Effects of Altered Sensory Input from the Neck on Cerebellar Function, Body Schema and Sensorimotor Integration

by

Julianne Baarbé

Submitted in Partial Fulfillment of the Requirements for the Degree Masters of Health Sciences at University of Ontario Institute of Technology, June 2015

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Abstract

Neck muscles have a high density of muscle spindle afferents and their input is critical for formulating the perception of head position relative to the body. Chronic alterations in afferent input from the neck may be studied in individuals with subclinical neck pain (SCNP), defined as non-severe recurrent neck pain lasting at least three months in the past year and testable on pain-free days so as to explore altered-afferent-input effects on cerebellar processing, upper extremity function and spatial awareness in the absence of pain. The first study tested participants with SCNP using transcranial magnetic stimulation to activate the cerebellar-thalamic-cortical circuit and produce cerebellar inhibition (CBI). SCNP participants were randomized to receive cervical manipulation or passive head movement (PHM), following which all participants completed a motor acquisition task. Healthy controls and SCNP participants who received manipulation showed significantly less CBI and improved motor performance whereas the SCNP group who received PHM showed no changes to CBI. The second study tested SCNP participants on upper extremity dart throwing. Three sets of ten darts were thrown at a slow-to-normal speed and three sets of ten darts were thrown at a fast speed. Compared to healthy participants, SCNP participants showed significantly greater elbow and forearm variability in motor selection, greater peak acceleration velocity of shoulder flexion-extension movement, and greater peak deceleration velocity of wrist movement. The third study looked at whether SCNP also impacted spatial awareness beyond an egocentric frame of reference, by measuring the response time to recognize objects which were rotated relative to their usual orientation. The SCNP group showed slower mental rotation at baseline and a smaller improvement when measured after four weeks (8.6%) in comparison to the healthy group (16.1%). These studies provide compelling evidence that chronic alterations in sensory input from the neck influences cerebellar integration leading to changes to upper extremity movement and spatial awareness of object orientation.

Keywords: altered sensory input, subclinical neck pain (SCNP), sensorimotor integration, cerebellum, body schema

Thesis supervisor: Professor Bernadette Murphy
Title: Head of Kinesiology, Professor, Faculty of Health Sciences
University of Ontario Institute of Technology

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.

Acknowledgements

I would like to take this opportunity to express my gratitude to my supervisor Professor Bernadette Murphy who has always supported my endeavours. You have opened up a world of scientific discovery to me, and I am grateful for this.

Thank you to Dr. Paul Yielder. Your knowledge of human neuroanatomy has formed the basis for much of my work. To Dr. Michael Holmes, thank you for helping me learn challenging biomechanics techniques and guiding this part of my thesis.

To Dr. Heidi Haavik, Director of Research at New Zealand College of Chiropractic. Your work has sparked many discoveries, and I am grateful for all your contributions.

To Julian Daligadu, previous student in the Human Neurophysiology and Rehabilitation Laboratory, thank you for helping me learn while I was still an undergraduate student. I truly believe your presence in the lab brought me to where I am today.

To my colleagues Chad Larabie, Ryan Gilley, Joseph Guirguis, and Devon Jarrett. Your motivation has inspired me, and your dedication to help in any way possible including running experiments and analyzing of data has been instrumental.

To all the students, colleagues and friends who participated in countless experiments. Thank you for coming to the school to participate even when you had exams, assignments, work, and other responsibilities. My thesis would not be possible without your dedicated support.

Special gratitude to University of Ontario Institute of Technology for being nearby when I needed a place to go to. Thank you to Ontario Graduate Scholarships and Canadian Institutes of Health Research for gracious funding support that helped to bring me to where I am today.

To the Australian Spinal Research Foundation, thank you for generously providing equipment which has aptly facilitated outcomes of my thesis. To the Natural Sciences and Engineering Research Council of Canada, thank you for generously supporting our research lab. To the Canadian Memorial Chiropractic College, thank you for generously providing software that I used to complete a large portion of data analysis for my thesis.

I also have tremendous gratitude to my mom, my dad, my nana, my papa, my oma, and my opa who have always been there when I needed them. To my siblings Jeremy, Jasper, Josiah, Justin, Jennessa, Jannelle, Joel, Jethro and Joylynn, thanks for your kind gestures and for just being there. It always cheers me up to have one of you close by.

Last, but not least, to my biggest supporter Hojjat, who is a talented researcher and friend. I hope we have a bright future together!

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Chapter 1: Introduction

1.1 Introduction

Each person has an internal map of the body in the brain that is created from past sensory experiences and that is used to interpret incoming sensory input and guide movement (Brownell, et al., 2010). The brain actively creates and uses this map, for instance to allow us to navigate through the darkness to a vehicle relying on our body's coordinate system. Small changes to this internal model can potentially alter motor skill and limb mechanics, particularly for tasks that require precision or large force demands.

The neck histologically contains many muscles, sensory receptors and nerves including the vagus (X) nerve, the accessory (XI) nerve and the cervical plexus. This high density of intricate neuromuscular structures makes the neck a relatively delicate structure and an important source of sensory input to numerous brain regions.

Muscle in the neck is a primary source of this sensory information to the brain and either changes to the sensory properties of the muscles, or the central control of this sensory input may affect the input received by the brain. It is known that the balance of input to the brain from the neck plays an important role both in the awareness of one's surroundings and in movement outcomes (Guerraz, et al., 2011; Haavik, et al., 2011; Kristjansson, et al., 2003; Lee, H.-Y., et al., 2008); further work will help to show how central control of sensory reception is impacted.

A key structure in the brain that plays an important role in the integration of incoming sensory input is the cerebellum. The cerebellum integrates sensory input to allow for learning of unfamiliar tasks and enhanced adaptation during complex, but more familiar, movements (Doyon, et al., 2003; Manzoni, 2005, 2007). Altered sensory input from the neck may result in changes to sensory integration by the cerebellum and may impact how the cerebellum channels this sensory input to form or implement new internal models.

My master’s thesis plans to explore how changes to central control of sensory reception arising from the neck affect performance, motor skill, spatial awareness, and cerebellar function. My hypothesis is that neck pain will alter the internal map of the body found in the brain, impacting sensory integration, cerebellar function and the motor response of the upper limb.

1.2 Altered Afferent Input

“Altered afferent input” is a term that is used to describe the sensory changes that occur when there are alterations to sensory input, or the central control of sensory input impacting the reception of this input. The cause-and-effect of altered afferent input is a debated topic since altered afferent input could be due to changes to the sensory receptor or alterations to the central control of this receptor. It is postulated that alterations occur with varying severity in a positive feedback manner. In this manner, changes to either a motor neuron, sensory receptor, or sensory apparatus may lead to altered central control of the principle receptor which causes further changes to sensory reception. For instance, one hypothesis is that abnormal (increased) firing of gamma motoneurons sets the sensitivity of the intrafusal muscle fibres, which leads to more frequent firing of the muscle spindle and increased tightness of the extrafusal muscle fibers and increased pain and tension (Johansson, et al., 1991).

Alterations that lead to overall changes in the central control of sensory reception can be further understood with disorders like multifocal muscular neuropathy, where changes to lower motor neuron pathways are known to cause sensory effects, although sensory effects are not necessarily considered to be part of the diagnosis or pathology of the disorder (Lambrecq, et al., 2009; Lievens, et al., 2009). Lambrecq et al. (2009) found that patients with multifocal muscular neuropathy reported paresthesias (tingling or prickly sensations) that tended to occur during episodes of more severe muscle weakening. These same patients indicated worsening of their sensory impairment as the disorder progressed. For instance, they reported numbness with loss of vibratory sensation, decreased pain and touch sensation accompanied by paresthesias, and pressure-induced pain in the arms (Lambrecq et al., 2009). These sensory effects occurred mainly in the region of the affected motor neuron, and worsening of sensory symptoms corresponded with changes to the amplitude of sensory nerve action potentials, although antibodies and cerebral spinal fluid samples indicated diagnosis of a motor neuropathy rather than a motor/sensory neuropathy (Lambrecq et al., 2009).

The progression of a more severe disease like multifocal muscular neuropathy which principally targets motor neurons provides important clues to the development and progression of less acute, but as prominent conditions. It is postulated that in these cases the neurology to the muscle is affected, meaning that altered afferent input originates from the central nervous system and is due to changes in the control of sensory processing rather than from actual changes in the sensory neuron or receptor (Lambrecq et al., 2009; Paulus, et al., 2008). These conditions may change the internal frame of reference in the brain and introduce conflicting input that alters the interpretation of sensory signals (Paulus et al., 2008) and impacts plasticity and adaptation of the body schema.

The body schema was first referred to as “postural schemata” by Head, et al. (1911-1912) who defined it as recognition of posture and passive movement that was possible through use of fresh proprioceptive and tactile sensations outside the foci of attention. More recently, the definition of body schema has extended to include visual and auditory sensory signals, along with signals of proprioception and other somatosensory inputs, which together provide multisensory representation(s) that allow for neural encoding of body representation via the reception of comprehensive, ongoing details of the body’s position (Holmes, et al., 2004). In a functional magnetic resonance imaging (fMRI) study, Chaminade, et al. (2005) found activation of the ipsilateral cerebellum and contralateral motor cortex when participants were asked to describe their observation of a limb orientation and its use. This activity of the cerebellum when participants described limb positions may be due to updating of an evolving postural and visual coordinate system, the input of which allows for comprehensive updating of bodily representations.

My research explores whether changes occur to motor performance on a motor sequence typing task and a multi-joint throwing task, as well as whether there are changes to cerebellar function. These effects will be studied in a group with recurrent subclinical neck pain (SCNP). That is, participants will have non-severe neck pain or muscle stiffness that has been recurrent over at least three months duration in the past year. These participants may also been classified as having Grade I to Grade III neck pain, following the categorical system suggested by the Neck Pain Task Force (Guzman, et al., 2008; Von Korff, et al., 1992). Although neck pain occurs with no known pathological change to sensory receptors or neurons, sensory effects have been particularly noted in this group (Lee, H., et al., 2004; Lee, H., et al., 2005; Lee, H.-Y. et al., 2008; Paulus et al., 2008). The cervical extensor muscles of SCNP patients have different motor control patterns than healthy individuals with the muscles having a lower flexion relaxation ratio (FRR) as compared to healthy controls, indicating the muscles are unable to properly relax during forward flexion (Murphy, et al., 2010). This continuous muscle activity is one source of altered sensory input to the cerebellum in SCNP. Furthermore, SCNP individuals are unable to further adapt their FRR in response to fatigue in the way that healthy controls are, providing evidence of altered motor control in SCNP. Evidence of altered processing of upper limb sensory input by SCNP individuals has been demonstrated by differential changes in median nerve somatosensory evoked potential amplitude in the N24 peak (which reflects activity in the cerebellum to somatosensory cortex pathway) following motor training as compared to healthy controls (Andrew, 2014). The advantage of recurrent SCNP compared to other models of altered afferent input is that participants can be studied on days when symptoms are minimal which minimizes the interference of confounding variables, such as pain. The non-severity of SCNP also makes it attractive for the study of sensory changes, since it allows for more sensitive discrimination of sensory/motor alterations and related effects to performance. It should also be noted that neck pain has high prevalence, and 30 to 50% of the general population has neck pain with more cases untreated than treated, a phenomenon referred to as the iceberg effect (Hogg-Johnson, et al., 2008). In contrast, conditions like multifocal muscular neuropathy are relatively rare and are treated in nearly every case, further supporting the use of SCNP to study chronic alterations to sensory input and the effects on cerebellar processing and body schema.

1.3 Challenges to Motor Skill

Perhaps the most readily observed effects of altered afferent input from recurrent neck pain include changes that occur to movement. Paulus et al. (2008) found that head position shifted towards the raised shoulder during passive shoulder elevation and away from the lowered shoulder during passive shoulder depression in participants with non-severe neck pain, whereas an opposite shift in head position occurred for asymptomatic participants. Trunk movements were also dramatically increased during active shoulder elevation in participants with neck pain compared to asymptomatic controls (Paulus et al., 2008).

Neck pain also occurs with reduced neck mobility, particularly with impaired range of motion during rotation (Cagnie, et al., 2007; Lee, H. et al., 2004; Lee, H. et al., 2005). The effect of reduced range of motion was exaggerated on repeated trials in participants with weekly or monthly pain. In contrast, participants without pain showed greater range of motion on repeated trials (Lee, H. et al., 2004; Lee, H. et al., 2005). Reduced range of motion on repeated trials has been referred to as sensitization and was found to occur in the neck pain participants during extension, right and left side flexion and left rotation, but was not seen in healthy participants (Lee, H. et al., 2004; Lee, H. et al., 2005).

Lee, H. et al. (2005) found that weekly neck pain corresponded with a greater sensitivity for distinguishing head movements compared to monthly or never/infrequent neck pain. In contrast, fatigue has been found to reduce detection of shoulder rotations so that more movement is needed before the shoulder rotation could be distinguished (Carpenter et al., 1998). This apparent dichotomy may be due to a greater reliance on proprioception in the fatiguing study whereas in the neck pain study participants had their eyes open. Pain may also be a confounding factor that may actually have enhanced participants’ attention (Liu et al., 2013).

Lomond, et al. (2010) tested 16 asymptomatic participants and 16 participants with chronic neck/shoulder pain on a reaching task where participants moved their arm from side to side to reach a target located at shoulder height (Figure 1.1). The task was terminated when participants could not maintain the desired rhythm (one movement per second), when participants rated the task difficulty as an eight on a zero to ten scale or when participants rated their pain as an eight on the zero to ten Numeric Rating Scale (NRS). Although participants were unaware of the criteria to terminate the task, participants with neck pain terminated the task sooner than asymptomatic participants (mean ± std. dev.: 4.1 ± 2.4 minutes compared to 7.5 ± 3.0 minutes). The asymptomatic participants also showed a clustered time to peak velocity following the task whereas the adults with chronic neck/shoulder pain showed no change (Figure 1.2). This study suggests that the healthy individuals learnt a strategy for performing the movement that was not learnt by the individuals with neck pain. In critique it should be noted that healthy participants had longer time to learn the motor strategy than participants with neck/shoulder pain which may have contributed to the clustered timing. A future study should look at motor strategies while controlling for differences in time while completing the task. The main theme however, regardless of time differences, is that participants with chronic neck/shoulder pain did not learn the motor strategy of their healthy counterparts.

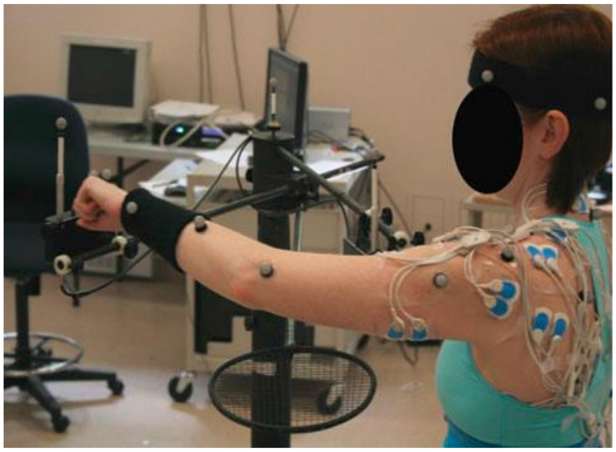

Figure 1.1 Setup for the reaching task performed by participants with chronic neck/shoulder pain and asymptomatic controls.

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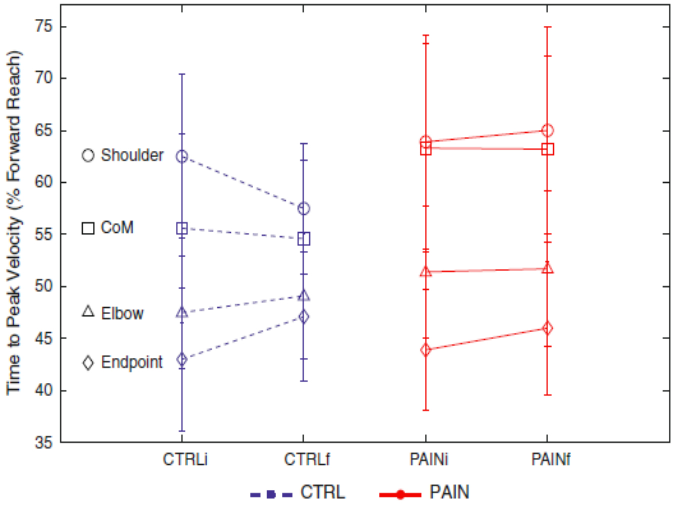

Figure 1.2 Time to peak velocity in participants with chronic neck/shoulder pain (red) and in asymptomatic participants (blue). Lines show changes from initial to final measurements. Custering of time to peak velocity is seen in final measurements of asymptomatic controls but not in final measurements of participants with chronic neck/shoulder pain.

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1.4 Challenges to Spatial Awareness

Neck pain may also impact one’s internal reference and affect judgement and spatial processing. Paulus et al. (2008) found that participants with neck pain judged their shoulder to be raised higher during passive shoulder elevation compared to asymptomatic controls. Haavik et al. (2011) found that participants with non-severe SCNP performed poorly when replicating elbow position with eyes closed compared to healthy controls.

Studies also show that with neck pain there is impaired ability to reposition the head to a neutral position (Kristjansson et al., 2003, Lee et al., 2008). For instance, Lee, H.-Y. et al. (2008) found that participants with neck pain showed more absolute error when positioning their head to a neutral position (e.g. comfortable position with head facing straight ahead) compared to a target (e.g. self-selected midpoint within the participant’s maximum range of motion).

The head’s position may also influence the body’s perception of itself in space and may be a source of altered representation in the body’s internal model. Paulus et al. (2008) found that participants with non-severe but recurrent neck pain repositioned their head more dramatically (e.g. with greater degree of displacement) away from the side where the trunk was bending than asymptomatic controls. Of interest, this more dramatic head positioning during passive shoulder elevation corresponded with greater trunk movement and perception of a higher shoulder during passive shoulder elevation (Paulus et al., 2008).

Guerraz et al. (2011) found that head posture greatly impacted participant’s ability to replicate an object using simple arm tracing. For this study, participants lay supine and were asked to view an object and then trace the shape of this object with their unseen index finger using elbow and shoulder movements (Figure 1.3). The tracing was completed in two conditions: with eyes closed and with eyes open (viewing only the object and not arm movements). When the head was tilted, there was a bias of spatial arm movements towards the opposite direction during both memory-guided and visually-guided movements (Figure 1.4). Two experiments were performed: specifically for the first experiment, the head was held straight while viewing the object and then tilted during tracing. In the second experiment, the head was tilted at 30 degrees during both viewing and tracing. Bias was seen in both instances as long as participants replicated the movements with their head tilted. The bias was not seen when participants replicated the movement with their head straight. When vision was added, bias decreased significantly for the leftward head tilt in both experiments. Notably, the participants perceived the tracing as being in line with their body even though the traces were biased by the head tilt (Guerraz et al., 2011).

The neck is connected to the head and changes to the head's position with neck pain (Paulus et al., 2008) may affect upper limb movements so that they are biased as occurred in the Guerraz et al. (2011) study. It is not clear whether the head's position is the determining factor to changes in awareness described in the previous studies, or whether the sensory receptors in the neck mediate the known effects to spatial awareness. Understandably, this is a topic worthy of more research.

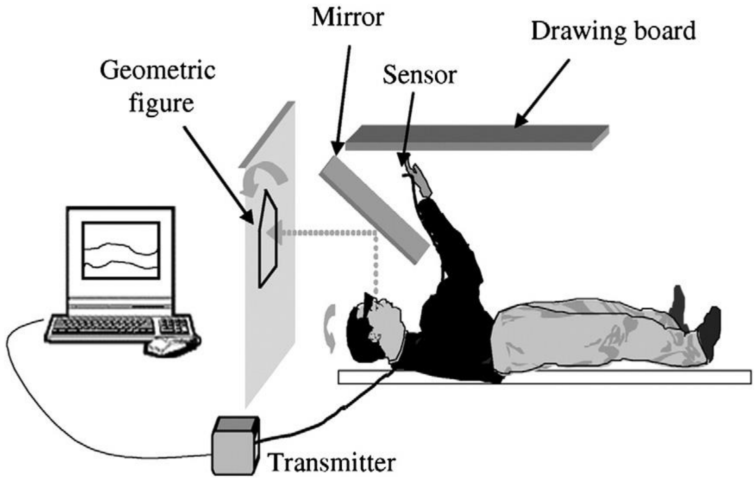

Figure 1.3. Participants viewed the object and replicated the image (seen or remembered) using primarily shoulder and elbow movements.

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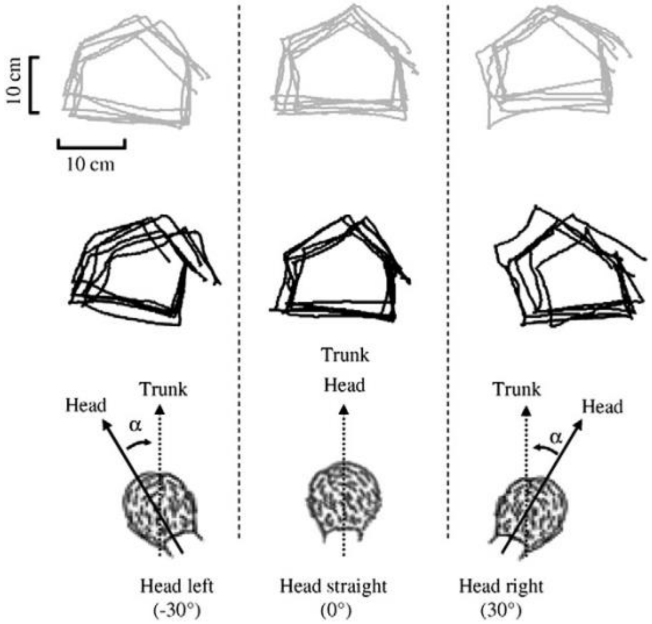

Figure 1.4. Arm traces when the head position was tilted left (-30º from the trunk), straight ahead (0º to the trunk), and right (30º from the trunk) for both visually-guided (grey traces) and memory-guided (black traces).

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1.5 Challenges to Mental Rotation

Altered sensory input from the neck may impact not only spatial mental representation of the body (Tsay, et al., 2015), but also the ability for mental rotation of objects. Mental rotation of the outward environment is a highly important task that is used in spatial navigation (Taylor, et al., 2008) as well as sport performance (Moreau, et al., 2011).

Previous work has shown that patients with cervical dystonia were slower in judging the laterality of a rotated hand, foot or eye patch, which are images related to their own bodies (Fiorio, et al., 2007). Limited knowledge however is available on how recurrent neck pain may impair mental rotation of outward objects that are beyond the immediate body. When patients with cervical dystonia were asked to judge the laterality of a rotated non-human image of a car, they showed a tendency for slower response times (Fiorio et al., 2007). The authors did not report significance in this study possibly because of the statistical design that they used which compared each angle of rotation using a 2 x 2 x 6 analysis of variance (ANOVA). Another past study showed that ability to mentally rotate an object improved with a single session of neck manipulation (Kelly, et al., 2000). The participants in this study all had low-grade recurrent neck pain and a comparison group of healthy participants would be needed to determine whether altered afferent input from the neck influences mental rotation skill (Chapter 5).

Mental rotation abilities may be strongly influenced by internal models that are formed by the cerebellum (Ito, 2008). Recent work using fMRI has shown activation in the left hemisphere of the cerebellum in lobule VII (Crus II), extending from lobules VI to VIIB, during a mental rotation task that involved recognizing whether an a rotated letter was presented in its normal or mirror image orientation (Stoodley, et al., 2012), suggesting that if there are impairments in mental rotation skill due to altered afferent input from the neck, that these impairments may also be seen by cerebellar changes.

1.6 Cerebellar Functioning

The cerebellum is a central integrator of sensory information and plays an important role in the formation of internal models to allow for learning of new tasks as well as adaptation during familiar but more complex movements (Doyon et al., 2003; Manzoni, 2005, 2007). In previous work, a novel method was developed to measure changes to cerebellar output (Baarbé, J., et al., 2014) This method involves the use of transcranial magnetic stimulation applied sequentially over the right cerebellum and contralateral primary motor cortex with an interstimulus interval of 5 milliseconds to inhibit motor evoked potentials, recorded from electromyographic (EMG) electrodes placed on the first dorsal interosseus of the right hand. The level that showed fifty percent inhibition was defined as cerebellar inhibition at fifty percent (CBI_{50}), and this level could be used to make comparisons following simple interventions such as a motor learning typing task (Baarbé, J. et al., 2014). In other preliminary work, we demonstrated that participants with SCNP tended to be more inhibited than healthy controls following learning of a simple motor learning typing task (Baarbé, J, et al., November 13, 2013). Daligadu, et al. (2013) completed similar work in participants with SCNP, showing that healthy participants tended to show no changes to cerebellar inhibition following motor learning, whereas participants with SCNP disinhibit after a combined intervention of motor learning and spinal manipulation. The principle difference between the the Baarbé et al and the Daligadu et al. (2013) studies is that the latter compared fewer stimulation intensities and did not compare at CBI_{50}, meaning the measure was less sensitive since averaged group effects do not necessarily reflect individual differences. The lack of change in the healthy particpants suggests either the motor learning task used was not challenging enough to lead to cerebellar changes or the cerebellar inhibition method was not sensitive enough and it is critical that these limitations be addressed in future work.

1.7 Muscle Activation Patterns

Lee, H. et al. (2004) and Lee, H. et al. (2005) found that muscle endurance was significantly less in SCNP participants who reported monthly or weekly pain compared to participants who experienced infrequent pain. In this line of thought, it is hypothesized that participants with SCNP will display changes to both the amplitude and duration of muscle activity. Variability of muscle activity may also be impaired in participants with SCNP. Following a fatiguing task Lomond et al. (2010) found that supraspinatus and upper trapezius variability in healthy adults increased whereas variability remained low in a chronic neck/shoulder pain group. Overall, supraspinatus activity was more variable (greater % of root mean squared EMG) in healthy adults than in adults with a chronic neck/shoulder disorder (Lomond et al., 2010).

1.7.1 Muscle activity in neck pain disorders

Szeto, et al. (2005) studied 23 females with neck or arm discomfort related to computer use and 20 asymptomatic females. EMG was recorded from the bilateral cervical erector spinae (CES), upper trapezii, lower trapezii, and anterior deltoids during the course of computer typing similar to what participant might experience in a typical work day. Participants who reported neck or arm discomfort had greater right upper trapezius activity and less CES activity than asymptomatic controls. Symptomatic females tended to show greater asymmetry between activity of their right and left upper trapezii than asymptomatic controls. Symptomatic participants also had a positive association between discomfort and upper right trapezii activity, with discomfort worsening in severity as participants progressed in the computer typing task. Increased upper right trapezius activity preceded ratings of greater discomfort, suggesting that altered muscle activity can be detected prior to onset of pain and discomfort.

