

Parameters for SEP Generation and Recording of Waveforms

According to the International Federation of Clinical Neurophysiologists (IFCN) updated recommendations, SEPs should be elicited through bipolar transcutaneous electrical stimulation consisting of a 0.1-0.2 ms square wave pulse on the skin over the peripheral nerve of interest through a constant current stimulator (Cruccu et al., 2008). Stimuli should be delivered at a rate of 2.47 Hz, a rate that does not lead to SEP peak attenuation (Fujii et al.). When target nerves are mixed (motor and sensory fibres), the stimulus intensity should exceed the motor threshold, resulting in a visible muscle twitch (Cruccu et al., 2008). Ensuring waveform reproducibility, SEPs are averaged between 500 and 2000 stimuli presentations to discriminates between noise and the actual potential (Cruccu et al., 2008; Murase et al., 2000). Early SEP peaks, referred to as short latency, are considered to be the most useful while later cortical waves (>45 ms) are more susceptible to changes due to cognitive factors (Cruccu et al., 2008).

SEP Peak Nomenclature and Generators

The nomenclature of evoked potentials is essential in understanding the data collected through the SEP technique. Peaks from waveforms are assigned a prefix representing their polarity, “P” or “N”, signifying positive or negative respectively. According to the IFCN, an upward wave deflection represents a negative polarity and is assigned the prefix “N”. Prefixes precede an integer which is based on the post stimulus latency (in milliseconds) at which each peak appears in a healthy population (Cruccu et al., 2008; Desmedt, 1988). This means, that the N24 peak reflects a negative deflection occurring at approximately 24 milliseconds (ms) following the stimulus, while the P14 peak reflects a positive deflection at 14 ms following the stimulus. The signals that are recorded reflect their underlying neural generators, confirmed through surgery and dipole source localization (Cruccu et al., 2008; Restuccia et al., 2001). Both the amplitude (µV) and latency (ms) of these peaks are useful in interpreting changes in neural activity when compared to normal populations or in response to interventions.

All recording electrodes should be placed according to the IFCN recommendations (Cruccu et al., 2008). A minimum of four channels is recommended: peripheral (Erb’s point) channel (N9), cervical channel (N11 and N13), parietal channel (P14 and N20) and frontal channel (P14-N18, P22-N24 and P22-N30 complexes). Recording EEG electrodes should be placed according to the 10-20 international EEG system, with cortical locations placed contralateral to the site of stimulation and an ipsilateral earlobe reference (Cruccu et al., 2008; Nuwer et al., 1994).

N9 Peak

The N9 peak is recorded at Erb's point, over the brachial plexus and represents a negative potential. Peripheral Erb's point electrodes should be placed within the angle formed by the posterior border of the clavicular head, the sternocleidomastoid muscle and the clavicle, with the reference electrode being either one of contralateral Erb's point, scalp electrode or ipsilateral earlobe (Cruccu et al., 2008; Desmedt, 1988). The neural generator of the N9 potential is thought to be in the peripheral nerve pathway close to, or in, the brachial plexus (Desmedt & Cheron, 1981).

N13 Peaks

The N13 SEP peak presents as an inflection of the N11 SEP peak. According to the IFCN, both the N11 and N13 peaks can be measured from the same channel. As such, the IFCN recommends that a recording spinal cervical electrode be placed over the 5th (Cv5), 6th (Cv6) or 7th (Cv7) cervical spinous process with a reference on the anterior neck at the level of the glottis or trachea (Cruccu et al., 2008; Haavik Taylor & Murphy, 2007a; Nuwer et al., 1994). The N13 SEP peak reflects the postsynaptic potential of the interneurons within the dorsal horn and midcervical cord (Desmedt & Cheron, 1981; Sonoo, Sakuta, Shimpo, Genba, & Mannen, 1991). The peak is generated at or near the first synaptic relay of the spinothalamic tract (Cruccu et al., 2008; Tinazzi et al., 2000).

P14 Peak

The neural generator of the P14 peak is located at or above the level of the foramen magnum, but below the cortex (Cruccu et al., 2008; Desmedt, 1988; Noel, Ozaki, & Desmedt, 1996; Sonoo et al., 1991) and is thought to be generated by the afferent volley in the medial lemniscus (Desmedt & Cheron, 1981). It is also thought to arise from the nucleus cuneatus, a wedge-shaped nucleus in the closed part of the medulla oblongata (Tinazzi et al., 2000). The P14 peak can be recorded from a contralateral frontal cephalic site with a non-cephalic reference (e.g. contralateral frontal cephalic to ipsilateral earlobe montage) (Cruccu et al., 2008; Rossi et al., 2003)

N18 Peak

The N18 component is a subcortical peak that can be recorded from a contralateral frontal cephalic site (6 cm anterior and 2 cm contralateral to Cz), which will be referred to as the Rossi site (Rossi et al., 2003). It can also be confounded with the cortical N20 peak which is recorded from a contralateral parietal cephalic site (2cm posterior to contralateral central scalp site C3/4, referred to as Cc') (Cruccu et al., 2008). The IFCN recommends a non-cephalic reference (e.g. cephalic to ipsilateral earlobe montage) (Cruccu et al., 2008). The N18 peak is a distinct elevation from baseline proceeding the P14 potential (Desmedt & Cheron, 1981). The neural generators of the N18 peak are thought to be located above the level of the spinal cord, in the brain stem, between the lower medulla and midbrain-pontine region (Noel et al., 1996; Sonoo et al., 1991). It has been suggested that there are numerous subthalamic generators of the N18 peak, specifically nuclei in the dorsal column medial lemniscus and accessory inferior olives (Manzano, Negrão, & Nóbrega, 1998; Noel et al., 1996; Sonoo et al., 1991). As such, the N18 peak has the potential to show changes in cerebellar activity.

N20 Peak

The parietal N20 SEP peak is generated in the primary somatosensory cortex (S1), representing neurons within Brodmann's area 3b in the posterior bank of the rolandic fissure (Mauguiere et al., 1999; Nuwer et al., 1994; Tinazzi et al., 2000). Recording electrodes are recommended 2 cm posterior to contralateral central scalp site C3/4, which is referred to as Cc' with a reference electrode placed on the ipsilateral earlobe (Cruccu et al., 2008; Haavik Taylor & Murphy, 2007a). The subcortical N18 peak may confound the N20 peak due to low-pass filters. To eliminate contamination from subcortical waves, a contralateral-ipsilateral montage may be used to determine the genuinity of the N20 peak, and may be utilized for monitoring purposes in clinical settings (Cruccu et al., 2008). Previous work has demonstrated changes in N20 peak amplitude following cervical spinal manipulation (Haavik-Taylor & Murphy, 2007).

P22 Peak

As with N18 the IFCN recommends recording from the contralateral frontal cephalic (Rossi) site, with a non-cephalic ipsilateral earlobe reference (Cruccu et al., 2008). Contrary from the N20 peak which originates in the primary somatosensory cortex, the positive deflection P22 is thought to be generated in the primary motor cortex (Desmedt & Cheron, 1981).

N24 Peak

The N24 is measured at the same recording electrode site as the N18, P22 and N30 peaks, however it is difficult to discern as it appears as a notch in the P22-N30 complex (Cruccu et al., 2008; Rossi et al., 2003). Previous work has demonstrated that by increasing the rate of stimulation of the peripheral nerve of interest, there is SEP peak attenuation of the N30 allowing the N24 peak to be more easily differentiated and accurately measureable (Fujii et al., 1994; Haavik Taylor & Murphy, 2007a). The N24 is not attenuated at increased stimulation rates (Fujii et al., 1994; Haavik Taylor & Murphy, 2007a). The neural generators of the N24 peak lie within the pathway between the cerebellum and the primary somatosensory cortex (Restuccia et al., 2001).

P25 Peak

A group of neurons within Brodmann's area 1 of S1 represent the parietal P25 SEP peak (Mauguiere et al., 1999). Recording electrodes are the same site where the parietal N20 peak is recorded; 2 cm posterior to contralateral central scalp site C3/4, which is referred to as Cc' with a reference electrode placed on the ipsilateral earlobe (Cruccu et al., 2008; Haavik Taylor & Murphy, 2007a).

N30 Peak

As with the N18, P22 and N24 peaks, the N30 is measured from the contralateral frontal cephalic Rossi site (Restuccia et al., 2001; Rossi et al., 2003). There is evidence to suggest that the N30 peak is related to a complex connection linking the thalamus, premotor areas, basal ganglia and primary motor cortex (Cebolla, Palmero-Soler, Dan, & Cheron, 2011; Kanovsky, Bares, & Rektor, 2003). The peak originates from the frontal lobe and the posterior wall of the central sulcus (Tinazzi et al., 2000). The N30 peak is therefore thought to reflect sensorimotor integration (Rossi et al., 2003). Previous work by Haavik Taylor and Murphy has demonstrated changes in the N30 peak following a repetitive motor activity (Haavik Taylor & Murphy, 2007a; Murphy, Taylor, Wilson, Oliphant, et al., 2003) and following high-velocity, low-amplitude cervical manipulation (Haavik Taylor & Murphy, 2010b).

Summary

Sensorimotor integration, the ability of the central nervous system to integrate sensory signals and formulate appropriate motor outputs from the muscles, is an increasing area of research. The study of sensorimotor integration is important in understanding both normal and maladaptive physiological function and may help explain why workers in jobs with high levels of repetitive activity and/or postural stress often injure themselves. It is known that the cerebellum provides optimal input-output needed for proper control of motor activity. Furthermore, it appears that the cerebellum is important in deciphering motor coding, movement anticipation, timing of motor commands, sensorimotor synchronization and changing the degree of muscle activation. A greater understanding of these changes may aid in developing appropriate treatment options for patients with movement disorders. Little is known on the effects of repetitive muscle activity on sensorimotor integration and the role of the cerebellum in this disorder. The cerebellum may be the perfect gate-way to understanding how ergonomic stress alters sensorimotor integration. With increased knowledge in this area, researchers may gain a better understanding of the human body and changes that occur due to ergonomic stresses.

References

Afifi, A., & Bergman, R. (2005). *Functional Neuroanatomy: Text and Atlas* (2nd ed.): The McGraw-Hill Companies.

Angel, R., Roylls, C., & Weinrich, M. (1984). Cerebral Evoked Potentials and Somatosensory Perception. *Neurology, 34*, 123-126.

Apps, R., & Garwicz, M. (2005). Anatomical and physiological foundations of cerebellar information processing. *Nature Reviews Neuroscience, 6*(4), 297-311.

Bloedel, J. (2004). Task-dependent role of the cerebellum in motor learning. *Progress in Brain Research, 143*, 319-329.

Bossé, J. (2012). *Motor Training and Cervical Spine Manipulation: Effects on Sensorimotor Integration.* Masters of Health Sciences, University of Ontario Institute of Technology.

Byl, N., Merzenich, M., Cheung, S., Bedenbaugh, P., Nagarajan, S., & Jenkins, W. (1997). A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. *Physical Therapy, 77*(3), 269-284.

Carroll, L. J., Hogg-Johnson, S., Van Der Velde, G., Haldeman, S., Holm, L. W., Carragee, E. J., . . . Peloso, P. M. (2008). Course and prognostic factors for neck pain in the general population. *European Spine Journal, 17*, 75-82.

Cebolla, A., Palmero-Soler, E., Dan, B., & Cheron, G. (2011). Frontal phasic and oscillatory generators of the N30 somatosensory evoked potential. *NeuroImage, 54*(2), 1297-1306.

Classen, J., Liepert, J., Wise, S., Hallett, M., & Cohen, L. (1998). Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology, 79*(2), 1117-1123.

Côté, P., Cassidy, J., & Carroll, L. (1998). The Saskatchewan health and back pain survey: the prevalence of neck pain and related disability in Saskatchewan adults. *Spine, 23*(15), 1689-1698.

Côté, P., Cassidy, J., & Carroll, L. (2001). The treatment of neck and low back pain: who seeks care? who goes where? *Medical Care, 39*(9), 956-967.

Côté, P., Cassidy, J., Carroll, L., & Kristman, V. (2004). The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain, 112*(3), 267-273.

Cowan, N. (2000). The magical number 4 in short-term memory: A reconsideration of mental storage capacity. *Behavioural and Brain Sciences, 24*, 87-185.

Craig, J. (1985). Tactile pattern perception and its perturbations. *Journal of Acoustical Society of America, 77*(1), 238-246.

Criscimagna-Hemminger, S., Bastian, A., & Shadmehr, R. (2010). Size of error affects cerebellar contributions to motor learning. *Journal of neurophysiology, 103*(4), 2275-2284.

Cruccu, G., Aminoff, M., Curio, G., Guerit, J., Kakigi, R., Mauguiere, F., . . . Garcia-Larrea, L. (2008). Recommendations for the clinical use of somatosensory-evoked potentials. *Clinical neurophysiology, 119*(8), 1705-1719.

Dawson, G. (1947). Cerebral responses to electrical stimulation of peripheral nerve in man. *Journal of Neurology, Neurosurgery & Psychiatry, 10*(3), 134-140.

Desmedt, J. (1988). Somatosensory evoked potentials *Human Event-Related Potentials* (Picton ed., pp. 245-360). Amsterdam: Elsevier.

Desmedt, J., & Cheron, G. (1981). Non-cephalic reference recording of early somatosensory potentials to finger stimulation in adult or aging normal: differentiation of widespread N18 and contralateral N20 from the prerolandic p22 and N30 components. *Electroencephalography and Clinical Neurophysiology, 52*(6), 553-570.

Desmond, J., & Fiez, J. (1998). Neuroimaging studies of the cerebellum: language, learning and memory. *Trends in Cognitive Sciences, 2*(9), 355-362.

Di Lazzaro, V., Molinari, M., Restuccia, D., Leggio, M., Nardone, R., Fogli, D., & Tonali, P. (1994). Cerebro-cerebellar interactions in man: neurophysiological studies in patients with focal cerebellar lesions. *Electroencephalography and Clinical Neurophysiology, 93*, 27-34.

Di Lazzaro, V., Restuccia, D., Molinari, M., Leggio, M., Nardone, R., Fogli, D., & Tonali, P. (1994). Excitability of the motor cortex to magnetic stimulation in patients with cerebellar lesions. *Journal of Neurology, Neurosurgery & Psychiatry, 57*, 108-110.

Donders, F. (1969). On the speed of mental processes. In W. Koster (Ed.), *Attention and performance II*. Amsterdam: North-Holland.

Donoghue, J., Hess, G., & Sanes, J. (1996). Substrates and mechanisms for learning in motor cortex. In J. Bloedel, T. Ebner & S. Wise (Eds.), *Acquisition of Motor Behavior in Vertebrates* (pp. 363–386). Cambridge, MA: MIT Press.

Ebner, T., & Pasalar, S. (2008). Cerebellum Predicts the Future Motor State. *Cerebellum, 7*(4), 583-588.

Falla, D., Bilenkij, G., & Jull, G. (2004). Patients with chronic neck pain demonstrate altered patterns of muscle activation during performance of a functional upper limb task. *Spine, 29*(13), 1436.

Fine, E., Ionita, C., & Lohr, L. (2002). The history of the development of the cerebellar examination. *Seminars in Neurology, 22*, 375-384.

Friston, K., Frith, C., Passingham, R., Liddle, P., & Frackowiak, R. (1992). Motor Practice and Neurophysiological Adaptation in the Cerebellum: A Positron Tomography Study. *Biological Sciences, 248*(1323), 223-228.

Fujii, M., Yamada, T., Aihara, M., Kokubun, Y., Noguchi, Y., Matsubara, M., & Malcolm, H. (1994). The effects of stimulus rates upon median, ulnar and radial nerve somatosensory evoked potentials. *Electroencephalography and Clinical Neurophysiology, 92*(6), 518-526.

Gasbarri, A., Pompili, A., Pacitti, C., & Cicirata, F. (2003). Comparative effects of lesions to the ponto-cerebellar and olivo-cerebellar pathways on motor and spatial learning in the rat. *Neuroscience, 116*(4), 1131-1140.

Grant, S., & Logan, G. (1993). The loss of repetition priming and automaticity over time as a function of degree of intial learning. *Memory & Cognition, 21*(5), 611-618.

Guadagnoli, M., & Lee, T. (2004). Challenge Point: A Framework for Conceptualizing the Effects of Various Practice Conditions in Motor Learning. *Journal of Motor Behavior, 36*(2), 212-224.

Haavik-Taylor, H., & Murphy, B. (2007). Cervical spine manipulation alters sensorimotor integration: a somatosensory evoked potential study. *Clinical Neurophysiology, 118*(2), 391-402.

Haavik, H., & Murphy, B. (2011). Subclinical Neck Pain and the Effects of Cervical Manipulation on Elbow Joint Position Sense. *Journal of manipulative and physiological therapeutics, 34*(2), 88-97.

Haavik, H., & Murphy, B. (2012). The role of spinal manipulation in addressing disordered sensorimotor integration and altered motor control. *Journal of Electromyography and Kinesiology*. doi: 10.1016/j.jelekin.2012.02.012

Haavik Taylor, H., & Murphy, B. (2006). *The effect of cervical spine manipulation on the ability to integrate somatosensory input following repetitive movements.* Paper presented at the Australian Neuroscience Society Annual Meeting, Sydney.

Haavik Taylor, H., & Murphy, B. (2007a). Altered cortical integration of dual somatosensory input following the cessation of a 20 min period of repetitive muscle activity. *Experimental Brain Research, 178*(4), 488-498.

Haavik Taylor, H., & Murphy, B. (2007b). *Selective changes in intracortical facilitation and inhibition following repetitive voluntary movement.* Paper presented at the International Brain Research Organization World Congree of Neuroscience Motor Control Satellite Meeting, Darwin, Northern Territory, Australia.