In another study, Falla, D. L., et al. (2004) recorded EMG from ten participants with a history of neck pain greater than one year and ten asymptomatic participants. Participants were asked to complete a craniocervical flexion task while EMG recorded activity of deep and surface cervical muscles. The results showed a linear increase in activity of deep cervical muscles as participants progressed in the task. However, this increase in deep muscle activity was found to be less than the activity of deep cervical muscles in asymptomatic controls. Superficial muscles including the sternocleidomastoid and anterior scalene muscles showed a trend, although insignificant, for increased muscle activity compared to asymptomatic controls.

In a similar study, Falla, D., et al. (2004) tested ten participants with a history of neck pain greater than one year and twelve asymptomatic participants. Participants were asked to complete fast unilateral arm flexion and extension in response to visual cues. EMG recorded activity of the deep cervical flexors, sternocleidomastoid, anterior scalenes, anterior deltoid and posterior deltoid muscles. Asymptomatic participants had an onset of deep cervical flexors, sternocleidomastoid and anterior scalene muscles less than 50 ms after the onset of EMG activity in the deltoid. However, participants with neck pain showed a delayed onset of deep cervical flexors, sternocleidomastoid and anterior scalene muscles.

The amplitude of cervical deep flexors and anterior scalenes was also lower in participants with neck pain compared to asymptomatic counterparts.

1.7.2 Muscle activity in cerebellar disorders

Patients with cerebellar lesions are also known to report distinct muscle activation patterns. On their affected side, cerebellar patients presented with a longer duration and slower rate of rise in their agonist muscle (biceps) during elbow flexion (Hore, et al., 1991). In their antagonist muscles (triceps), the patients showed delayed onset and delayed peak activity with a peak velocity that was on average larger than on the affected side (Hore et al., 1991). Overall, the patients showed decreased peak acceleration and increased peak deceleration on their affected side. It can be critiqued that in this study, Hore et al. (1991) excluded three participants who did not show dysmetria and only six of the nine cerebellar patients with dysmetria were studied. Flament, et al. (1986) however found similar results when he taught monkeys to quickly and accurately flex their elbows. Monkeys with cerebellar lesions demonstrated hypermetria with several peaks in velocity whereas controls had only one peak in velocity. Similar to Hore et al. (1991), cerebellar monkeys had a decreased peak acceleration with prolonged activation of the biceps. They also showed an increase in peak deceleration in the triceps with delayed onset of muscle activity and shorter duration. This is analogous to using gas and brake pedals in a car. Compared to healthy participants, participants with cerebellar lesions apply less pressure to the gas pedal (less agonist muscle activity – e.g. they maintain their foot on the gas pedal for a longer time). When it is time to decelerate, participants with cerebellar lesions do not step on the brake as quickly (slower antagonist muscle activity), but decelerate faster with the foot on the brake pedal for a shorter length of time.

A strength of the Flament et al. (1986) study is that the anatomical involvement was controlled to the dentate nucleus responsible for output from the cerebellum, unlike human studies where participants are included with cerebellar lesions that arise from many different sources. For instance, Hallett, et al. (1975) measured 20 human subjects with cerebellar lesions during fast elbow flexion and noted three remarkable groups: in the first group, six out of the 20 patients showed prolonged muscle activity of the biceps as well as a tendency to overshoot; in the second group, seven of 20 patients showed prolonged activity of the biceps and triceps; and in the third group, two out of 20 patients showed prolonged activity of triceps but not of biceps. The subjects from the Hallett et al. (1975) study were from a heterogonous group with lesions which included cerebellar degeneration, multiple sclerosis, dementia, and surgical removal of cancerous tumors. Some of these disorders would have affected systems other than the cerebellum or the pathway of sensory input to the cerebellum.

It should be noted that the monkeys in the Flament et al. (1986) study were well-trained on the elbow flexion task before the cerebellar lesion, but they showed the same characteristic muscle activation patterns noted in the Hore et al. (1991) study. The key theme is that cerebellar changes lead to specific patterns of muscle activation that give important clues to the changes that occur with disordered central processing of sensory information.

1.8 Effects of Altered Afferent Input on Multimodal Processing

Altered sensory input from the neck may also interfere with the ability to process sensory input from other senses. In a previous study, Rock, et al. (1964) presented an object to participants who both felt and saw its shape. When the shape was visually distorted with optical lenses, the participant showed a strong tendency to be biased by the visual illusion and would draw the shape or match the shape with what they saw instead of with the true representation.

Combining visual and haptic senses however results in more sensitive discrimination than haptic stimuli alone. Ernst, et al. (2002) found that when visual noise was high, less weight was placed on visual information, and participants showed a greater tendency to respond inaccurately. Combining visual and haptic stimuli allowed for overall improvement to accuracy, and when there was high noise, improved discrimination (Ernst et al., 2002). However, when a sense is less reliable or provides contradictory information, combining of stimuli may become problematic.

1.8.1 The central nervous system's response to adjust for sensory mismatches

Hogendoorn, et al. (2009) found that when contradiction was imposed between proprioception of the hand's location and a visual afterimage, the visual afterimage of the hand disappeared. The central nervous system may silence certain types of contradictory information, but it is also possible that the central nervous system responds to contradictory information through plasticity and sensorimotor transformations. For instance, when there is contradictory information, the central nervous system may try to align sensory information relative to other sources of sensory information, or else adapt motor output to the muscles (e.g. less contraction to more accurately reach the target).

In order to investigate the contribution of plasticity between sensory neurons when participants were imposed with mismatched sensory input, van der Kooij, et al. (2013) completed a study imposing mismatches between proprioception and vision. Participants pointed towards a target with their unseen hand. The researchers then manipulated the relationship between proprioception and vision by imposing erroneous visual feedback about the target's location. The sensory relationship between proprioceptive input and vision was held constant so that plasticity between sensory images could be created; however, movement patterns varied so that participants were not able to learn an optimal motor plan for the movements. It was found that partial alignment (up to ~ 60%) occurred between proprioception and the "visual image," meaning that participants corrected their responses in the presence of visual feedback towards the adjusted visual image up to 60% the distance of the visual feedback. A smaller degree of alignment occurred (~30%) between proprioception and vision when the visual feedback accurately depicted the target's location, suggesting that prior to feedback the participants were already responding accurately, most likely due to prior plasticity between proprioception and vision before the task began. The biases found in pointing toward the target occurred in different directions for all participants, but showed consistent placements on separate days for individual participants.

Similarly, Cressman, et al. (2009) found that participants learnt to adjust the location of their hand following training with knowledge of results (KR) of their hand's position that was distorted 4 cm to the right or rotated 30 degrees toward the right. Learning of a motor strategy was prevented by varying the location of KR and showing KR only at the end of the trial when participants had reached the estimated location. When asked to estimate the location of their hand, participants partially adjusted their hand in the direction of the distorted KR, accounting for ~25% of the absolute size of the distortion. This indicates that plasticity occurs in the relationship between two senses to facilitate a “sensory map” that contributes *partially* to the sensorimotor transformation. It has been suggested that the need to re-plasticize mismatched information may also impact motor learning (Henriques, et al., 2012).

1.8.2 Sensory mismatches between two or more senses

Typically when a sensory modality is less reliable or provides contradictory information, less weight is placed on the unreliable sense (Bresciani, et al., 2008; Oie, et al., 2002). Bresciani et al. (2008) explored this concept by presenting rapid stimuli in sequence (50 milliseconds duration with 50 milliseconds intervals between stimuli) and asking participants to discriminate the number of events. Participants were asked to focus on a target stimuli (tactile, visual, and/or auditory) while the same number of events or a contradictory number of events was presented in the background using one or more of the remaining two modalities (e.g. tactile and/or vision if audition was the selected target modality). Bresciani et al. (2008) found that the participant’s variability (computed as standard deviation of responses within a target modality) was found to correlate inversely with the relative importance the participants placed on the modality to complete the task. For example, participants displayed greater variability within tactile and vision when reporting the number of events they perceived, as well as a greater tendency to respond inaccurately and be biased by contradictory information when focusing on these modalities. In contrast, participants showed less variability when using audition as well as a greater tendency to respond correctly to this stimulus and be less biased by contradictory information (Bresciani et al., 2008).

1.9 Summary and Relevance to Thesis

Altered sensory input in the form of recurrent neck pain muscle can have a multitude of effects on motor skill, spatial awareness, muscle activation patterns, and multimodal processing. It is thought that neck pain affects sensory input to the brain and may cause altered central control that leads to maladaptation in the motor control of muscles. However, research is still needed to explore effects that may occur in cerebellar function, and the impact on motor skill acquisition, motor performance and mental rotation. My research will focus on this area of study in participants with SCNP who have a relatively non-severe condition, in order to more thoroughly assess effects that occur from altered central control of afferent information.

Understanding central changes of SCNP, along with outward behavioural and sensory aspects has potential to improve our understanding of the interaction between central processing and sensory reception influencing performance, activity and participation of Canadians.

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Chapter 2: Technical Considerations for Thesis

2.1 Introduction to Chapter

This document outlines technical considerations for my thesis “Effects of altered sensory input from the neck on cerebellar function, body schema and sensorimotor integration.” In particular, this document introduces magnetic brain stimulation and motion capture, including background on each modality, its current application within research and its potential for use in my master’s thesis. It is recognized that in covering the technical background that consideration could also be given to specific methodological procedures. However, this has been covered elsewhere. For further reading, the reader may refer to the methodology sections that may be found in Chapters 3 and 4.

2.2 Introduction and Theoretical Background

Altered afferent feedback from the neck may have profound effects to movement, reaction time and coordination. This has been seen in studies that have shown simple rotation and flexion of the head and neck affects elbow joint position sense (Knox, et al., 2005), and vibration of muscles in the neck to induce an illusory movement of the head also affects elbow joint position sense (Knox, J., et al., 2006). Neck pain also impacts perception and placement of the elbow and forearm (Haavik, et al., 2011; Knox, J. J., et al., 2006). Biomedical signals are signals that may be collected, stored, and analyzed. The theoretical background of which plays a fundamental role in the special significance of the signal. Particular emphasis may be placed on the physical explanation for how the signal is generated, quality assurance for when the signal data is collected, procedures to filter and process the acquired data, and boundaries for what the signal may or may not describe within the particular study. The technical aspects of the aforementioned provide a comprehensive and analytical background to discuss the study of upper limb motor control, displacement and velocity as in my thesis.

2.3 Relevance and Significance to Thesis

This chapter reviews the relevant theoretical background for the neurophysiological and biomechanical techniques used in this thesis Background in biomedical signals, physiology, as well as experimental techniques is fundamental and necessary for reasonable discussion on potential effects of distorted feedback from the neck, such as in people with neck pain or muscle tightness (see Figure 1). In this manuscript, I propose the following that **1)** cerebellar and motor cortical function may be studied using transcranial magnetic stimulation (TMS) and applying a special technique called cerebellar inhibition at fifty percent (CBI_{50}), and **2)** coordination and motor control of the upper limb may be assessed through a dart throwing task assessing translational and angular kinematics of movement using infrared-emitting markers and a Northern Digital Instruments (NDI) sensor system.

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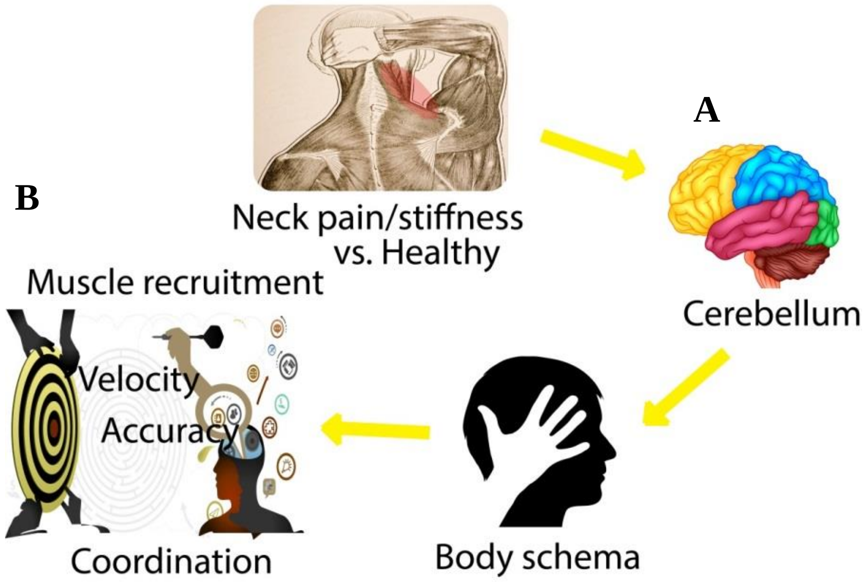

Figure 2.1 This manuscript proposes that as a consequence of neck pain and neck muscle tightness that changes will be seen to CBI$_{50}$ following motor learning as measured through TMS (A), and coordination and velocity measured through infrared-emitting markers using the NDI sensor system, as well as timing and magnitude of muscle activity measured through EMG will be affected (B).

2.4 Neurophysiological Signals

2.4.1 Transcranial Magnetic Stimulation

The brain may be activated non-invasively through either an electrical current applied to the brain or through an alternating magnetic field applied perpendicularly. In the mid-to-late 1900s, high-voltage electrical capacitors were initially used to stimulate brain tissue. This method was unpleasant and painful, and researchers were beginning to find that alternating magnetic fields also could activate brain tissue. Transcranial magnetic stimulation (TMS) was developed in 1985 when Barker and colleagues discharged a capacitor into coil that could activate brain tissue and elicit a motor response (Barker, A. T., et al., 1985; Barker, A., et al., 1985). With TMS, an alternating current within a coil generates a magnetic file that produces an electrical current in underlying neural tissue. This process leads to activation of neural tissue that can be seen either through a noticeable muscle twitch or through motor evoked potentials (MEPs) recorded by electromyography (EMG) of a distal hand muscle (Roth, et al., 2013). The magnetic field is strong and reaches strengths of up to 2 Tesla (Hallett, 2007). Pulse durations however are relatively short with a rise time of 100 µs and duration of 1 ms (Magstim, 2011).

2.4.2 Signal Application within Research

Applications of TMS include using the stimulator to activate and inhibit brain tissue, and in this way map areas of brain activity (Hallett, 2007). Within TMS research, individual cells are *not* targeted, but rather functional brain regions, due to the intermediate resolution of TMS both spatially and temporally (Walsh, et al., 2000). For this reason, quality assurance of the TMS signal includes using coils with a more focal stimulation point (Hallett, 2007) and visual inspection of traces for latency changes.

TMS has also been used extensively in the study of human motor control (Reis, et al., 2008). Of particular interest, TMS has been used to measure cortical changes that occur following motor learning paradigms, with consideration given to cortical changes of the motor cortex (Classen, et al., 1998; Liepert, et al., 1998; Pascual-Leone, et al., 1995; Sugawara, et al., 2013) and the cerebellum and motor cortex in tandem (Baarbé, et al., 2014; Daligadu, et al., 2013).

The application of TMS in research may either be single pulse TMS or repetitive TMS involving a train of pulses (rTMS) (Hallett, 2007). Single pulse TMS allows activation of brain tissue in a safe and controlled manner. Delivering a train of TMS pulses to neural tissue interrupts brain function allowing for valuable study that is distinct from simple activating or inhibiting of brain regions performed with single pulse TMS and has its own ethical and safety considerations (Rossi, et al., 2009; Wassermann, 1998).

2.4.3 Physiological Considerations

A main physiological theme throughout this study is the cerebellum. Monophasic TMS applied to the cerebellum five to eight milliseconds prior to a monophasic TMS stimulus over the motor cortex inhibits motor evoked potentials recorded from a distal limb muscle, typically the first dorsal interossius (FDI). This technique was pioneered by Ugawa and colleagues (1995) , who used a double cone coil due to its potential for deeper stimulation. Later, Daskalakis, et al. (2004) called the procedure cerebellar inhibition or CBI (Daskalakis et al., 2004).

Projections from the cerebellum to the motor cortex extend from the dentate nucleus to the motor thalamus through the superior cerebellar peduncle (Holdefer, et al., 2000). This pathway is known as the dentate-thalamo-cortical pathway and is an excitatory pathway (Holdefer et al., 2000). Projections however from Purkinje cells that synapse within the dentate nucleus are inhibitory leading to the inhibitory effect of cerebellar inhibition (Grimaldi, et al., 2013).

The cerebellum contains over half of the neurons in the brain and is highly influential in balance, coordination of body movement and affective (emotional) responses (Kandel, et al., 2012; Manto, et al., 2012). The cerebellum is also highly involved in timing of limb movements, and creation of forward internal models that predict the sensory effects that occur from movement (in this way reducing relatively large time delays for receiving sensory input from potentially distal afferent sources such as the hand) (Manto et al., 2012). The cerebellum has also been shown to be involved in motor sequence learning as well as finger-tapping as demonstrated through functional magnetic resonance imaging and positron emission tomography (Doyon, et al., 2002; Olsson, et al., 2008; Penhume, et al., 2002; Stoodley, et al., 2012; Witt, et al., 2008). This literature supports that cerebellar function may be studied using functional tasks similar to the tasks in the above literature and applying the CBI technique.

2.4.4 Proposed Features and Use of Signal for Thesis

Daligadu et al. (2013) tested people with neck pain and healthy people with the CBI technique before and after a combined intervention of treatment (neck pain group only) and motor acquisition (neck pain group and healthy group) (Daligadu et al., 2013). The study found that the CBI curve was more inhibited in people with neck pain compared to healthy controls, with a decrease to CBI following the treatment and motor acquisition intervention. Healthy participants who performed only motor acquisition showed no change in CBI (Daligadu et al., 2013).

CBI at fifty percent (CBI_{50}) was piloted by Baarbé et al. (2014) as a method to study changes following simple interventions. The level of stimulator output that elicits fifty percent inhibition (CBI_{50}) and stimulator levels that are 5% and 10% adjacent to CBI_{50} was used as a level for comparison following a motor acquisition task (Baarbé et al., 2014). Significant disinhibition was seen at CBI_{50} and at 5% and 10% stimulator output above CBI_{50} following a motor acquisition task similar to tasks shown to activate the cerebellum from previous fMRI and PET studies (Baarbé et al., 2014).

Following the same line of thought as Daligadu et al. (2013), it is hypothesized that disinhibition of CBI_{50} will occur differently in people with neck pain following treatment and motor acquisition compared to people with neck pain who do not receive treatment. This background frames current development in my thesis work to elucidate differences in CBI_{50} in people with neck pain compared to healthy people following motor acquisition.

2.4.5 Quality Assurance

CBI has previously been used to study changes following motor learning paradigms (Baarbé et al., 2014; Daligadu et al., 2013). However, deep penetration of the electrical field is necessary to activate Purkinje cells, and stimulations often result in the concomitant activation of surrounding muscles. For these reasons, CBI technique can result in signals that are "contaminated" by background EMG, cervical root activity and other physiological sources of noise (Baarbé et al., 2014).

Depending on physical properties of the head and neck, cerebellar TMS may activate the corticospinal tract through the cervicomedullary junction, and great care must be given to this potential confounding factor. In a lengthy article, Fisher and colleagues outline their methods and findings for producing CBI and conclude that there may be confounding effects in the use of CBI for study of cerebellar physiology due to potential activation at the spinal cord and antidromic activity of corticospinal tract (Fisher, et al., 2009). However, Baarbé et al. (2014) describe procedures to minimize potential contamination of the trace. These procedures include visually inspecting each trace at a high gain while looking for cervical root activity and cervicomedullary motor evoked potentials within the range of 14 – 18 ms following the cerebellar stimulation. Baarbé et al. (2014) also recommends individualizing stimulator intensities since CMEPs are often found at higher intensities of stimulator output, and cerebellar inhibition may be possible at lower intensities.

Another confounding factor is the potential for both physiological and electromagnetic noise. Suggestions to minimize noise include ensuring coil components are tangent to participant`s head (Roth et al., 2013), ensuring participant’s upper limb and hand are relaxed, ensuring return currents have an “exit” point as far away as possible from participant’s head as possible (Roth et al., 2013), and ensuring EMG leads are at right angles to the main TMS cable. Researchers must attend to these procedures very carefully and report these potential confounding variables when applying CBI to the study of cerebellar function.

2.5 Kinematic Signals

2.5.1 Motion analysis

Various biomechanical and movement analysis techniques have been used to track gait, posture and movement. These techniques range from very simple techniques that measure movement in only one plane, to more advanced techniques that measure displacement and depth over time. For instance, Haavik et al. (2011) used a simplistic technique to measured arm angle in only one plane, which meant that participants had to lie on their backs while researchers measured elbow angle with an electrogoniometer. In another series of articles, (McNaughton, et al. (2004); Timmann, et al. (2008); Timmann, et al. (2000)) used a magnetic field search-coil technique to track movement during arm throws. Participants sat within a three orthogonal, high-frequency, alternating magnetic field system and movements were tracked through search coils attached to body segments. A sampling frequency of 1000 Hz was used which is very high considering that human movement is relatively slow and can be sampled at low sampling frequencies ranging between 32 and 64 Hz (personal communication, Dr. Holmes). The magnetic field used in these studies is also very sensitive to aerials such as metal in the immediate environment, for instance from the grid used to detect accuracy of throws. Although potential for noise is high with this technique, values for velocity and acceleration were extremely high, which is likely due to noise (greater than 1000 degrees/second (s) for velocity, and greater than 50 000 degrees/s^2 for acceleration) and methods to filter the data (e.g. low pass filter) were not described in this article series (Timmann et al., 2008).

These various methods for movement analysis demonstrate that although techniques may share similarities in their capacities to track limb segments in one or more planes, movement analysis techniques have different features for signal generation, degree of accuracy and resolution, as well as in their ease of use. One technique for motion analysis involves infrared-light emitted from markers placed on body segments and detected by a special sensor system. This technique involves the placement of three or more special infrared-emitting markers onto a rigid body which is then placed on body segments to be tracked during movement. Examples include the 3D Investigator (NDI, Waterloo, Ontario) with accuracy of 0.4 mm and a spatial resolution of 0.01 mm and the Optotrak Certus (NDI, Waterloo, Ontario) with accuracy of 0.1 mm and a spatial resolution of 0.01 mm.

2.5.2 Signal Generation

The 3D Investigator system (NDI, Waterloo, Ontario) works through the emission of infrared light from markers containing an infrared light emitting diode (IRED). Each diode is made of special semiconductor material with two layers separated by a depletion zone. When a voltage source is applied, positive charges travels across the depletion zone, and the interaction of positive charges with free electrons creates photons that are emitted from the source as infrared light. This infrared light travels from its source and is then detected by special position sensors.

As a participant moves their limbs, the signal source is displaced and may shift to a different depth. The 3D motion capture system detects the amount of time necessary for the infrared signal to travel from the markers to the capture system, using the speed of light (3.0×10^8 meters per second) as a constant to allow for calculations of displacement and depth.

$$\frac{3.0 \times 10^8 \text{ meters}}{1 \text{ second}} \times n \text{ seconds} = d \text{ meters}$$

Figure 2.2. Equation to determine depth of infrared signal source emitted from markers placed on specific limb segments

2.5.3 Essential Characteristics

Infrared light is emitted as electromagnetic waves that have a longer wavelength (700 nm to 1 mm) compared to visible light (400 nm to 700 nm). This longer wavelength falls just below red light on the visible light spectrum where it for the most part escapes human detection. Properties of infrared emission fall under a branch in physics known as optics, which is study that is primarily concerned with characteristics of light. Similar to other electromagnetic light, infrared light shares properties of attenuation, reflection, refraction and absorption.

Attenuation refers to the gradual decline in light intensity that occurs over distance. Due to the sensitivity of NDI sensors, attenuation is not a concern in most motion analysis cases, and although there is a decrease in intensity at greater distances, the increased distance is proportional to an increase in the area where the light intensity can be detected (inverse square law), allowing the markers to be detected at greater distances from the sensor. For this reason, an increased distance of the sensor is often recommended. Reflection refers to light "bouncing" off of surfaces (and in some cases causing scattering of the beam), and this property of light may need to be considered if shiny or white objects are introduced into the experimental setup. Refraction refers to the light bending when it passes through mediums of different densities and in most experimental cases is of little concern. Absorption however occurs when light is taken up by a medium. This absorption may occur if clothing or body segments block the light from the sensors.

2.5.4 Physiological Considerations

A main application of 3D motion analysis is to record and analyze human movement and determine kinematic relationships of limbs relative to each other. Motion capture and analysis may also be used to explain and represents activity of muscles and the degrees of freedom that are possible from tissues and biological systems interacting together. Panjabi (1992) previously outlined that dysfunction brought about by spine instability is an end product of the passive musculoskeletal subsystem, which includes ligaments, joint articulations, and passive components of muscle, the active musculoskeletal subsystem, which includes contractile muscle fibers, and the neural subsystems which include α-motorneurons and γ-motorneurons, as well as sensory nerve fibers originating from muscle spindles and Golgi tendon organs (Panjabi, 1992). Neural subsystems may also include higher level processes such as integration of sensory signals by the cerebellum. Movement is a complex interplay of many subsystems and collection and analysis of motion shows how these subsystems work together. Neck pain may alter any one of these subsystems and cause deviations in the motion signal. The motion signal allows for determining the overall "net" function for how all subsystems work together. The dependent variables collected may also help to show whether particular physiological subsystems are affected.

2.5.5 Signal Application within Research

Gait variability in older adults in response to auditory stimuli is a topic of great interest and has previously been explored through 3D motion capture (Kaipust, et al., 2013). The analysis in the Kaipust et al. (2013) study is based on the theory that older adults display reduced complexity during movement (similar to reduced variability in other systems such as the heart). For this study, older adults and young adults walked on a treadmill with infrared-emitting markers placed as rigid bodies above the knee on the thigh, above the ankle on the shank, on the sacrum, and on the foot. 3D Investigators (NDI, Waterloo, Ontario) were used to assess stride length, step width and stride interval. A Detrended Fluctuation Analysis (DFA) was then performed in Matlab (MathWorks, Massachusetts, USA) which assessed long-range, power-law correlations over time. This method divided the data into time windows and then calculated the logarithm of fluctuation within the window plotted relative to the logarithm of the size of the window. The data was then "detrended" by calculating the best-fitted line for each window and subtracting this from the data, and using these new plots to calculate root mean square fluctuation. The relationship of root mean square fluctuations were then compared across the data series to provide a relationship of fluctuation occurring across time. In this case, linear and quadratic relationships were assessed, with a quadratic relationship representing balance in variability between complexity and predictability where the apex represents an optimal level that balances both complexity and predictability. It was determined that this quadratic relationship was seen when adults listened to the more complex auditory stimuli (Kaipust et al., 2013).

In another study, Gams, et al. (2011) discuss how they used the 3D Investigator (NDI, Waterloo, Ontario) to create algorithms of human stability that could then be applied to a robotic leg. Infrared-emitting markers were placed on the hip, knee and ankle of humans, and data was collected as humans performed squats. The algorithm was then effectively applied to maintain stability in a robotic leg during squatting movements on both flat and inclined surfaces (Gams et al., 2011).