Haavik Taylor, H., & Murphy, B. (2008). Altered sensorimotor integration with cervical spine manipulation. *Journal of Manipulative and Physiological Therapeutics, 31*(2), 115-126.

Haavik Taylor, H., & Murphy, B. (2009). *Selective changes in cerebellar-cortical processing following motortraining*. Paper presented at the Australian Neuroscience Society 29th Annual Meeting, Canberra, Australia.

Haavik Taylor, H., & Murphy, B. (2010a). Altered central integration of dual somatosensory input after cervical spine manipulation. *Journal of manipulative and physiological therapeutics, 33*(3), 178-188.

Haavik Taylor, H., & Murphy, B. (2010b). The effects of spinal manipulation on central integration of dual somatosensory input observed after motor training: a crossover study. *Journal of manipulative and physiological therapeutics, 33*(4), 261-272.

Haldeman, S., Carroll, L., & Cassidy, J. D. (2010). Findings from the bone and joint decade 2000 to 2010 task force on neck pain and its associated disorders. *Journal of Occupational and Environmental Medicine, 52*(4), 424.

Harrington, D., Lee, R., Boyd, L., Rapcsak, S., & Knight, R. (2004). Does the representation of time depend on the cerebellum? Effect of cerebellar stroke. *Brain, 127*, 561-574.

Hauptmann, B., & Karni, A. (2002). From primed to learn: the saturation of repetition priming and the induction of long-term memory. *Cognitive Brain Research, 13*, 313-322.

Herzog, W., Scheele, D., & Conway, P. (1999). Electromyographic responses of back and limb muscles associated with spinal manipulative therapy. *Spine, 24*(2), 146-153.

Hogg-Johnson, S., Van Der Velde, G., Carroll, L., Holm, L., Cassidy, J., Guzman, J., . . . Carragee, E. (2009). The Burden and Determinants of Neck Pain in the General Population:: Results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine, 33*(4S), S39-S51.

Holmes, G. (1939). The cerebellum of man. *Brain, 62*, 1-30.

Hoy, D. G., Protani, M., De, R., & Buchbinder, R. (2010). The epidemiology of neck pain. *Best Practice & Research Clinical Rheumatology, 24*, 783-792.

Ide, J. S., & Li, C. R. (2011). A cerebellar thalamic cortical circuit for error-related cognitive control. *NeuroImage, 54*, 455-464.

Ivry, R., Keele, S., & Diener, H. (1988). Dissociation of the lateral and medial cerebellum in movement itming and movement execution. *Experimental Brain Research, 73*, 167-180.

Jenkins, I., Brooks, D., Nixon, P., Frackowiak, R., & Passingham, R. (1994). Motor Sequence Learning: A Study with Positron Emission Tomography. *The Journal of Neuroscience, 14*(6), 3775-3790.

Kandel, E., Schwartz, J., & Jessell, T. (2000). *Principles of Neural Science* (4th ed.). New York: McGraw-Hill Professional Publishing.

Kanovsky, P., Bares, M., & Rektor, I. (2003). The selective gating of the N30 cortical component of the somatosensory evoked potentials of median nerve is different in the mesial and dorsolateral frontal cortex: evidence from intracerebral recordings. *Clinical Neurophysiology, 114*(6), 981-991.

Kawashima, R., Okuda, J., Umetsu, A., Sugiura, M., Inoue, K., Suzuki, K., . . . Yamadori, A. (2000). Human Cerebellum Plays an Important Role in Memory-Timed Finger Movement: An fMRI Study. *Journal of Neurophysiology, 83*, 1079-1087.

Kim, D., Shin, M., Lee, K., Chu, K., Woo, S., Kim, Y., . . . Roh, J. (2004). Musical training induced functional reorganization of the adult brain: Functional magnetic resonance imaging and transcranial magnetic stimulation study on amateur string players. *Human Brain Mapping, 23*(4), 188-199.

Laforce, R., & Doyon, J. (2001). Distinct Contribution of the Striatum and Cerebellum to Motor Learning. *Brain and Cognition, 45*(2), 189-211.

Lalanne, K., Lafond, D., & Descarreaux, M. (2009). Modulation of the flexion-relaxation response by spinal manipulative therapy: a control group study. *Journal of Manipulative and Physiological Therapeutics, 32*(3), 203-209.

Leggio, M., Tedesco, A., Chiricozzi, F., Clausi, S., Orsini, A., & Molinari, M. (2008). Cognitive sequencing impairment in patients with focal or atrophic cerebellar damage. *Brain, 131*, 1332-1343.

Logan, G. (1985). Skill and automaticity: Relations, implications, and future directions. *Canadian Journal of Psychology, 39*, 367-386.

Logan, G. (1988). Toward an Instance Theory of Automatization. *Psychological Review, 95*(4), 492-527.

Logan, G. (1990). Repetition Priming and Automaticity: Common Underlying Mechanisms? *Cognitive Psychology, 22*, 1-35.

Logan, G. (1992). Attention and Preattention in Theories of Automaticity. *The American Journal of Psychology, 105*(2), 317-339.

Logan, G. (1995). The Weibull Distribution, the Power law, and the Instance Theory of Automaticity. *Psychological Review, 102*(4), 751-756.

Lundy-Ekman, L. (2007). *Neuroscience: Fundamentals for Rehabilitation* (3rd ed.). St. Louis, MI: Saunders Elsevier.

Manchikanti, L., Singh, V., Datta, S., Cohen, S. P., & Hirsch, J. A. (2009). Comprehensive Review of Epidemiology, Scope, and Impact of Spinal Pain. *Pain Physician, 12*, E35-E70.

Manto, M. (2005). The wide spectrum of spinocerebellar ataxias. *Cerebellum, 4*, 2-6.

Manto, M., & Bastian, A. J. (2007). Cerebellum and the deciphering of motor coding. *The Cerebellum, 6*, 3-6.

Manzano, G., Negrão, N., & Nóbrega, J. (1998). The N18 component of the median nerve SEP is not reduced by vibration. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 108*(5), 440-445.

Manzoni, D. (2005). The cerebellum may implement the appropriate coupling of sensory inputs and motor responses: evidence from vestibular physiology. *The Cerebellum, 4*(3), 178-188.

Manzoni, D. (2007). The cerebellum and sensorimotor coupling: looking at the problem from the perspective of vestibular reflexes. *The Cerebellum, 6*(1), 24-37.

Mauguiere, F., Allison, T., Babiloni, C., Buchner, H., Eisen, A., Goodin, D., . . . Nuwer, M. (1999). Somatosensory evoked potentials. The International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology - Supplement, 52*, 79-90.

Michaelson, P., Michaelson, M., Jaric, S., Latash, M., Sjölander, P., & Djupsjöbacka, M. (2003). Vertical posture and head stability in patients with chronic neck pain. *Journal of Rehabilitation Medicine, 35*(5), 229-235.

Miller, G. (1956). The Magical Number Seven, Plus or Minus Two: Some Limits on Our Capacity for Processing Information. *The Psychological Review, 63*, 81-97.

Millers, D. (2007). *How Our Brain Works: The Construction and Functionality of Your Brain Presented and Explained*: iUniverse.

Molinari, M., Filippini, V., & Leggio, M. (2002). Neuronal plasticity of interrelated cerebellar and cortical networks. *Neuroscience, 111*(4), 863-870.

Molinari, M., Leggio, M., & Thaut, M. (2007). The cerebellum and neural networks for rhythmic sensorimotor synchronization in the human brain. *The Cerebellum, 6*(1), 18-23.

Moulton, E., Schmahmann, J., Becerra, L., & Borsook, D. (2010). The cerebellum and pain: integrator or active participator? *Brain Research Reviews, 65*, 14-27.

Murase, N., Kaji, R., Shimazu, H., Katayama-Hirota, M., Ikeda, A., Kohara, N., . . . Rothwell, J. (2000). Abnormal premovement gating of somatosensory input in writer's cramp. *Brain, 123*(9), 1813-1829.

Murphy, B., Bossé, J., & Daligadu, J. (2008). *The Effect of Repetitive Typing on Cerebellar Evoked Potentials.* Paper presented at the University of Ontario Summer Research Conference, University of Ontario Institute of Technology in Oshawa, Ontario, Canada.

Murphy, B., Dawson, N., & Slack, J. (1995). Sacroiliac joint manipulation decreases the H-reflex. *Electromyography and Clinical Neurophysiology, 35*(2), 87-94.

Murphy, B., Marshall, P., & Taylor, H. (2010). In Press: The cervical flexion-relaxation ratio: reproducibility and comparison between chronic neck pain patients and controls. *Spine*.

Murphy, B., Taylor, H., Wilson, S., Knight, J., Mathers, K., & Schug, S. (2003). Changes in median nerve somatosensory transmission and motor output following transient deafferentation of the radial nerve in humans. *Clinical Neurophysiology, 114*(8), 1477-1488.

Murphy, B., Taylor, H., Wilson, S., Oliphant, G., & Mathers, K. (2003). Rapid reversible changes to multiple levels of the human somatosensory system following the cessation of repetitive contractions: a somatosensory evoked potential study. *Clinical Neurophysiology, 114*(8), 1531-1537.

Murphy, B., Taylor, H. H., & Marshall, P. W. (2010). The Effect of Spinal Manipulation on the Efficacy of a Rehabilitation Protocol for Patients With Chronic Neck Pain: A Pilot study. *Journal of Manipulative and Physiological Therapeutics, 33*(3), 168-177.

Nixon, P., & Passingham, R. (2001). Predicting sensory events: The role of the cerebellum in motor learning. *Experimental Brain Research, 138*, 251-257.

Noel, P., Ozaki, I., & Desmedt, J. (1996). Origin of N18 and P14 far-fields of median nerve somatosensory evoked potentials studied in patients with a brain-stem lesion. *Electroencephalography and Clinical Neurophysiology, 98*(2), 167-170.

Nuwer, M., Aminoff, M., Desmedt, J., Eisen, A., Goodin, D., Matsuoka, S., . . . Vibert, J. (1994). IFCN recommended standards for short latency somatosensory evoked potentials. Report of an IFCN committee. International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology, 91*(1), 6.

Parsons, L., Bower, J., Gao, J., Xiong, J., Li, J., & Fox, P. (1997). Lateral cerebellar hemispheres actively support sensory acquisition and discrimination rather than motor control. *Learning & Memory, 4*, 49-62.

Pascual-Leone, A., & Torres, F. (1993). Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. *Brain, 116*, 39-52.

Poldrack, R., & Gabrieli, J. (2001). Characterizing the neural mechanisms of skill learning and repetition priming. Evidence from mirror reading. *Brain, 124*, 67-82.

Ramnani, N. (2006). The primate cortico-cerebellar system: anatomy and function. *Nature Reviews: Neuroscience, 7*, 511-522.

Ramnani, N., Behrens, T. E. J., Johansen-Berg, H., Richter, M. C., Pinsk, M. A., Andersson, J. L. R., . . . Thompson, A. J. (2006). The evolution of prefrontal inputs to the cortico-pontine system: diffusion imaging evidence from Macaque monkeys and humans. *Cerebral Cortex, 16*(6), 811-818.

Restuccia, D., Valeriani, M., Barba, C., Le Pera, D., Capecci, M., Filippini, V., & Molinari, M. (2001). Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions. *Brain, 124*(4), 757-768.

Richardson-Klavehn, A., & Bjork, R. (1988). Measures of Memory. *Annual Reviews of Psychology, 39*, 475-543.

Rossi, S., della Volpe, R., Ginanneschi, F., Ulivelli, M., Bartalini, S., Spidalieri, R., & Rossi, A. (2003). Early somatosensory processing during tonic muscle path in humans: relation to loss of proprioception and motor 'defensive' strategies. *Clinical Neurophysiology, 114*(7), 1351-1358.

Rovee-Collier, C. (1997). Dissociations in Infant Memory: Rethinking the Development of Implicit and Explicit Memory. *Psychological Review, 104*(3), 467-498.

Schacter, D. (1987). Implicit Memory: History and Current Status. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 13*(3), 501-518.

Schmahmann, J. (1991). An Emerging Concept: The Cerellar Contribution to Higher Function. *Archives of Neurology, 48*(11), 1178-1187.

Schmahmann, J. (1996). From Movement to Thought: Anatomic Substrates of the Cerebellar Contribution to Cognitive Processing. *Human Brain Mapping, 4*, 174-198.

Schmahmann, J. (1997). *The cerebellum and cognition* (Vol. 41). San Diego: Academic Press.

Schmahmann, J., Doyon, J., Toga, A., Petrides, M., & Evans, A. (2000). *MRI Atlas of the Human Cerebellum*. San Diego: Academic Press.

Schmahmann, J., & Pandyat, D. (1997). The cerebrocerebellar system. *International review of neurobiology, 41*, 31-60.

Schmidt, R., & Lee, T. (2011). *Motor Control and Learning: A Behavioural Emphasis* (5th ed.). Windsor: Human Kinetics.

Schneider, W., & Shiffrin, R. (1977). Controlled and Automatic Human Processing: I. Detection, Search, and Attention. *Psychological Review, 84*, 1-66.

Shaffer, L. (1975). Multiple attention in continuous verbal tasks. *Attention and performance, 5*, 157-167.

Shiffrin, R., & Schneider, W. (1977). Controlled and Automatic Human Information Processing: II. Perceptual Learning, Automatic Attending, and a General Theory. *Psychological Review, 84*(2), 127-190.

Snell, R. (1997). *Clinical neuroanatomy for medical students* (4th ed.). Philadelphia, PA: Lippincott-Raven Publishers.

Soldan, A., Habeck, C., Gazes, Y., & Stern, Y. (2010). Neural mechanisms of repetition priming of familiar and globally unfamiliar visual objects. *Brain Research, 1343*, 122-134.

Sonoo, M., Sakuta, M., Shimpo, T., Genba, K., & Mannen, T. (1991). Widespread N18 in median nerve SEP is preserved in a pontine lesion. *Electroencephalography and Clinical Neurophysiology, 80*(3), 238-240.

Sperling, G. (1960). The infromation available in brief visual presentations. *Psychological Monographs: General and Applied, 74*(11), 1-29.

Stoodley, C., & Schmahmann, J. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *Neuroimage, 44*(2), 489-501.

Suter, E., McMorland, G., Herzog, W., & Bray, R. (1999). Decrease in quadriceps inhibition after sacroiliac joint manipulation in patients with anterior knee pain. *Journal of Manipulative and Physiological Therapeutics, 22*(3), 149-153.

Suter, E., McMorland, G., Herzog, W., & Bray, R. (2000). Conservative lower back treatment reduces inhibition in knee-extensor muscles: A randomized controlled trial. *Journal of Manipulative and Physiological Therapeutics, 23*(2), 76-80.

Tesche, C., & Karhu, J. (1997). Somatosensory evoked magnetic fields arising from sources in the human cerebellum. *Brain Research, 744*(1), 23-31.

Thach, W. (1972). Cerebellar output: Properties, synthesis and uses. *Brain Research, 40*, 89-102.

Timmann, D., Depper, J., Maschke, M., Kolb, F., Böring, D., Thilmann, A., & Diener, H. (2002). Motor deficits cannot explain impaired cognitive associative learning in cerebellar patients. *Neuropsychologia, 40*, 788-800.

Tinazzi, M., Fiaschi, A., Rosso, T., Faccioli, F., Grosslercher, J., & Aglioti, S. M. (2000). Neuroplastic Changes Related to Pain Occur at Multiple Levels of the Human Somatosensory System: A Somatosensory-Evoked Potentials Study in Patients with Cervical Radicular Pain. *The Journal of Neuroscience, 20*(24), 9277-9283.

Tinazzi, M., Zanette, G., Polo, A., Volpato, D., Manganotti, P., Bonato, C., . . . Fiaschi, A. (1997). Transient deafferentation in humans induces rapid modulation of primary sensory cortex not associated with subcortical changes: a somatosensory evoked potential study. *Neuroscience Letters, 223*(1), 21-24.

Tinazzi, M., Zanette, G., Volpato, D., Testoni, R., Bonato, C., Manganotti, P., . . . Fiaschi, A. (1998). Neurophysiological evidence of neuroplasticity at multiple levels of the somatosensory system in patients with carpal tunnel syndrome. *Brain, 121*(9), 1785-1794.

Verillo, R. (1985). Psychophysics of vibrotactile stimulation. *Journal of Acoustical Society of America, 77*(1), 225-232.

Walker Bone, K., Palmer, K., Reading, I., Coggon, D., & Cooper, C. (2004). Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. *Arthritis & Rheumatism, 51*(4), 642-651.

Wolf, U., Rapoport, M., & Schweizer, T. (2009). Evaluating the Affective Component of the Cerebellar Cognitive Affective Syndrome. *Journal of Neuropsychiatry and Clinical Neurosciences, 21*(3), 245-253.

Xu, D., Lui, T., Ashe, J., & Bushara, K. (2006). Role of the olivo-cerebellar system in timing. *Journal of Neuroscience, 26*, 5990-5995.

SECTION 2: PROPOSED RESEARCH

Proposed Research Framework

The proposed thesis will explore two areas of research in human neurophysiology, with two separate experiments. The overall objective of this research is to look at the efficacy of chiropractic treatment of neck pain in neural processing of new complex motor training tasks. In order to address this objective, there are three main steps: develop an appropriate complex motor training task; test the new task against a simple motor task and; apply the new task to test chiropractic efficacy. The first experiment aims to test a new complex motor training task compared to a simple motor task, testing the automaticity theory of attention related movement in a motor training paradigm and its effects on sensorimotor integration in a healthy population. The second experiment aims to determine whether manipulation of dysfunctional cervical joints will result in sensorimotor integration altering cerebellar peaks (N18 and N24) as well as sensorimotor integration peaks (N30 and P40) in response to a complex motor training. The proposed experiments will adopt a similar framework for experimental design as employed by Murphy et al (Murphy, Taylor, Wilson, Oliphant, et al., 2003). Due to the apparent link between computer use and neck pain, and the fact that the University of Ontario Institute of Technology, where the research is being conducted, is a laptop based university, the students provide an ideal subject pool.