Motion capture systems like the 3D Investigator (NDI, Waterloo, Ontario) have also been used to track timing during perturbations (Hur, et al., 2013). For instance, markers may be applied to inanimate objects allowing researchers to determine both the onset of the perturbation and timing of stabilization (Hur et al., 2013).

The 3D Investigator (NDI, Waterloo, Ontario) has also been used to track movement of the hand in patients with multiple sclerosis (Esteki, et al., 1994). For this, infrared-emitting markers were placed on the index finger and patients with multiple sclerosis and healthy participants were directed to complete reaching movements towards a target. Data was used to calculate both the accuracy (mean location of hand placement with respect to the target) and precision (standard deviation of hand placemen with respect to the target). Thalamic deep brain stimulation was then applied in order to assess how stimulation may be used to improve motor control of the hand in patients. The study found that accuracy and precision was greatest in healthy participants, followed by participants with multiple sclerosis who had deep brain stimulation, with greatest error seen in participants with multiple sclerosis who did *not* have deep brain stimulation (Esteki et al., 1994).

2.5.6 Proposed Features and Use of Signal for Thesis

My master thesis seeks to address whether coordination and motor control of the upper limb may be assessed on a dart throwing task using infrared-emitting markers and a 3D Investigator system (NDI, Waterloo, Ontario). The NDI 3D Investigator system has excellent accuracy (0.4 mm) and spatial resolution (0.01 mm) and is reputable for its use in motion analysis (Esteki et al., 1994; Gams et al., 2011; Hur et al., 2013; Kaipust et al., 2013). The system captures detailed data on individual segment and joints relative to each other, allowing for analysis in six degrees of freedom including in the anterior/posterior directions, medial/lateral directions, and superior/inferior directions. Millisecond accuracy is also maintained, and the system may be paired with electromyography to compare joint kinematics alongside muscle activity. The use of infrared light in oppose to magnetic fields reduces sources of noise introduced by magnetic fields as seen in throwing studies described above (McNaughton et al., 2004; Timmann et al., 2008; Timmann et al., 2000). The 3D Investigator signal also may be filtered with a low-pass Butterworth filter that removes low-frequency noise, such as caused by movement, and smooths the signal. These features make the 3D Investigator a tool of choice in the field of motion analysis.

2.5.7 Quality Assurance

The NDI motion capture signal contains coordinates in three planes including the sagittal plane (*x* axis), coronal plane (*y* axis), and transverse plane (*z* axis) (Figure 3). Magnitude of angular displacement is understood as degrees of rotation of an axis around its corresponding axis in the reference segment, where perfect alignment of the two axes in a straight line is 0 degrees. Magnitude of rotation is never perfect, since it is assumes there is perfect alignment when the limb is straight. Careful placement of the rigid bodies during analysis helps to reduce this error ensuring that the angle produced by the rigid bodies are in line with angles of limb segments.

Filtering of the signal with a low pass Butterworth filter is also helpful to reduce unwanted low frequency artifacts from movement and smooth the signal (Najarian, et al., 2012).

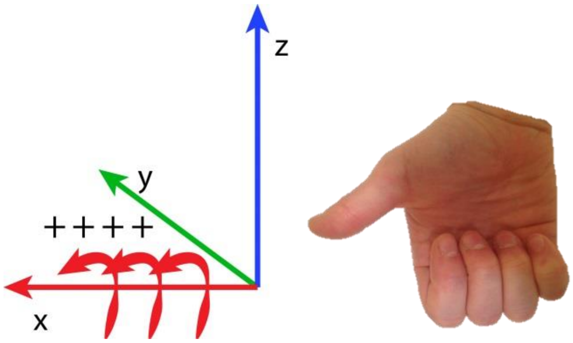

Figure 2.3. Right hand rule depicting direction of movement around an axis. When the thumb is pointed in the direction of the axis and rotation occurs in the direction of the curled fingers, rotation is positive, whereas rotation in the opposite direction of the fingers is negative. Typically, the coordinate system aligns so that the *x* axis points laterally, the *y* axis anteriorly, and the *z* axis upward.

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Chapter 3: Neck Pain Alters the Response of the Cerebellum Following Motor Training

3.1 Introduction to Chapter

Substantial evidence suggests that neck pain has implications for sensorimotor function. People with neck pain experience loss of acuity in proprioception (Kristjansson, et al., 2003; Lee, H.-Y., et al., 2008), poor smoothness of movement (Sjölander, et al., 2008), and altered interpretation of proprioceptive signals (Paulus, et al., 2008)

The cerebellum plays a key role in receiving sensory input and processing this input to predict sensory consequences of movement for online motor corrections. This function allows corrections to be made prior to the time physically needed to receive sensory feedback from distal sources such as the hand (Manto, et al., 2012). Sensory encoding by the cerebellum may be impaired in neck pain. A recent study demonstrated that there were differential changes in the amplitude of upper limb somatosensory evoked potential (SEP) peaks related to the cerebellum-primary somatosensory cortex (S1) pathway following motor learning in SCNP individuals as compared to healthy controls (Andrew, 2014). However, evidence of cerebellar dysfunction leading to altered motor control in SCNP is inconclusive. Cerebellar inhibition (CBI) is a technique that involves transcranial magnetic stimulation applied over the cerebellum 5 ms prior to stimulation over the motor cortex (M1). Previous work found marked differences in cerebellar inhibition (CBI) in neck pain participants following a combined intervention of *spinal manipulation* and *upper limb motor training* (Daligadu, et al., 2013). Unexpectedly, healthy people who completed an intervention of *motor training only* showed no changes to CBI (Daligadu et al., 2013). For this study, levels of stimulator output were constant at 70%, 80% and 90% preventing individualization for participants who were smaller or more easily excited, which may have accounted for the lack of change in the healthy group, and the interventions differed between healthy and neck pain groups. CBI at fifty percent (CBI_{50}) was piloted as a method to study CBI changes more thoroughly (Baarbé, et al., 2014). Comparisons are made when inhibition reaches fifty percent (CBI_{50}) and at stimulator outputs 5 and 10% above CBI_{50}. Using this technique, significant disinhibition was seen at CBI_{50} and at stimulator outputs 5 and 10% above CBI_{50} following motor training of a typing task in healthy participants (Baarbé et al., 2014), suggesting the CBI_{50} technique is more sensitive than the technique used in Daligadu et al. (2013). With this new found technique, I set out in this study to compare CBI_{50} in healthy and neck pain participants to observe their cerebellar responses. In order to determine whether SCNP was a cause or an effect of altered cerebellar inhibition to M1, I also compared the effects of treating areas of neck dysfunction prior to the motor training task with a control intervention. The overall goal of this research study was to determine the nature of cerebellar changes in people with neck pain and to use spinal manipulation to determine if these changes could be reversed by treating areas of neck dysfunction.

3.2 Abstract

Cerebellar inhibition at fifty percent (CBI_{50}) was measured in participants with subclinical neck pain (SCNP) and healthy participants in order to quantify the impact of SCNP on cerebellar function in response to motor training. To determine whether SCNP was a cause or an effect of altered cerebellar inhibition to the motor cortex (M1), the effects of treating areas of neck dysfunction prior to the motor training task were compared to a control intervention that was also delivered prior to motor training in the SCNP group.

Twenty-seven volunteers (16 women, range 18 – 27 years) with subclinical neck pain and twelve healthy volunteers (2 women, range 20-27 years) participated in the study. Neck pain participants were randomized so that fourteen participants comprised the manipulation group (8 women, range 18 – 27 years) and thirteen participants comprised the neck pain control group (8 women, range 19 – 24 years). Cerebellar inhibition (CBI) at increasing intensities, along with test motor evoked potentials (test MEPs) and resting threshold (RTh), were measured *before* and *after* a therapeutic intervention of spinal manipulation (manipulation group) or passive head movement (neck pain controls), and upper limb motor acquisition (all participants). The motor acquisition task involved typing eight letter sequences of the letters Z, D, F, P using right index finger abduction-adduction (e.g. Z,D,P,Z,F,P,D,D). CBI was normalized as the percentage of the test MEP amplitude pre and post-intervention conditions, and CBI$_{50}$ was determined as CBI at fifty percent. Comparisons were then made at CBI$_{50}$ and at 5 and 10% stimulator output above CBI$_{50}$ (CBI$_{50}$+5% and CBI$_{50}$+10%). A main interaction of group on pre vs. post was seen ($F_{2,72} = 11.247$, $P < 0.001$), as was a main effect of pre vs. post ($F_{1,72} = 37.378$, $P < 0.001$). Significant differences were found between groups on their post-intervention measurements ($F_{2,75.1} = 20.957$, $P < 0.001$) with significant higher CBI magnitudes found in the manipulation group than in neck pain controls (146 ± 95% manipulation vs. 58 ± 33% neck pain controls, $P < 0.001$) and in healthy participants than in neck pain controls (98 ± 49% healthy vs. 58 ± 33% neck pain controls, $P < 0.001$). Marked differences to CBI were seen between manipulation, healthy and neck pain individuals post intervention. Neck pain may impair the normal cerebellar response to upper limb motor acquisition, and manipulation may restore cerebellar responses to normal levels.

3.3 Introduction

Neck pain is a common and debilitating problem, and experts estimate 30 to 50% of the general population experiences this condition (Hogg-Johnson, et al., 2008). Neck pain has been found to correspond with altered muscle recruitment patterns (Falla, et al., 2004; Szeto, et al., 2005), decreased proprioceptive acuity to position the head to a neutral position (Kristjansson et al., 2003; Lee, H.-Y. et al., 2008), poor smoothness of movement (Sjölander et al., 2008) and altered interpretation of proprioceptive signals (Paulus et al., 2008). Participants with neck pain also show sensitization of the neck (Lee, H., et al., 2005), which is decreased range of motion that occurs on subsequent trials and has no mechanical explanation. These studies suggest that neck pain has sensory implications that influence how the central nervous system receives and processes sensory input.

Subclinical neck pain (SCNP) has been studied in previous studies (Haavik, et al., 2011; Lee, H., et al., 2004; Lee, H. et al., 2005; Lee, H.-Y. et al., 2008), where it is described as mild-to-moderate recurrent neck pain for which participants have not yet sought treatment. SCNP has been found to occur alongside decreased muscle endurance (Lee, H. et al., 2004; Lee, H. et al., 2005), decreased range of motion (Lee, H. et al., 2004) and impaired cervical kinesthesia (Lee, H.-Y. et al., 2008). Due to its recurrent nature, SCNP provides an opportunity to explore neurophysiologic dysfunction without the confounding effect of current pain, which has been shown in previous studies to affect measures of sensorimotor integration and motor control (Rossi, et al., 2003; Strutton, et al., 2005; Waberski, et al., 2008). SCNP may influence sensory encoding of the cerebellum. A recent study demonstrated that there were differential changes in the amplitude of upper limb somatosensory evoked potential peaks related to the cerebellum-somatosensory cortex (S1) pathway following motor learning in SCNP individuals as compared to healthy controls (Andrew, 2014). However, evidence of cerebellar dysfunction leading to altered motor control in SCNP is inconclusive.

The cerebellum receives and integrates sensory information before modulating output through Purkinje cells to cortical regions. This allows for the learning of smooth, continuous movements and for the formation of sensorimotor representations such as body schema (Popa, et al., 2013). Alterations in sensory input such as occurs in neck pain may be sufficient to change the plasticity of the cerebellum to motor and somatosensory cortices (Doyon, et al., 2003; Doyon, et al., 2002).

A previous study found alterations in cortical and cerebellar motor processing in a neck pain group following spinal manipulation and motor training using a transcranial magnetic stimulation (TMS) technique called cerebellar inhibition (CBI) (Daligadu et al., 2013). However this study had several limitations. One important limitation was that the control group consisted of healthy individuals. The study lacked a neck pain control group who did not receive treatment, making it hard to discriminate whether the treatment or the neck pain was responsible for the observed changes in cerebellar inhibition between the neck pain and healthy group. An additional challenge was that the healthy people who completed an intervention of *motor training only* showed no changes to CBI (Daligadu et al., 2013) when past research using fMRI has shown changes in cerebellar excitability in healthy participants who completed a similar task (Doyon et al., 2002). The authors suggested that this may have been because levels of stimulator output for the cerebellar coil were held constant at 70%, 80% and 90% of stimulator output for all participants, preventing individualization for participants who were smaller or more easily excited, which may have accounted for the lack of change in the healthy group (Daligadu et al., 2013).

CBI at fifty percent (CBI_{50}) was developed as a method to study CBI changes more precisely (Baarbé et al., 2014) which involves applying a protocol that is individualized to each participant's inhibition profile. CBI is collected at varying intensities, and comparisons are made when inhibition reaches fifty percent of the test motor evoked potential (test MEP) referred to as CBI_{50} and at stimulator outputs 5 and 10% above CBI_{50}. Using this technique, significant disinhibition was seen following completion of a novel motor acquisition typing task in healthy participants (Baarbé et al., 2014), suggesting the CBI_{50} technique is more sensitive than the technique used by Daligadu et al. (2013).

CBI has previously been studied as a way to assess functional connectivity and plasticity between the cerebellum and motor cortex (M1) (Daskalakis, Zafiris J, et al., 2004; Pinto, et al., 2001; Ugawa, et al., 1995). The cerebellum transfers input that aids the reorganization and plasticity of cortico-striatal regions (Doyon, et al., 2005; Doyon et al., 2003; Doyon et al., 2002). More recently, the cerebellum has been shown to form internal models that help automate the performance of cognitive activities (Ito, 2008). Thus, altered sensory input in patients with neck pain may affect output of the cerebellum to the somatosensory and cerebral cortices and thereby influence plasticity of representations required for motor tasks. One study in SCNP patients found decreased elbow joint position sense relative to healthy controls (Haavik et al., 2011). A single treatment session led to improved upper limb joint position sense relative to an SCNP group who received a control intervention, suggesting that body representation may be altered in SCNP patients and that normalizing afferent input from the neck may influence the body schema (Haavik et al., 2011).

In this study, we set about to explore alterations to motor training-induced plasticity from the cerebellum in participants with neck pain to explore how altered sensory input due to neck pain affects the cerebellar response when participants complete an upper limb typing task. We considered upper limb motor training using a novel motor acquisition task, and we individualized each stimulus intensity using the technique described in Baarbé et al. (2014). Spinal manipulation has been found to transiently increase firing of muscle spindle afferents in a feline model, upon which, afferent input firing from the affected region lessens in frequency relative to baseline (Pickar, et al., 2006; Reed, et al., 2015). Spinal manipulation thus represents a means of changing afferent input from muscle spindles to the central nervous system. In order to be able to determine whether any alterations in motor performance and cerebellar processing observed in SCNP participants are a cause or an effect of altered sensory input from the neck, we compared two SCNP groups. One group performed motor training after receiving spinal manipulation and the second group performed motor training after having their neck palpated and moved in a manner to mimic neck manipulation but who were not actually manipulated.

To test how altered sensory input modulates the control of the cerebellum on motor and somatosensory cortices, we applied the CBI_{50} technique through a magnetic stimulus to the cerebellum applied five milliseconds in advance of a stimulus over M1 before and after a novel motor acquisition task.

3.4 Materials and Methods

3.4.1 Participants

Twenty-seven participants (16 women, range 18 – 27 years) with recurrent neck pain, but minimal acute pain on the day of testing, participated in the study. Neck pain was graded between Grade 1 to Grade 3 on the Chronic Pain Grading Scale (Guzman, et al., 2009; Von Korff, et al., 1992), which categorizes pain intensity and disability between a grade of 0, meaning the participant experienced minimal neck pain and no disability in the previous six months, and a grade of 4, which meant that the participant experienced severe neck pain and disability in the previous six months. Participants with neck pain were randomized to one of two groups. Fourteen participants (8 women, range 18 - 27 years) who would receive a spinal manipulation by a registered chiropractor were part of the spinal manipulation group, and thirteen participants (8 women, range 19 – 24 years) who would receive a passive head movement (PHM) control comprised a second group. Participants also had to be right-handed, and had a mean score (± standard deviation) on the Edinburgh Handedness Inventory of 76.8 ± 20.7 in the spinal manipulation group and 73.9 ± 19.8 in the PHM group (Oldfield, 1971).

Data was also collected from twelve healthy controls (2 women, range 20 – 27 years) who did not have neck pain on the day of testing or history of neck pain. These participants all had very low grading on the Chronic Pain Grading Scale (no more than zero disability points and a characteristic pain intensity score $\leq$ 23). Participants also had to be right-handed, and had a mean score (± standard deviation) of 65.0 ± 31.8 on the Edinburgh Handedness Inventory. Ethical approval was obtained from the university ethics committee, and the study was performed in keeping with the human right principles set out in the Declaration of Helsinki (WMA, 2013).

3.4.2 Neck Pain Characteristics

Frequency, duration, and location of neck pain, as well as the severity of neck pain was detailed by neck pain participants. To measure severity of neck pain, participants were shown a 10 cm Visual Analog Scale and were asked to indicate pain at the time of testing and to indicate the level of severity experienced during flare-ups in the previous six months. Participants also indicated functional limitations on activities of daily living using the Patient-Specific Functional Scale (Stratford, 1995; Westaway, et al., 1998).

3.4.3 Exclusion Criteria

Exclusion to participate included major structural injuries or anomalies to the cervical spine including disk herniation or fracture. As well, participants were excluded if they had received manual therapy or care for their neck in the previous three months. Other exclusion items included inflammatory or system conditions (e.g. rheumatoid arthritis or infection), trauma or other severe injury to the spine, radicular arm pain, hypermobility, intake of anti-coagulant medication or bleeding disorders, history of stroke or cancer in the past five years, and vertigo or dizziness. Participants also completed a TMS safety checklist with exclusion items including prior head injury, history of epilepsy, prior heart condition, recent intake of neuroactive medication, pregnancy, and metal implants in the head or upper body (e.g. pacemakers).

3.4.4 Experimental Protocol

All the participants were asked to attend a session in which the technique cerebellar inhibition at fifty percent (CBI_{50}) previously described (Baarbé et al., 2014) was measured.

CBI technique involves application of TMS over the cerebellum ipsilateral to the right hand as well as application of TMS over M1 on the contralateral (left-hand) side. When TMS is applied over the left M1, a muscle twitch volley is produced that is recorded from a distal hand muscle of the right hand. The combination of cerebellar and M1 stimulations at an interstimulus intervals 5 – 8 milliseconds apart causes inhibition of the M1 muscle twitch volleys (Pinto et al., 2001; Ugawa et al., 1995).

Participants sat upright on a chair with their right arm resting on a pillow on their lap. Motor evoked potentials (MEPs) were recorded from the first dorsal interosseus of the right of hand using disposable Ag/AgCl electrodes (Figure 3.1). MEPs were amplified (x 1000) and band-pass filtered (20 - 1000 Hz) through a Cambridge Electronic Design 1902 amplifier (CED, Cambridge, England), before sampled at 5 000 Hz with a CED 1401 (CED, Cambridge, England) and recorded as a digital signal (Signal 4.08, CED, Cambridge, England).

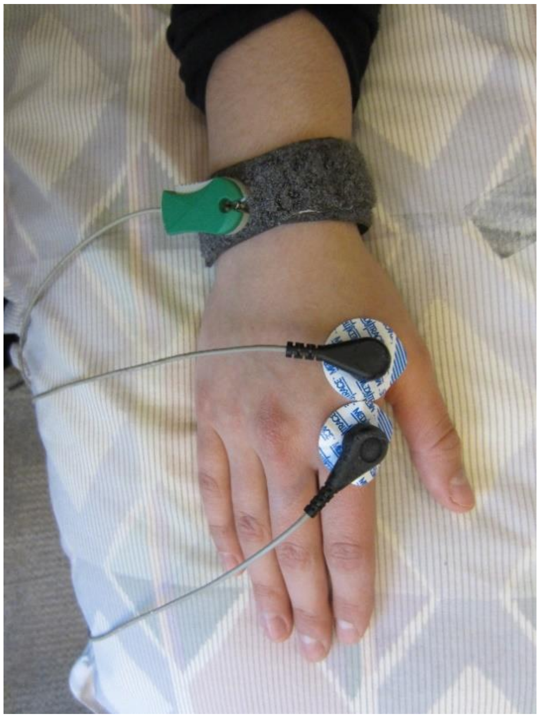

Figure 3.1 MEPs were recorded from the first dorsal interosseus of the right of hand using disposable Ag/AgCl electrodes.

3.4.5 Transcranial magnetic stimulation

Two coils were used in the experiment. The first coil, a double cone coil (11 cm diameter), was strapped to the cerebellum ipsilateral to the right hand at the midline between the inion and the external auditory meatus at the level of, or slightly above the level of, the inion to elicit optimal MEP suppression as described by Ugawa et al. (1995). This coil connected to a Magstim Bistim (Magstim Co., Whitland, Dyfed, UK) which channels the voltage from two Magstim 200^2 units together so that the output is 13% greater than output from a single unit (Magstim, 2002). The second coil was a figure-of-eight coil (9 cm diameter) held over M1 on the contralateral (left-hand) side. The handle of this second coil was held in a posterior direction approximately 45 degrees from the sagittal plane by a researcher with at least one year of experience. This coil was connected to a Magstim 200^2 (Magstim Co., Whitland, Dyfed, UK) and stimulator output was adjusted to elicit test MEPs ~ 0.5 mV in peak-to-peak amplitude (Figure 3.2). A test MEP of ~ 0.5 mV in peak-to-peak amplitude was selected since test MEPs less than 1 mV have been shown to be the most consistent in their sensitivity for showing cerebellar inhibition (Daskalakis, Z.J., et al., 2004; Ugawa et al., 1995).

Figure 3.2 The figure-of-eight coil was held over the contralateral M1 and the double-cone coil was strapped over the ipsilateral cerebellum at the midline between the inion and the external auditory meatus at the level of, or slightly above the level of, the inion (Ugawa et al., 1995).

3.4.6 Cerebellar Inhibition

Once the optimal sites for stimulation had been found, the test MEP amplitude was found from the average of sixteen MEPs elicited by the figure-of-eight coil over M1. CBI was then elicited by firing of the double-cone coil 5 ms in advance of the figure-of-eight coil. Ten cerebellar-M1 MEPs were elicited and averaged at each of three to seven Magstim Bistim stimulator intensities (an average of five cerebellar intensities were used depending on when inhibition had reached fifty percent). Using the technique described in (Baarbé et al., 2014), CBI_{50} was determined as the stimulator output of the double cone coil that would elicit a MEP fifty percent of the test MEP. CBI_{50} during the experiment was estimated, but in the case of overestimating the stimulus for the fifty percent level (Fisher, et al., 2009), additional CBI was measured at stimulator intensities above and below CBI_{50}. Once CBI had been collected, resting threshold (RTh) was determined as the stimulator intensity that would elicit five out of ten significant MEPs with peak-to-peak amplitude equal to or greater than 50 µV. This entire protocol with the inclusion of RTh and test MEP collections was repeated before and after manipulation or PHM (as randomized at the beginning of the study) and upper limb motor acquisition.

3.4.7 Spinal Manipulation

Clinical indicators of altered function at individual spinal segments include restricted intersegmental range of motion, palpable muscle tension at the intervertebral level, and tenderness to palpation of the joint (Fryer, et al., 2004; Hubka, et al., 1994). A pragmatic approach was applied where a practicing registered chiropractor applied treatment to the regions of palpable tenderness and restricted movement in the cervical spine that were most noticeable and considered likely to contribute to the patient’s pain.

The manipulations performed involved high-velocity, low-amplitude spinal manipulation. All treated areas of the neck region were documented, and recorded on the patient's file, alongside the frequency, location, duration and severity described by the patient. For the duration of the brief time of the treatment (five to ten minutes), the patient was moved to a reclining treatment chair. EMG electrodes were kept on the patient, and the only change made was that the leads were unplugged from the base. Care was taken to ensure that the participant returned to the same state as before the intervention.

3.4.8 Control Conditions

Procedures were also carried out in two control conditions. The first control condition was for participants with neck pain who were randomized to receive the control. Similar to the patients in the manipulation group, light palpation was applied to the neck. The head was gently moved into lateral flexion and rotation in a similar manner to the actual neck manipulation, without applying the high-velocity, low-amplitude manipulative thrust. This condition was carried out to ensure that the changes that were measured after the manipulation were not simply due to the passage of time, or due to the activation of muscle spindles, joint receptors or cutaneous touch that would occur as the neck is positioned for cervical spine manipulation. Control participants were also moved to the reclining chair, similar to the manipulation patients described above. Once participants received the intervention, they then completed the motor sequence acquisition task before completing the final CBI measurements. The second control condition was healthy participants who complete only the motor acquisition task. To determine whether the passive head movement may have had an effect on the CBI response, a small number of healthy participants were also given passive head movement prior to completing the motor training task. This did not impact their CBI response following motor learning.

3.4.9 Motor Acquisition Task

Following the manipulation and control conditions, all participants were asked to learn a motor task by typing randomized eight-letter sequences of the letters Z, P, D, and F (Z,D,P,Z,F,P,D,D) as quickly and as accurately as possible. This task was performed on specially-designed keyboard to encouraged right index finger adduction-abduction to reach individual keys (Figure 3.3). E-Prime 2.0 software (Psychology Software Tools, Sharpsburg, Pennsylvania) was used for writing the program and as a platform to implement the task. This task takes participants ~15 minutes to complete and was selected as similar tasks have been shown to activate the cerebellum (Doyon et al., 2002; Penhume, et al., 2002). Performance on the task was measured as the response time to press each key sequentially as well as the accuracy of each key selection. To determine performance, participants completed ten instances of eight-letter sequences at the beginning of the experiment (before CBI) and at the start and end of the motor acquisition task. EMG electrodes placed on the first dorsal interosseous recorded background muscle activity while completing the task. Following completion of the motor acquisition task, all participants completed the procedure for CBI a second time.

Figure 3.3 Keyboard for motor acquisition task. Participants typed randomized eight-letter sequences of the letters Z, P, D, and F (Z,D,P,Z,F,P,D,D) as quickly and as accurately as possible for ~ 15 minutes.

3.4.10 Data Analysis

As described in Baarbé et al. (2014), the traces were carefully examined at high gain for instances of extraneous activity (cervicomedullary evoked potentials (CMEPs), cervical root activity, antidromic activity). Previous work has identified CMEPs elicited from double-cone stimulations over the inion and recorded from the first dorsal interosseus to have a latency of ~ 18 ms and cervical root activity to have a latency of ~ 15 ms (Martin, et al., 2009). Whereas, CBI ideally should elicit inhibited MEPs that have a latency ~ 21 ms from stimulation of M1 (Martin et al., 2009) which in our experiments was ~ 26 ms from stimulation over the cerebellum considering the 5 ms interval from the cerebellum stimulus (double-cone coil) to the M1 stimulus (figure-of-eight coil). Individual traces that showed extraneous activity, along with traces that showed background muscle activity before or following stimulation, were removed so that 8 to 10 MEPs were averaged for each level of stimulus intensity (Baarbé et al., 2014). Only one participant out of forty-two participants tested showed CMEP and cervical root activity throughout collection and his data could not be used in analysis (< 3% of individuals tested). Two other participants showed EMG activity in the trace leading up to stimulation and their data was also removed so that of forty-two participants tested, thirty-nine were used in final analysis (14 manipulation, 13 neck pain participants and 12 healthy controls).

3.4.11 Normalization

Average peak-to-peak amplitude was found for each level of stimulus intensity and these averages were divided by the test MEP for each participant for each intensity of CBI (Baarbé et al., 2014). Previous work had found that CBI decreases at increasing level of stimulator intensities and that by selecting a standardized level such as the fifty-percent mark, the comparisons could be individualized for each participant (Baarbé et al., 2014) CBI_{50} was used as the level for comparisons, as well as CBI at simulator output intensities 5 and 10% above CBI_{50} (termed CBI_{50}+5% and CBI_{50}+10%) (Baarbé et al., 2014).

3.4.12 Statistical Analysis

Repeated-measures, 2 x 3 x 3 mixed-design analysis of variance (ANOVA) was used to assess significance. Within-subject variables included time (pre-intervention vs. post-intervention) and stimulator intensities (CBI_{50}, CBI_{50}+5% and CBI_{50}+10%). The between-subjects factor was group (manipulation group, neck pain control and healthy controls). Post-hoc one-way ANOVAs and independent samples *t* tests were used compare the levels where significance is seen in the mixed-design ANOVA.

Mean response time on the motor sequence acquisition task was found for each participant, and assessed with a repeated-measures, 3 x 3 mixed-design ANOVA. The within group factor included time (baseline, pre-task condition, vs. post-task condition), and the between group factor included group (manipulation group, neck pain controls, and healthy controls). Post-hoc repeated-measures ANOVAs and paired-sample *t* tests were used to compare the levels where significance is seen in the mixed-design ANOVA. For all statistical tests, the *P* value was set to 0.05, and statistical analysis was performed through SPSS Statistics 22 (International Business Machines Corporation, Armonk, New York).

3.5 Results

3.5.1 Participant Characteristics

The neck pain characteristics for the manipulation group and neck pain control group are summarized in Table 3.1. Independent samples *t* tests performed on all measurements showed no differences between the two groups, with the exception of day-to-day functionality on the Patient-Specific Functional Scale which showed patient's perception of greater loss to function to be greater in neck pain participants who received manipulation than in neck pain controls (5.6 ± 2.4 manipulation vs. 8.0 ± 2.4 neck pain controls, *P* = 0.017).

Table 3.1 Neck pain characteristics for the manipulation group and neck pain controls.

Neck Pain Characteristic	**Neck Pain Manipulation (Mean ± Std. Dev.)**	**Neck Pain Control (Mean ± Std. Dev.)**
Frequency of Neck Pain (days per months)	14.5 ± 8.8	16.9 ± 9.1
Duration of Neck Pain (years)	3.2 ± 2.2	1.6 ± 1.5
Neck Pain Intensity in Past 6 Months (Visual Analog scale)	6.4 ± 2.1	5.6 ± 2.1
Neck Pain Intensity at Current Time (Visual Analog scale)	2.8 ± 2.0	3.4 ± 2.5
Patient-Specific Functional Scale (0 indicating loss of function and 10 indicating no losses to functionality)	5.6 ± 2.4	8.0 ± 2.4
Chronic Pain Grade Scale score (0 absence of pain or disability to 4 severe pain and disability)	1.7 ± 0.6	1.5 ± 0.7
Disability Days (days per month)	5.4 ± 8.2	2.2 ± 3.3

3.5.2 RTh and Test MEPs

No differences were seen before or after the intervention in RTh. The mean RTh (± std. dev.) before the intervention was 43.3 ± 7.5% of maximal stimulator output and 43.0 ± 7.0% maximal stimulator output following the intervention (*P* = 0.60 for between pre vs. post main effects and *P* = 0.75 for group interaction effects). Similarly, no differences were seen in the stimulator intensity that would elicit test MEP of ~ 0.5 mV in peak-to-peak amplitude. Mean test MEP stimulator intensity (± std. dev.) was 48.6 ± 8.4% maximal stimulator output before the intervention and 48.8 ± 8.3% post intervention ($P = 0.32$ for pre vs. post main effects and $P = 0.80$ for interaction effects).

Manipulation may have unique effects on M1 excitability (Haavik-Taylor, et al., 2007, 2008) and so the manipulation group was assessed separately using paired *t* tests. No difference was seen for either RTh or test MEP stimulator intensity pre and post manipulation and motor training.

3.5.3 Cerebellar Inhibition

Raw traces from representative participants from all three groups may be seen in Figure 3.4. The grey lines show the test MEP which was measured in each condition pre- and post-intervention. The red lines show CBI_{50} which was the MEP produced by firing the cerebellar coil and then the M1 coil 5 ms later. In the pre-intervention state, all participants showed a CBI_{50} (red line) that was fifty percent of the original test MEP (grey line). Following the intervention, neck pain controls show no change to CBI, whereas healthy increased the magnitude of their CBI and neck pain manipulation showed an exceeding great increase to their inhibition levels.

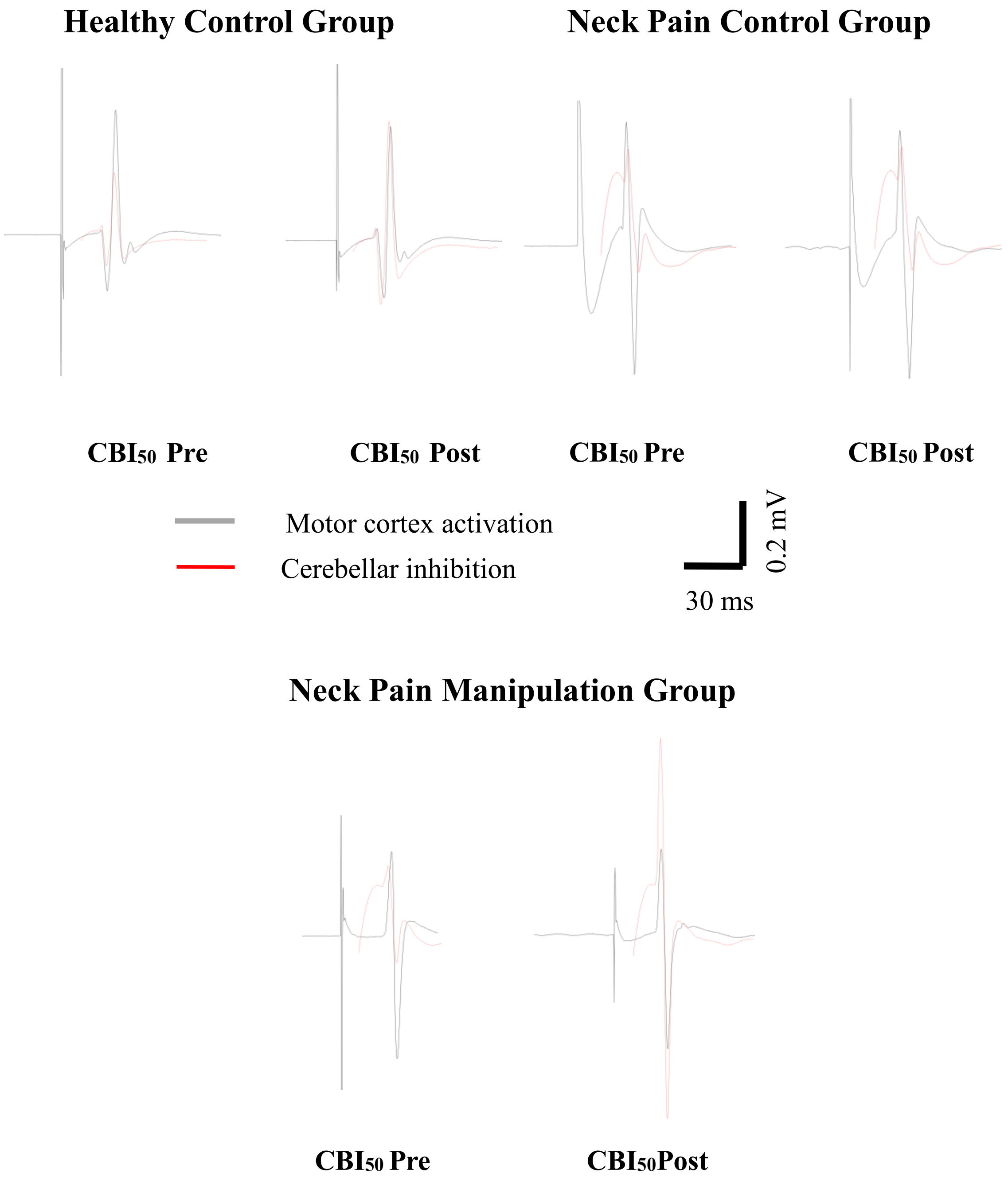

Figure 3.4 Raw traces from representative participants from all three groups showing CBI_{50} at pre- and post-motor training, as relative to raw traces of M1 activation. At pre-motor training CBI is fifty percent of M1 activation. Following motor training, an increased amplitude is seen representing less inhibition in the manipulation and healthy groups. Little change in CBI is seen following motor training in the neck pain control group.

A main interaction of group on pre vs. post was seen ($F_{2,72} = 11.247$, $P < 0.001$), as was a main effect of pre vs. post ($F_{1,72} = 37.378$, $P < 0.001$). Post hoc Welch ANOVA tests showed there were significant differences between groups on their post-intervention measurements ($F_{2,75.1} = 20.957$, $P < 0.001$). Post hoc Welch *t* tests showed significant higher CBI magnitudes in healthy than in neck pain controls (98 ± 49% healthy vs. 58 ± 33% neck pain controls, $P < 0.001$). The manipulation group also showed a significantly higher CBI magnitudes than neck pain controls (146 ± 95% manipulation vs. 58 ± 33% neck pain controls, $P < 0.001$). When manipulation and healthy participants were compared, the manipulation group showed significantly higher CBI magnitudes than the healthy group (146 ± 95% manipulation vs 98 ± 49% healthy, $P = 0.006$). No significant differences were seen between groups on pre-intervention measurements.

Post hoc paired *t* tests comparing pre- vs. post-intervention in each of the groups showed a significant increase in the magnitude of inhibition from pre to post in healthy participants (an increase from 45 ± 22% pre to 98 ± 49% post, $P < 0.001$) (Figure 3.5). As well, the manipulation group showed a significant increase in their magnitudes of inhibition (an increase from 56 ± 32% pre to 146 ± 95% post, $P < 0.001$) (Figure 3.6). Neck pain controls showed no increases to their magnitudes of inhibition (57 ± 21% pre and 58 ± 33% post, $P = 0.86$) (Figure 3.7).

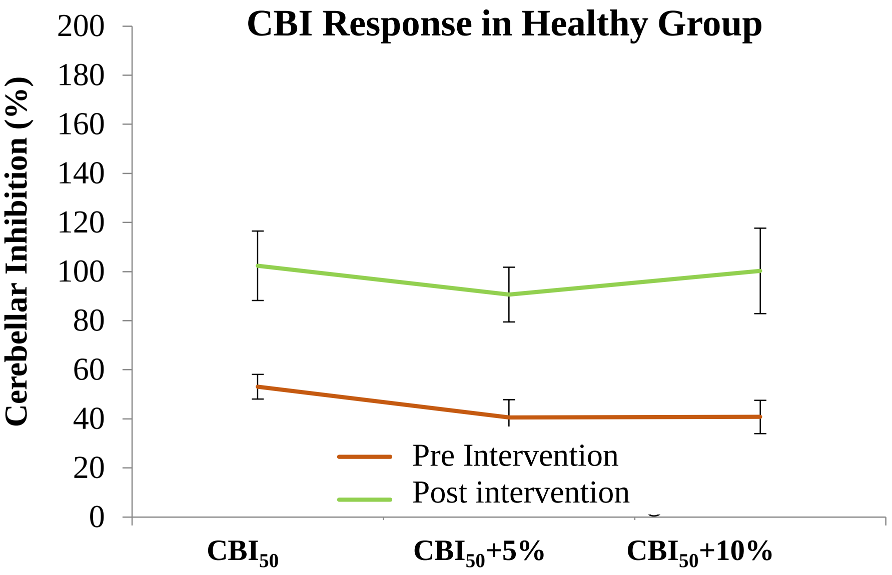

Figure 3.5 Mean CBI response in healthy group pre and post motor training. Error bars represent standard error of the mean.

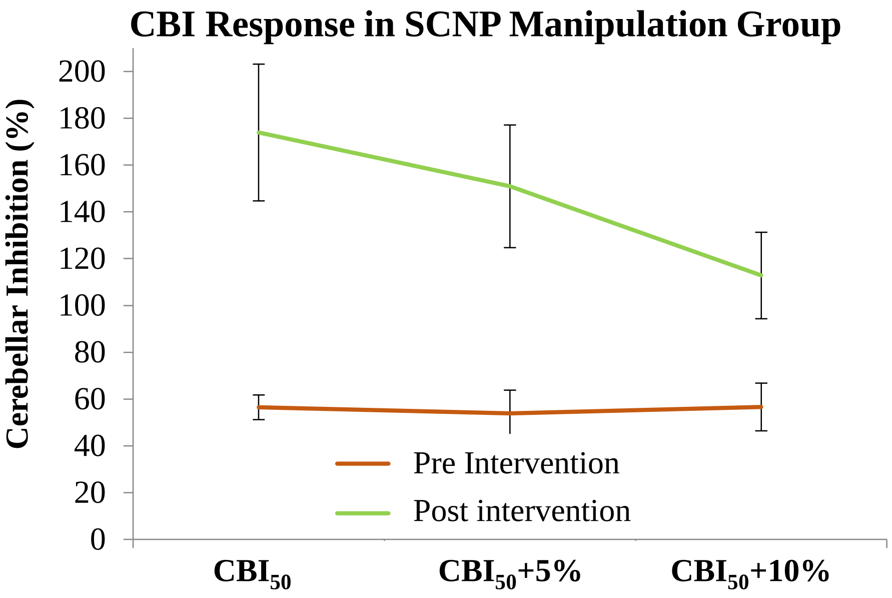

Figure 3.6 Mean CBI response in manipulation group pre and post the combined intervention of spinal manipulation motor training. Error bars represent standard error of the mean.

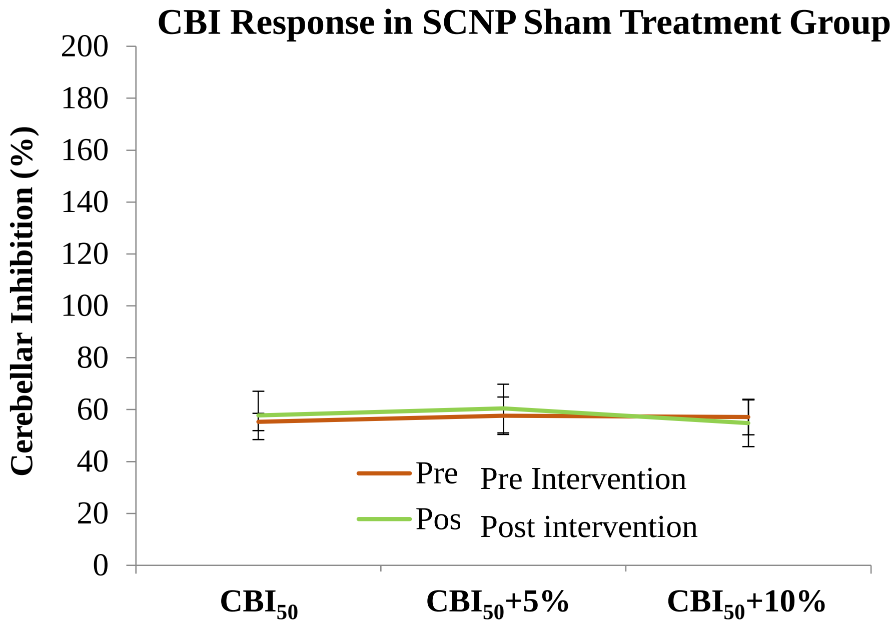

Figure 3.7 Mean CBI response in neck pain control group pre and post the combined intervention of PHM and motor training. Error bars represent standard error of the mean.

3.5.4 Motor Acquisition Task

Participants showed a main effect of response time across the three conditions (baseline, pre-task vs. post-task conditions) ($F_{2,70}$ = 51.563, $P < 0.001$, no interaction effect). Post hoc paired *t* tests showed significantly faster response time from the baseline condition to the pre-task condition, which was an increase in speed from a mean response time of 808.2 ± 223.7 ms at baseline to a mean response time of 712.6 ± 151.1 ms for the pre-task condition ($P < 0.001$). Mean response time also significantly increased in speed from a pre-task mean response time of 724.5 ± 166.6 ms to a post-task mean response time of 625.7 ± 149.3 ms ($P < 0.001$).

Post hoc repeated-measures ANOVA comparing response time across the three conditions for each group showed a significant effect of time for healthy participants ($F_{2,20}$

= 14.031, $P < 0.001$), and the post hoc paired t tests showed a significantly faster response time from baseline to the pre-task condition (869.4 ± 288.1 ms vs. 704.2 ± 151.6 ms, $P = 0.009$) and from pre- to post-task conditions (743.6 ± 198.9 ms vs. 647.6 ± 153.3 ms, $P = 0.034$).

Manipulation participants showed a significant effect of time ($F_{1.3,17.4} = 40.338$, $P < 0.001$), and their response times were found to be significantly faster from baseline to pre-task conditions which was the period of time in which they received a manipulation. The increase in speed following the manipulation was from 800.2 ± 214.0 ms baseline to 711.3 ± 171.8 ms pre-task, $P = 0.003$). Following completions of the motor training task, an increase in speed occurred from 711.3 ± 171.8 ms pre-task to 609.2 ms post-task, $P < 0.001$).

The neck pain participants also showed a significant effect of time ($F_{2,24} = 11.186$, $P < 0.001$). However, no increases in speed occurred from baseline to pre-task conditions which was the period of time when they received PHM (765.0 ± 173.2 ms baseline vs. 721.1 ± 138.3 ms pre-test, $P = 0.20$). Once motor training had been completed, neck pain control participants showed an increased in speed from the pre-task condition to the post-task condition (721.1 ± 138.3 ms pre-task condition vs. 623.4 ± 145.5 ms post-task condition, $P = 0.005$) (Figure 3.8).

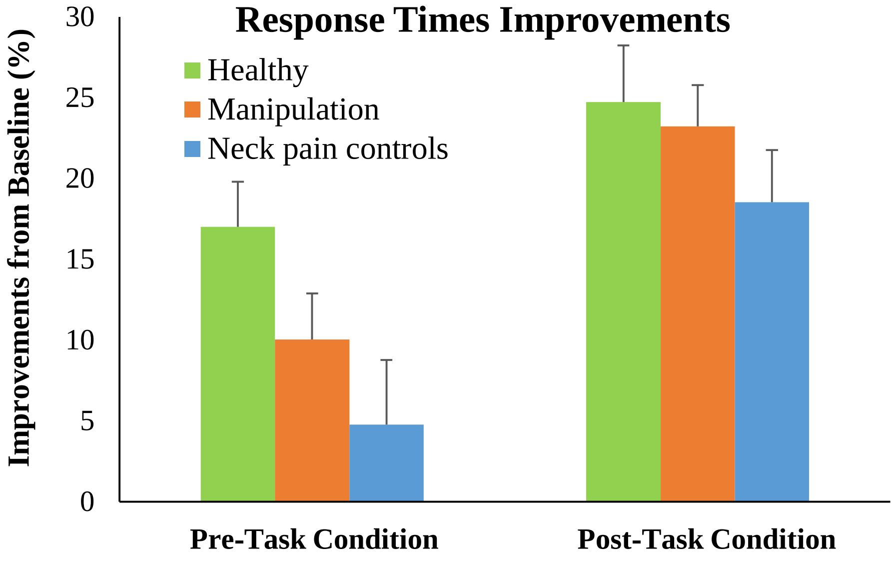

Figure 3.8 Mean response times in all three groups showing the percentage improvement from baseline [(baseline – pre-task)/baseline * 100) or (baseline – post-task)/baseline * 100)]. Improvements are seen in all three groups but the greatest improvements from baseline are seen in the healthy and manipulation groups. The major difference between the manipulation group and neck pain controls is that the manipulation group had received manipulation whereas neck pain groups had received PHM. The Pre-Task Condition bars show changes in response time following manipulation and PHM in neck pain participants from a reference baseline of 0. Improvement was significant following manipulation (*P* = 0.003) but not following PHM (*P* = 0.20). Error bars represent standard error of the mean.

3.6 Discussion

Marked differences were seen in CBI for the SCNP treatment group and the healthy individuals following the completion of a motor training task. Spinal manipulation greatly impacted the cerebellar response to motor training in individuals with neck pain so that the manipulation group showed the greatest magnitudes of post intervention CBI. The healthy group showed the next greatest magnitudes of post-intervention CBI, and no differences were seen to CBI in neck pain controls. Motor acquisition occurred in all individuals as evidenced by improved response times. However, when looking at changes in response time following the manipulation, significant improvements were seen in the manipulation group whereas improvements for the SCNP group who received PHM prior to motor learning were not significant.

The increased magnitude of the CBI response in the manipulation group (above 100%) indicates that it is more than a dis-inhibition of Purkinje cell input to M1 interneurons, but may in fact be due to facilitation of neurons further upstream in the cerebellar-M1 pathway (Reis, et al., 2008). Future work is needed to explore this concept of facilitation in more depth.

The difference between the manipulation and neck pain controls was unlikely to be caused by differences in neck pain characteristics between the two groups. All objective "physical" traits in the two neck pain groups including the frequency, duration and intensity of their neck pain showed no differences. Furthermore the reported number of disability days showed no differences. As well, the two neck pain groups had similar age ranges and number of females. There was a difference in the Patient-Specific Functional Scale, which is a subjective score. The greater perceived loss of function on day-to-day tasks in the manipulation group may have occurred because individuals in the manipulation group knew they were being treated and were more "tuned in" to their neck issues and hence reported greater restrictions to their activities. Alternately, the manipulation group may genuinely have experienced a greater loss of function. The experiment was carried out very carefully so that the only major difference between the two groups was the type of care they received. The manipulation group received a spinal manipulation by a registered chiropractor and they completed an upper limb motor training task, whereas the neck pain controls received a PHM, also delivered by the same chiropractor who palpated the joints and moved and challenged the neck at joint end range, similar to setting up for neck manipulations but without delivering the actual manipulative thrust. The PHM was very similar to low level mobilizations delivered by many manual therapists. Indeed several participants reported feeling a bit better after the PHM suggesting that it was a good control for both therapist patient interaction effects as well as the physiological effects of moving the neck passively.

Additionally, the participants had no idea of the type of results that were expected with respect to CBI so expectancy was unlikely to have affected the results between the two SCNP groups. The increase to CBI levels in the manipulation group is of such a high magnitude and a sufficient number of participants were tested that this increase is unlikely to be attributed to unplanned experimental bias.

Motor learning has been shown to lead to changes in M1 excitability (Lotze, et al., 2003). For this reason, we selected a task that was novel to participants and had limited predictability so as to challenge cerebellar connections rather than simply *hardwire* a simple movement in the motor cortex. Doyon et al. (2003) explains that for early stages of motor sequence learning (similar to the task that we had the participants complete), the deep cerebellar nuclei and cortex is more active and in later stages of motor learning the cortico-striatal layers of the brain become more active. We only tested the participants for a brief period of time early in their learning stage as compared to the Doyon et al. (2002) study, and we ensured that the task had sufficient novelty (had not been used for previous training purposes). Furthermore, changes to M1 excitability could not have contributed to the findings since RTh was the same across all conditions pre and post intervention. The stimulator output for the test MEP was also found to be the same across all conditions pre and post motor training.

We also wanted to be sure that the PHM did not influence motor training or CBI measurements (so that we could effectively compare neck pain controls with healthy participants, and also more effectively understand the manipulation which was expected to influence both motor training and CBI), and so a small number of healthy participants were given a PHM and no differences to the CBI response were seen in these individuals. Similar improvements to response time for the motor acquisition task were also seen between neck pain controls and healthy groups suggesting similar “performance” in both groups. Thus, it is unlikely that PHM had any major influence on motor learning or the CBI response to motor training. Thus we suggest that the presence of neck pain influenced the lack of cerebellar response to motor training in neck pain controls.

Another study (Daligadu et al., 2013) also showed that the CBI magnitude increased with a combined intervention of manipulation and motor training which supports our finding of increased CBI magnitude with the same intervention. Our study extends the Daligadu et al. (2013) study by individualizing the levels selected at fifty percent of the test MEP, as well as by including a neck pain control group who received passive head movement. In the Daligadu et al. (2013), healthy participants showed no changes to their inhibition levels following motor training. Our findings however showed that the healthy group had an increase to CBI levels following motor training, which is likely due to the more precise method used in this current study which individualized the CBI protocol to the 50 percent inhibition level for each participant. In a related study, participants completed a control condition of no activity and there were no changes in CBI levels whereas changes were seen in a healthy experimental group (Baarbé et al., 2014). We applied the same individualizing technique as in Baarbé et al. (2014) and we produced similar findings in a healthy population, suggesting that CBI_{50} method produces robust and reproducible findings, further confirming that the changes observed between groups were due to changes in the cerebellar-M1 pathways.

The cerebellum receives and integrates large amounts of sensory information from joints, tendons and muscles including those from the intervertebral regions of the neck (Manzoni, 2007). This input to the cerebellum becomes integrated for timing of limb movements, and creation of forward internal models to predict the sensory consequences of movement milliseconds prior to the movement (Manto et al., 2012). The cerebellum is also highly active in motor learning and motor adaption (Doyon et al., 2005; Doyon et al., 2003; Doyon et al., 2002). Small muscles across cervical vertebrae indicate minute details of change using the mechanosensory properties of muscle including properties of collagen and titin which are highly involved in mechanosensation (Eckes, et al., 2004; Tirrell, et al., 2012). The findings of this study have shown that SCNP results in significant changes in the cerebellar response to motor training as well as impairs response time to complete a motor sequence task, even though participants were tested on pain free days. This suggests that there are significant differences in SCNP participants to their capability to transfer and process sensations from the neck to the cerebellum leading to changes in cerebellar excitability and greater inhibition, as well as reduced performance.