Both conventional and faster rate SEPs will be elicited in a controlled experimental design to investigate the role of the cerebellum in altered sensorimotor integration previously observed following cervical spine manipulation (Haavik-Taylor & Murphy, 2007; Haavik Taylor & Murphy, 2006; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2010a, 2010b) and repetitive motor activity (Haavik Taylor & Murphy, 2006, 2007a, 2007b; Murphy et al., 2008; Murphy, Taylor, Wilson, Oliphant, et al., 2003).

Simple and Complex Motor Training Tasks

The effect of a simple and complex motor task on cerebellar peaks and sensorimotor integration will be investigated in Experiment 1. The intervention will consist of a repetitive typing task where subjects will be required to press keys on an external numeric keyboard with the middle three fingers consecutively for 20 minutes. The simple motor task will consist of pressing three keys in order, e.g. 7, 8, 9 in ascending order while the complex motor task will consist of a more complex sequencing of the same three numbers utilized in the simple motor task e.g. 9, 9, 7, 8, 7, 8, etc. In order to monitor and analyze motor training effects, all subjects will be required to press the keys in the pattern for either the simple or complex motor task for two minutes both pre and post intervention. Reaction time and accuracy will be analyzed to determine motor training.

The purpose of the repetitive typing tasks is that it is testing the automaticity theory of attention related to movement. In the simple task, the response of the participant is learned very quickly, then becomes automated or done effortlessly, no longer requiring conscious attention. In the complex test, a context has been created where automaticity is much more difficult to develop, requiring more conscious effort and attention. By constantly presenting an unpredicted key press sequence in a random order, the participant is forced to use more attentional resources, and thus the response and reaction times will be longer and movement response will not be automated.

Cervical Manipulation and Passive Head Movement Interventions

Cervical manipulation intervention

The effect of cervical spinal manipulation on cerebellar activity and sensorimotor integration in response to a complex motor task will be investigated in Experiment 2. The intervention, cervical spinal manipulation, will be high velocity, low amplitude thrusts. During manipulation, the spine will be held in lateral flexion, slight rotation and slight extension and will be carried out by a registered chiropractor. In order to ensure that manipulation is successful for individual subjects, the cervical spines of subject's will be checked after each adjustment to determine if the subsequent levels still require adjusting. Following the intervention, post-intervention dependent variables, SEPs, will be collected, recorded and analyzed.

Passive head movement control

Since subjects cannot be exposed to the motor training task more than once, a control group will also participate in Experiment 2. The control intervention will consist of a passive movement of the subject's head that will be carried out by the same chiropractor who performs the cervical adjustments in the adjustment intervention. The passive head movement control intervention involves the subject's head being passively laterally flexed, and slightly extended and rotated to a position that the chiropractor would normally manipulate that person's cervical spine, and then return the subjects head back to neutral position. This will be repeated for both the left and right sides and will be performed prior to the complex motor training task from Experiment 1. Following the intervention, post-intervention dependent variables, SEPs, will be collected, recorded and analyzed.

Experimental Protocol

The protocol for SEPs collection and repetitive activity will be adapted from previous work by Haavik Taylor and Murphy (Haavik-Taylor & Murphy, 2007; Haavik Taylor & Murphy, 2006, 2007a; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2009; Haavik Taylor & Murphy, 2010b; Murphy et al., 2008; Murphy, Taylor, Wilson, Oliphant, et al., 2003) and the IFCN guidelines (Cruccu et al., 2008).

Significance of Research

The study of sensorimotor integration has received increasing interest within the past decade. SMI is important in understanding physiological function and may be useful in explaining the recurring injury states of individuals with high levels of repetitive activity in their occupation. As discussed earlier, the adult human central nervous system retains its ability to reorganize itself in response to altered afferent input (Classen et al., 1998; Haavik Taylor & Murphy, 2007a, 2007b; Murphy et al., 2008; Murphy, Taylor, Wilson, Oliphant, et al., 2003; Tinazzi et al., 1997; Tinazzi et al., 1998). Due to this ability, repetitive muscle activity may alter sensory and motor processing, leading to changes in sensorimotor integration (Murphy, Taylor, Wilson, Knight, et al., 2003). A greater understanding of neurological changes due to repetitive muscular activity may aid in the development of appropriate treatment options for patients with movement disorders as well as allow researchers to gain a better understanding of the human body and changes that occur due to ergonomic stresses.

The effect of chiropractic adjustments on cerebellar function and its contribution to sensorimotor integration as well as how it interacts with the basal ganglia, cortex and periphery, needs to be addressed in the context of altered afferent input from the spine and the effects of chiropractic adjustments. The proposed research themes that will be investigated in Dr. Bernadette Murphy's Human Neurophysiology and Rehabilitation Laboratory will focus on the connection between chiropractic care, cerebellar function and sensorimotor integration as well as repetitive motor activity, cerebellar function and sensorimotor integration. The experiments planned will expand on previous work by Dr. Murphy (Haavik-Taylor & Murphy, 2007; Haavik Taylor & Murphy, 2006, 2007a, 2007b; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2009; Haavik Taylor & Murphy, 2010a, 2010b; Murphy et al., 2008; Murphy, Taylor, Wilson, Oliphant, et al., 2003) by looking specifically at changes in cerebellar processing. This will in turn provide useful information to researchers by expanding knowledge and understanding of the impact of chiropractic adjustments on the spine and nervous system by demonstrating the effects of spinal adjustments on changes in how incoming sensory information is processed as well as changes in central neural control of upper limb muscles. The proposed research aims to identify challenges which limit the translation of research into making statements about the health benefits of chiropractic care. Furthermore, the research is unique in that it focuses and will compliment pioneer work by researchers Dr. Bernadette Murphy, Dr. Heidi Haavik (formerly Taylor) and colleagues.

A greater understanding of the mechanisms of the changes in SMI and the role of the cerebellum in SMI will aid clinicians to understand who is most likely to benefit from chiropractic care. In addition, it will aid in identification of patients with distorted SMI who may require chiropractic care in combination with other approaches. This is important since it may provide a rationale for long-term care of individuals with chronic or recurring neck and back pain in order to normalize sensory information to reduce or eliminate the cycle of recurrence. Furthermore, this research will provide information on the effects of repetitive strain injury, occupational overuse syndrome and repetitive muscular activity on neural processing and daily functions. Thus, this research may help to shift away from pain management to disease prevention models to prevent the development of chronic pain and enhance function to decrease the risk of injury in occupation, recreational and domestic settings. This research aims to provide evidence to help change policy and shift to a preventative approach.

References

Classen, J., Liepert, J., Wise, S., Hallett, M., & Cohen, L. (1998). Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology, 79*(2), 1117-1123.

Cruccu, G., Aminoff, M., Curio, G., Guerit, J., Kakigi, R., Mauguiere, F., . . . Garcia-Larrea, L. (2008). Recommendations for the clinical use of somatosensory-evoked potentials. *Clinical neurophysiology, 119*(8), 1705-1719.

Haavik-Taylor, H., & Murphy, B. (2007). Cervical spine manipulation alters sensorimotor integration: a somatosensory evoked potential study. *Clinical Neurophysiology, 118*(2), 391-402.

Haavik Taylor, H., & Murphy, B. (2006). *The effect of cervical spine manipulation on the ability to integrate somatosensory input following repetitive movements.* Paper presented at the Australian Neuroscience Society Annual Meeting, Sydney.

Haavik Taylor, H., & Murphy, B. (2007a). Altered cortical integration of dual somatosensory input following the cessation of a 20 min period of repetitive muscle activity. *Experimental Brain Research, 178*(4), 488-498.

Haavik Taylor, H., & Murphy, B. (2007b). *Selective changes in intracortical facilitation and inhibition following repetitive voluntary movement.* Paper presented at the International Brain Research Organization World Congree of Neuroscience Motor Control Satellite Meeting, Darwin, Northern Territory, Australia.

Haavik Taylor, H., & Murphy, B. (2008). Altered sensorimotor integration with cervical spine manipulation. *Journal of Manipulative and Physiological Therapeutics, 31*(2), 115-126.

Haavik Taylor, H., & Murphy, B. (2009). *Selective changes in cerebellar-cortical processing following motortraining*. Paper presented at the Australian Neuroscience Society 29th Annual Meeting, Canberra, Australia.

Haavik Taylor, H., & Murphy, B. (2010a). Altered central integration of dual somatosensory input after cervical spine manipulation. *Journal of manipulative and physiological therapeutics, 33*(3), 178-188.

Haavik Taylor, H., & Murphy, B. (2010b). The effects of spinal manipulation on central integration of dual somatosensory input observed after motor training: a crossover study. *Journal of manipulative and physiological therapeutics, 33*(4), 261-272.

Murphy, B., Bossé, J., & Daligadu, J. (2008). *The Effect of Repetitive Typing on Cerebellar Evoked Potentials.* Paper presented at the University of Ontario Summer Research Conference, University of Ontario Institute of Technology in Oshawa, Ontario, Canada.

Murphy, B., Taylor, H., Wilson, S., Knight, J., Mathers, K., & Schug, S. (2003). Changes in median nerve somatosensory transmission and motor output following transient deafferentation of the radial nerve in humans. *Clinical Neurophysiology, 114*(8), 1477-1488.

Murphy, B., Taylor, H., Wilson, S., Oliphant, G., & Mathers, K. (2003). Rapid reversible changes to multiple levels of the human somatosensory system following the cessation of repetitive contractions: a somatosensory evoked potential study. *Clinical Neurophysiology, 114*(8), 1531-1537.

Tinazzi, M., Zanette, G., Polo, A., Volpato, D., Manganotti, P., Bonato, C., . . . Fiaschi, A. (1997). Transient deafferentation in humans induces rapid modulation of primary sensory cortex not associated with subcortical changes: a somatosensory evoked potential study. *Neuroscience Letters, 223*(1), 21-24.

Tinazzi, M., Zanette, G., Volpato, D., Testoni, R., Bonato, C., Manganotti, P., . . . Fiaschi, A. (1998). Neurophysiological evidence of neuroplasticity at multiple levels of the somatosensory system in patients with carpal tunnel syndrome. *Brain, 121*(9), 1785-1794.

SECTION 3: MANUSCRIPT 1 -
A COMPARISON OF SOMATOSENSORY PROCESSING CHANGES FOLLOWIN THE PERFORMANCE OF A SIMPLE VERSUS COMPLEX MOTOR TRAINING TASK

A comparison of somatosensory processing changes following the performance of a simple versus complex motor training task

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Abstract

Background

Altered afferent input to the CNS leads to plastic changes in how it responds to further input. There is evidence to suggest that a period of repetitive voluntary movement such as simple repetitive typing, results in changes in transmission of somatosensory afferent information. More complex motor training tasks are useful in determining neural contributions to motor skill learning such as number sequence learning. This study sought to compare the effects of a simple and complex motor training task on neural processing.

Methods

We recorded spinal, brainstem and cortical somatosensory evoked potentials (SEP) to median nerve stimulation before and after a simple repetitive and complex motor training typing task.

Results

There were significant increases in the P14-N18 and P22-N30 SEP complexes following the complex motor training task while there was a significant decrease in the P22-N24 SEP complex following both training tasks.

Conclusions

The results suggest that the more complex motor training task produces differential behavioural and neural changes as compared to simple motor training tasks.

KEYWORDS

Somatosensory evoked potentials (SEP); motor learning; cerebellum; sensorimotor integration (SMI)

Introduction

It is known that altered afferent input to the CNS leads to plastic changes in how it responds to subsequent input (Byl et al., 1997; Classen et al., 1998; Haavik Taylor & Murphy, 2007a; Murphy, Taylor, Wilson, Knight, et al., 2003; Murphy, Taylor, Wilson, Oliphant, et al., 2003; Pascual-Leone & Torres, 1993; Tinazzi et al., 1997; Tinazzi et al., 1998). Altered CNS changes have been shown to outlast the period of altered input and induce organizational changes in both the primate and human cortex (Byl et al., 1997; Classen et al., 1998; Haavik Taylor & Murphy, 2007a, 2007b; Murphy, Taylor, Wilson, Oliphant, et al., 2003). Previous studies have demonstrated that a period of repetitive voluntary movement, in the form of a typing task, results in changes in transmission of somatosensory afferent information (Haavik Taylor & Murphy, 2007a, 2007b; Murphy, Taylor, Wilson, Oliphant, et al., 2003). These studies focused on the effects of simple repetitive typing sequences, tasks which require little attention and result in automatic processing.

Automatic processing is a subtopic in the study of attention (Logan, 1985, 1988, 1990). Regardless of stage of performance, whether novice or expert, attention plays a key role in performance, but it is also a limitation to learning (Logan, 1990). The theory of automaticity gets around the limitations of attention by stating that automatic processing demands little attention, making it effortless and requiring little conscious thought (Logan, 1988, 1990, 1992). According to the instance theory, automaticity is a continuum. Thus, regardless of degree of automaticity, the same qualitative effects should be observed (Logan, 1988, 1992). As individuals are exposed to more sessions, the degree of effect may change, but the qualitative effects remain the same. Accordingly, if a positive effect was observed after one session, a positive effect should also be observed following several sessions, however, the degree of positivity may vary. Additionally, the introduction of a different task will interfere with retrieval (Logan, 1990). Complex tasks are an example of retrieval interference. In a complex test, an environment is created where automaticity is virtually impossible to develop. By always presenting an unpredictable key press sequence in a random order, the participant is forced to use more attentional resources, and thus the response and response times will be longer and movement response will not be automated. However, learning outcomes may differ. In neurophysiological studies, the comparison between simple and complex typing sequences has not been investigated.

More complex typing tasks, categorized as motor skill learning tasks can be used conjunction with electrophysiological techniques to investigate the contributions that various brain areas such as the cerebellum and sensorimotor cortex make to motor skill learning. Sequence learning, used in conjunction with neuroimaging techniques, not only demonstrates learning by a decreased response time from stimulus to onset of response but also decreases in superior cerebellar and deep nuclear region activation (Desmond & Fiez, 1998). While simple repetitive motor tasks result in attenuation of sensorimotor processing and bilateral activation of the cerebellar cortex as well as premotor cortex, lateral thalamus and deep cerebellar nuclei (Friston et al., 1992; Haavik Taylor & Murphy, 2007a, 2007b; Murphy, Taylor, Wilson, Oliphant, et al., 2003), more complex motor sequence tasks have been shown to result in significant increases in activation in the bilateral cerebellar hemispheres and bilateral ventral thalamus as well as the deep cerebellar nuclei (Jenkins et al., 1994). Regardless of complexity, activations are greatest following prelearned sequences, demonstrating the role of the cerebellum in the automaticity and learning of motor tasks (Friston et al., 1992; Jenkins et al., 1994). Additionally, the olivo-cerebellar system has been shown to play a role in timing, further explaining its role in motor control as well as nonmotor cognitive functions (Harrington et al., 2004; Ivry et al., 1988; Xu et al., 2006).

Somatosensory evoked potentials (SEP) are electrical potentials induced by physiological or electrical stimulation of somatosensory receptors or their axons (Angel, Roylls, & Weinrich, 1984; Mauguiere et al., 1999). By combining SEP protocols with motor learning paradigms, changes in neural processing resulting from motor learning can be investigated (Angel et al., 1984). It has been understood for a number of years that the cerebellum is important in motor learning, but more recent evidence suggests that the role of the cerebellum is to process sensory inputs in order to prepare motor responses to predictable sensory events (Nixon & Passingham, 2001). Neural activity in pathways involving the cerebellum can be quantified using short latency SEPs. The use of SEPs combined with a motor learning paradigm will add to our understanding of neurophysiological changes following simple repetitive and complex motor learning tasks.

This study sought to investigate whether the performance of a simple repetitive typing task compared to a complex task of varying number sequence presentations results in differing processing changes in the somatosensory system. Comparisons of SEP peak amplitude changes from median nerve stimulation could give better insight to the role of sensorimotor integration areas including the cerebellum in processing of somatosensory information following two differing motor tasks.

Methods

Participants

Thirteen participants (three women and ten men), aged 19-28 (mean age 22.2), participated in this study. The study was a paired experimental design where participants were allocated into both the SIMPLE and COMPLEX typing task groups, thus no age-matching was necessary, with a minimum 48 hours between each session. All participants consented to two experimental sessions and were required to have no history of neurological disease. Informed consent was obtained and the study was approved by the ethical committee at the University of Ontario Institute of Technology.

Participant no.	Gender	Age	Handedness
1	F	20	R
2	M	23	R
3	M	25	R
4	M	21	R
5	M	23	R
6	F	21	R
7	M	28	R
8	M	22	L
9	F	21	R
10	M	21	R
11	M	22	R
12	M	22	R
13	M	19	R

Table 1: Study participant age, gender and handedness details

Stimulation of median nerve

Stimuli consisted of electrical square pulses, 1ms in duration delivered at rates of 2.47Hz and 4.98Hz through Ag/AgCl ECG conductive adhesive electrodes (MEDITRACE™ 130 by Ludlow Technical Products Canada Ltd., Mansfield, MA) (impedance <5 kΩ) placed over the median nerve at the wrist of the right hand, with anode proximal. SEPs were recorded at the two rates since the slow rate 2.47Hz does not lead to SEP peak attenuation (Fujii et al., 1994) and the fast rate 4.98Hz attenuates the N30 SEP peak resulting in the N24 SEP peak being accurately measurable (Fujii et al., 1994). The stimulus intensity was increased until motor threshold was achieved for each individual participant. Motor threshold was defined as the lowest stimulation intensity that evoked a visible muscle contraction of the abductor pollicis brevis muscle.