Tilting of the head is known to affect spatial placement of the hand (Guerraz, et al., 2011) and changes detection of head and neck position (Knox, J. J., et al., 2005). Neck vibration affects the ability to accurately replicate elbow and forearm positions (Knox, J., et al., 2006) and SCNP individuals have impaired upper limb joint position sense (Haavik et al., 2011) and motor performance (Taylor, et al., 2008). These changes in upper limb proprioception with changes in input from the neck are likely due to the brain using mismatched information from the neck to update the body schema, a process which involves encoding by the cerebellum. It is likely that the lack of cerebellar disinhibition in the neck pain control group in response to motor training was due to the influence of altered sensory input to the cerebellum from receptors in the joints and intrinsic muscles of the neck. Manipulation appeared to restore the cerebellar disinhibition response and also improved motor performance response times. Normalizing the sensory input from the spine through treatment of areas showing restricted intersegmental movement may have led to increased excitability of the cerebellum and a subsequent decrease in the inhibition from the cerebellar to M1 in response to motor learning, as well as enabling a greater improvement in performance.

CBI was measured ~ 20 minutes following manipulation, and future work should look at how long lasting manipulation influences the cerebellar response to motor training. It would also be important to know the implications of these findings for the learning of complex upper limb tasks as well as the potential of neck pain to increase injury risk in the workplace.

In conclusion, neck pain was found to lower the magnitude of cerebellar responses and impaired the response time to complete a motor sequence task compared to healthy participants. An acute session of manipulation increased the magnitude of cerebellar responses as well as improved response time. This study suggests neck pain may impair reception of sensory input which influences cerebellar output and motor processing, which may be restored even above that of healthy participants with manipulation.

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Chapter 4: Subclinical Neck Pain Impacts 3D Kinematics of Upper Extremity Dart Throwing

4.1 Introduction to Chapter

Previous work has shown that altered sensory input to the neck as a result of pain or fatigue leads to decreased upper limb proprioception (Haavik, et al., 2011; Zabihhosseinian, Holmes, & Murphy, 2015). As well, studies have shown tilting of the head affects spatial placement of the hand during unseen tracing tasks (Guerraz, et al., 2011). More recently, studies have found that low grade neck pain is associated with changes to cerebellar inhibition (CBI) which is a measured of inhibition to motor output recorded from a distal hand muscle (Chapter 3) (Baarbé, et al., 2015; Daligadu, et al., 2013). Low grade ongoing neck pain has also been shown to lead to differential changes in the amplitude of upper limb somatosensory evoked potential (SEP) peaks related to the cerebellum-somatosensory cortex pathway following motor learning (Andrew, 2014).

These findings bear significance in light of studies which have shown cerebellar sensory neurons encode both the movement and position of limb endpoint (Bosco, et al., 1996; Casabona, et al., 2004; Giaquinta, et al., 1999). Patterns of activity in Purkinje cells and nuclear cells of the cerebellum specifically have been attributed to certain limb postures (Casabona et al., 2004), such as changes to the firing frequency of Purkinje cells and interpositus nucleus cells when limb position of anesthetized rats was displaced (Casabona et al., 2004). Altered sensory input in neck pain has the same potential to influence encoding within cells of the cerebellum. The aforementioned findings of altered spatial awareness and motor performance in neck pain as well as CBI changes in the same individuals may be due to neck pain encoding altered sensory signals from the neck.

Overarm dart throwing is a complex upper extremity task that requires coordination and timing between joints of the shoulder, elbow and wrist. Dart throwing may have many possible degrees of freedom and muscle actions related to performance. Subjects with cerebellar lesions fail to release balls at the peak time in an overarm throw movement, leading to slower throws (McNaughton, et al., 2004) including slower elbow extension velocity and acceleration, absence of elbow extension deceleration at the end of the throw, and slower wrist flexion velocity (Timmann, et al., 2008). Recent work has demonstrated altered neck muscle function in individuals with SCNP (Zabihhosseinian, Holmes, Ferguson, et al., 2015). The altered sensory input from neck muscles and joints due to neck pain would be likely to alter the body schema and influence the capacity of the cerebellum for error detection and feedforward correction of upper limb movements. Should there be a relationship between altered sensory input due to low levels of ongoing neck pain and encoding in the cerebellum leading to poor motor performance, participants with neck pain would be predicted to display differences to a healthy group in kinematic patterns, including greater total distance traveled (e.g. variability) while learning the task, as well as differences to their performance once the task has been learnt.

4.2 Abstract

Changes to sensory input from the neck have been shown to alter spatial awareness and proprioceptive acuity, as well as patterns of neck muscle activation, but few studies have been performed looking at complex upper limb movements that are directed at an outward goal and that require accuracy and precision for successful execution. The cerebellum encodes kinematics including position and velocity, and is involved in predicting sensory and motor consequences of movements. Overarm dart throwing is a task that requires coordination and timing between joints of the shoulder, elbow and wrist, and is a task that is highly dependent on intact cerebellar function. Changes in spatial awareness, proprioceptive acuity and cerebellar inhibition have previously been seen in people with low grade recurrent neck pain, and it is predicted that people with low levels of recurrent neck pain will display differences in kinematic patterns of movement compared to healthy people during an overarm dart throwing task. Fourteen participants with subclinical neck pain (9 women, range 19 – 24 years) and fourteen healthy controls (7 women, range 20 – 26 years), all novice to dart throwing, participated in the study. Participants were instructed to throw three sets of ten darts at a slow-normal speed, and three sets of ten darts at fast speed. Participants with neck pain showed increased total distance of the hand’s trajectory during the throw, as well as increased variability in elbow and forearm motor selection. Peak acceleration velocity of the shoulder and peak deceleration velocity of the wrist was found to be faster in participants with neck pain. These findings suggest that sensorimotor disturbances of neck pain have a neural origin that also influences motor control.

4.3 Introduction

Sensory input from the neck may have profound implications on upper limb motor control. Previous work has shown that tilting of the head affects spatial placement of the hand (Guerraz et al., 2011). Displacement to head and neck location (Knox, J. J., et al., 2005) as well as vibration applied to neck muscles (Knox, J., et al., 2006) have been found to affect the ability to accurately replicate elbow and forearm positions. A recent study also demonstrated that there were differential changes in the amplitude of upper limb SEP peaks related to the cerebellum-S1 pathway following motor learning (Andrew, 2014).

Subclinical neck pain (SCNP) refers to mild-to-moderate recurrent neck pain for which participants have not yet sought treatment. Individuals have been shown to have poor upper limb proprioception in the presence of SCNP (Haavik et al., 2011) as well as various sensorimotor effects including decreased cervical kinesthesia and muscle endurance (Lee, H., et al., 2004; Lee, H., et al., 2005; Lee, H.-Y., et al., 2008). Individuals with SCNP provide an ideal opportunity to explore the influence of altered sensory input from the neck on upper limb motor control since pain is recurrent and participants can be tested on pain free days, without the confounding effect of current pain, which has been shown in previous studies to affect measures of sensorimotor integration and motor control (Rossi, et al., 2003; Strutton, et al., 2005; Waberski, et al., 2008).

Purkinje cells of the cerebellum of rhesus monkeys have shown consistent patterns of spiking that correlated independently with kinematics of upper limb position and velocity (Hewitt, et al., 2011). Purkinje cell spiking encodes kinematic signals and motor errors signals onto the same cells (Popa, et al., 2012). Spike firing of motor errors specifically encode errors of position, direction and distance, and these motor error signals demonstrate two phases including a predictive spike in the leading phase prior to the error parameter and a feedback spike in the lagging phase following error execution (Popa et al., 2012).

The cerebellum receives input from joints, tendons and muscles in the neck and this input becomes integrated for timing of limb movements, the creation of forward internal models that predict the sensory consequences of movement (Figure 4.1), reducing the relatively large time delays for receiving sensory input from distal afferent sources such as the hand (Manto, et al., 2012). In humans, cerebellar inhibition (CBI), as measured by transcranial magnetic stimulation, has shown differences in SCNP participants in response to an upper limb motor acquisition task as compared to responses seen in healthy participants (Baarbé et al., 2015).

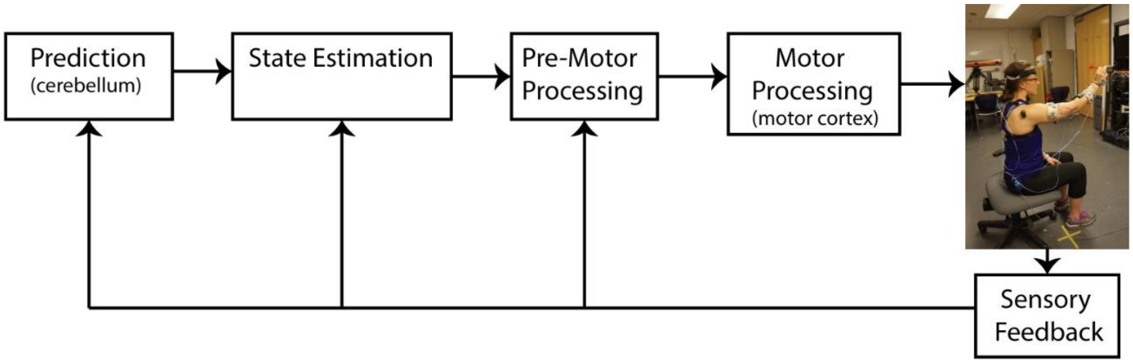

Figure 4.1 Schematic of cerebellar involvement in movement leading to sensory feedback of movement outcomes. Alterations to sensory feedback of movement may alter both prediction and state estimation.

The ability of the cerebellum to encode kinematic limb movements (Hewitt et al., 2011; Popa et al., 2012) may facilitate the process of the cerebellum to update predictive motor and sensory plans (Manto et al., 2012). If this is the case, sensorimotor changes in SCNP (Haavik et al., 2011; Kristjansson, et al., 2003; Lee, H. et al., 2004; Lee, H. et al., 2005; Lee, H.-Y. et al., 2008; Paulus, et al., 2008) are likely a result of motor adaptation of the cerebellum in the presence of conflicting sensory input from the neck.

Throwing is a skill which is highly dependent on intact cerebellar function. Subjects with cerebellar lesions failed to release balls at the peak time in overarm throwing, leading to slower ball speeds (McNaughton et al., 2004) and resulting in slower elbow extension velocity and acceleration, absence of elbow extension deceleration at the end of the throw, and slower wrist flexion velocity (Timmann et al., 2008). Dart throwing is a task with a specific outcome that has been used extensively in motor control literature (Lohse, et al., 2010; Müller, et al., 2004; Nasu, et al., 2014; Smeets, et al., 2002). This task involves elbow flexion and forearm pronation at the beginning of the throw, leading to elbow extension and forearm supination, as well as slight increases to shoulder flexion towards the end of the throw (Lohse et al., 2010) and motion around the arch of the wrist (Moritomo, et al., 2007). The latter movement is referred to as dart thrower's motion (DTM) and is the primary axis of rotation for wrist movements during dart throwing (Moritomo et al., 2007). DTM involves the motion arc from wrist extension/radial deviation to wrist flexion/ulnar deviation. The arc of DTM provides the wrist with the greatest range of motion, and is considered to be the common movement of the wrist in many ergonomic tasks (Moritomo et al., 2007).

Should there be a relationship between altered sensory input in SCNP individuals and encoding of these signals by the cerebellum, participants with neck pain would be predicted to display kinematic differences as compared to a healthy group during dart throwing as well as increased variability in the movement patterns during the throw. These differences could include the total distance of the hand's trajectory, variability to select the motor pathway, and displacement and velocity of joints. Total distance traveled by the hand's trajectory and variability in motor selection would likely be the greatest in neck pain participants while learning the task due to conflicting sensory signals and the increased need for exploration and exploitation of task parameters. Joint displacement and velocity would likely show differences across all movements due to cerebellar encoding of mismatched input from the neck, which influences spatial awareness and may alter the movement patterns of throwing.

4.4 Methodology

4.4.1 Participants

Fourteen volunteers (9 women, range 19 – 24 years) who were novice to dart throwing and had recurrent neck pain, but minimal acute pain on the day of testing, participated in the study. Neck pain was graded between Grade I to Grade III on the Chronic Pain Grading Scale (Guzman, et al., 2009; Von Korff, et al., 1992), which categorizes pain intensity and disability between a grade of 0, meaning the participant experienced minimal neck pain and no disability in the previous six months, and a grade of IV, which meant that the participant experienced severe neck pain and disability in the previous six months. Participants also had to be right-handed, and had a mean score (± standard deviation) on the Edinburgh Handedness Inventory of 70.8 ± 17.1, which categories extreme left-handedness as -100 and extreme right-handedness as +100 (Oldfield, 1971).

Data was also collected from fourteen healthy controls (7 women, range 20 – 26 years) who did not have neck pain on the day of testing or a history of neck pain, and who were also novice to dart throwing. These participants all had a very low grading on the Chronic Pain Grading Scale (no more than zero disability points and a characteristic pain intensity score $\leq$ 13). Participants had to be right-handed, and had a mean score (± standard deviation) of 82.6 ± 15.4 on the Edinburgh Handedness Inventory. Ethical approval was obtained from the university ethics committee, and the study was performed in keeping with the human right principles set out in the Declaration of Helsinki (WMA, 2013).

4.4.2 Neck Pain Characteristics

Frequency, duration, and location of neck pain, as well as the severity of neck pain was detailed by neck pain participants. To measure severity of neck pain, participants were shown a 10 cm Visual Analog Scale and were asked to indicate pain at the time of testing and to indicate the level of severity experienced during flare-ups in the previous six months. Participants also indicated functional limitations on activities of daily living using the Patient-Specific Functional Scale (Stratford, 1995; Westaway, et al., 1998).

4.4.3 Exclusion Criteria

Exclusion to participate included major structural injuries or anomalies to the cervical spine or shoulder including disk herniation, dislocation or fracture. As well, participants were excluded if they had received manual therapy or care for their neck pain in the previous three months. Other exclusion items included inflammatory or system conditions (e.g. rheumatoid arthritis or infection), trauma or other severe injury to the spine, radicular arm pain, hypermobility, intake of anti-coagulant medication or bleeding disorders, history of stroke or cancer in the past five years, and vertigo or dizziness.

4.4.4 Experimental Protocol

The participant faced a dart board, on a throwing line which was 2.37 m from the front of the dart board following international standards of dart throwing (WFD, 2007). An initial learning curve was expected and for this reason, participants were asked to throw three sets of ten darts at a slow-to-normal speed. The darts were handed to the participant one at a time for each set (Figure 4.2). Once the slow-to-normal speed sets were completed, participants threw three sets of ten darts at fast speeds. In order to control for excess trunk movement, participants were told to limit movement of their thorax. Care was taken to ensure that participants had adequate rest of 30 seconds or more between each set to prevent the onset of muscle fatigue during the throws. During the fast throws, participants were instructed to “throw fast”. In anticipation that accuracy would decrease with fast throws and that some participants may hesitate to throw at fast speeds, participants were instructed that even if their throws were less accurate, to still “throw fast”.

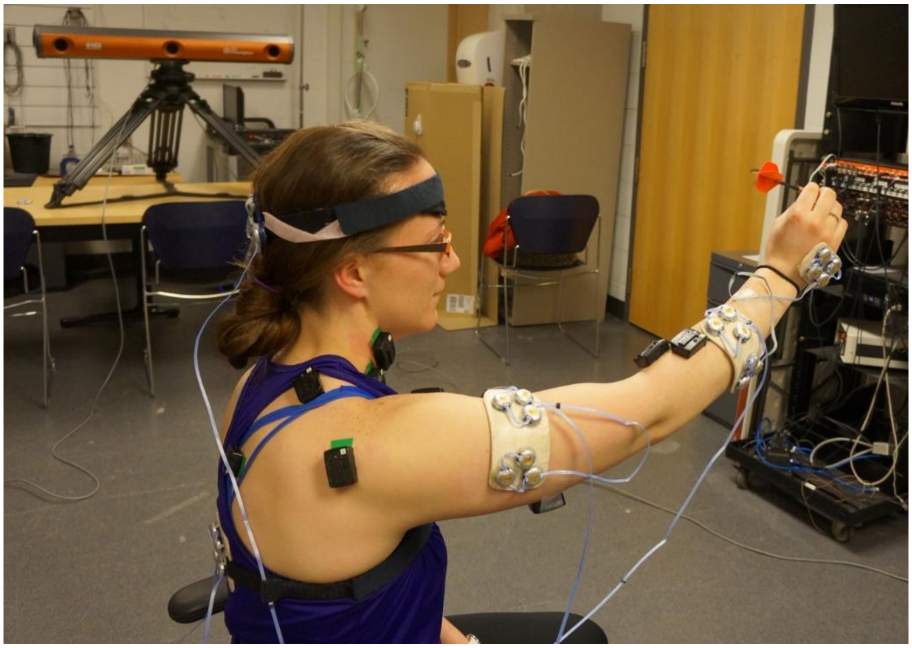

Figure 4.2 A participant whose dart throw is over midway through the throw cycle.

4.4.5 Three-Dimensional Kinematics

Upper extremity kinematics were measured during the task using the 3D Investigator motion capture system (Northern Digital Inc. [NDI], Waterloo, Ontario). Infrared-emitting markers were configured in sets of three or more markers on rigid bodies placed on the mid-segmental regions of the right upper arm, right forearm, right hand, posteriorly on the thoracic region of the spine, and the inion (Figure 4.2). Characterizing the length of each segment was done by landmarking bony prominences relative to each rigid body configuration (Table 4.1). Movements were recorded at a sampling rate of 64 Hz (First Principles, Version 1.2.4, NDI, Waterloo, Ontario).

Table 4.1 Proximal and distal prominences used to characterize the length of each segment.

Segment	**Proximal Prominences**		**Distal Prominences**	
	Lateral	**Medial**	**Lateral**	**Medial**
Right Hand	Radial styloid	Ulnar styloid	Thumb	Tip of middle finger
Right Forearm	Lateral epicondyle	Medial epicondyle	Radial styloid	Ulnar styloid
Right Upper Arm	Right acromion (middle prominence)		Lateral epicondyle	Medial epicondyle
Thorax	Right ASIS	Left ASIS	Right acromion	Left acromion
Head	Left acromion (for axes to align)	Right acromion (for axes to align)	Left top of head	Right top of head

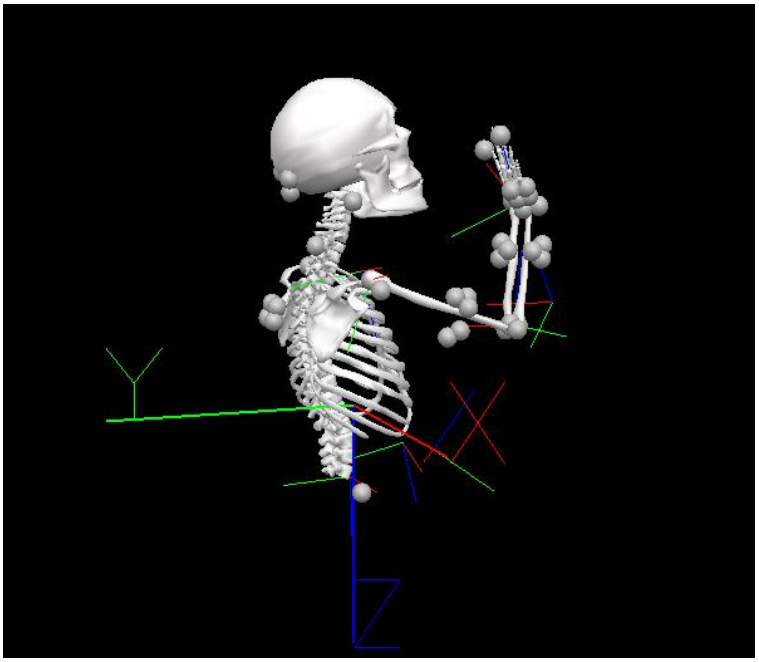

Figure 4.3 Skeleton made from rigid body configurations and segment characterization as displayed in Visual3D (Version 5.01.6, C-Motion, Maryland, USA)

4.4.6 Data Analysis

Kinematic data was processed using Visual3D (Version 5.01.6, C-Motion, Maryland, USA). The coordinate system was set so that X pointed medial-lateral, Z pointed inferior-superior and Y pointed anterior-posterior (Figure 4.3). Joint angles were assessed using the X-Y-Z Cardan rotational sequence. Kinematic data was cubic spline interpolated (Howarth, et al., 2010) and filtered with a second-order, dual-pass Butterworth filter that had a low-pass cut-off frequency of 6 Hz that reflected 1 second of data at both the beginning and ends of the data. Onset and offset of the throw cycle were then identified. Onset was defined as the time at which the hand was in its most posterior position where the elbow was most flexed just prior to exerting force into the throw, and offset was defined as the time at which the hand was in its most anterior position which occurs following dart release when the elbow is fully extended (Martin, T., et al., 2001). This offset was selected because we sought to determine the extent of sensorimotor effects on movement for the entire range of motion without attempting to correlate accuracy. Previous work had already determined that precision in timing of ball release is a main factor in prism adaptation (Martin, T. et al., 2001) and in high-low inaccuracies (Hore, et al., 1996), and it was not our goal to repeat these studies but rather to find out whether an altered body schema of the upper limb in the presence of neck pain affects kinematics of a directed movement.

Data was time-course normalized as a percentage of the throw cycle so that the data for each throw, trial and participant had 101 data points. Increased variance in the neck pain group was expected for slow-to-normal speed throws when participants were learning the task and for this reason, once the data was normalized, total movement distance of the distal hand in all three axis for slow-normal speed throws was further analyzed using MATLAB (R2014a, MathWorks, Natick, MA). If significance was seen in total movement travelled, total on-axis distance would then be assessed as the total distance of the distal hand within the major plane of motion (anterior-posterior motion), and total off-axis distance travelled would be assessed as the distance travelled outside the major plane of motion (e.g. movement travelled within the medial-lateral and inferior-superior planes). Time-course analysis looked at variability, measured as standard deviation around the mean of each trial for each participant, during the first 20% of slow-normal speed and fast speed throws for each velocity of the major joint movements during the throw. This time phase represents the time in which participants had to select the movement pattern they would implement for the remainder of the throw and would be important for determining altered motor control in movement selection.

Patterns of altered motor control would also be apparent by changes in peak joint displacement and velocity. Peaks were assessed for both slow-normal speed and fast throws for each of the major joint movements within the throw.

Major joint movements that were assessed for differences included elbow flexion-extension, forearm pronation-supination as well as DTM of the wrist. Shoulder abduction-adduction and shoulder flexion-extension were also assessed to determine differences in performance and movement patterns, since the shoulder is the proximal joint involved in the throw and thus more sensitive to indicate central changes to sensorimotor integration in the presence of neck pain.

4.4.7 Statistical Analysis

Slow-normal speed throws were assessed separately from fast throws. A 2 x 3 mixed design repeated-measures analysis of variance (ANOVA) tested significance for total distance, peak displacements and peak velocities for each joint. The repeated within-subject factor tested trial (three slow-normal speed trials, or in a separate ANOVA three fast trials) vs. the between subjects factor of group (neck pain vs. healthy). Post hoc repeated-measures ANOVA and paired *t* tests tested findings of significance from the original ANOVA.

The initiation of the throwing cycle is most likely to reflect initial awareness of upper limb joint position sense. We thus tested the influence of neck pain vs. healthy and trial on standard deviations for the first 20% of the throw cycle using a two-way 2 x 3 ANOVA. Post hoc independent samples *t* tests were applied when significance was found in the original ANOVA. For all statistical tests, the *p* value was set to 0.05, and statistical analysis was performed through SPSS Statistics 22 (International Business Machines Corporation, Armonk, New York).

4.5 Results

Out of 14 SNCP and 14 healthy participants, one participant was removed due to a problem with the tracking system and another participant experienced an unexpected episode of neck pain that contraindicated her inclusion in the healthy group. Fourteen SCNP volunteers (9 women, range 19 – 24 years) and twelve healthy volunteers (5 women, range 20 – 26) were included for final analysis.

4.5.1 Neck Pain Characteristics

Neck pain was experienced by SCNP participants on average one out of every two days. The intensity of neck pain ranged from 0.32 to 7.10 cm as measured on a 10 cm Visual Analog Scale. Loss of function on activities of daily living ranged from 2.5 to 10 on a scale of 0 to 10, with 0 indicating complete loss of functional ability on activities of daily living and 10 indicating no loss of function. Days lost due to disability from pain ranged from 0 to 20 days. Mean and standard deviations of neck pain scores are shown in Table 4.2.

Table 4.2 Neck pain characteristics in neck pain group

Neck Pain Characteristic	**Mean ± Standard Deviation**
Frequency of Neck Pain (days per months)	15.2 ± 8.6
Duration of Neck Pain (years)	2.2 ± 1.9
Neck Pain Intensity (Visual Analog Scale)	3.0 ± 2.1
Chronic Pain Grade Scale score (0 absence of pain or disability to IV severe pain and disability)	1.5 ± 0.7 Ranges from Grade I to III
Patient-Specific Functional Scale (0 minimal function on activities of daily living to 10 perfect functional ability on activities of daily living)	7.4 ± 2.8
Disability Days (days per month)	2.7 ± 5.2

4.5.2 Trajectory of Throw

Plots of the trajectory of the hand are shown in Figure 4.4. This figure demonstrates hand displacement in all three axes for slow-normal speed throws of neck pain and healthy participants. Our approach was to quantify and more fully understand the nature of these trajectories, as well as determine the kinematic and variable differences between the two groups leading to differences in the throw trajectories, in order to determine whether sensorimotor dysfunction brought about by neck pain could be a likely contributing factor to these differences.

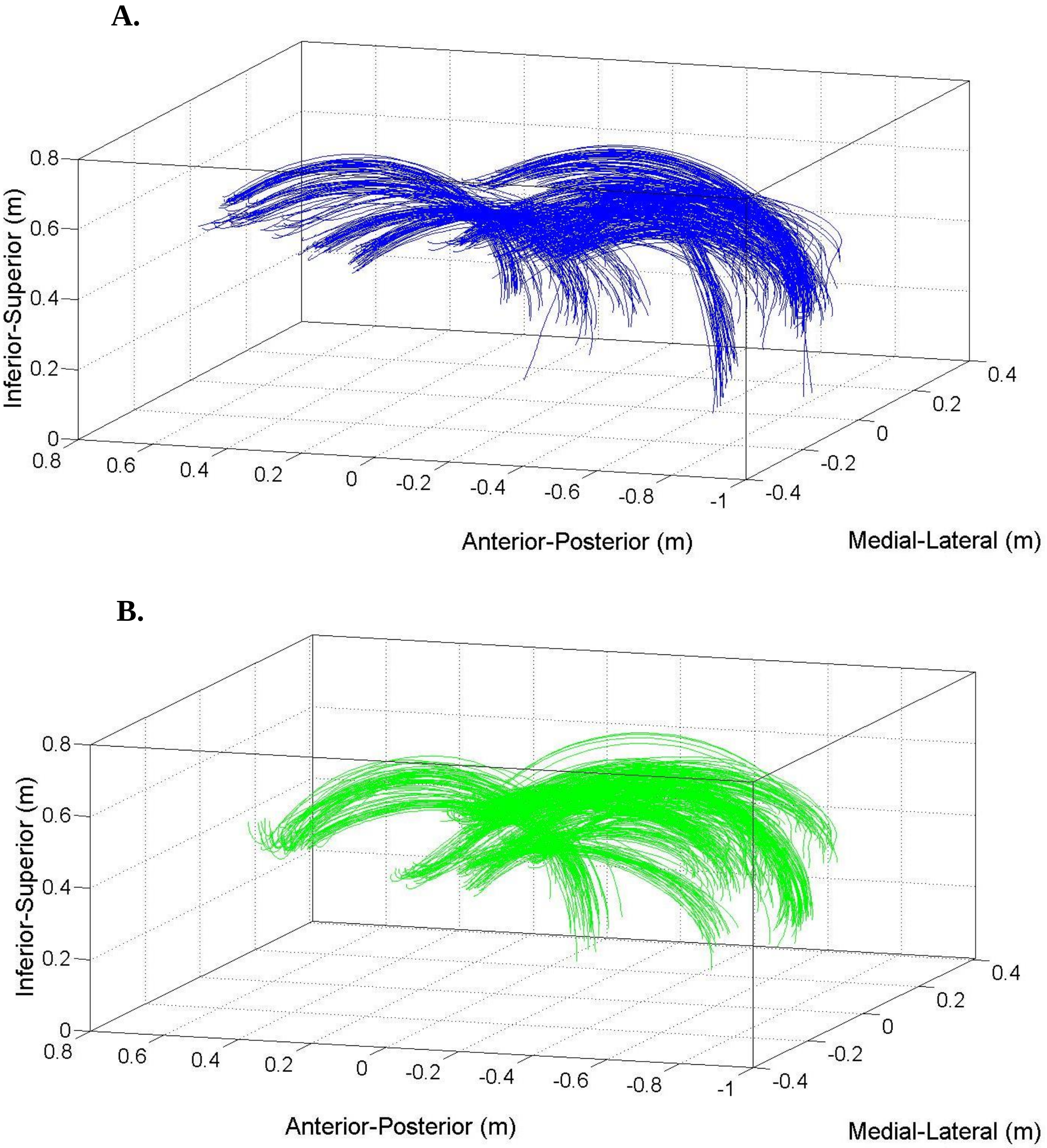

Figure 4.4 Trajectory of hand showing displacement in all three axes for the slow-to-normal speed throws of neck pain participants (A) and healthy participants (B).

4.5.3 Variance in Trajectory of Throw

Total distance travelled by the distal hand showed a significant interaction of group X trial ($F_{2,23} = 3.517$, $P = 0.046$). As shown in Figure 4.5, greater distance was travelled by neck pain participants with an increase to the distance travelled from the first to second trials in neck pain participants, whereas healthy participants had slightly decreased distance over the first and second trials and increased their distance only at the third trial (1.18 ± 0.26 m healthy vs. 1.21 ± 0.21 m neck pain).

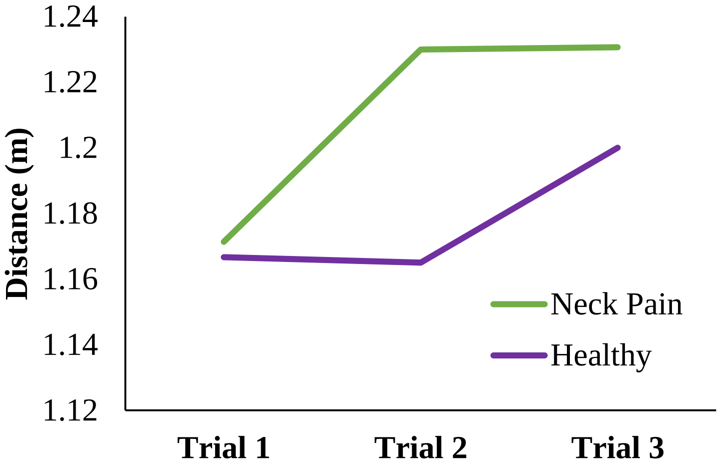

Figure 4.5 Distance of trajectory for slow throws showing a significant interaction of group X trial ($P < 0.05$).

This finding prompted further analysis, and so the on-axis distance (e.g. distance in the anterior-posterior direction of the throw) was compared to “off-axis” distance travelled (e.g. the distance travelled in the medial-lateral and superior-inferior axes). It was found that the total on-axis distance travelled showed a significant main effect of trial ($F_{2,23} = 3.934$, $P = 0.034$), with neck pain participants showing this main effect ($F_{2,12} = 4.907$, $P = 0.028$), but not healthy participants (Figure 4.6). In particular, neck pain participants increased on-axis distance travelled by the hand from trial one to trial two (*P* = 0.01) (0.70 m ± 0.08 trial one; 0.73 m ± 0.07 trial two; 0.72 m ± 0.08 trial three), whereas healthy participants had total greater distance travelled in the on-axis anterior-posterior direction (0.74 m ± 0.11 healthy vs. 0.72 m ± 0.07 neck pain), and they increased the distance travelled sequentially at every trial (0.72 m ± 0.11 trial one; 0.73 m ± 0.12 trial two; 0.75 m ± 0.11).

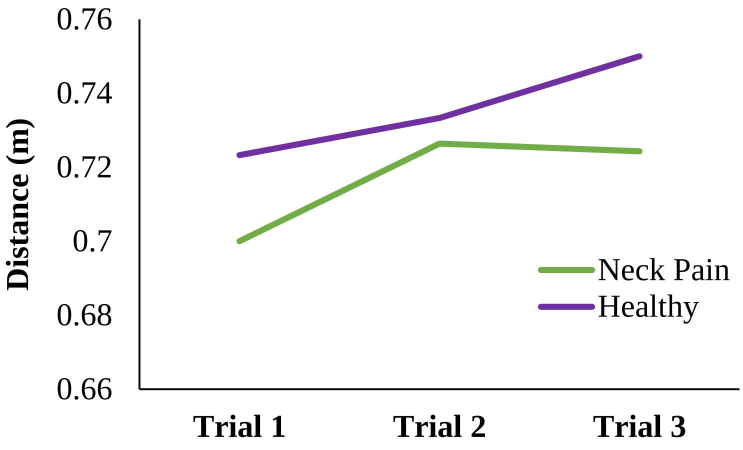

Figure 4.6 Total on-axis distance for slow throws showing a main effect trial ($P < 0.05$).

Off-axis distance of the distal hand travelled in the medial-lateral and superior-inferior directions showed a significant interaction of group X trial ($F_{2,23} = 3.679$, $P = 0.041$). As shown in Figure 4.7, overall off-axis distance for neck pain participants showed an increased distance from the first to second trial, whereas healthy participants showed a decreased off-axis distance from the first to second trial (0.49 ± 0.18 m neck pain vs. 0.44 ± 0.16 m healthy).

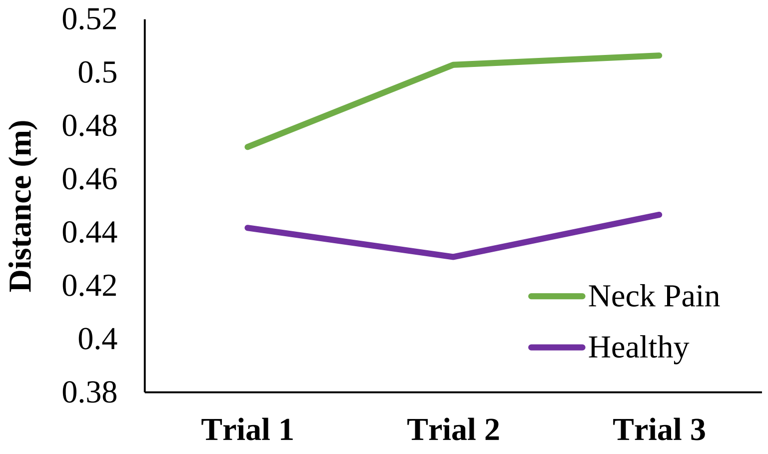

Figure 4.7 Total off-axis distance for slow throws showing a main effect trial ($P < 0.05$).

4.5.4 Variance in Motor Selection

Time-course analysis looking at variability during the first 20% of slow-normal speed throws showed a significant main effect of group (neck pain vs. healthy) for elbow flexion-extension velocity ($F_{1,72} = 4.124$, $P = 0.046$). Neck pain participants showed larger variability in elbow flexion-extension velocity with a mean standard deviation for the first 20% of the throw 29.25 ± 18.11 °/sec for neck pain (mean ± std. dev.) and 21.24 ± 15.77 °/sec (mean ± std. dev.) for healthy (Figure 4.8). Forearm pronation-supination velocity also showed a significant main effect of group ($F_{1,72} = 6.994$, $P = 0.010$). Post hoc independent samples *t* tests showed neck pain participants had an overall significantly greater standard deviation for the first 20% of the throw when they selected the movement pattern they would implement for the remainder of the throw [$P = 0.006$; 25.75 ± 16.37 °/sec neck pain (mean ± std. dev.) and 17.45 ± 9.10 °/sec healthy (mean ± std. dev.)] (Figure 4.9).

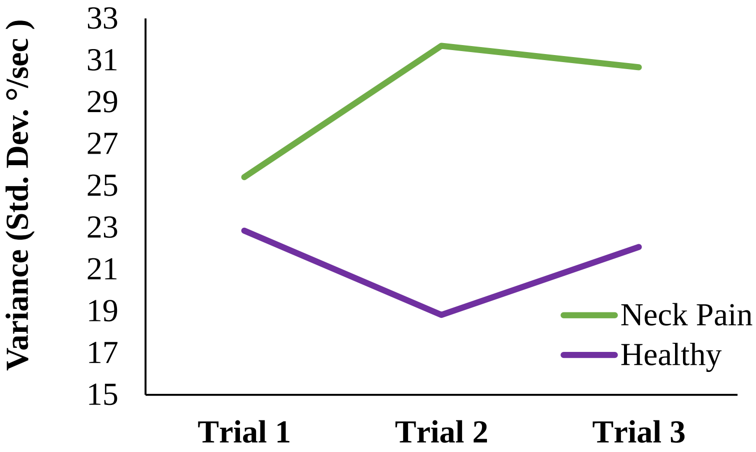

Figure 4.8 Variability during the first 20% of slow-normal speed throws showed a significant main effect of group (neck pain vs. healthy) for elbow flexion-extension velocity (*P* < 0.05).

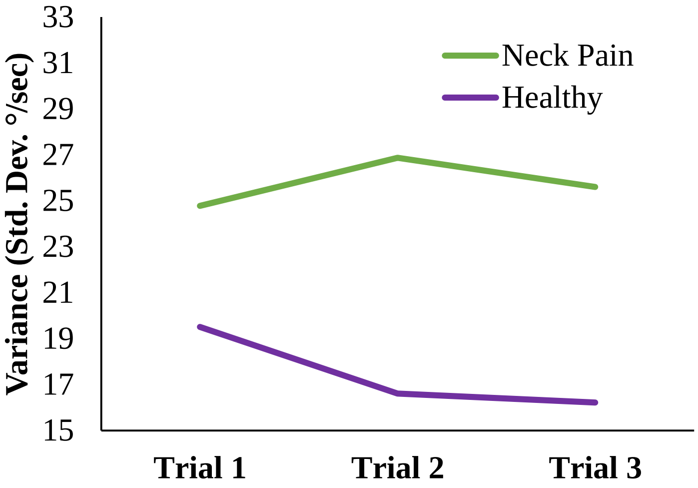

Figure 4.9 Variability during the first 20% of slow-normal speed throws showed a significant main effect of group (neck pain vs. healthy) for forearm pronation-supination velocity ($P \leq 0.01$).

4.5.5 Forearm Displacement and Velocity

Forearm motion started in a pronated position at the beginning of the throw and ended in a supinated position at the end of the throw. Peak forearm supination, which occurred at the end of the throw cycle, showed a significant interaction of neck pain X trial for fast throws ($F_{2,23}$ = 4.673, P = 0.020). As shown in Figure 4.10, mean peak supination in neck pain participants decreased from the second to third trial, whereas peak supination increased in healthy participants between their second and third trials (9.40 ± 15.78° neck pain and 6.31 ± 9.78° healthy) (Figure 4.10). Forearm velocity for fast throws also showed a significant interaction of neck pain X trial ($F_{2,48}$ = 4.916, P = 0.011). As shown in Figure 4.11, neck pain participants showed less peak forearm velocity in their fast throws with decreasing velocity over trial than healthy participants who had increased velocity over trial (334.25 ± 134.52 °/sec neck pain and 376.91 ± 132.56 °/sec healthy).

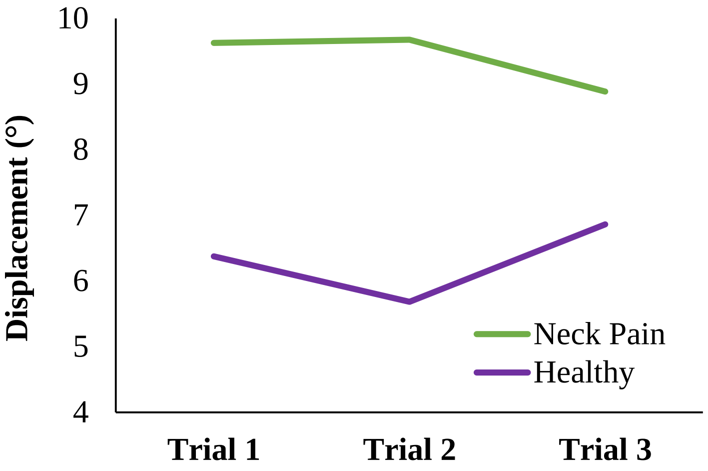

Figure 4.10 Peak forearm supination showed a significant interaction of neck pain X trial for fast throws $P < 0.05$).

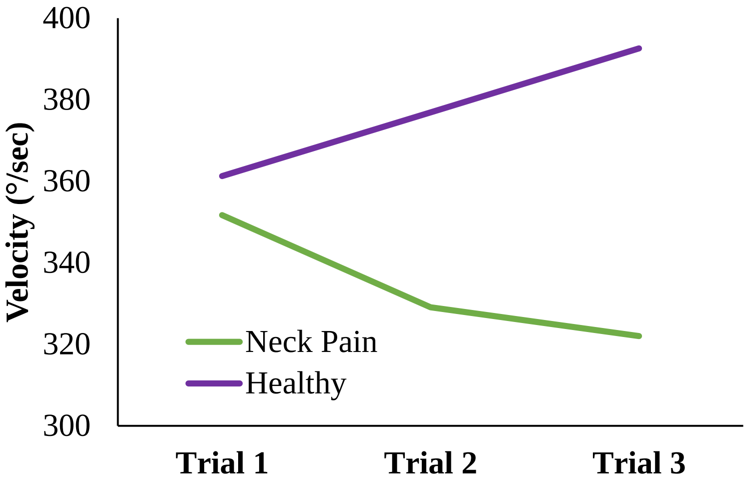

Figure 4.11 Forearm velocity showed a significant interaction of neck pain X trial for fast throws ($P < 0.05$).

4.5.6 Dart Thrower's Motion (Displacement and Velocity)

DTM is the major axis of rotation for wrist movement during dart throwing and motion around this axis involves the arc of travel from wrist extension and radial deviation to wrist flexion and ulnar deviation (Moritomo et al., 2007). During the dart throw, the wrist rotates from extension and radial deviation at the beginning of the throw to wrist flexion and ulnar deviation at the end of the throw when the dart is released. Peak DTM of the wrist in flexion and ulnar deviation showed a significant interaction of neck pain X trial during fast throws ($F_{1.5,35.2} = 3.710$, $P = 0.047$). Neck pain and healthy showed similar displacements into the DTM flexion/ulnar deviation (-21.52 ± 27.04° and -21.55 ± 16.09° for the neck pain and healthy groups, respectively) (e.g. negative values represent a DTM consisting of wrist flexion/ulnar deviation which occurs towards the end of the throw whereas positive values represent a DTM consisting of wrist extension/radial deviation which occur at the beginning of the throw). However, unlike healthy participants, neck pain participants showed a main effect of trial ($F_{1.3,16.5} = 5.150$, $P = 0.030$) across the three throws, with a significantly increased DTM flexion/ulnar deviation rotation across the first to third trial ($P = 0.028$; -16.77 ± 25.62° trial one, -19.54 ± 25.02° trial two, and -28.27 ± 30.74° trial three) (Figure 4.12).

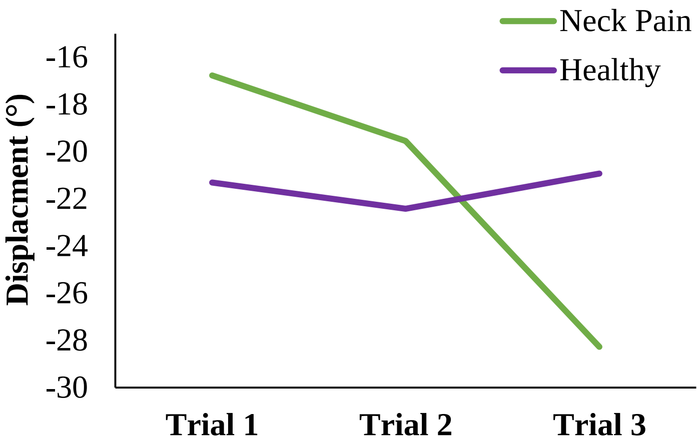

Figure 4.12 Peak DTM flexion showed a significant interaction of neck pain X trial for fast throws ($P < 0.05$). Values that are more negative represent greater wrist flexion/ulnar deviation.

Peak DTM velocity may be considered in two parts: (1) the most negative velocity which represents peak velocity of extension-flexion motion during the throw and (2) the most positive velocity which represents deceleration of the wrist following release of the dart. The latter peak is due to the wrist's response within the throw when deceleration of the extension-flexion motion reaches a peak velocity. No changes were seen to the peak negative velocity during the throw (eg. the velocity that is reached at dart release). However, peak velocity of deceleration showed a significant interaction of neck pain X trial for slow ($F_{2,48} = 4.656$, $P = 0.014$) and fast throws ($F_{2,23} = 4.456$, $P = 0.023$). The neck pain group showed significantly faster peak deceleration velocity than healthy during slow throws across all trials (*P* = 0.005; 152.95 ± 101.01° neck pain and 99.79 ± 58.08° healthy) and at the third trial (*P* = 0.033; 170.03 ± 104.47° neck pain and 93.05 ± 58.79° healthy) (Figure 4.13, Panel A). For fast throws, the neck pain group also showed significantly faster peak deceleration velocity across all three trials (*P* = 0.030; 198.61 ± 190.53° neck pain and 120.65 ± 98.91° healthy) (Figure 4.13, Panel B).

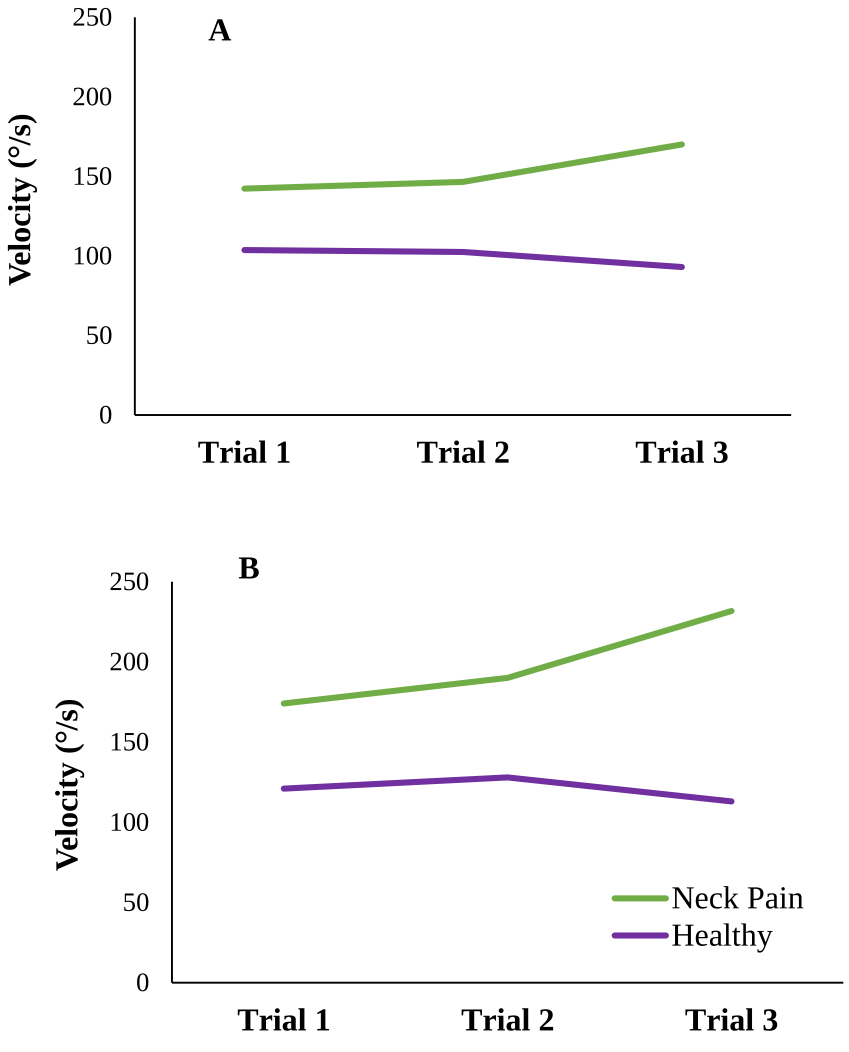

Figure 4.13 Peak DTM deceleration velocity for slow-normal speed throws (A) and fast throws (B) showing a significant interaction of neck pain X trial ($P < 0.05$ for both conditions)

4.5.7 Shoulder Velocity

A main effect of neck pain vs. healthy was seen for peak shoulder flexion-extension velocity during slow ($F_{1,72} = 13.091$, $P = 0.001$) and fast throws ($F_{1,72} = 37.973$, $P < 0.001$). Peak shoulder flexion-extension velocity for slow slows reached an overall greater peak velocity in neck pain vs. healthy for slow throws ($P < 0.001$; 139.39 ± 64.88° neck pain and 94.14 ± 37.97° healthy) and for fast throws ($P < 0.001$; 160.01 ± 51.70° neck pain and 97.62 ± 32.00° healthy) (Figure 4.14, Panel A). Neck pain participants were also significantly faster for fast throws on trial one ($P = 0.001$; 153.54 ± 54.14° neck pain and 89.07 ± 28.45° healthy) (Figure 4.14, Panel B). No changes were seen to peak deceleration speed when the shoulder extended or “dropped” following dart release.

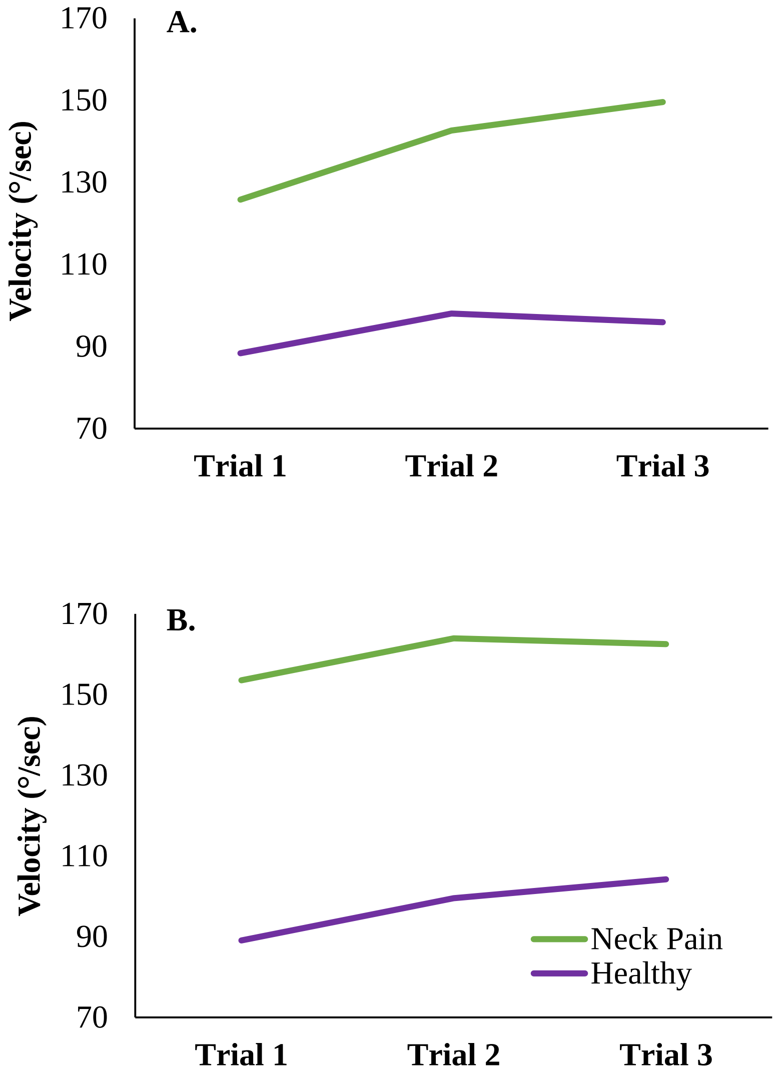

Figure 4.14 Peak shoulder flexion-extension velocity showed a main effect of group (neck pain vs. healthy) for slow and fast throws ($P < 0.001$ for both conditions).

4.6 Discussion

The challenges of altered spatial awareness (Lee, H.-Y. et al., 2008), altered proprioceptive acuity (Haavik et al., 2011; Paulus et al., 2008) and decreased cerebellar inhibition (Baarbé et al., 2015) are characteristically seen in people with neck pain. People with neck pain are also predicted to have altered motor control in upper limb overarm throwing. Upon carrying out a dart throwing task, participants with SCNP showed increased total distance travelled by the hand’s trajectory in all directions and an increase in off-axis movements (e.g. movements in the medial-lateral and superior-inferior directions). In contrast, healthy participants had lower total distance travelled, and they tended to have lower off-axis movement, but greater on-axis movements (e.g. movement in the anterior-posterior direction). Participants with SCNP showed an increased variance in elbow and forearm velocity for the first 20% of the throw compared to healthy participants. As well, SCNP as well as faster peak acceleration velocity of the shoulder and a faster peak deceleration velocity of the wrist, as well as tendencies for greater peak forearm supination and tendency for lower peak forearm pronation-supination velocity.

The throw cycle used to assess data in this study was determined by defining onset as maximum translational displacement of the hand in the posterior direction (also where elbow flexion was the greatest) and offset as maximum translational displacement of the hand in the anterior position. Previous work has shown that timing of release occurs approximately 13.5 ms before the maximum of the superior-inferior trajectory of the hand (Smeets et al., 2002). Our pilot data showed specifically that the offset landmark we had used in our study was approximately 8-12 ms later than the inferior-superior landmark used in the Smeets et al. (2002) study, meaning that by selecting this landmark we were analyzing data approximately 21-26 ms following dart release, a period of time that is characterized by full elbow extension and deceleration of joint velocities.