SEP recording parameters

SEP recoding electrodes (1.8288m Traditional Lead, 10mm disc, 2mm hole gold cup EEG electrodes, Grass Technologies, An Astro-Med, Inc. Subsidiary, Rockland, MA) (impedance <5 kΩ) were placed according to the International Federation of Clinical Neurophysiologists (IFCN) recommendations. Recording electrodes were placed on the ipsilateral Erb's point, over C5 spinous process (Cv5), the anterior neck (tracheal cartilage), 2cm posterior to contralateral central C3/4, which will be referred to as Cc', and a frontal cite (6cm anterior and 2cm contralateral to Cz), which will be referred to as the Rossi site (Rossi et al., 2003). The C5 spinous process was referenced to the trachea while all other electrodes were referenced to the ipsilateral earlobe. A 1.8288m Traditional Lead, 10mm disc, 2mm hole gold cup EEG electrode was also used as a ground, placed in the mouth of participants.

Data collection

During the data recording sessions, participants were seated in a quiet room, on a La-Z-Boy™ chair to minimize any movement of recording electrodes and were instructed to sit still and as quiet as possible. During the SEP recordings, the lights in the room were turned off and participants' eyes were open. The SEP signal was amplified (gain 10,000), filtered (0.2-1000 Hz) and stored on a laboratory computer for later retrieval. A total of 1500 sweeps were averaged per stimulation rate using a purpose written Signal® configuration (Cambridge Electronic Design, Cambridge, UK). Far-field potentials require a higher number of averaged sweeps, however 500 sweeps can reliably record peripheral Erb's and cortical SEP peaks (Mauguiere et al., 1999; Nuwer et al., 1994). The averaged waveform was displayed in an analysis window from which the amplitudes of the specific waveforms of interest were measured. SEP peak amplitudes were measured according to the IFCN guidelines (Cruccu et al., 2008). We identified and analyzed the following SEP components: the peripheral N9, the spinal N11 and N13, the far-field P14-18 complex, the parietal N20 (P14-N20 complex) and P25 (N20-P25 complex) and the frontal N24 (P22-N24 complex) and N30 (P22-N30 complex). SEPs were recorded before and after a typing task intervention which consisted of two separate tasks performed on different days with a minimum 48 hours between sessions.

Typing motor task interventions

Custom E-Prime (Psychology Software Tools, Inc., Pittsburgh, PA) software was utilized to prompt participants through the typing task interventions while recording dependent variables. The typing task interventions were separated into two tasks: a simple and a complex task. Each subject completed both tasks separately on different days with a minimum 48 hours between sessions. The intervention consisted of a repetitive typing task in which participants were required to press keys on an external numeric keyboard with the middle three fingers (digits 2-4) consecutively for 20 minutes. The baseline condition was rest, and SEP peak amplitudes following this condition were compared to SEP peak amplitudes following two other conditions. The first condition was a simple repetitive typing task in which participants performed a sequence of keypresses comprised of three moves, e.g. 7, 8, 9 in ascending order, performed using digits 2-4 on their right hand. The second condition was a more complex motor typing task which involved performing more complex sequences of keypresses comprised of six moves using the same three numbers utilized in the simple motor task. There were a total of fifteen six-number sequences randomized in the complex task. In order to monitor and analyze motor training effects, all subjects were required to press the keys in the pattern for either the simple or complex motor task, depending on which session they were completing on that day, for two minutes both pre and post intervention. Response time (RT) and accuracy (ACC) were analyzed to determine motor training.

The purpose of the repetitive typing tasks was that it tested the automaticity theory of attention related to movement. In the simple task, the response of the participant is learned very quickly, and then becomes automated or done effortlessly, no longer requiring conscious attention. In the complex test, a context is created where automaticity is much more difficult to develop, requiring more conscious effort and attention. By constantly presenting an unpredicted key press sequence in a random order, the participant is forced to use more attentional resources, and thus the response times will be longer and movement response will not be automated.

Data analysis

Participants were familiarized with the electrical stimulation needed to elicit SEPs while determining motor threshold, eliminating the need to discard any sweeps within the first data collection SEP trial. Once data was acquired, peak amplitudes were measured from peak to the proceeding peak from the averaged waveform for each SEP peak.

In order to compare the magnitude of the difference between the two motor training tasks all pre SEP peak amplitudes were normalized to 1 and subsequent post amplitudes were expressed relative to 1 for each subject for both the simple and complex typing tasks. Pre scores of 1 were compared with adjusted post-simple and post-complex amplitudes and exported to IBM SPSS Statistics. To look at the overall effect of typing for both conditions a repeated measures analysis of variance (ANOVA) was performed using IBM SPSS Statistics with factors time (pre and post intervention) and task (simple vs. complex). Behavioural data collected across the two experiments included means of response time (RT) and accuracy (ACC) for each subject, pre and post motor training. An ANOVA was performed with factors time (pre and post) and task (simple vs. complex) using IBM SPSS Statistics program. Statistical significance was set at $P \leq 0.05$. An inclusion criteria for data to be further analyzed was that the N9 SEP peak differed by no more than 10% between pre and post trials. This is because the N9 measures the peripheral afferent volley at the level of the brachial plexus and in order to be able to measure changes in centrally generated SEP peaks to the intervention, it is critical that the peripheral volley is stable. Three participant's data did not fit this inclusion criteria and thus were not included in the final analysis.

Results

The final data analysis included ten right-handed participants comprised of eight men and two women for the SEP data while all thirteen subjects were included in the analysis of behavioural data.

The repeated measures ANOVA revealed significant main effects for the N18 and N30 peaks for task [F = (9,2) 7.22 ($p = 0.025$)] and [F = (9,2) 8.58 ($p = 0.017$)] and the N24 peak for time [F = (9,2) 5.72 ($p = 0.041$)] (Figure 4). The brainstem P14-N18 complex increased by 21.0%

following the complex task compared to 2.1% for the simple task while the P22-N30 complex increased by 20.0% following the complex task compared to 6.0% for the simple task.

Figure 5 depicts the pre and post-motor training SEP peaks for one individual participant. Note the increase in the P14-N18 and P22-N30 complexes following the complex typing task. Behavioural data revealed significant main effects for trials across RT for both time [F = (12,2) 53.29 (*p*<0.001)] and task [F = (12,2) 59.09 (*p*<0.001)]. Figure 6 shows mean ACC changes across all trials while Figure 7 depicts significant RT changes for both time and task.

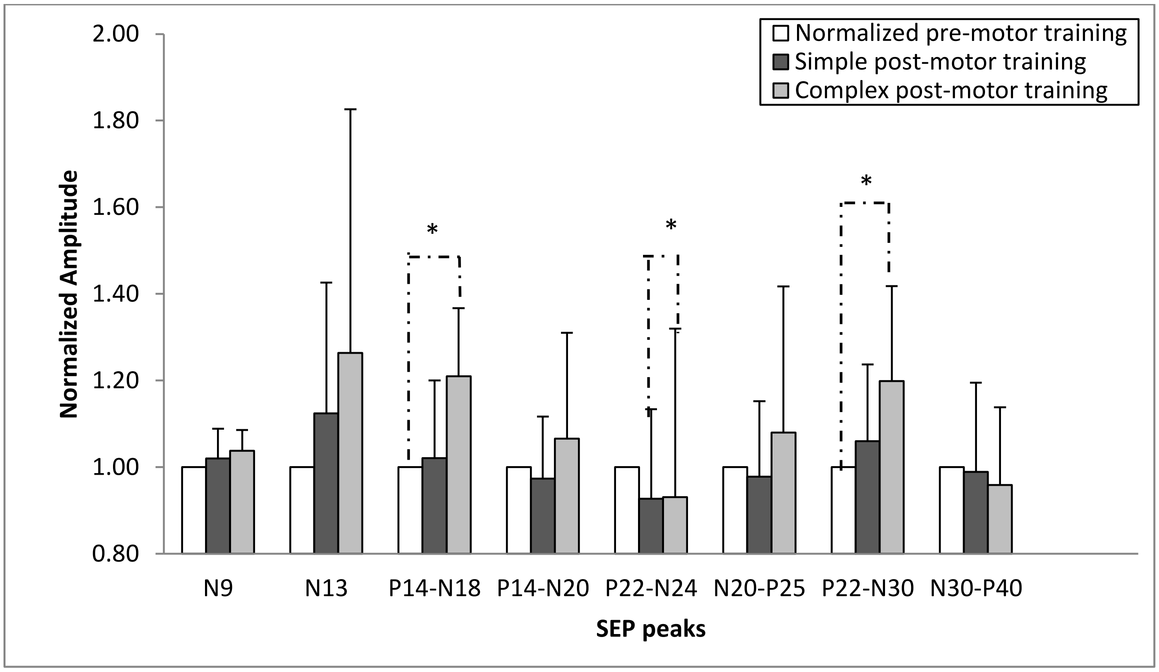

Figure 2: Normalized mean amplitude changes for the simple & complex typing interventions + SD. Pre-values were normalized to 1. * indicates significant changes from baseline for the repeated measures ANOVA comparing both time (pre and post) and task (simple vs. complex).

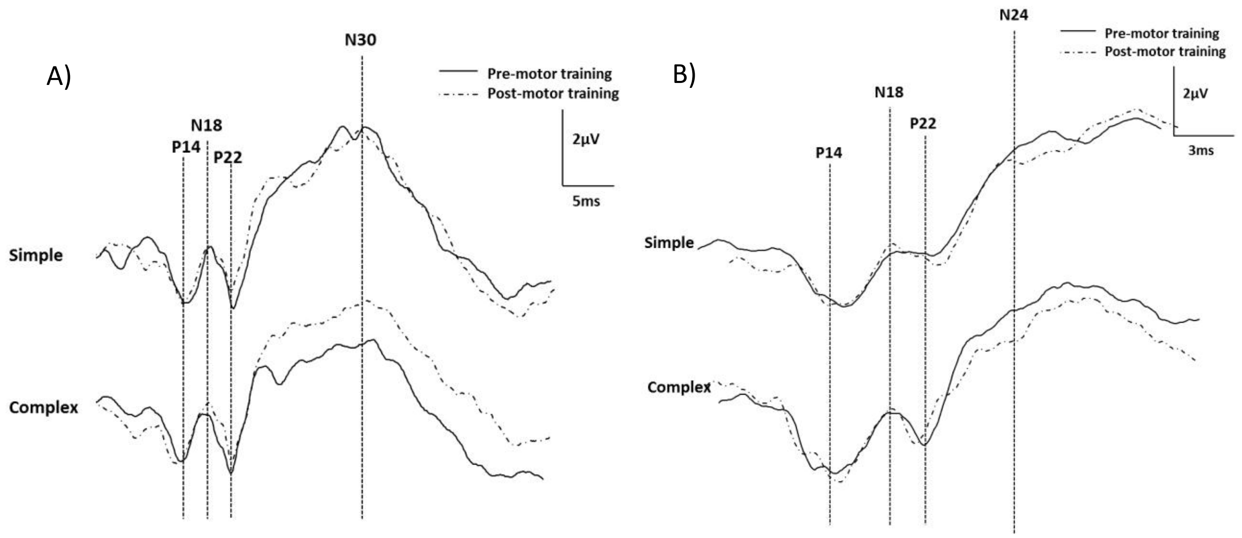

Figure 3: The pre and post-motor training SEP peaks for one individual participant.
Note the significant increase in the P14-N18 and P22-N30 complexes following the complex typing task as well as the significant decrease in the P22-N24 complex post-motor training for both typing tasks.

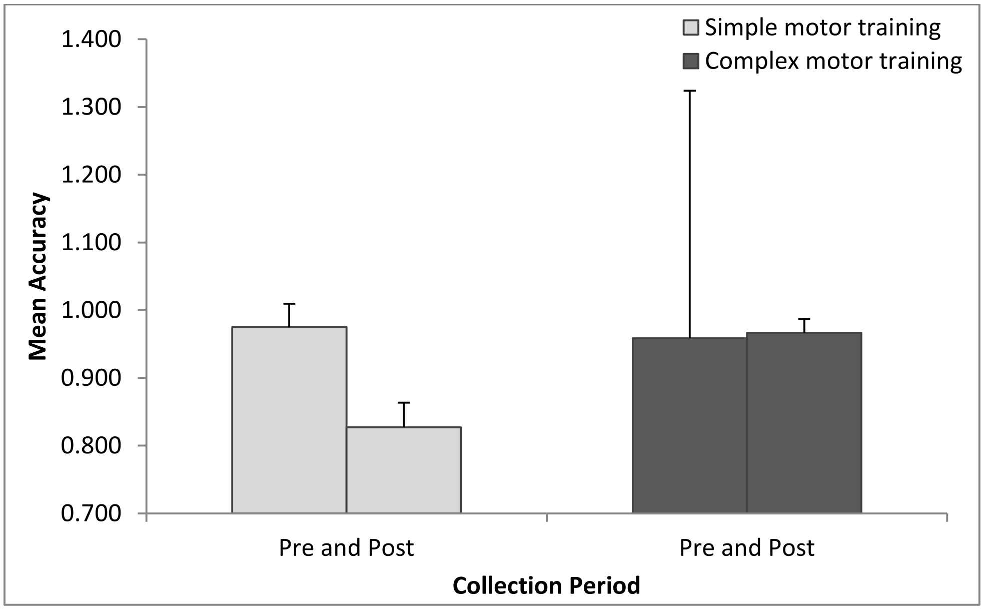

Figure 4: Accuracy (ACC).
The mean accuracy is shown for both the time trials (pre and post) and task where an accuracy of 1 depicts a perfect score. There were no significant improvements in accuracy over time for both motor training interventions.

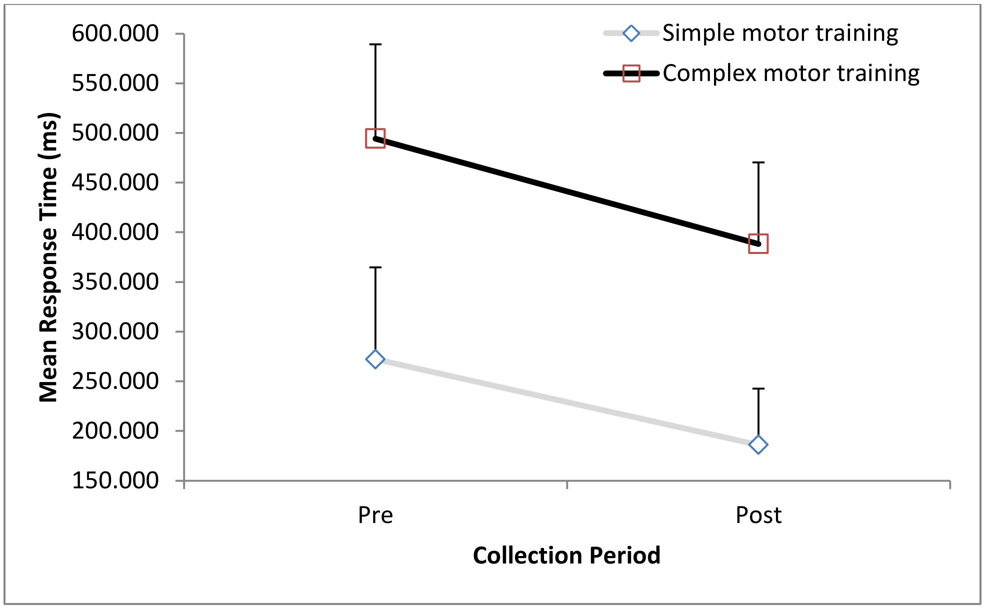

Figure 5: Response time (RT).
The change in response time over the 2 time trials is shown for both the simple (grey line) and complex (black line) conditions. There were significant main effects for both time and task indicating the participants learned to respond more quickly following the motor training task.

Discussion

The large change in the N18 and N30 SEP peak amplitudes for the complex typing task compared to the simple task suggests that exposure to a complex motor task results in changes in neural activation beyond what is necessary to perform the simple typing task alone. In comparison, the significant decrease in the N24 SEP peak amplitudes following both typing tasks suggest that the specific neural structures representative of that SEP peak are involved in motor training, regardless of degree of difficulty.

The N18 SEP peak reflects activity in the brain stem between the lower medulla and midbrain-pontine regions (Manzano et al., 1998; Noel et al., 1996) and within the olivo-cerebellar pathways (Noel et al., 1996). The increase in amplitude for the complex group may reflect a decrease in inhibition at the level of the cuneate nucleus (Manzano et al., 1998), which may be reflective of the mechanism by which the cerebellum is involved in learning of complex motor tasks. While the central nervous system is mainly controlled by inhibition, the simple group did not show any significant changes in the N18 peak suggesting that more complex motor tasks may have had a modulatory effect on inhibitory control of the olivo-cerebellar pathway. Sensorimotor integration (SMI) is important in task learning and motor training. There is evidence to suggest that the N30 SEP peak represents a complex connection between various SMI regions such as the thalamus, premotor areas, basal ganglia and primary motor cortex (Cebolla et al., 2011; Kanovsky et al., 2003; Rossi et al., 2003). The larger increase in amplitude following the complex motor task suggests, along with the N18 changes, that there is an increase in neural activity specific to sensorimotor integration regions following more complex motor tasks.

The most interesting finding is that the N24 SEP peaks decreased significantly following both typing tasks. The N24 peak reflects activation of neurons within the pathway between the cerebellum and the primary somatosensory cortex (Restuccia et al., 2001). The significant decrease in activation following both the simple and complex tasks may reflect an increase in inhibition of neurons within that pathway, indicative of their role in both motor training and motor learning. Furthermore, this result suggests that the neurons within this pathway play a role in motor training regardless of task difficulty. The findings from these experiments propose a decrease in inhibition within the olivo-cerebellar pathway followed by the opposite, an increase in inhibition, within the cerebellar-primary somatosensory cortex pathway during motor training task. The combination of the N18 results and N24 results gives an interesting depiction of the activation of neural structures and the role of the cerebellum in motor training tasks. No previous work has demonstrated both cerebellar and SMI activation changes when comparing simple and complex motor tasks.

Previous studies have demonstrated changes in somatosensory information processing following typing tasks involving repetitive voluntary movement (Haavik Taylor & Murphy, 2007a, 2007b; Murphy, Taylor, Wilson, Oliphant, et al., 2003). However, these studies focused on the effects of simple repetitive typing sequences which require little attention, resulting in automatic processing (Logan, 1988, 1990, 1992). Complex tasks are an example of retrieval interference. The complex task adopted in this study created an environment where automaticity was impossible to attain, by always presenting a random, unpredictable key press sequence. Previous work by Murphy et al. looked at the effects of a simple repetitive typing task where participants were required to perform a typing task using keys 7, 8 and 9 using the second to forth digits of the dominant hand in ascending order (Murphy, Taylor, Wilson, Oliphant, et al., 2003). This is the first study to compare the neurophysiological effects of simple and complex typing sequences. The main interest was to see whether a more complex task would induce more and/or different changes in neurophysiological activity when compared to a simple repetitive typing task.

Similar to previous findings, the simple repetitive motor task resulted in minimal changes in sensorimotor processing and attenuation of cerebellar cortex activation (Friston et al., 1992; Haavik Taylor & Murphy, 2007a, 2007b; Murphy, Taylor, Wilson, Oliphant, et al., 2003)). However, contrary to previous findings, the simple repetitive task did not induce a decrease in amplitude of the P14-N18 peak (Murphy, Taylor, Wilson, Oliphant, et al., 2003). Instead, a significant decrease was observed in the P22-N24 peak for both tasks. The complex motor sequence task showed a significant increase in the P14-N18 SEP peak, representing activity within the olivo-cerebellar pathway. Along with the N18, the N24 peak represents neurons within the pathway between the cerebellum and the primary somatosensory cortex (Restuccia et al., 2001). Similar findings to the N18 results have been observed by Jenkins et al. with increases in bilateral cerebellar activation following more complex motor sequence tasks (Jenkins et al., 1994). The observed changes in the P14-N18 and P22-N24 complexes suggest that the cerebellum plays a key role in integrating and learning complex motor tasks, far beyond its role in simple motor tasks.

The behavioural data revealed significant changes in RT for both time and task while no significant changes were observed for ACC. However, there was an overall improvement in

ACC for the complex motor task following the 20 minute training period while there was a large decrease in accuracy for the simple motor task. Possible explanations for the decrease in ACC for the simple task could be participant fatigue as well as loss of concentration. With the complex task, there were 15 6-digit sequences that were randomized. Participants utilized more attentional resources to perform the task, which in turn may have stimulated neural structures, as observed with the increased in P14-N18 and P22-N30 SEP peaks and decrease in the P22-N24 SEP peak. The significant improvement in RT for both tasks suggests that participants learned to respond more quickly following the 20 minute motor training task.

Strengths

Strength in this study is found in that it coupled previous work with simple repetitive motor training tasks with more complex motor learning tasks. This is the first study of its kind to compare simple repetitive typing with a novel complex typing task for both neurophysiological changes as well as behavioural changes. The results suggest that the complex task involves more networking between neural structures and may be used as a measure of behavioural changes when coupled with different interventions.

Limitations

One issue that may be of concern due to the low subject numbers is the failure to observe improvement of the N13 SEP peak with both tasks may reflect a type II error given the increase observed in both following motor training. This peak can be more variable between subjects and tends to require greater subject numbers before concluding that there is no statistical difference. Future considerations could include further data collection from more participants in order to eliminate doubt that true changes are missed.

Conclusion

The results suggest that the more complex task may be a useful tool in recording and observing behavioural and neural changes following specific interventions. A future direction would be to couple this novel task with cervical spine manipulation to observe changes in neural processing and performance in participants with chronic subclinical neck pain.

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References

Angel, R., Roylls, C., & Weinrich, M. (1984). Cerebral Evoked Potentials and Somatosensory Perception. *Neurology, 34*, 123-126.

Byl, N., Merzenich, M., Cheung, S., Bedenbaugh, P., Nagarajan, S., & Jenkins, W. (1997). A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. *Physical Therapy, 77*(3), 269-284.

Cebolla, A., Palmero-Soler, E., Dan, B., & Cheron, G. (2011). Frontal phasic and oscillatory generators of the N30 somatosensory evoked potential. *NeuroImage, 54*(2), 1297-1306.

Classen, J., Liepert, J., Wise, S., Hallett, M., & Cohen, L. (1998). Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology, 79*(2), 1117-1123.

Cruccu, G., Aminoff, M., Curio, G., Guerit, J., Kakigi, R., Mauguiere, F., . . . Garcia-Larrea, L. (2008). Recommendations for the clinical use of somatosensory-evoked potentials. *Clinical neurophysiology, 119*(8), 1705-1719.

Desmond, J., & Fiez, J. (1998). Neuroimaging studies of the cerebellum: language, learning and memory. *Trends in Cognitive Sciences, 2*(9), 355-362.

Friston, K., Frith, C., Passingham, R., Liddle, P., & Frackowiak, R. (1992). Motor Practice and Neurophysiological Adaptation in the Cerebellum: A Positron Tomography Study. *Biological Sciences, 248*(1323), 223-228.

Fujii, M., Yamada, T., Aihara, M., Kokubun, Y., Noguchi, Y., Matsubara, M., & Malcolm, H. (1994). The effects of stimulus rates upon median, ulnar and radial nerve somatosensory evoked potentials. *Electroencephalography and Clinical Neurophysiology, 92*(6), 518-526.

Haavik Taylor, H., & Murphy, B. (2007a). Altered cortical integration of dual somatosensory input following the cessation of a 20 min period of repetitive muscle activity. *Experimental Brain Research, 178*(4), 488-498.

Haavik Taylor, H., & Murphy, B. (2007b). *Selective changes in intracortical facilitation and inhibition following repetitive voluntary movement.* Paper presented at the International Brain Research Organization World Congree of Neuroscience Motor Control Satellite Meeting, Darwin, Northern Territory, Australia.

Harrington, D., Lee, R., Boyd, L., Rapcsak, S., & Knight, R. (2004). Does the representation of time depend on the cerebellum? Effect of cerebellar stroke. *Brain, 127*, 561-574.

Ivry, R., Keele, S., & Diener, H. (1988). Dissociation of the lateral and medial cerebellum in movement itming and movement execution. *Experimental Brain Research, 73*, 167-180.

Jenkins, I., Brooks, D., Nixon, P., Frackowiak, R., & Passingham, R. (1994). Motor Sequence Learning: A Study with Positron Emission Tomography. *The Journal of Neuroscience, 14*(6), 3775-3790.

Kanovsky, P., Bares, M., & Rektor, I. (2003). The selective gating of the N30 cortical component of the somatosensory evoked potentials of median nerve is different in the mesial and dorsolateral frontal cortex: evidence from intracerebral recordings. *Clinical Neurophysiology, 114*(6), 981-991.

Logan, G. (1985). Skill and automaticity: Relations, implications, and future directions. *Canadian Journal of Psychology, 39*, 367-386.

Logan, G. (1988). Toward an Instance Theory of Automatization. *Psychological Review, 95*(4), 492-527.

Logan, G. (1990). Repetition Priming and Automaticity: Common Underlying Mechanisms? *Cognitive Psychology, 22*, 1-35.

Logan, G. (1992). Attention and Preattention in Theories of Automaticity. *The American Journal of Psychology, 105*(2), 317-339.

Manzano, G., Negrão, N., & Nóbrega, J. (1998). The N18 component of the median nerve SEP is not reduced by vibration. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 108*(5), 440-445.

Mauguiere, F., Allison, T., Babiloni, C., Buchner, H., Eisen, A., Goodin, D., . . . Nuwer, M. (1999). Somatosensory evoked potentials. The International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology - Supplement, 52*, 79-90.

Murphy, B., Taylor, H., Wilson, S., Knight, J., Mathers, K., & Schug, S. (2003). Changes in median nerve somatosensory transmission and motor output following transient deafferentation of the radial nerve in humans. *Clinical Neurophysiology, 114*(8), 1477-1488.

Murphy, B., Taylor, H., Wilson, S., Oliphant, G., & Mathers, K. (2003). Rapid reversible changes to multiple levels of the human somatosensory system following the cessation of repetitive contractions: a somatosensory evoked potential study. *Clinical Neurophysiology, 114*(8), 1531-1537.

Nixon, P., & Passingham, R. (2001). Predicting sensory events: The role of the cerebellum in motor learning. *Experimental Brain Research, 138*, 251-257.

Noel, P., Ozaki, I., & Desmedt, J. (1996). Origin of N18 and P14 far-fields of median nerve somatosensory evoked potentials studied in patients with a brain-stem lesion. *Electroencephalography and Clinical Neurophysiology, 98*(2), 167-170.

Nuwer, M., Aminoff, M., Desmedt, J., Eisen, A., Goodin, D., Matsuoka, S., . . . Vibert, J. (1994). IFCN recommended standards for short latency somatosensory evoked potentials. Report of an IFCN committee. International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology, 91*(1), 6.

Pascual-Leone, A., & Torres, F. (1993). Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. *Brain, 116*, 39-52.

Restuccia, D., Valeriani, M., Barba, C., Le Pera, D., Capecci, M., Filippini, V., & Molinari, M. (2001). Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions. *Brain, 124*(4), 757-768.

Rossi, S., della Volpe, R., Ginanneschi, F., Ulivelli, M., Bartalini, S., Spidalieri, R., & Rossi, A. (2003). Early somatosensory processing during tonic muscle path in humans: relation to loss of proprioception and motor 'defensive' strategies. *Clinical Neurophysiology, 114*(7), 1351-1358.

Tinazzi, M., Zanette, G., Polo, A., Volpato, D., Manganotti, P., Bonato, C., . . . Fiaschi, A. (1997). Transient deafferentation in humans induces rapid modulation of primary sensory cortex not associated with subcortical changes: a somatosensory evoked potential study. *Neuroscience Letters, 223*(1), 21-24.

Tinazzi, M., Zanette, G., Volpato, D., Testoni, R., Bonato, C., Manganotti, P., . . . Fiaschi, A. (1998). Neurophysiological evidence of neuroplasticity at multiple levels of the somatosensory system in patients with carpal tunnel syndrome. *Brain, 121*(9), 1785-1794.

Xu, D., Lui, T., Ashe, J., & Bushara, K. (2006). Role of the olivo-cerebellar system in timing. *Journal of Neuroscience, 26*, 5990-5995.

SECTION 4: MANUSCRIPT 2 -
THE EFFECT OF SPINAL MANIPULATION ON MOTOR LEARNING IN A COHORT OF PARTICIPANTS WITH SUBCLINICAL NECK PAIN

The effect of spinal manipulation on motor learning in a cohort of participants with subclinical neck pain

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Abstract

Background

There is a growing body of evidence to suggest that spinal dysfunction may affect central neural processing, potentially leading to maladaptive plastic changes. Previous work has demonstrated that spinal manipulation alters central nervous system excitability as well as sensory processing in subjects with subclinical neck pain (SCNP). SCNP is defined as recurring neck dysfunction such as stiffness and pain but for which the sufferers have not yet sought any treatment for. This study sought to investigate the immediate effects of spinal manipulation on CNS processing in SCNP as well as processing following a complex motor training task.

Methods

We recorded somatosensory evoked potentials (SEP) following median nerve stimulation before and after passive head movement, spinal manipulation and subsequently a motor training.

Results

There was a significant increase in the P22-N30 complex following passive head movement and N30-P40 complex following manipulation. Significant changes were observed in the cortical N20-P25 (increase) following the motor training task in the manipulation group. Behavioural data revealed significant main effects across all trials for response time (RT).

Conclusion

This work has shown a decrease in subcortical and increase in cortical SEP amplitudes following a cervical spine manipulation intervention in neck pain participants. It has also shown that a complex motor training task induces changes in neural processing, supporting previous work. The increase in amplitude of the N30-P40 SEP peak following motor learning for the manipulation group suggests that manipulation plays a modulatory role in afferent processing that takes place during early motor learning.

KEYWORDS: Cervical spine manipulation; somatosensory evoked potentials; motor training

Introduction

Despite being one of the most common treatments for back and neck pain, little is understood about the biological mechanisms for the efficacy of manual spinal manipulation. Neck pain has increased in prevalence over the years with an annual prevalence between 30% and 50% (Côté et al., 1998; Côté et al., 2004; Haldeman et al., 2010; Hogg-Johnson et al., 2009; Manchikanti et al., 2009). Neck pain is likely to be significantly underestimated in the literature as many individuals experience recurring neck dysfunction, stiffness and pain on a regular basis, but it is not yet severe enough to seek treatment (Haavik & Murphy, 2011).

Research in the area of neck pain and spinal dysfunction suggests that even mild dysfunction as evidenced by recurrent neck pain and stiffness may affect central neural processing, potentially leading to maladaptive plastic changes, which may explain how these disorders become and/or remain chronic (Falla et al., 2004; Haavik-Taylor & Murphy, 2007; Haavik & Murphy, 2012; Haavik Taylor & Murphy, 2006; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2010b; Michaelson et al., 2003; Murphy B et al., 2010). There is also evidence demonstrating that spinal manipulation alters central nervous system excitability, cognitive and sensory processing and motor output (Haavik-Taylor & Murphy, 2007; Herzog et al., 1999; Murphy et al., 1995). A growing body of evidence suggests that spinal manipulation may aid in the potential issues that arise with spinal dysfunction, having a positive neuromodulatory effect (Haavik & Murphy, 2012; Haavik Taylor & Murphy, 2008; Haavik Taylor & Murphy, 2010a, 2010b; Herzog et al., 1999; Murphy et al., 1995; Suter et al., 1999, 2000).

It is known that altered afferent input to the central nervous system (CNS) leads to changes in how it responds to subsequent input (Byl et al., 1997; Pascual-Leone & Torres, 1993; Tinazzi et al., 1997; Tinazzi et al., 1998). These changes can occur following increases and decreases in input (Byl et al., 1997) and can lead to both inhibition and facilitation of neural input. Thus, it is possible that the presence of subclinical neck pain may represent a form of altered afferent input which leads to central neural plastic changes by altering afferent input to the CNS.

The study of SMI has also increased dramatically within the last decade, with emerging evidence of maladaptive plastic changes in movement disorders such as overuse injuries and following repetitive movements (Byl et al., 1997; Classen et al., 1998; Haavik Taylor & Murphy, 2007a, 2007b; Kim et al., 2004; Murphy, Taylor, Wilson, Oliphant, et al., 2003). SMI is an essential process required when learning skills and performing new tasks. Impaired SMI may be useful in explaining injury in occupations with significant amounts of repetitive muscular activity. Although it appears that changes are essential for normal functioning, undesirable changes may also occur due to the plastic nature of the central nervous system. The plasticity of the brain refers to its ability to change based on experience and exposure to new tasks. If these maladaptive changes can be monitored and measured, a greater understanding of these changes may aid in better diagnostic tools and refinement of treatment options for patients with movement disorders, overuse injuries such as repetitive strain injury and other musculoskeletal syndromes such as vertebral dysfunction and pain.

It has been understood for a number of years that the cerebellum is a key structure involved in motor learning, balance and coordination, however, more recent evidence suggests more of a processing role in sensory processing in preparation for motor responses (Nixon & Passingham, 2001). Neural activity in pathways involving the cerebellum can be quantified using short latency somatosensory evoked potentials (SEP). SEPs are elicited by physiological or electrical stimulation of peripheral nerves and subsequent recording of the result neural activity through surface electrodes (Angel et al., 1984; Mauguiere et al., 1999). The amplitudes of various SEP peaks reflect processing of different neural structures. By combining SEP protocols with motor training paradigms, changes in neural processing resulting from motor training can be investigated (Angel et al., 1984). When coupled with treatment interventions such a spinal manipulation, there are various more degrees of interaction that may be observed, giving more insight to how altered afferent input modulates neural activity and how effective treatment may change the brains ability to process new motor skills. The use of SEPs combined with both an intervention and motor training paradigm will add to our understanding of how neck pain impacts early somatosensory processing, and could aid in the development of novel rehabilitative strategies.

Methods

Participants

Fourteen participants (five women and nine men), aged 19-29 years (mean age 22.4) participated in the cervical spine manipulation portion of this study (see Table 2 & 3), and thirteen aged-matched participants (three women and ten men), aged 19-28 years (mean age 22.2), participated in the passive head movement portion of this study. The study was a between-group experimental design. Participants performed the same complex motor learning sequence in both experiments. All participants consented to being treated by a certified chiropractor and were required to have chronic and recurring neck pain as determined through health history examination by the associated chiropractor of this study. Informed consent was obtained and the study was approved by the ethical committee at the University of Ontario Institute of Technology.