We had selected this offset because we sought to determine the extent of sensorimotor effects of neck pain for the entire range of motion. Selecting the full range of motion allows for seeing the acceleration to peak velocity, which is a landmark of release time (Smeets et al., 2002), as well as deceleration of the throw which is impaired in cerebellar patients (Timmann et al., 2008). Moreover our selection of offset is unlikely to have affected our results. SCNP and healthy participants had similar speeds in elbow extension and similar movement times for the throw, and so offset at the end range of motion is unlikely to have affected our findings of greater total trajectory distance in SCNP. Variability in motor selection was measured in the first 20% of the throw, and since our onset represented the true beginning of the throw (Smeets et al., 2002), this variability is highly unlikely to have been affected by offset.

The findings of greater peak acceleration velocity of the shoulder and greater peak deceleration velocity of the wrist means that neck pain participants had either a greater acceleration/deceleration respectively or a longer duration of acceleration/deceleration. Findings of muscle activity as a result of cerebellar lesions have shown differences in the onset, magnitude, and duration of acceleration, as well as in magnitude and duration of deceleration.

Subjects who had cerebellar lesions also failed to release balls at the peak time in arm movement leading to slower throws (McNaughton et al., 2004). Typically patients with cerebellar lesions are more affected in the execution of unpredictable tasks (synchronized finger-tapping) and less affected by continuous tasks (circle drawing) (Molinari, et al., 2007; Spencer, et al., 2003). Molinari et al. (2007) points out that coordination studies show similar errors in speed, precision, and timing, and these errors occur due to insufficient sensory input (Bower, et al., 2003; Molinari et al., 2007). Although the cerebellum is active during temporal processing, it does not engage in temporal processing as its sole function; the cerebellum plays a more complex and global role in the learning of unfamiliar, novel tasks, error correction, and sensory processing (Molinari et al., 2007).

The role of the cerebellum in motor adaptation has been demonstrated in studies where visual feedback is altered through the use of prismatic lenses (Baizer, et al., 1999; Hashimoto, et al., 2015; Martin, T. a., et al., 1996; Martin, T. et al., 2001). When a new task is learnt or when adaptation is necessary (such as occurs with altered sensory input from the neck), visual, vestibular, and proprioceptive functions integrate together so that adaption and automaticity is possible (Manzoni, 2007). Manzoni (2007) points out that among the models that account for cerebellar function there is a common element: Motor commands create various degrees of cerebellar output as determined by the learned relationship between input and output and the parameters of the task. For these reasons, the cerebellum is considered an integral part of learning and automaticity since without the cerebellum motor commands do not readily adapt and increased attention is needed to execute learned behaviour (Block, et al., 2012; Manzoni, 2007; Thach, et al., 1992).

Patterns of cerebellar activity have been seen that correlate with the angle of the limb and the direction of limb placement (Casabona et al., 2004). A review of early studies found that phasic activity and tonic activity correlate with joint angle and joint position respectively (Casabona et al., 2004). These patterns of phasic and tonic activity were particularly evident in mossy fibres and granule cells, the input cells of the cerebellum (Casabona et al., 2004). Spiking of Purkinje cells of the cerebellum have shown correlation with kinematic signals including position and velocity (Popa et al., 2012). Likewise, studies have shown that spiking of cerebellar sensory neurons encode both the movement and position of limb endpoint (Bosco et al., 1996; Giaquinta et al., 1999). Patterns of activity in Purkinje cells and nuclear cells have also been attributed to certain postures (Casabona et al., 2004). In one study, the firing rate of Purkinje cells and interpositus nucleus cells show a strong tendency for modulated activity when the limb position of anesthetized rats was displaced (Casabona et al., 2004). Modulated activity was strongest in the neurons along the anteroposterior axis (i.e. sagittal plane) (Casabona et al., 2004). These findings are in line with the internal model theory that network patterns are learned and repeated in a predictable manner (Casabona et al., 2004; Ito, 2006)(8, 18). The importance of this is that plastic changes occur to the central nervous system as the cerebellum encodes limb range of motion. Altered sensory input from the neck due to low grade ongoing neck pain may be a source for misguided information about the location of limb endpoint and alter ability for smooth continuous movements.

Future research should consider the duration of accelerations and decelerations and their magnitudes, onsets and time of peaks. Muscle activity is also an important indicator of changes to timing and control of upper limb movements. Future work may look at the onset and amplitude of muscle activity which indicate the timing and magnitude of forces produced during the movement. Kinetics of movement include the interaction joint torques that come into play during the throw. Future work may consider joint force and moment that are constituents of the movement.

In conclusion, this study found SCNP participants show an increased total distance of the hand’s trajectory during the throw, as well as increased off-axis movement and increased variability during elbow and forearm motor selection. SCNP participants also showed greater peak acceleration velocity of the shoulder and peak deceleration velocity of the wrist. The position and velocity of limb segments are encoded through spiking of

Purkinje cells in the cerebellum. These findings suggest that sensorimotor disturbances of neck pain have a neural origin that also influences motor control.

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Chapter 5: Neck Pain Impairs the Ability to Perform a Mental Rotation Task

Adapted from submitted publication:

Baarbé, J., Holmes, M., Murphy, H., Haavik, H., & Murphy, B. Subclinical neck pain impairs the ability to perform a mental rotation task: a four week longitudinal study with a healthy control group comparison. *Journal of Manipulative and Physiological Therapeutics.* Award-winning paper.

5.1 Introduction to Chapter

An increasing body of knowledge has found that pain influences the reweighing of sensory input with less weight placed on sensory input from painful regions and more weight placed on sensory input from nonpainful regions (Tsay, et al., 2015). This imbalance of input has central effects that likely implicate the cerebellum which is involved in motor adaptation via the reception and integration of sensory signals. Altered sensory input as a result of neck pain may influence this ability of the cerebellum for adaptation to changes beyond the immediate body. Previous work on neck pain participants has shown differences in cerebellar inhibition between neck pain and healthy participants (Chapter 3), and it is hypothesized that the performance of neck pain participants on outwardly-directed tasks is also implicated. The cerebellum is highly regarded for its role not only in motor adaptive processes, but also in cognitive function (Stoodley, et al., 2012). Recent work using functional magnetic resonance imaging (fMRI) has shown activation in the left hemisphere of the cerebellum in lobule VII (Crus II), extending from lobules VI to VIIB, during a mental rotation task that involved recognizing whether an a rotated letter was presented in its normal or mirror image orientation (Stoodley et al., 2012).

Sensory signals to the cerebellum include kinematic signals that provide information about position and velocity of body parts (Hewitt, et al., 2011) as well as predictive signals that carrying information about the forthcoming motor errors along with feedback signals that transfer information on motor errors already executed (Popa, et al., 2012). Neck pain participants who threw darts showed greater peak acceleration velocity of the shoulder and peak deceleration velocity of the wrist while throwing as well as increased variance during elbow and forearm motor selection (Chapter 4). These effects may have been due to altered sensory input from the neck impacting the cerebellum leading to a defect of the cerebellum in spatial processing. Previous work has shown that patients with cervical dystonia were slower in judging the laterality of a rotated hand, foot or eye patch, which are images related to their own bodies (Fiorio, et al., 2007). Altered sensory signals to the neck, thus, are highly likely to be part of processes that influence the immediate body schema.

Limited knowledge is available on how neck pain may impair visual-spatial awareness beyond the immediate body. Mental rotation of the outward environment is a highly important task that is used in spatial navigation (Taylor, et al., 2008) as well as sport performance (Moreau, et al., 2011), and thus, altered sensory signals to the neck may impair not only the ability to mentally rotate outward objects, but also perform well in complex spatial environments. One study asked patients with cervical dystonia to judge the laterality of a rotated non-human image of a car, and they showed a tendency for slower response times (Fiorio et al., 2007). The testing of mental rotation skill in a neck pain population is important to determine influences that are specific to this group. Neck pain participants were tested without pain on the day of testing as the presence of pain itself is known to influence measures of sensorimotor integration and motor control (Rossi, et al., 2003; Strutton, et al., 2005; Waberski, et al., 2008). The presence of neuroplastic changes as a result of altered sensory signals from the neck (rather than the presence of pain) was predicted to influence mental rotation skill, and for this reason, participants were tested on days when they were without pain to allow for a more robust interpretation of spatial mental representation in the presence of recurrent neck pain.

5.2 Abstract

The ability to mentally rotate objects and the frame of reference of those objects is critical for executing correct and skillful movements, and is particularly important for object recognition, spatial navigation and movement planning. Altered sensory feedback from the neck, such as occurs with neck pain, may impair this ability to mentally rotate because of changes to cerebellar connections and an altered body schema. Mental rotation skill was tested in individuals with subclinical neck pain (SCNP) and in healthy controls in a longitudinal study comparing performance scores at baseline and after four weeks. Twenty-six volunteers (13 SCNP; 12 controls) participated in this study. SCNP participants had scores of mild to moderate on the Chronic Pain Grade Scale and controls had minimal or no pain. For the mental rotation task, participants were presented with an object (letter 'R') on a computer screen presented randomly in either normal or backwards parity at various orientations (0˚, 45˚, 90˚, 135˚, 180˚, 225˚, 270˚, 315˚). Participants had to indicate the object's parity by pressing 'N' for normal or 'B' for backwards. Each orientation for normal and backward parities was presented 5 times and the average response time for all letter presentations was calculated for each participant, at baseline and four weeks later. Healthy participants had mean response times (± standard deviations) of 994.4 ± 211.9 ms at baseline vs. 834.0 ± 183.3 ms at four weeks. The SCNP group had mean response times

of 1220.9 ± 294.5 ms at baseline vs. 1115.8 ± 220.8 ms at four weeks. The overall improvement for both groups was significant ($F_{1, 23} = 8.93$; $P = 0.006$), and response times were significantly different between groups, both at baseline ($P < 0.05$) and at four weeks ($P < 0.05$). Healthy participants performed better than the SCNP group at both time points. SCNP may impair the ability to perform a complex mental rotation task involving cerebellar connections, possibly due to an altered body schema.

5.3 Introduction

The concept of an altered body schema in individuals with chronic pain has become a recent area of interest, with the altered schema extending to peripersonal space (Moseley, et al., 2012). Mental rotation of an object is a complex task requiring prediction and cerebellar involvement (Creem-Regehr, et al., 2007; Popa, et al., 2013), and one past study showed that ability to mentally rotate an object improved with a single session of neck manipulation (Kelly, et al., 2000). Neck pain has been shown to impact upper limb proprioception (Haavik, et al., 2011), and recent neurophysiological studies suggest that individuals with neck pain may have altered cerebellar processing (Baarbé, et al., 2015; Daligadu, et al., 2013).

Subclinical neck pain (SCNP) (Lee, H., et al., 2004; Lee, H., et al., 2005; Lee, H.-Y., et al., 2008) refers to mild-to-moderate recurrent neck pain for which participants have not yet sought treatment. Individuals with SCNP show decreases in neck range of motion, cervical kinesthesia and muscle endurance (Lee, H. et al., 2004; Lee, H. et al., 2005; Lee, H.-Y. et al., 2008). Individuals with SCNP provide an opportunity to explore neurophysiologic dysfunction without the confounding effect of current pain, which has been shown in previous studies to affect measures of sensorimotor integration and motor control (Rossi et al., 2003; Strutton et al., 2005; Waberski et al., 2008).

Recent work using transcranial magnetic stimulation (Daligadu et al., 2013) found that cerebellar function is altered in individuals with SCNP in comparison to healthy controls. Normally the cerebellum disinhibits in order to allow learning of new motor skills. This ability is impaired in individuals with low level neck pain. This raises the possibility that altered cerebellar processing of afferent input may contribute to alterations in other cerebellar dependent functions such as kinesthetic and spatial awareness.

The cerebellum is important in both feedback and feedforward models of motor control, using afferent feedback to update body schema to maintain accuracy of feedforward control of movement (Popa et al., 2013), and it also plays a critical role in spatial processing and object recognition (Picazio, et al., 2013). The study by Picazio et al. (2013) used continuous theta burst stimulation (cTBS) to decrease cerebellar hemispheric excitability in healthy adult participants performing a mental rotation task. Mental rotation is the ability to rotate mental representations of two or three dimensional figures rapidly and accurately. Mental rotation ability is important for a number of other abilities such as acquiring spatially complex skills, object recognition, problem solving, and action planning (Creem-Regehr et al., 2007). Mental rotation is also used in flight navigation (Taylor et al., 2008) as well as sport performance (Moreau et al., 2011). In the study by Picazio et al (2013), decreasing the input from the left cerebellar hemisphere using cTBS led to slower mental rotation response times for both an embodied mental rotation task requiring an egocentric mental rotation strategy and an abstract mental rotation task which required an allocentric strategy, as compared to sham cTBS.

The involvement of the cerebellum in mental rotation is intriguing in light of an older study that showed that upper cervical manipulation enhanced mental rotation ability in individuals with neck joint dysfunction compared to a group receiving a sham treatment (Kelly et al 1995). Altered kinesthetic awareness is known to occur in SCNP participants (Haavik et al., 2011; Lee, H. et al., 2005; Lee, H.-Y. et al., 2008) and it now seems likely that this may extend to altered spatial awareness of objects. If mental rotation ability is impaired in individuals with recurrent neck pain relative to healthy controls, it would suggest that the altered cerebellar processing could be contributing to not only a disrupted body schema but disruptions in spatial recognition of objects.

Therefore the aim of the current study was to compare a group of individuals with recurrent neck pain to a healthy control group and to follow-up this comparison at four weeks in the absence of any treatment for the neck pain group. We hypothesized that those in the SCNP group would have slower response times when performing mental rotation, and that this would not be explained by changes in movement time (indicated by response time when the object was presented in normal orientation at 0 degrees of rotation). Furthermore we hypothesized that although both groups would improve over time due to task familiarity, the SCNP group would still show decreased mental rotation ability relative to the control group after four weeks.

5.4 Methods

5.4.1 Participants

Thirteen participants (8 women; age 21.2 ± 1.9 years) with self-reported neck pain, but minimal acute pain on the day of testing, participated in the study. These participants were classified as Grade I to III on the Chronic Pain Grading Scale which categorizes pain intensity and disability between a grade of 0, meaning the participant had minimal pain in the previous six months, and a grade of IV, which would mean very severe pain intensity and disability in the previous six months (Guzman, et al., 2009; Von Korff, et al., 1992). All participants were right-handed with a mean score (± standard deviation) of 71.6 ± 18.2 on the Edinburgh Handedness Inventory (Oldfield, 1971).

Data was also collected from a healthy control group of twelve participants (3 women; 21.9 ± 2.1 years) without neck pain or a history of neck pain/injury. These participants had an Edinburgh Handedness Inventory score (± standard deviation) of 73.0 ± 30.5 and very low grading on the Chronic Pain Grade Scale (zero disability points and characteristic pain intensity score $\leq$ 23).

Exclusion to participate included major structural injuries or anomalies to the cervical spine including disk herniation or fracture. As well, participants were excluded if they had received care for their neck condition in the past three months. Other exclusion items included inflammatory or system conditions (e.g. rheumatoid arthritis or infection), trauma or other severe injury to the spine, radicular arm pain, hypermobility, intake of anti-coagulant medication or bleeding disorders, history of stroke or cancer in the past five years, and vertigo or dizziness. Neck pain participants also had to detail the history, frequency, duration, location, and severity at the time of testing and during flare-ups in the previous six months, as well as functional ability to participate in activities of daily living. Ethical approval was obtained from the university ethics committee, participants provided informed consent prior to participating, and the study was performed in keeping with the human right principles set out in the Declaration of Helsinki.

5.4.2 Experimental Protocol

The participants attended two sessions, at baseline and at four weeks later. At each session they were seated in a comfortable chair facing a laptop computer (ThinkPad T500 series, Lenovo, Beijing, China). A fixation point would appear on the screen, and at random intervals of 200 to 400 ms, the letter ‘R’ was presented. ‘R’ was randomly presented in either backwards (‘Я’) or normal orientation, at various degrees of rotation (0˚,45˚, 90˚, 135˚, 180˚, 225˚, 270˚, 315˚) (Figure 5.1). The letter ‘R’ was chosen as past research has demonstrated that there was no difference between males and females in the ability to perform mental rotation of letters and polygons (Cohen, et al., 1989). Since we did not know at the outset the number of males and females that would end up in each group, we wanted to be sure that differences in male and female participation numbers between the groups would not influence group results.

Participants had to indicate the object’s orientation by pressing ‘N’ for normal or ‘B’ for backwards with their dominant hand index finger which was positioned proximate to the computer key pad. These two letters are adjacent to each other on the key pad which meant that there would be no difference in the time required to reach each letter. Following the participant’s judgement as to normal or backwards orientation, a visual prompt was presented saying "Press any key to continue." Each orientation was presented five times and the response time from object presentation to key press was measured using E-prime software (Psychology Software Tools [PST], Sharpsburg, USA). The average response time to all letter presentations was calculated for each participant both at baseline and when they repeated the task four weeks later.

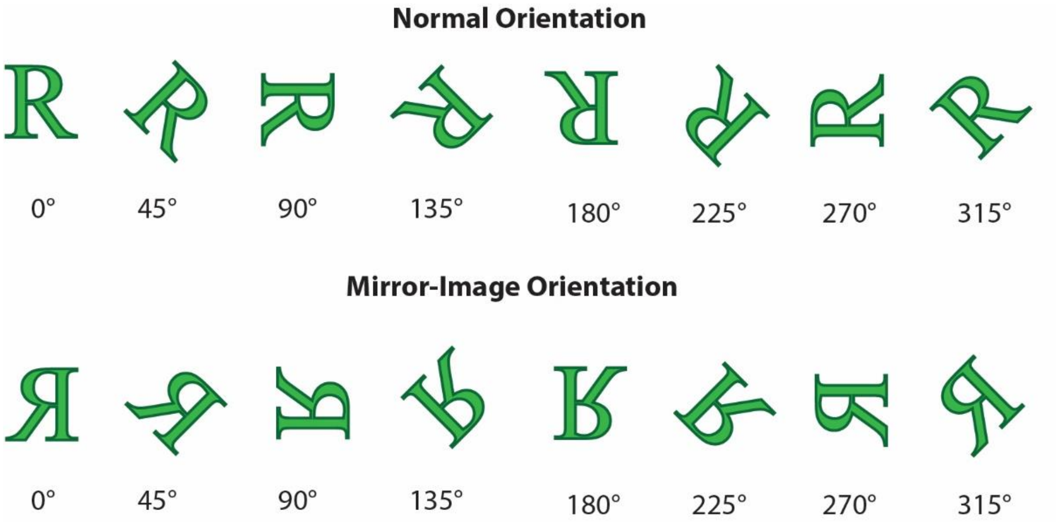

Figure 5.1 The letter ‘R’ at various orientation angles in both its normal and mirror-image orientations.

5.4.3 Simple Response Time

Figure 5.2 demonstrates events of response time, which mainly include (1) time for recognizing the stimulus, (2) time for cognitively rotating the stimulus and (3) time for motor initiation and movement. In order to determine any differences between neck pain and healthy in the time they needed to recognize the stimulus and initiate the movement, which are processes separate from cognitive mental rotation, the response time to respond to letter ‘R’ in normal orientation at 0˚ was analyzed and called “simple response time.” This measure would more purely indicate response time to perform the task without demands on cognitive resources to rotate the image, so as to provide a way to compare whether recognition and movement time, rather than mental rotation ability, was different between the two groups.

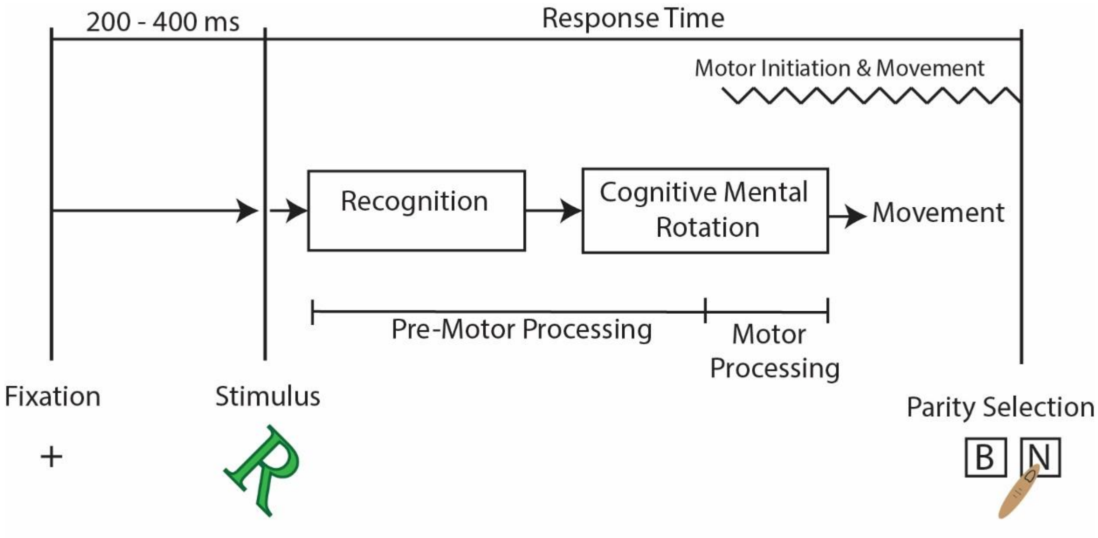

Figure 5.2 Response time begins at the presentation of a stimulus and includes recognition, the cognitive function of rotating an object, as well as time for motor initiation and movement until the participant has selected their desired response.

5.4.4 Data Collection and Analysis

The data was collected and stored within E-Studio software (PST, Sharpsburg, USA). The first presentation of each rotation angle for the forward and mirror-image chiral forms were removed from analysis since these were considered to be part of the warm-up while participants were still learning the task. The remaining trials were averaged to determine response time to identify either the normal or mirror-image chiral form and accuracy of the selection (expressed as percent correct).

5.4.5 Statistical Analysis

Changes in mental rotation response time over time were assessed using a two-way repeated-measures analysis of variance (ANOVA). The average mental rotation response time between the two groups were compared at baseline and at four weeks using unpaired *t* tests. Accuracy between neck pain and healthy at baseline and at four weeks was assessed using Chi-square tests.

Simple response time was tested at baseline and at four weeks using a two-way repeated-measures ANOVA to compare differences in response time between normal and mirror-image chiral forms. Self-paced delay between trials (the time that elapsed from presentation of the screen “Press any key to continue” until participants responded) was also assessed with a two-way repeated-measures ANOVA to ensure that any improvements following the four weeks were not due to changes in mental processing time between trials.

5.5 Results

The neck pain group pain characteristics are summarized in Table 5.1, and mean response times for each orientation angle of ‘R’ in its normal parity is shown in Figure 5.3. There was a main effect of time for mental rotation response time ($F_{1, 23} = 8.93$; $P = 0.006$ with no significant interaction) (see Figure 5.4). The baseline mental rotation response time was significantly faster ($P < 0.05$) for healthy vs. SCNP groups (994.4 ± 211.9 ms vs. 1220.9 ± 294.5 ms). At four weeks, mental rotation time improved for the healthy group to 834.0 ± 183.3 ms, a 160.4 ± 156.0 ms (or 16.1%) improvement, while the SCNP group improved to 1115.8 ± 220.8 ms, a 105.0 ± 263.6 ms (or 8.6%) improvement.

Table 5.1 Neck pain group characteristics at baseline and after four weeks (results are presented as mean ± standard deviation).

Neck Pain Characteristic	**Baseline**	**Week Four**
Frequency of Neck Pain (days per months)	13.9 ± 8.1	12.55 ± 9.1
Duration of Neck Pain (years)	2.3 ± 2.0	N/A
Neck Pain at Present Time: (Visual Analog scale)	2.8 ± 2.2	3.06 ± .39
Chronic Pain Grade Scale score (0 to 4 minimal to severe)	1.46 ± 0.78	1.42 ± 0.79

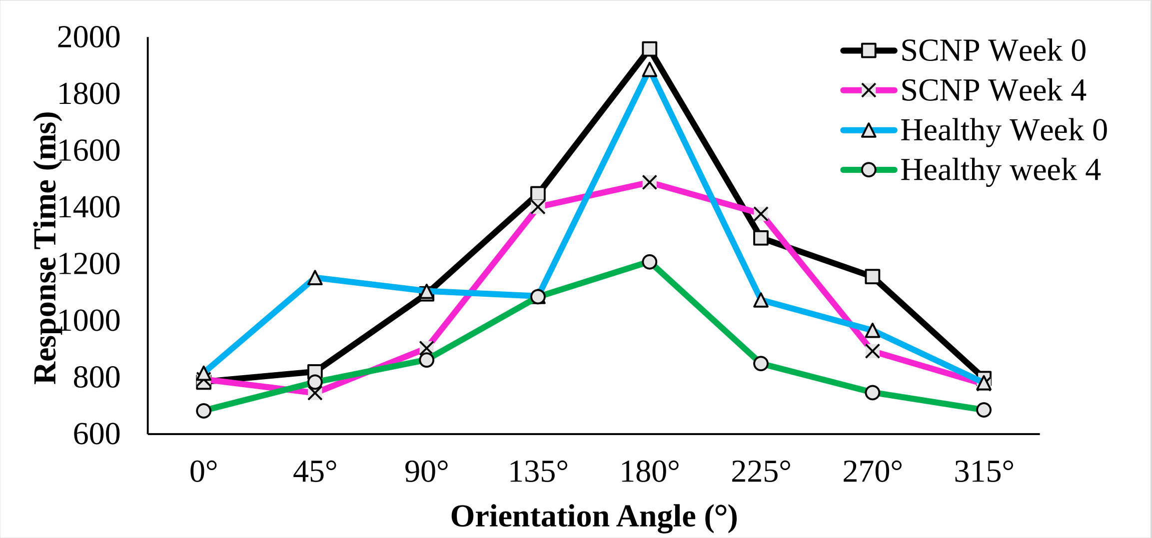

Figure 5.3 Average response times (ms) for each orientation angle of ‘R’ in its normal parity for neck pain and control groups at baseline (Week 0) and following four weeks in the absence of any intervention.