Participant no.	Gender	Age	Handedness
1	F	20	R
2	M	23	R
3	M	25	R
4	M	21	R
5	M	23	R
6	F	21	R
7	M	28	R
8	M	22	L
9	F	21	R
10	M	21	R
11	M	22	R
12	M	22	R
13	M	19	R

Table 2: Study participant age, gender and handedness details (passive head movement experiment)

Participant no.	Gender	Age	Handedness
1	F	21	R
2	F	19	R
3	F	21	R
4	M	25	R
5	M	22	L
6	F	19	R
7	M	21	R
8	M	29	R
9	M	21	R
10	M	21	R
11	M	29	R
12	M	23	R

13	M	20	R
14	F	22	R

Table 3: Study participant age, gender and handedness details (manipulation experiment)

Somatosensory Evoked Potentials

SEP recoding electrodes (1.8288m Traditional Lead, 10mm disc, 2mm hole gold cup EEG electrodes, Grass Technologies, An Astro-Med, Inc. Subsidiary, Rockland, MA) (impedance <5 kΩ) were placed according to the International Federation of Clinical Neurophysiologists (IFCN) recommendations. Recording electrodes were placed on the ipsilateral Erb's point, over C5 spinous process (Cv5), the anterior neck (tracheal cartilage), 2cm posterior to contralateral central C3/4 (Cc'), and a frontal cite (6cm anterior and 2cm contralateral to Cz) (F) (Rossi et al., 2003). The C5 spinous process was referenced to the trachea while all other electrodes were referenced to the ipsilateral earlobe. A 1.8288m Traditional Lead, 10mm disc, 2mm hole gold cup EEG electrode was also used as a ground, placed in the mouth of participants. Ag/AgCl conductive adhesive recording electrodes (MEDITRACE™ 130 by Ludlow Technical Products Canada Ltd., Mansfield, MA) (impedance <5 kΩ) were placed over the median nerve at wrist of the right hand with anode proximal.

SEPs were recorded at rates of 2.47Hz and 4.98Hz since the slow rate 2.47Hz does not lead to SEP peak attenuation (Fujii et al., 1994) while the fast rate 4.98Hz attenuates the N30 SEP peak resulting in the N24 SEP peak being accurately measurable (Fujii et al., 1994). Stimulus intensity varied between individuals and was increased until motor threshold was achieved which was defined as the lowest stimulation intensity that evoked a visible muscle contraction of the abductor pollicis brevis muscle.

Data collection

To minimize any movement of recording electrodes during the data recording sessions, participants were seated on a comfortable La-Z-Boy™ chair and instructed to remain as still and quiet as possible. Participants were discouraged from talking while SEPs recordings took place. During the SEP recordings, the lights in the room were turned off and participants' eyes were open.

SEP signals were amplified (gain 10,000), filtered (0.2-1000 Hz) and stored on a password protected computer for later retrieval. A total of 1500 sweeps were averaged per stimulation rate using a specifically written Signal® configuration (Cambridge Electronic Design, Cambridge, UK). SEP peak amplitudes were measured according to the IFCN guidelines (Cruccu et al., 2008). We identified and analyzed the following SEP components: the peripheral N9, the spinal N11 and N13, the far-field P14-18 complex, the parietal N20 (P14-N20 complex) and P25 (N20-P25 complex) and the frontal N24 (P22-N24 complex) and N30 (P22-N30 complex). SEPs were recorded before and after a passive head movement (PHM) or cervical spine manipulation (SM) intervention and again following a complex typing task (described in the previous article).

Cervical spine manipulation and passive head movement interventions

Cervical manipulation intervention

The SM intervention consisted of high velocity, low amplitude thrusts carried out by a registered chiropractor. During manipulation, the spine was laterally flexed, slightly rotated and extended. In order to ensure that manipulation was successful for individual subjects, the cervical spines of participants were checked after each adjustment to determine if the subsequent levels still required adjusting. Following the intervention, post-intervention dependent variables, SEPs, were collected, recorded and analyzed.

Passive head movement control

A control group with similar demographics including neck pain level participated in the PHM experiment since participants could not be exposed to the motor training task more than once. The control intervention consisted of a passive movement of the participant's head, carried out by the same chiropractor who performed the cervical adjustments in the manipulation intervention. The passive head movement control intervention involved the participant's head being passively laterally flexed, and slightly extended and rotated to a position that the chiropractor would normally manipulate the cervical spine, and then returned the participant's head back to a neutral position. This was repeated for both the left and right sides and performed prior to the complex motor training task from described in the previous article. Following the intervention, post-intervention dependent variables, SEPs, were collected, recorded and analyzed.

Data analysis

During data collection, the averaged waveform for each SEP peak was displayed in a separate window. Peak amplitudes were measured from peak to the proceeding peak form the averaged waveform. An inclusion criteria for data to be further analyzed was a change of less than 10% for the N9 SEP peak between pre and post trials. The N9 measures the peripheral afferent volley at the level of the brachial plexus. In order to measure changes in centrally generated SEP peaks following the intervention, the peripheral volley must remain stable. If a participants N9 SEP peak differed by more than 10%, their data was not included in the final analysis. Based on the inclusion criteria, two participants were removed from the passive head movement study while one participant was removed from the manipulation study. The final analysis included eleven participants in the passive head movement experiment and thirteen participants in the manipulation experiment.

SEP peak amplitudes were normalized in order to compare the percentage difference following the interventions and following motor training. All pre SEP peak amplitudes were normalized to 1 and subsequent post amplitudes expressed relative to 1 and were exported to IBM SPSS Statistics where two separate repeated measures analysis of variance (ANOVA) were performed for both the passive head movement and manipulation interventions. Each ANOVA compared the pre-intervention amplitudes with the post-intervention amplitudes and the pre-motor training amplitudes with the post-motor training amplitudes. Behavioural data collected across the two experiments for the motor training task were also collected and analyzed. Two separate ANOVAs were performed in IBM SPSS Statistics for the manipulation and passive head movement groups, each with factors time (pre and post) and task (simple vs. complex) for both reaction time (RT) and accuracy (ACC). Statistical significance was set at $P \leq 0.05$.

Results

Analysis revealed a significant increase of 3.8% in the N20-P25 complex following cervical spine manipulation [F = (12,2) 6.61; p = 0.02]. Figure 8 depicts the amount of change in SEP peak amplitudes relative to baseline + standard deviation (SD) following the passive head movement and manipulation interventions. The repeated measures ANOVA revealed a statistically significant increase of 18.0% in the P22-N30 complex following motor training for the passive head movement group [F = (10,2) 8.87; p = 0.01]. Significant main effects were also found in the N30-P40 complex with an increase by 12.6% following motor training in the manipulation group [*F* = (12,2) 4.68; *p* = 0.05]. Changes in peak amplitudes relative to baseline following the motor training task are displayed in Figure 9. Figure 10 depicts pre and post-motor training as well as pre and post-intervention SEP peaks for one individual participant.

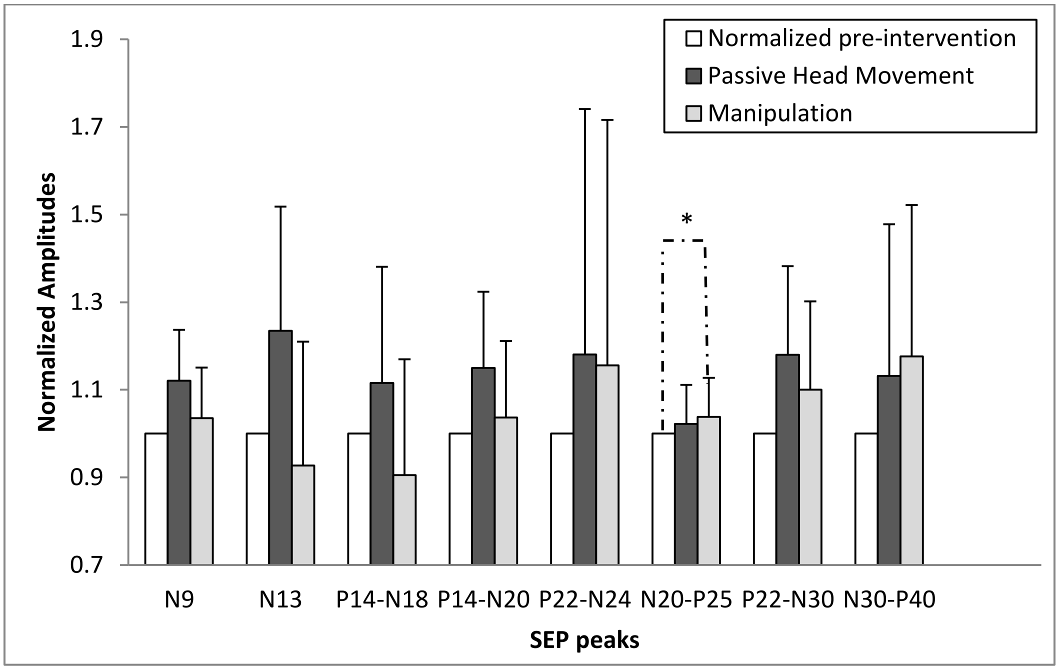

Figure 6: Normalized amplitude changes following the interventions + SD.
Pre-values were normalized to 1. * indicates significant changes comparing the pre and post SEP peak amplitudes for both interventions.

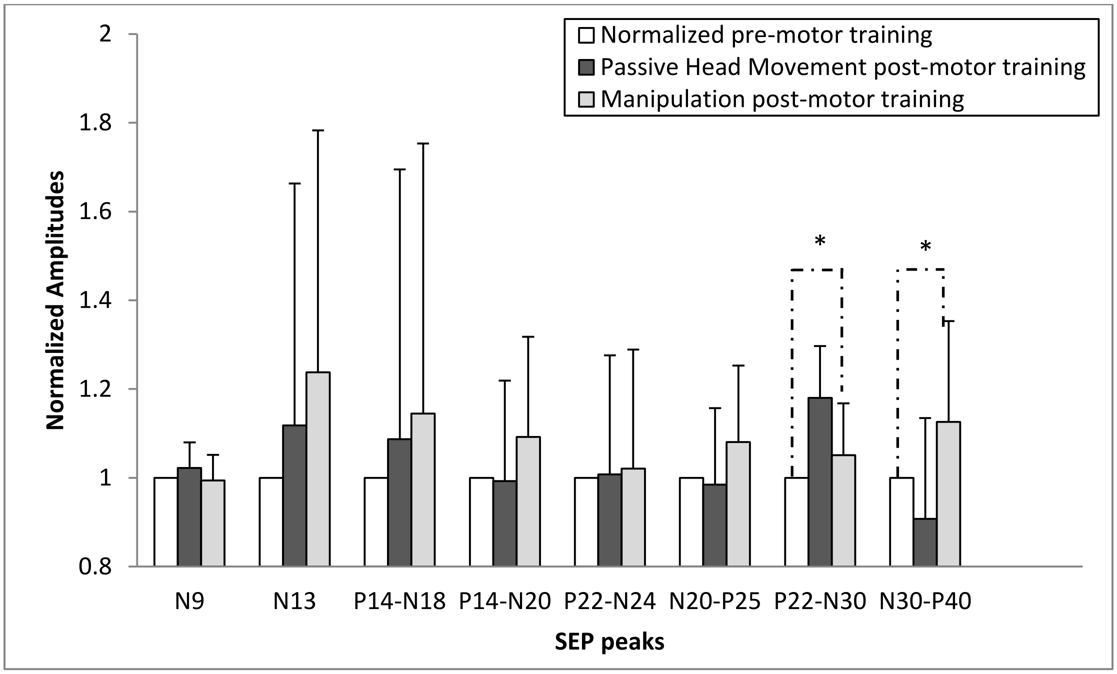

Figure 7: Normalized amplitude changes following motor training + SD.
Pre-values were normalized to 1. * indicates significant changes comparing the pre and post-motor training SEP peak amplitudes for both interventions.

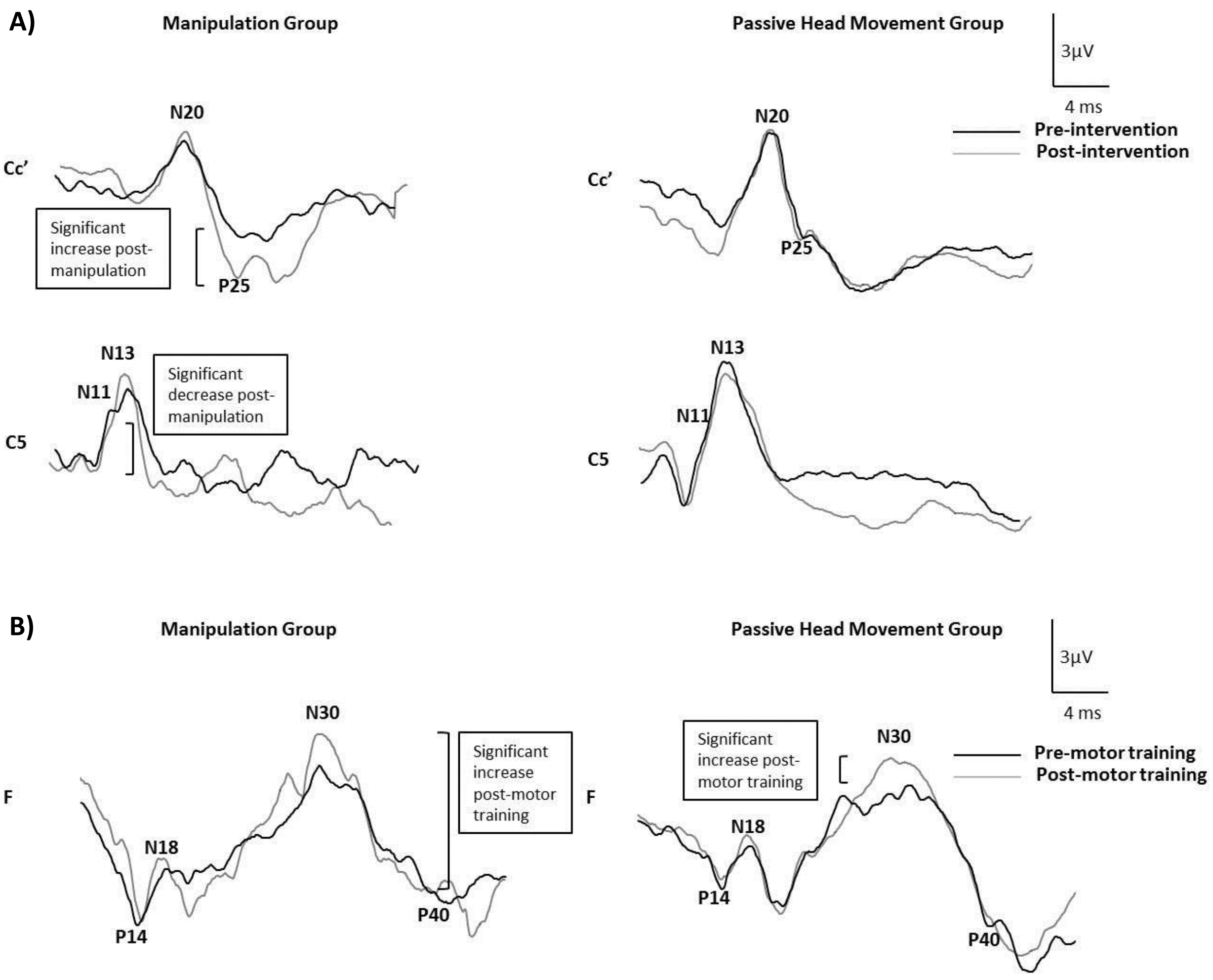

Figure 8: Significant SEP peak changes for one representative participant following (A) the PHM and SM intervention and (B) the motor training intervention.
Note the significant increase in the N30-P40 complex following motor training for the manipulation group as well as the increase in the P22-N30 complex for the passive head movement group. A significant increase was also found for the N20-P25 complex and decrease for the N11 post-manipulation.

Behavioural data revealed significant main effects across all trials for RT specific to time [*F* = 77.34 (12,1); $p < 0.001$]. No significant effects were found for accuracy across all trials. Figure 11 and 12 show the mean ACC and RT changes across all trials.

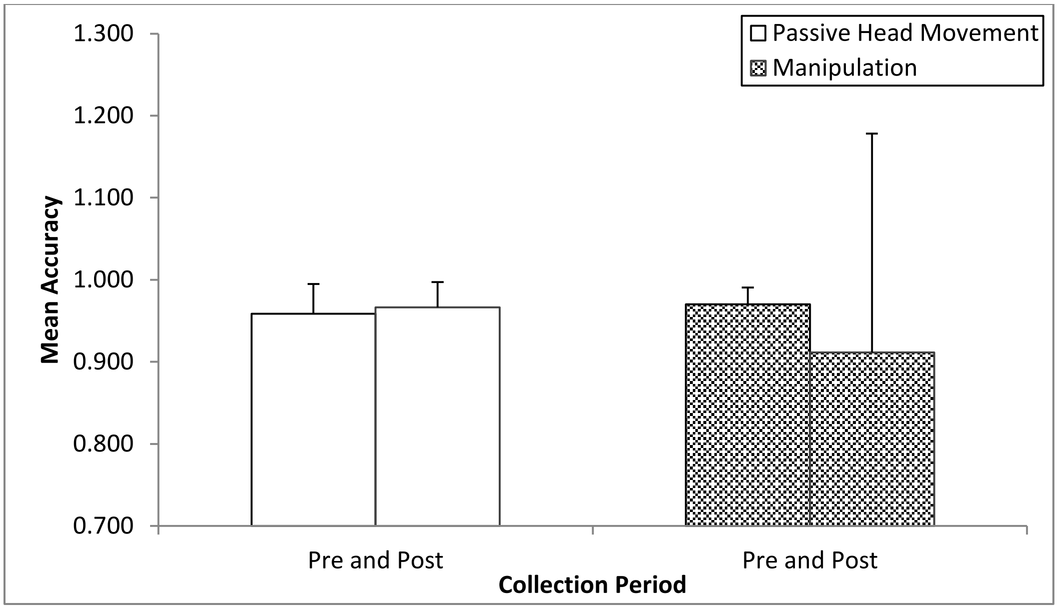

Figure 9: Mean accuracy (ACC).
The mean accuracy is shown for time (pre and post) and intervention (passive head movement and manipulation).

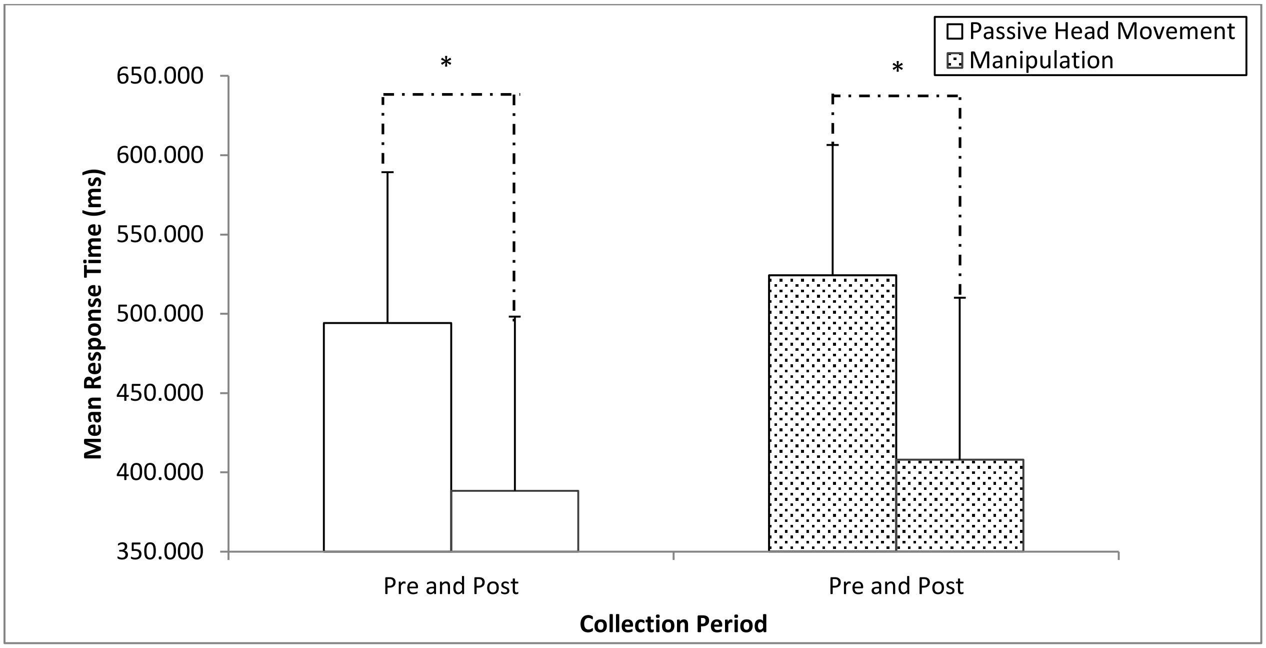

Figure 10: Response time (RT).
The improvement in response time is shown over time for both interventions. There were significant main effects observed in response time over time but not specific to task. This indicates that participant response times were improved following the motor training task for both interventions.

Discussion

It is known that altered afferent input to the central nervous system (CNS) leads to changes in how it responds to subsequent input (Byl et al., 1997; Pascual-Leone & Torres, 1993; Tinazzi et al., 1997; Tinazzi et al., 1998). These changes can occur following increases and decreases in input (Byl et al., 1997) and can lead to both inhibition and facilitation of neural input. Thus, it is possible that the presence of subclinical neck pain may represent a form of altered afferent input which leads to central neural plastic changes by altering afferent input to the CNS.

The study of SMI has also increased dramatically within the last decade, with emerging evidence of maladaptive plastic changes in movement disorders such as overuse injuries and following repetitive movements (Byl et al., 1997; Classen et al., 1998; Haavik Taylor & Murphy, 2007a, 2007b; Kim et al., 2004; Murphy, Taylor, Wilson, Oliphant, et al., 2003). SMI is an essential process required when learning skills and performing new tasks. Impaired SMI may be useful in explaining injury in occupations with significant amounts of repetitive muscular activity. Although it appears that changes are essential for normal functioning, undesirable changes may also occur due to the plastic nature of the central nervous system. The plasticity of the brain refers to its ability to change based on experience and exposure to new tasks. If these maladaptive changes can be monitored and measured, a greater understanding of these changes may aid in pre-diagnostics and development of appropriate treatment options for patients with movement disorders, overuse injuries such as repetitive strain injury and other musculoskeletal syndromes such as vertebral dysfunction and pain.

Our results have shown attenuation an increase in amplitude in cortical SEP complexes. The only significant changes observed in the passive head movement group were observed within the cortical P22-N30 complex. Recently, authors have suggested that the N30 SEP component is related to a complex neural loop connecting various SMI regions including the basal ganglia, thalamus, premotor areas and primary motor cortex (Cebolla et al., 2011; Kanovsky et al., 2003; Rossi et al., 2003). Similar to findings from the previous article, the significant increase in the P22-N30 complex amplitude was found following the complex motor training task. However, this result was only observed in the passive head movement group and not the manipulation group. A possible explanation is that neck pain results in altered afferent input since information is processed on a distorted "map" of the body. Manipulation corrects this problem, resulting in a change in neural processing. This result corroborates previous work demonstrating greater changes in the P22-N30 complex following more complex motor training tasks compared to a simple repetitive typing task (Bossé, 2012). As expected from the first study, there were no other changes following passive head movement. All other significant changes occurred following manipulation, demonstrating its effect in altering neural processing in patients with neck pain.

The cortical N20-P25 complex, representing a group of neurons within Brodmann's area 1 of the primary somatosensory cortex (Mauguiere et al., 1999) increased significantly following manipulation. This finding suggests an increase in activation of neurons within Brodmann's area 1, indicating increased activation within the primary somatosensory cortex. The demonstration of altered processing that we observed following manipulation suggests that plastic changes along the neural pathway occur immediately following manipulation, affecting both cortical and subcortical regions.

The typing task induced cortical changes for both interventions. As previously discussed; the P22-N30 complex increased significantly for the passive head movement group while the N30-P40 complex in the manipulation group increased significantly following the complex typing task. The N30-P40 results indicate that there were SMI effects following motor training that were attributable to the manipulation. For the behavioural data, our results showed significant main effects for RT for time, not specific to the intervention. This verifies results from the previous study indicating that the motor training resulted in participants learning to respond quicker and thus justifies its use in this study to evaluate the efficacy of cervical spine manipulation on motor learning. There were no significant changes observed in accuracy. This may be explained by the high pre-motor training leaving little room for improvement as well as participant feedback that the task could have been more engaging. Although accuracy and response time were the same for both groups, the presence of peak amplitude changes suggests that there was increased processing in those specific brain regions, demonstrating the modulatory effects of manipulation on brain activity and potentially how the brain processes new task information.

Strengths

Our findings are unique for two reasons. The results showed changes in cortical peaks following manipulation only. The second is that this is the first study of its kind to combine the effects of cervical spine manipulation on neck pain participants with a complex motor training paradigm to measure the effects of the intervention on neural processing. Previous work by

Murphy et al. has looked at the effects of a simple repetitive typing tasks alone (Haavik Taylor & Murphy, 2007a, 2007b; Haavik Taylor & Murphy, 2009; Murphy, Taylor, Wilson, Oliphant, et al., 2003) as well as manipulation (Haavik-Taylor & Murphy, 2007; Haavik Taylor & Murphy, 2006; Haavik Taylor & Murphy, 2010a, 2010b; Murphy B et al., 2010). However, the combination of a complex motor training task and manipulation has yet to be investigated, making this a novel study. These findings are important as they suggest that SCNP can influence the way in which the brain processes information during motor learning. This is of great potential importance for athletes, musicians and industries if the presence of SCNP affects the response to motor learning.

Limitations

A limitation of this study is the possibility of a type II error for the changes in some SEP peaks. Almost all SEP peak amplitudes seemed to increase following the passive head movement, while decreases were seen in the N13 and P14-N18 SEP complexes following manipulation. This suggests that these decreases may represent genuine effects of the manipulation, suggesting that more participants should be tested to determine whether these changes persist. Another issue is that while the complex task resulted in improved response time for both the passive head movement and manipulation groups, there were no improvements in accuracy. Future work should explore variations of this task and utilize motor learning paradigms which measure retention and transfer to determine if there is any correlation between changes in SEP peak amplitudes and subsequent retention and transfer of motor learning.

Conclusion

This work has shown an increase in cortical SEP amplitudes following a cervical spine manipulation intervention in neck pain participants. It has also shown that a complex motor training task induces changes in neural processing, supporting previous work. The increase in processing of the N30-P40 SEP peak following motor learning for the manipulation group suggests that manipulation plays a modulatory role in afferent processing.

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References

Afifi, A., & Bergman, R. (2005). *Functional Neuroanatomy: Text and Atlas* (2nd ed.): The McGraw-Hill Companies.

Angel, R., Roylls, C., & Weinrich, M. (1984). Cerebral Evoked Potentials and Somatosensory Perception. *Neurology, 34*, 123-126.

Apps, R., & Garwicz, M. (2005). Anatomical and physiological foundations of cerebellar information processing. *Nature Reviews Neuroscience, 6*(4), 297-311.

Bloedel, J. (2004). Task-dependent role of the cerebellum in motor learning. *Progress in Brain Research, 143*, 319-329.

Bossé, J. (2012). *Motor Training and Cervical Spine Manipulation: Effects on Sensorimotor Integration.* Masters of Health Sciences, University of Ontario Institute of Technology.

Byl, N., Merzenich, M., Cheung, S., Bedenbaugh, P., Nagarajan, S., & Jenkins, W. (1997). A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. *Physical Therapy, 77*(3), 269-284.

Carroll, L. J., Hogg-Johnson, S., Van Der Velde, G., Haldeman, S., Holm, L. W., Carragee, E. J., . . . Peloso, P. M. (2008). Course and prognostic factors for neck pain in the general population. *European Spine Journal, 17*, 75-82.

Cebolla, A., Palmero-Soler, E., Dan, B., & Cheron, G. (2011). Frontal phasic and oscillatory generators of the N30 somatosensory evoked potential. *NeuroImage, 54*(2), 1297-1306.

Classen, J., Liepert, J., Wise, S., Hallett, M., & Cohen, L. (1998). Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology, 79*(2), 1117-1123.

Côté, P., Cassidy, J., & Carroll, L. (1998). The Saskatchewan health and back pain survey: the prevalence of neck pain and related disability in Saskatchewan adults. *Spine, 23*(15), 1689-1698.

Côté, P., Cassidy, J., & Carroll, L. (2001). The treatment of neck and low back pain: who seeks care? who goes where? *Medical Care, 39*(9), 956-967.

Côté, P., Cassidy, J., Carroll, L., & Kristman, V. (2004). The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain, 112*(3), 267-273.

Cowan, N. (2000). The magical number 4 in short-term memory: A reconsideration of mental storage capacity. *Behavioural and Brain Sciences, 24*, 87-185.

Craig, J. (1985). Tactile pattern perception and its perturbations. *Journal of Acoustical Society of America, 77*(1), 238-246.

Criscimagna-Hemminger, S., Bastian, A., & Shadmehr, R. (2010). Size of error affects cerebellar contributions to motor learning. *Journal of neurophysiology, 103*(4), 2275-2284.

Cruccu, G., Aminoff, M., Curio, G., Guerit, J., Kakigi, R., Mauguiere, F., . . . Garcia-Larrea, L. (2008). Recommendations for the clinical use of somatosensory-evoked potentials. *Clinical neurophysiology, 119*(8), 1705-1719.

Dawson, G. (1947). Cerebral responses to electrical stimulation of peripheral nerve in man. *Journal of Neurology, Neurosurgery & Psychiatry, 10*(3), 134-140.

Desmedt, J. (1988). Somatosensory evoked potentials *Human Event-Related Potentials* (Picton ed., pp. 245-360). Amsterdam: Elsevier.

Desmedt, J., & Cheron, G. (1981). Non-cephalic reference recording of early somatosensory potentials to finger stimulation in adult or aging normal: differentiation of widespread N18 and contralateral N20 from the prerolandic p22 and N30 components. *Electroencephalography and Clinical Neurophysiology, 52*(6), 553-570.

Desmond, J., & Fiez, J. (1998). Neuroimaging studies of the cerebellum: language, learning and memory. *Trends in Cognitive Sciences, 2*(9), 355-362.

Di Lazzaro, V., Molinari, M., Restuccia, D., Leggio, M., Nardone, R., Fogli, D., & Tonali, P. (1994). Cerebro-cerebellar interactions in man: neurophysiological studies in patients with focal cerebellar lesions. *Electroencephalography and Clinical Neurophysiology, 93*, 27-34.

Di Lazzaro, V., Restuccia, D., Molinari, M., Leggio, M., Nardone, R., Fogli, D., & Tonali, P. (1994). Excitability of the motor cortex to magnetic stimulation in patients with cerebellar lesions. *Journal of Neurology, Neurosurgery & Psychiatry, 57*, 108-110.

Donders, F. (1969). On the speed of mental processes. In W. Koster (Ed.), *Attention and performance II*. Amsterdam: North-Holland.

Donoghue, J., Hess, G., & Sanes, J. (1996). Substrates and mechanisms for learning in motor cortex. In J. Bloedel, T. Ebner & S. Wise (Eds.), *Acquisition of Motor Behavior in Vertebrates* (pp. 363–386). Cambridge, MA: MIT Press.

Ebner, T., & Pasalar, S. (2008). Cerebellum Predicts the Future Motor State. *Cerebellum, 7*(4), 583-588.

Falla, D., Bilenkij, G., & Jull, G. (2004). Patients with chronic neck pain demonstrate altered patterns of muscle activation during performance of a functional upper limb task. *Spine, 29*(13), 1436.

Fine, E., Ionita, C., & Lohr, L. (2002). The history of the development of the cerebellar examination. *Seminars in Neurology, 22*, 375-384.

Friston, K., Frith, C., Passingham, R., Liddle, P., & Frackowiak, R. (1992). Motor Practice and Neurophysiological Adaptation in the Cerebellum: A Positron Tomography Study. *Biological Sciences, 248*(1323), 223-228.

Fujii, M., Yamada, T., Aihara, M., Kokubun, Y., Noguchi, Y., Matsubara, M., & Malcolm, H. (1994). The effects of stimulus rates upon median, ulnar and radial nerve somatosensory evoked potentials. *Electroencephalography and Clinical Neurophysiology, 92*(6), 518-526.

Gasbarri, A., Pompili, A., Pacitti, C., & Cicirata, F. (2003). Comparative effects of lesions to the ponto-cerebellar and olivo-cerebellar pathways on motor and spatial learning in the rat. *Neuroscience, 116*(4), 1131-1140.

Grant, S., & Logan, G. (1993). The loss of repetition priming and automaticity over time as a function of degree of intial learning. *Memory & Cognition, 21*(5), 611-618.

Guadagnoli, M., & Lee, T. (2004). Challenge Point: A Framework for Conceptualizing the Effects of Various Practice Conditions in Motor Learning. *Journal of Motor Behavior, 36*(2), 212-224.

Haavik-Taylor, H., & Murphy, B. (2007). Cervical spine manipulation alters sensorimotor integration: a somatosensory evoked potential study. *Clinical Neurophysiology, 118*(2), 391-402.

Haavik, H., & Murphy, B. (2011). Subclinical Neck Pain and the Effects of Cervical Manipulation on Elbow Joint Position Sense. *Journal of manipulative and physiological therapeutics, 34*(2), 88-97.

Haavik, H., & Murphy, B. (2012). The role of spinal manipulation in addressing disordered sensorimotor integration and altered motor control. *Journal of Electromyography and Kinesiology*. doi: 10.1016/j.jelekin.2012.02.012

Haavik Taylor, H., & Murphy, B. (2006). *The effect of cervical spine manipulation on the ability to integrate somatosensory input following repetitive movements.* Paper presented at the Australian Neuroscience Society Annual Meeting, Sydney.

Haavik Taylor, H., & Murphy, B. (2007a). Altered cortical integration of dual somatosensory input following the cessation of a 20 min period of repetitive muscle activity. *Experimental Brain Research, 178*(4), 488-498.

Haavik Taylor, H., & Murphy, B. (2007b). *Selective changes in intracortical facilitation and inhibition following repetitive voluntary movement.* Paper presented at the International Brain Research Organization World Congree of Neuroscience Motor Control Satellite Meeting, Darwin, Northern Territory, Australia.

Haavik Taylor, H., & Murphy, B. (2008). Altered sensorimotor integration with cervical spine manipulation. *Journal of Manipulative and Physiological Therapeutics, 31*(2), 115-126.

Haavik Taylor, H., & Murphy, B. (2009). *Selective changes in cerebellar-cortical processing following motortraining*. Paper presented at the Australian Neuroscience Society 29th Annual Meeting, Canberra, Australia.

Haavik Taylor, H., & Murphy, B. (2010a). Altered central integration of dual somatosensory input after cervical spine manipulation. *Journal of manipulative and physiological therapeutics, 33*(3), 178-188.

Haavik Taylor, H., & Murphy, B. (2010b). The effects of spinal manipulation on central integration of dual somatosensory input observed after motor training: a crossover study. *Journal of manipulative and physiological therapeutics, 33*(4), 261-272.

Haldeman, S., Carroll, L., & Cassidy, J. D. (2010). Findings from the bone and joint decade 2000 to 2010 task force on neck pain and its associated disorders. *Journal of Occupational and Environmental Medicine, 52*(4), 424.

Harrington, D., Lee, R., Boyd, L., Rapcsak, S., & Knight, R. (2004). Does the representation of time depend on the cerebellum? Effect of cerebellar stroke. *Brain, 127*, 561-574.