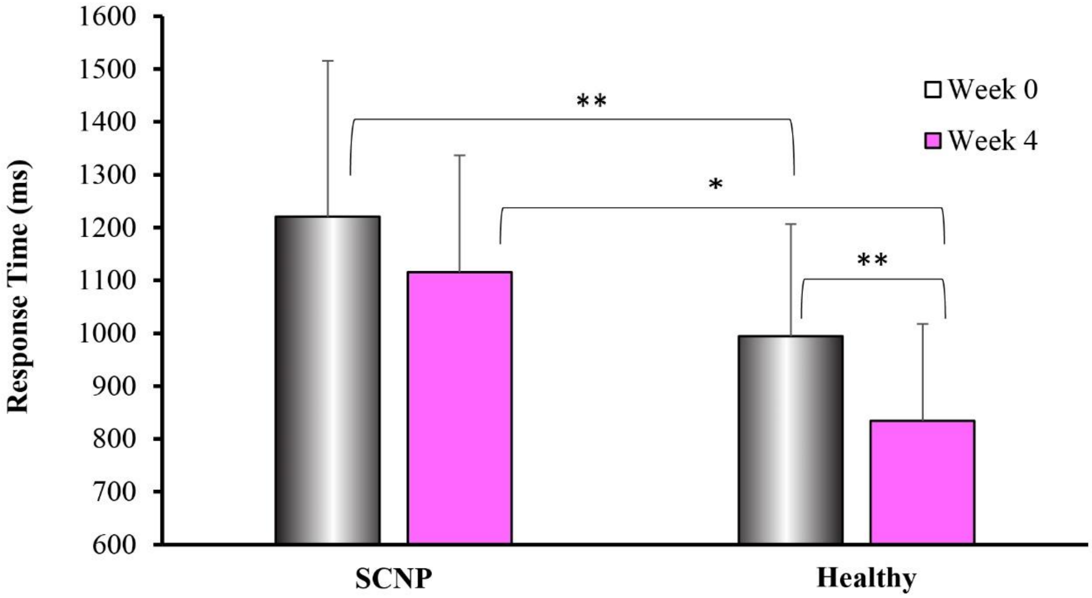

Figure 5.4 Average response times (ms) for neck pain and control groups at baseline (Week 0) and four week follow-up in the absence of any intervention (*$P < 0.05$, **$P < 0.01$). Error bars represent standard deviations.

The average of the simple response time for the letter 'R' presented at 0˚ of rotation at baseline was 783.7 ± 191.7 ms for the neck pain group and 815.1 ± 311.9 ms for the healthy group, while at week four it was 793.4 ± 320.3 ms for the neck pain group and 682.3 ± 150.3 ms for the healthy group (Figure 5.5). There was no difference in this "simple" response time over the four weeks and no significant differences between groups for the response time when the letter was not rotated.

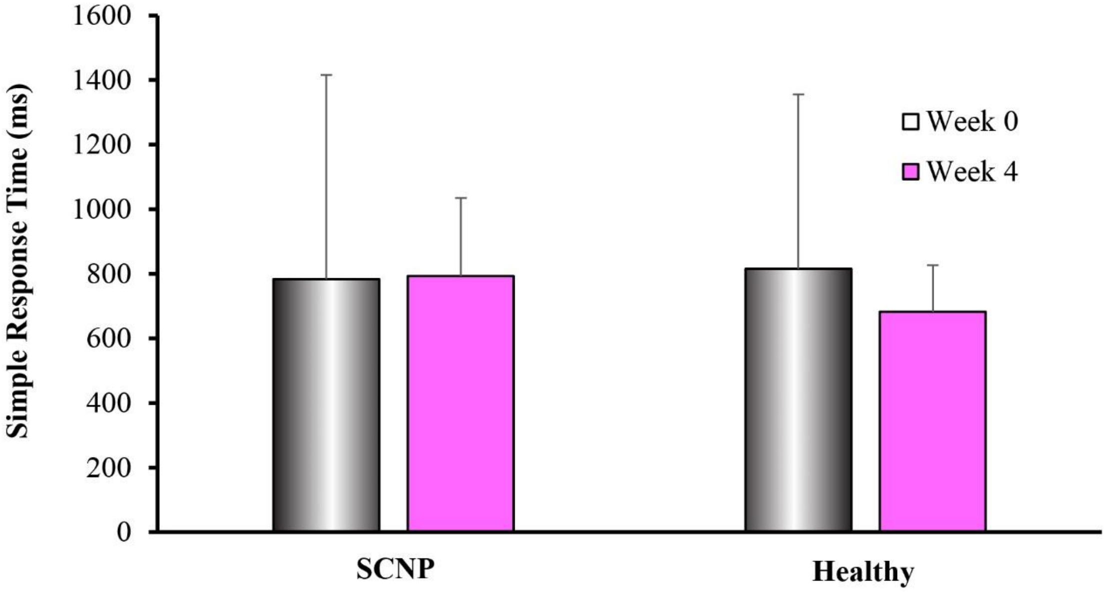

Figure 5.5 Average simple response times (ms) for the neck pain and healthy groups to recognize shape in normal orientation at 0 degrees. Error bars represent standard deviations.

There were no differences between the neck pain and healthy groups for accuracy scores at 0 weeks, but at four weeks the healthy group improved from 93.5 ± 8.5% accurate at baseline to 95.9 ± 3.5% at four weeks, while the neck pain group declined in their accuracy from 94.7 ± 4.7% accurate at baseline to 93.5 ± 7.3% at four weeks ($X^2 = 4.24$, $P = 0.039$) (Figure 5.6). Neck pain participants had an average self-timed delay between events of 363.8 ± 170.8 ms at baseline and 382.8 ± 214.9 at four weeks. The healthy participants had an average self-timed delay between events of 433.6 ± 190.2 ms at baseline and 438.0 ± 224.0 ms at four weeks (Figure 5.7). No differences were seen in this self-time delay over the four week period, and there were no significant differences between the two groups.

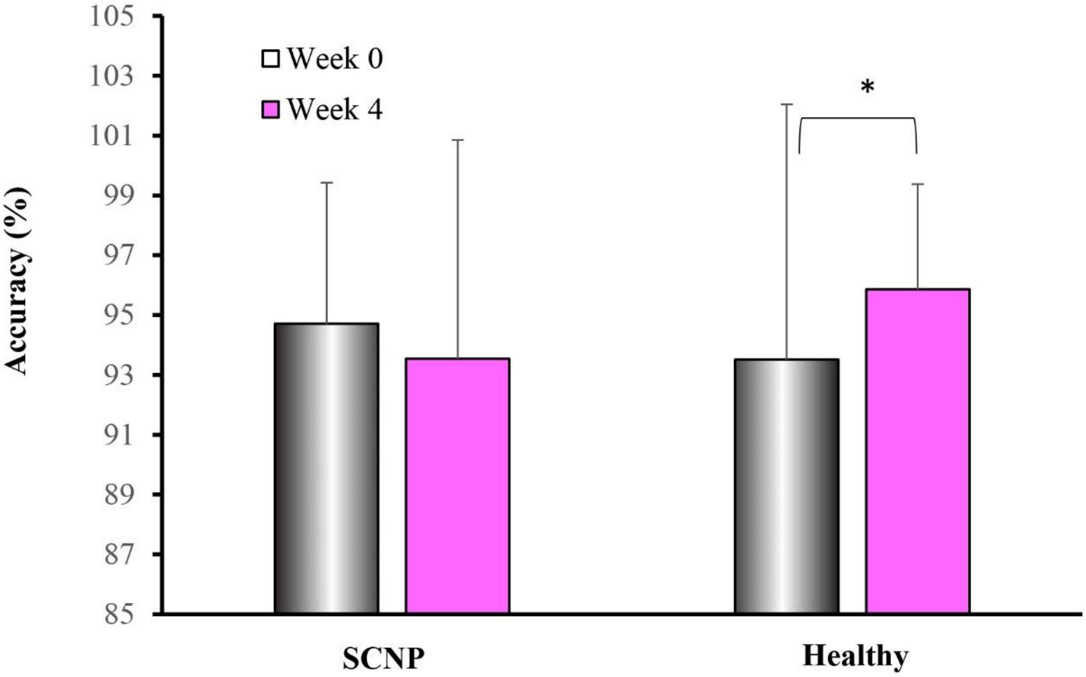

Figure 5.6 Accuracy of mental rotation performance (*$P < 0.05$). Error bars represent standard deviations.

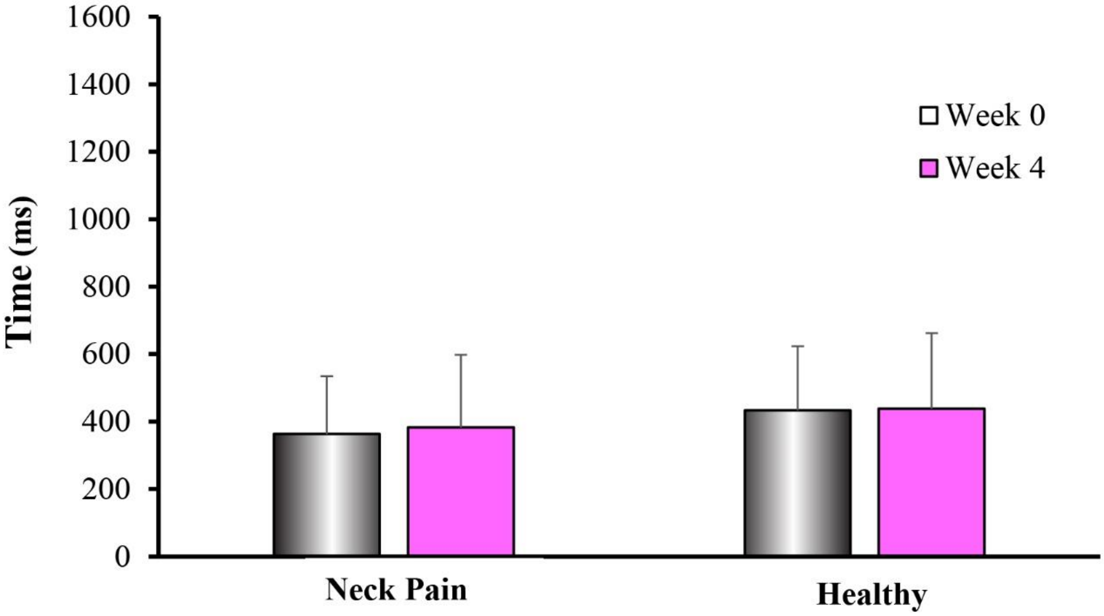

Figure 5.7 Average time (ms) between events at baseline and four weeks for SCNP and healthy control participants. Error bars represent standard deviations.

5.6 Discussion

The main finding of this study was that, as hypothesized, the SNCP group had significantly slower mental rotation response times than healthy controls both at baseline and after four weeks. Although both groups improved in response time over four weeks, as predicted the healthy group improved more (16.1%) than the control group (8.6%). Participants in the healthy group also had significantly greater accuracy at four weeks as compared to participants in the SCNP group, who performed slightly worse than baseline. These results suggest that neck joint dysfunction significantly impairs cognitive processing. This impairment is unlikely due to the presence of pain itself since the study population had minimal symptoms on the day they participated in this study.

These results are unlikely to be due to differences in response time between letter presentations, or due to differences in movement time between participants. There was no change in the self-paced delay between events, indicating that participants were not taking more or less time between stimulus presentations after four weeks (i.e. they weren't just improving because they were faster at the task, but they were actually better at performing the mental rotations). Additionally there was no difference between the groups or between baseline and four weeks in the response time for the letter 'R' presented in its normal orientation. The response time during a mental rotation task is a made up of the pre-motor response time to recognize a stimulus, the motor response time from stimulus recognition to the onset of muscle activity and movement time from when the arm begins to move to press the keys. The similarity in response time to recognize the letter 'R' in its normal upright orientation at 0 degrees means that there was no difference between groups in the combination of time to recognize the stimulus and initiate movement (Figure 5.2), indicating that the neck pain group did not have slower mental rotation response times because they were moving more slowly due to their neck problem.

During mental rotation, pre-motor response time increases linearly as object orientation angle increases, suggesting that subjects mentally rotate the object into congruence before responding (Shepard, et al., 1971). Therefore, the longer mental rotation response times in the neck pain group in the face of unchanged response times for the letter in its normal orientation indicates that SCNP participants are taking longer to mentally rotate the object into congruence before responding, rather than changing their movement speed. We suspect that this is due to altered cerebellar function in the neck pain group. Recent work has shown altered cerebellar function in SCNP individuals (Baarbé et al., 2015; Daligadu et al., 2013). A transcranial magnetic stimulation study demonstrated that SCNP patients do not show disinhibition in response to a motor learning task while healthy control participants disinhibit significantly (Baarbé et al., 2015). Furthermore, there is decreased kinesthesia in SCNP populations for both the upper limb (Haavik et al., 2011) and neck (Lee, H. et al., 2004; Lee, H. et al., 2005; Lee, H.-Y. et al., 2008). This suggests that the altered sensory input from the neck may be leading to altered kinesthesia as a result of an altered body schema which is partially encoded in the cerebellum.

One way that that central nervous system controls movement is by creating an internal model of the body and using this model to predict the sensory consequences of the movement (Shadmehr, et al., 2010). There is growing evidence that the cerebellum plays a critical role in creating this internal model (Shadmehr et al., 2010). The simple spike firing of cerebellar Purkinje cells is highly correlated with movement kinematics (Hewitt et al., 2011). A recent study in monkeys demonstrated that cerebellar Purkinje neurons demonstrate firing properties consistent with signalling feedforward internal predictions used for compensatory movements, as well as receiving sensory feedback about actual movements to monitor performance (Popa et al., 2013).

Mental rotation tasks typically require either manipulation of the frame of reference of the participant (egocentric frame of reference) or rotations of the object’s frame of reference (allocentric frame of reference). In a previous study, Creem-Regehr et al. (2007) compared performance and fMRI activation on two different mental rotation tasks, one requiring rotation of the involved body-part (hand) and the other requiring body (perspective) transformations. They found that both types of tasks created activation in the lateral occipital areas, inferior and superior parietal cortex, and the cerebellum (Creem-Regehr et al., 2007). Further weight to the importance of the cerebellum in the ability to perform mental rotation tasks was provided by the cTBS study by Picazio et al. (2013), which demonstrated that decreasing input from the left cerebellar hemisphere using cTBS led to slower mental rotation response times for both an embodied mental rotation task requiring an egocentric mental rotation strategy and an abstract mental rotation task which required an allocentric strategy.

Neck pain is known to impact our internal reference frame, affecting spatial judgement and processing. Paulus, et al. (2008) found that participants with neck pain judged their shoulder to be raised higher during passive shoulder elevation compared to asymptomatic controls. Haavik et al. (2011) found that participants with non-severe SCNP performed poorly when replicating elbow position with eyes closed compared to healthy controls. Participants with neck pain also show an impaired ability to reposition the head to a neutral position (Kristjansson, et al., 2003; Lee, H.-Y. et al., 2008). Lee, H.-Y. et al.

(2008) found that participants with neck pain showed more absolute error when positioning their head to a neutral position (e.g. comfortable position with head facing straight ahead) compared to a target (e.g. self-selected midpoint within the participant's maximum range of motion).

The head's position may also influence the body's perception of itself in space and may be a source of altered representation in the body's internal model. Paulus et al. (2008) found that participants with non-severe, but recurrent neck pain, repositioned their head more dramatically (e.g. with greater degree of displacement) away from the side where the trunk was bending than asymptomatic controls. Of interest, this more dramatic head positioning during passive shoulder elevation corresponded with greater trunk movement and perception of a higher shoulder during passive shoulder elevation (Paulus et al., 2008).

Guerraz, et al. (2011) found that head posture greatly impacted participant's ability to replicate an object using simple arm tracing. For this study, participants lay supine and were asked to view an object and then trace the shape of this object with their unseen index finger using elbow and shoulder movements. The tracing was completed in two conditions: with eyes closed and with eyes open (viewing only the object and not arm movements or the tracing). When the head was tilted, there was a bias of spatial arm movements towards the opposite direction during both memory-guided and visually-guided movements. Two experiments were performed: specifically for the first experiment, the head was held straight while viewing the object and then tilted during tracing. In the second experiment, the head was tilted at 30 degrees during both viewing and tracing. Bias was seen in both instances as long as participants replicated the movements with their head tilted. The bias was not seen when participants replicated the movement with their head straight. When vision was added (to view arm movements and tracing), bias decreased significantly for the leftward head tilt in both experiments. Notably, the participants perceived the tracing as being in line with their body even though the traces were biased by the head tilt (Guerraz et al., 2011). A recent study found that changing visual feedback altered the amount of pain-free neck rotation in a group of chronic neck pain patients (Harvie, et al., 2015). This indicates an increased reliance on visual input in this group, possibly because their internal body schema or body map is not accurately calibrated, leading to altered integration of sensory input.

In conclusion, mental rotation ability, which is partially encoded by the cerebellum along with body schema, is compromised in individuals with recurrent neck pain. This impairment is unlikely due to the presence of pain itself since the study population had minimal symptoms on the day they participated in this study. It is therefore possible that people who are developing neck pain have disrupted sensorimotor function of the neck that even without current pain can disrupt processing and integration of other sensory inputs.

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Chapter 6: Conclusions

6.1 Summary of Findings

This thesis set out to explore systematically the influences of chronic alterations in afferent input from the neck, as demonstrated by SCNP participants. Recurrent subclinical neck pain (SCNP) is defined as non-severe recurrent neck pain lasting at least three months in the past year. The overall hypothesis was that chronic alterations in afferent input from the neck would lead to an altered body schema, resulting in altered cerebellar processing, changes in upper limb function and changes in spatial mental representations.

Pain creates neural and biomechanical adaptations which are hard to entangle from the effects of altered afferent input from the neck on body schema. Individuals with SCNP represent an interesting model because they enable the chronic effects of altered input from the neck to be studied on days when participants are pain free.

To explore the influence of SCNP on cerebellar processing in the first study "Neck Pain Alters the Response of the Cerebellum Following Motor Training" (Chapter 3), I looked at the effects of motor training on cerebellar inhibition (CBI) in both healthy and neck pain participants. To determine whether SCNP was a cause or an effect of potential alterations of cerebellar inhibition to the motor cortex, I compared the effects of treating areas of neck dysfunction prior to motor training vs. the effects of a control intervention of light palpations to the neck prior to motor training. For this, I applied the technique CBI at fifty percent (CBI_{50}), and I studied changes in participants' CBI response at fifty percent inhibition (CBI_{50}) and at stimulator outputs 5 and 10% above CBI_{50}.

The specific hypothesis of study one was that SCNP participants would show greater CBI_{50} following motor learning than healthy participants. A single session of spinal manipulation would restore CBI_{50} to the same level as healthy participants. I hypothesized that if alterations to the feedback of sensory input from the neck were not a source of altered sensory feedback to the neck that there would be no difference in CBI_{50} between SCNP participants and healthy participants and a single session of spinal manipulation session would have no impact on CBI_{50} measures.

My findings support my hypothesis. Study one found that following completion of the motor training task, SCNP participants who received manipulation significantly increased the magnitude of CBI (e.g. they were more dis-inhibited). SCNP participants also improved their motor acquisition performance following manipulation. In contrast, SCNP participants who were randomized to the control conditions and received only light palpations and mobilization to the neck, showed no changes to CBI, nor did they show any improvements to motor acquisition following passive head movement.

The cerebellum encodes kinematics including position and velocity, and is involved in predicting sensory and motor consequences of movements. Given the changes in cerebellar function seen in the first study, I wanted to see whether SCNP impacted performance on an upper limb task that is highly reliant on the cerebellum. Overarm dart throwing is a task that requires coordination and timing between joints of the shoulder, elbow and wrist, and is a task that is highly dependent on intact cerebellar function. In the second study “Subclinical Neck Pain Impacts 3D Kinematics of Upper Extremity Dart Throwing” (Chapter 4), I compared upper limb kinematics and variability between novice dart throwers who were healthy and those with SCNP.

I hypothesized that should there be a relationship between altered afferent input from the neck in SCNP participants and altered cerebellar encoding as was found in

Chapter 3, SCNP participants would show kinematic differences compared to healthy participants during an upper extremity dart throwing task, as well as increased variability in movement patterns. Specifically, I hypothesized that there would be increased total distance in the hand's trajectory as measured from three axes, as well as increase variability to select the motor pathway in the first 20% of the throw. These differences would be seen while SCNP participants learnt the task (during the first three throws) due to conflicting signals from the neck and the increased need for exploration and exploitation of task parameters. I also hypothesized that SCNP participants would show differences in joint displacement and velocity across joint movements during the throw. The null hypothesis of study one was that SCNP participants would show no differences in kinematics or variability compared to healthy participants.

I found that participants with SCNP showed increased total distance of the hand's trajectory during slow-normal speed throws, as well as increased variability in elbow and forearm motor selection for slow-normal speed throws. Peak acceleration velocity of the shoulder was found to be faster in participants with neck pain for both slow-normal speed and fast throws, and peak deceleration velocity of the wrist was also found to be faster in SCNP participants for slow-normal speed and fast throws.

The differences that I found in SCNP participants to their total distance travelled and variability of motor selection for slow-normal speed throws indicate that learning in SCNP participants occurred differently than it did for healthy participants. Findings of greater peak velocity, greater distance travelled, tendency for greater forearm supination and tendency for lower peak forearm pronation-supination velocity indicate that SCNP participants had to exert more effort into the throw than healthy participants. These findings together suggest that sensorimotor disturbances of neck pain influence the efficiency and control of movement.

Mental rotation is the ability to rotate mental representations of two or three dimensional figures rapidly and accurately. The ability to mentally rotate objects and the frame of reference of those objects is a critical for many activities. Mental rotation of the outward environment is a highly important task that is used for executing correct and skillful movements, and is particularly important for object recognition, spatial navigation and movement planning. The cerebellum is important in both feedback and feedforward models of motor control, using afferent feedback to update body schema to maintain accuracy of feedforward control of movement (Popa, et al., 2013), and it also plays a critical role in spatial processing and object recognition (Picazio, et al., 2013). A study by Picazio et al. (2013) used continuous theta burst stimulation (cTBS) to decrease cerebellar hemispheric excitability in healthy adult participants performing a mental rotation task and found that it decreased performance. Given the effects of SCNP on cerebellar function observed in study one and the effects on a throwing task highly dependent on cerebellar function seen in study two, I sought to determine whether SCNP also impacted the capacity for mental rotation. If mental rotation ability is impaired in individuals with recurrent neck pain relative to healthy controls, it would suggest that the altered cerebellar processing could be contributing to not only a disrupted body schema but disruptions in spatial recognition of objects.

In study three “Neck Pain Impairs the Ability to Perform a Mental Rotation Task” (Chapter 5), I tested mental rotation skill in individuals with SCNP and in healthy controls. To determine whether mental rotation ability naturally improved over time in SCNP participants relative to healthy controls, I performed a longitudinal study comparing performance scores at baseline and after four weeks in SCNP and healthy controls.

I hypothesized that those in the SCNP group would have slower response times when performing mental rotation, and that this would not be explained by changes in movement time. Furthermore, I hypothesized that although both groups would improve over time due to task familiarity, the SCNP group would still show decreased mental rotation ability relative to the control group after four weeks.

I found that, as hypothesized, the SNCP group had significantly slower mental rotation response times than the healthy group both at baseline and after four weeks. Both groups showed improvements to response time over four weeks. However, the healthy group improved more (16.1%) than the SCNP group (8.6%). No differences were seen to response time between groups or over four weeks when the object was at 0 degrees of rotation, suggesting that improvements are not likely to be due to either the time needed to recognize the letter or to movement time that is needed to press the key. Participants in the healthy group also had significantly greater accuracy at four weeks as compared to participants in the SCNP group, who performed slightly worse than baseline.

Taken as a whole, these three studies provide compelling evidence that altered afferent input from the joints and muscles of the neck due to recurrent SCNP influences cerebellar integration of that input leading to altered cerebellar disinhibition in response to motor training. Altered signals to the neck in SCNP also influence the body schema, leading to changes in upper limb kinematics when learning a new motor task, and a decreased capacity for mental rotation of external objects.

6.2 Implications of Findings

Even low levels of ongoing neck pain appear to inhibit the cerebellar response, and lead to altered motor performance. This thesis suggests the concept that altered sensory input from the neck due to SCNP affects cerebellar processing, upper limb performance and spatial mental representations. Spinal manipulation, as oppose to mobilization techniques, may be sufficient to normalize sensory input from the neck and restore altered cerebellar processing and motor performance.

This work is of critical significance, as it suggests that ongoing changes in afferent feedback from the neck may influence motor performance and spatial awareness. This could mean that changes in afferent input from the neck, as occur in neck pain, may potentially set people up for upper limb injuries due to altered kinematics, and also influence accuracy and performance of the upper limb. This has tremendous implications for industry and sport where small errors can have large consequences, influencing both productivity and safety.

6.3 Future Directions

Future work should explore the costs of altered sensory input in neck pain to see whether individuals compensate through loss of attention, time on the task or cognitive resources. If less efficiency is found in neck pain, it may be due to a re-weighting of sensory input so less importance (and thus less information) is provided from painful areas such as the neck. The implications may be a reliance on other sources of input. The neuroplastic changes that facilitate this process may decrease timing efficiency for completing tasks since increasing the reliance on less useful sources of input (than input from the neck) may result in more transfer time and processing time in the brain.

For this reason, the speed-accuracy trade-off due to altered sensory input in neck pain participants is another aspect that may be researched more. In this thesis, I found that SCNP participants have altered cerebellar processing (Chapter 3), which likely means that more attentional focus is required to complete tasks. I also found that greater peak velocities were reached in SCNP participants during an upper limb throwing task suggesting lower movement efficiency. A fundamental question that remains is whether accuracy in SCNP individuals is maintained at a loss of speed. SCNP participants may show an all-or-nothing response where greater attention is applied as well as greater accuracy at the cost of time to facilitate learning until either the task is learnt or sensory input to the neck is normalized. Theoretically, healthy people whose sensory input to the neck is already normalized will have a more flexible focus of attention that allows them to shift focus more easily. Thus, future research should look at whether SCNP individuals are able to perform more than one task together, or whether they are able to perform reasonably well on a task that they are applying only moderate amounts of attention to compared to healthy participants.

Spinal manipulation may help speed the process of normalizing sensory input to the neck and may improve performance times, thus reducing the speed/accuracy trade-off. Future work should elucidate more the nature of the chiropractic manipulation and its implications for functional real-world tasks.

Future work may also look at multisensory input in SCNP. If the brain re-weights input so that painful areas of the neck are given less weight and non-painful areas are given more weight, this might interfere with proprioception as sensory input from the from neck joints, muscles and tendons is weighted less and other senses such as sight or sound are weighted more. Multisensory processing is an important part of adaptation, and SCNP may influence the multisensory skills which allow adaption to new or unfamiliar environments.

6.4 Conclusion

In conclusion, what I have found suggests that chronic alterations in afferent input from the neck appears to lead to an altered body schema, as evidenced by altered cerebellar processing, changes in upper limb function and changes in spatial mental representations of external objects. The fact that these changes were measured in SCNP participants on days that they were pain free is important as it suggests that recurrent neck pain leads to chronic alterations in sensorimotor integration that persist even when pain is absent. Ongoing changes in afferent feedback from the neck such as occurs in SCNP may influence timing of tasks, movement efficiency as well as spatial awareness of the environment. This could potentially set people up for upper limb injuries while learning motor tasks, as well as influence the accuracy and performance of the upper limb. This knowledge potentially has many implications to industry and sport, since it suggests that SCNP individuals who learn new tasks or perform on well-learnt tasks may be at risk for injuries or for errors that influence their safety and productivity.

6.5 References

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