Hauptmann, B., & Karni, A. (2002). From primed to learn: the saturation of repetition priming and the induction of long-term memory. *Cognitive Brain Research, 13*, 313-322.

Herzog, W., Scheele, D., & Conway, P. (1999). Electromyographic responses of back and limb muscles associated with spinal manipulative therapy. *Spine, 24*(2), 146-153.

Hogg-Johnson, S., Van Der Velde, G., Carroll, L., Holm, L., Cassidy, J., Guzman, J., . . . Carragee, E. (2009). The Burden and Determinants of Neck Pain in the General Population:: Results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine, 33*(4S), S39-S51.

Holmes, G. (1939). The cerebellum of man. *Brain, 62*, 1-30.

Hoy, D. G., Protani, M., De, R., & Buchbinder, R. (2010). The epidemiology of neck pain. *Best Practice & Research Clinical Rheumatology, 24*, 783-792.

Ide, J. S., & Li, C. R. (2011). A cerebellar thalamic cortical circuit for error-related cognitive control. *NeuroImage, 54*, 455-464.

Ivry, R., Keele, S., & Diener, H. (1988). Dissociation of the lateral and medial cerebellum in movement itming and movement execution. *Experimental Brain Research, 73*, 167-180.

Jenkins, I., Brooks, D., Nixon, P., Frackowiak, R., & Passingham, R. (1994). Motor Sequence Learning: A Study with Positron Emission Tomography. *The Journal of Neuroscience, 14*(6), 3775-3790.

Kandel, E., Schwartz, J., & Jessell, T. (2000). *Principles of Neural Science* (4th ed.). New York: McGraw-Hill Professional Publishing.

Kanovsky, P., Bares, M., & Rektor, I. (2003). The selective gating of the N30 cortical component of the somatosensory evoked potentials of median nerve is different in the mesial and dorsolateral frontal cortex: evidence from intracerebral recordings. *Clinical Neurophysiology, 114*(6), 981-991.

Kawashima, R., Okuda, J., Umetsu, A., Sugiura, M., Inoue, K., Suzuki, K., . . . Yamadori, A. (2000). Human Cerebellum Plays an Important Role in Memory-Timed Finger Movement: An fMRI Study. *Journal of Neurophysiology, 83*, 1079-1087.

Kim, D., Shin, M., Lee, K., Chu, K., Woo, S., Kim, Y., . . . Roh, J. (2004). Musical training induced functional reorganization of the adult brain: Functional magnetic resonance imaging and transcranial magnetic stimulation study on amateur string players. *Human Brain Mapping, 23*(4), 188-199.

Laforce, R., & Doyon, J. (2001). Distinct Contribution of the Striatum and Cerebellum to Motor Learning. *Brain and Cognition, 45*(2), 189-211.

Lalanne, K., Lafond, D., & Descarreaux, M. (2009). Modulation of the flexion-relaxation response by spinal manipulative therapy: a control group study. *Journal of Manipulative and Physiological Therapeutics, 32*(3), 203-209.

Leggio, M., Tedesco, A., Chiricozzi, F., Clausi, S., Orsini, A., & Molinari, M. (2008). Cognitive sequencing impairment in patients with focal or atrophic cerebellar damage. *Brain, 131*, 1332-1343.

Logan, G. (1985). Skill and automaticity: Relations, implications, and future directions. *Canadian Journal of Psychology, 39*, 367-386.

Logan, G. (1988). Toward an Instance Theory of Automatization. *Psychological Review, 95*(4), 492-527.

Logan, G. (1990). Repetition Priming and Automaticity: Common Underlying Mechanisms? *Cognitive Psychology, 22*, 1-35.

Logan, G. (1992). Attention and Preattention in Theories of Automaticity. *The American Journal of Psychology, 105*(2), 317-339.

Logan, G. (1995). The Weibull Distribution, the Power law, and the Instance Theory of Automaticity. *Psychological Review, 102*(4), 751-756.

Lundy-Ekman, L. (2007). *Neuroscience: Fundamentals for Rehabilitation* (3rd ed.). St. Louis, MI: Saunders Elsevier.

Manchikanti, L., Singh, V., Datta, S., Cohen, S. P., & Hirsch, J. A. (2009). Comprehensive Review of Epidemiology, Scope, and Impact of Spinal Pain. *Pain Physician, 12*, E35-E70.

Manto, M. (2005). The wide spectrum of spinocerebellar ataxias. *Cerebellum, 4*, 2-6.

Manto, M., & Bastian, A. J. (2007). Cerebellum and the deciphering of motor coding. *The Cerebellum, 6*, 3-6.

Manzano, G., Negrão, N., & Nóbrega, J. (1998). The N18 component of the median nerve SEP is not reduced by vibration. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 108*(5), 440-445.

Manzoni, D. (2005). The cerebellum may implement the appropriate coupling of sensory inputs and motor responses: evidence from vestibular physiology. *The Cerebellum, 4*(3), 178-188.

Manzoni, D. (2007). The cerebellum and sensorimotor coupling: looking at the problem from the perspective of vestibular reflexes. *The Cerebellum, 6*(1), 24-37.

Mauguiere, F., Allison, T., Babiloni, C., Buchner, H., Eisen, A., Goodin, D., . . . Nuwer, M. (1999). Somatosensory evoked potentials. The International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology - Supplement, 52*, 79-90.

Michaelson, P., Michaelson, M., Jaric, S., Latash, M., Sjölander, P., & Djupsjöbacka, M. (2003). Vertical posture and head stability in patients with chronic neck pain. *Journal of Rehabilitation Medicine, 35*(5), 229-235.

Miller, G. (1956). The Magical Number Seven, Plus or Minus Two: Some Limits on Our Capacity for Processing Information. *The Psychological Review, 63*, 81-97.

Millers, D. (2007). *How Our Brain Works: The Construction and Functionality of Your Brain Presented and Explained*: iUniverse.

Molinari, M., Filippini, V., & Leggio, M. (2002). Neuronal plasticity of interrelated cerebellar and cortical networks. *Neuroscience, 111*(4), 863-870.

Molinari, M., Leggio, M., & Thaut, M. (2007). The cerebellum and neural networks for rhythmic sensorimotor synchronization in the human brain. *The Cerebellum, 6*(1), 18-23.

Moulton, E., Schmahmann, J., Becerra, L., & Borsook, D. (2010). The cerebellum and pain: integrator or active participator? *Brain Research Reviews, 65*, 14-27.

Murase, N., Kaji, R., Shimazu, H., Katayama-Hirota, M., Ikeda, A., Kohara, N., . . . Rothwell, J. (2000). Abnormal premovement gating of somatosensory input in writer's cramp. *Brain, 123*(9), 1813-1829.

Murphy, B., Bossé, J., & Daligadu, J. (2008). *The Effect of Repetitive Typing on Cerebellar Evoked Potentials.* Paper presented at the University of Ontario Summer Research Conference, University of Ontario Institute of Technology in Oshawa, Ontario, Canada.

Murphy, B., Dawson, N., & Slack, J. (1995). Sacroiliac joint manipulation decreases the H-reflex. *Electromyography and Clinical Neurophysiology, 35*(2), 87-94.

Murphy, B., Marshall, P., & Taylor, H. (2010). In Press: The cervical flexion-relaxation ratio: reproducibility and comparison between chronic neck pain patients and controls. *Spine*.

Murphy, B., Taylor, H., Wilson, S., Knight, J., Mathers, K., & Schug, S. (2003). Changes in median nerve somatosensory transmission and motor output following transient deafferentation of the radial nerve in humans. *Clinical Neurophysiology, 114*(8), 1477-1488.

Murphy, B., Taylor, H., Wilson, S., Oliphant, G., & Mathers, K. (2003). Rapid reversible changes to multiple levels of the human somatosensory system following the cessation of repetitive contractions: a somatosensory evoked potential study. *Clinical Neurophysiology, 114*(8), 1531-1537.

Murphy, B., Taylor, H. H., & Marshall, P. W. (2010). The Effect of Spinal Manipulation on the Efficacy of a Rehabilitation Protocol for Patients With Chronic Neck Pain: A Pilot study. *Journal of Manipulative and Physiological Therapeutics, 33*(3), 168-177.

Nixon, P., & Passingham, R. (2001). Predicting sensory events: The role of the cerebellum in motor learning. *Experimental Brain Research, 138*, 251-257.

Noel, P., Ozaki, I., & Desmedt, J. (1996). Origin of N18 and P14 far-fields of median nerve somatosensory evoked potentials studied in patients with a brain-stem lesion. *Electroencephalography and Clinical Neurophysiology, 98*(2), 167-170.

Nuwer, M., Aminoff, M., Desmedt, J., Eisen, A., Goodin, D., Matsuoka, S., . . . Vibert, J. (1994). IFCN recommended standards for short latency somatosensory evoked potentials. Report of an IFCN committee. International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology, 91*(1), 6.

Parsons, L., Bower, J., Gao, J., Xiong, J., Li, J., & Fox, P. (1997). Lateral cerebellar hemispheres actively support sensory acquisition and discrimination rather than motor control. *Learning & Memory, 4*, 49-62.

Pascual-Leone, A., & Torres, F. (1993). Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. *Brain, 116*, 39-52.

Poldrack, R., & Gabrieli, J. (2001). Characterizing the neural mechanisms of skill learning and repetition priming. Evidence from mirror reading. *Brain, 124*, 67-82.

Ramnani, N. (2006). The primate cortico-cerebellar system: anatomy and function. *Nature Reviews: Neuroscience, 7*, 511-522.

Ramnani, N., Behrens, T. E. J., Johansen-Berg, H., Richter, M. C., Pinsk, M. A., Andersson, J. L. R., . . . Thompson, A. J. (2006). The evolution of prefrontal inputs to the cortico-pontine system: diffusion imaging evidence from Macaque monkeys and humans. *Cerebral Cortex, 16*(6), 811-818.

Restuccia, D., Valeriani, M., Barba, C., Le Pera, D., Capecci, M., Filippini, V., & Molinari, M. (2001). Functional changes of the primary somatosensory cortex in patients with unilateral cerebellar lesions. *Brain, 124*(4), 757-768.

Richardson-Klavehn, A., & Bjork, R. (1988). Measures of Memory. *Annual Reviews of Psychology, 39*, 475-543.

Rossi, S., della Volpe, R., Ginanneschi, F., Ulivelli, M., Bartalini, S., Spidalieri, R., & Rossi, A. (2003). Early somatosensory processing during tonic muscle path in humans: relation to loss of proprioception and motor 'defensive' strategies. *Clinical Neurophysiology, 114*(7), 1351-1358.

Rovee-Collier, C. (1997). Dissociations in Infant Memory: Rethinking the Development of Implicit and Explicit Memory. *Psychological Review, 104*(3), 467-498.

Schacter, D. (1987). Implicit Memory: History and Current Status. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 13*(3), 501-518.

Schmahmann, J. (1991). An Emerging Concept: The Cerellar Contribution to Higher Function. *Archives of Neurology, 48*(11), 1178-1187.

Schmahmann, J. (1996). From Movement to Thought: Anatomic Substrates of the Cerebellar Contribution to Cognitive Processing. *Human Brain Mapping, 4*, 174-198.

Schmahmann, J. (1997). *The cerebellum and cognition* (Vol. 41). San Diego: Academic Press.

Schmahmann, J., Doyon, J., Toga, A., Petrides, M., & Evans, A. (2000). *MRI Atlas of the Human Cerebellum*. San Diego: Academic Press.

Schmahmann, J., & Pandyat, D. (1997). The cerebrocerebellar system. *International review of neurobiology, 41*, 31-60.

Schmidt, R., & Lee, T. (2011). *Motor Control and Learning: A Behavioural Emphasis* (5th ed.). Windsor: Human Kinetics.

Schneider, W., & Shiffrin, R. (1977). Controlled and Automatic Human Processing: I. Detection, Search, and Attention. *Psychological Review, 84*, 1-66.

Shaffer, L. (1975). Multiple attention in continuous verbal tasks. *Attention and performance, 5*, 157-167.

Shiffrin, R., & Schneider, W. (1977). Controlled and Automatic Human Information Processing: II. Perceptual Learning, Automatic Attending, and a General Theory. *Psychological Review, 84*(2), 127-190.

Snell, R. (1997). *Clinical neuroanatomy for medical students* (4th ed.). Philadelphia, PA: Lippincott-Raven Publishers.

Soldan, A., Habeck, C., Gazes, Y., & Stern, Y. (2010). Neural mechanisms of repetition priming of familiar and globally unfamiliar visual objects. *Brain Research, 1343*, 122-134.

Sonoo, M., Sakuta, M., Shimpo, T., Genba, K., & Mannen, T. (1991). Widespread N18 in median nerve SEP is preserved in a pontine lesion. *Electroencephalography and Clinical Neurophysiology, 80*(3), 238-240.

Sperling, G. (1960). The infromation available in brief visual presentations. *Psychological Monographs: General and Applied, 74*(11), 1-29.

Stoodley, C., & Schmahmann, J. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *Neuroimage, 44*(2), 489-501.

Suter, E., McMorland, G., Herzog, W., & Bray, R. (1999). Decrease in quadriceps inhibition after sacroiliac joint manipulation in patients with anterior knee pain. *Journal of Manipulative and Physiological Therapeutics, 22*(3), 149-153.

Suter, E., McMorland, G., Herzog, W., & Bray, R. (2000). Conservative lower back treatment reduces inhibition in knee-extensor muscles: A randomized controlled trial. *Journal of Manipulative and Physiological Therapeutics, 23*(2), 76-80.

Tesche, C., & Karhu, J. (1997). Somatosensory evoked magnetic fields arising from sources in the human cerebellum. *Brain Research, 744*(1), 23-31.

Thach, W. (1972). Cerebellar output: Properties, synthesis and uses. *Brain Research, 40*, 89-102.

Timmann, D., Depper, J., Maschke, M., Kolb, F., Böring, D., Thilmann, A., & Diener, H. (2002). Motor deficits cannot explain impaired cognitive associative learning in cerebellar patients. *Neuropsychologia, 40*, 788-800.

Tinazzi, M., Fiaschi, A., Rosso, T., Faccioli, F., Grosslercher, J., & Aglioti, S. M. (2000). Neuroplastic Changes Related to Pain Occur at Multiple Levels of the Human Somatosensory System: A Somatosensory-Evoked Potentials Study in Patients with Cervical Radicular Pain. *The Journal of Neuroscience, 20*(24), 9277-9283.

Tinazzi, M., Zanette, G., Polo, A., Volpato, D., Manganotti, P., Bonato, C., . . . Fiaschi, A. (1997). Transient deafferentation in humans induces rapid modulation of primary sensory cortex not associated with subcortical changes: a somatosensory evoked potential study. *Neuroscience Letters, 223*(1), 21-24.

Tinazzi, M., Zanette, G., Volpato, D., Testoni, R., Bonato, C., Manganotti, P., . . . Fiaschi, A. (1998). Neurophysiological evidence of neuroplasticity at multiple levels of the somatosensory system in patients with carpal tunnel syndrome. *Brain, 121*(9), 1785-1794.

Verillo, R. (1985). Psychophysics of vibrotactile stimulation. *Journal of Acoustical Society of America, 77*(1), 225-232.

Walker Bone, K., Palmer, K., Reading, I., Coggon, D., & Cooper, C. (2004). Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. *Arthritis & Rheumatism, 51*(4), 642-651.

Wolf, U., Rapoport, M., & Schweizer, T. (2009). Evaluating the Affective Component of the Cerebellar Cognitive Affective Syndrome. *Journal of Neuropsychiatry and Clinical Neurosciences, 21*(3), 245-253.

Xu, D., Lui, T., Ashe, J., & Bushara, K. (2006). Role of the olivo-cerebellar system in timing. *Journal of Neuroscience, 26*, 5990-5995.

THESIS SUMMARY

Altered afferent input from dysfunctional neck joints has become a growing area of study. Research on the effects of cervical spine manipulation, specifically in individuals with subclinical neck pain; have revealed changes in neural processing attributable to the intervention. The effects of manipulation on motor learning in individuals with SCNP have not been investigated until now. Study 1 demonstrated that a complex motor training task induced greater changes in neural structures involved in sensorimotor integration as well as the cerebellum than did a simple repetitive typing task. The study also revealed significant decreases in response time for both tasks. The observed changes suggest that the more complex task may be a useful tool in recording and observing behavioural and neural changes following specific interventions. These preliminary results needed to be coupled with cervical spine manipulation to observe changes in neural processing and performance in participants with subclinical neck pain. Study 2 was the first to couple a novel complex motor training task with cervical spine manipulation and a passive head movement control. The most notable finding of this study was that significant decreases in subcortical peaks and increases in cortical peaks were observed following cervical spine manipulation. Additionally, increases in peaks related to SMI were observed for both groups. This finding corroborated with the findings from study 1 that the complex motor training task induced changes in neural processing specific to SMI.

These preliminary findings need to be extended in both laboratory and clinical studies, however, this research could significantly impact the development of pain management and preventative measures within work and home settings.

With the advancement in technology in school, home and work settings, there is an increase chance that individuals will suffer from acute, subclinical and chronic neck and back pain placing a large burden on the health care system and personal life as it may lead to decreased work place performance and limitations in daily activity. These studies suggest that even a single session of manipulation of dysfunctional joints results in alterations in processing of subsequent afferent input. They also suggest that a novel complex motor training task may be an aid in determining individual ability to learn new tasks with various neck joint impairments.

By better understanding the mechanisms by which various treatments can alter neck pain, preventative measures of neck pain can be put in place and save valuable time, money and resources in treating by catching it before it becomes chronic. These studies will help to provide data for further investigations of the efficacy of a complex motor training task with other interventions for neck pain on individual abilities to process and perform novel tasks.