



Swansea University
Prifysgol Abertawe



Cronfa - Swansea University Open Access Repository

This is an author produced version of a paper published in :
Journal of Bodywork and Movement Therapies

Cronfa URL for this paper:
<http://cronfa.swan.ac.uk/Record/cronfa33672>

Paper:

Whelan, G., Johnston, R., Millward, C. & Edwards, D. (2017). The immediate effect of osteopathic cervical spine mobilization on median nerve mechanosensitivity: A triple-blind, randomized, placebo-controlled trial. *Journal of Bodywork and Movement Therapies*
<http://dx.doi.org/10.1016/j.jbmt.2017.05.009>

This article is brought to you by Swansea University. Any person downloading material is agreeing to abide by the terms of the repository licence. Authors are personally responsible for adhering to publisher restrictions or conditions. When uploading content they are required to comply with their publisher agreement and the SHERPA RoMEO database to judge whether or not it is copyright safe to add this version of the paper to this repository.

<http://www.swansea.ac.uk/iss/researchsupport/cronfa-support/>

Title page

The Immediate Effect of Osteopathic Cervical Spine Mobilization on Median Nerve Mechanosensitivity: a Triple-Blind, Randomized, Placebo-Controlled Trial

Gary Whelan^a M.Ost

Ross Johnston, M.Sc. B.Sc. (Hons) Ost Med, DO^b

Charles Millward, ND DO^c

Darren J. Edwards B.Sc. M.Sc. Ph.D.^{d*}

^a *Osteopath, College of Human & Health Sciences, Swansea University, Singleton Park, Swansea, Wales, SA2 8PP*

^b *Senior Lecturer, College of Human & Health Sciences, Swansea University, Singleton Park, Swansea, Wales, SA2 8PP*

^c *Lecturer, College of Human & Health Sciences, Swansea University, Singleton Park, Swansea, Wales, SA2 8PP*

^d *Lecturer, College of Human & Health Sciences, Swansea University, Singleton Park, Swansea, Wales, SA2 8PP*

* *Corresponding author. Tel: +44 (0) 1792 604185*

E-mail address: d.j.edwards@swansea.ac.uk

Abstract

Background: Neurodynamics is a clinical medium for testing the mechanical sensitivity of peripheral nerves which innervate the tissues of both the upper and lower limb. Currently, there is paucity in the literature of neurodynamic testing in osteopathic research, and where there is research, these are often methodologically flawed, without the appropriate comparators, blinding and reliability testing. **Aims:** This study aimed to assess the physiological effects (measured through Range of Motion; ROM), of a commonly utilized cervical mobilization treatment during a neurodynamic test, with the appropriate methodology, i.e., compared against a control and sham. Specifically, this was to test whether cervical mobilization could reduce upper limb neural mechanical sensitivity. **Methodology:** Thirty asymptomatic participants were assessed and randomly allocated to either a control, sham or mobilization group, where they were all given a neurodynamic test and ROM was assessed. **Results:** The results showed that the mobilization group had the greatest and most significant increase in ROM with Change-Left $p < 0.05$ and Change-Right $p < 0.05$ compared against the control group, and Change-Left $p < 0.01$ and Change-Right $p < 0.05$ compared against the sham group. **Conclusions:** This study has highlighted that, as expected, cervical mobilization has an effect at reducing upper limb neural mechanical sensitivity. However, there may be other factors interacting with neural mechanosensitivity outside of somatic influences such as psychological expectation bias. Further research could utilize the methodology employed here, but with other treatment areas to help develop neural tissue research. In addition to this, further exploration of psychological factors should be made such as utilizing complex top-down cognitive processing theories such as the neuromatrix or categorization theories to help further understand cognitive biases such as the placebo effect, which is commonly ignored in osteopathic research, as well as other areas of science, and which would further complete a holistic perspective.

Keywords

Osteopathy; Neurodynamics; Mechanosensitivity; Neurophysiological Mechanism;

Mobilization; Nerve Tension; Range of Motion

Introduction

Studying neck pain and identifying ways in which to remediate this pain and increase mobility is extremely important and significant to osteopathic practice. This includes studies which focus on asymptomatic participants, as the generalizability, and therefore external validity, between asymptomatic and clinical populations have been found to be high. This is where, for example, similar positive outcomes have been found when using the same interventions such as a lateral glide (iii) mobilization technique between both clinical (lateral epicondylalgia) and non-clinical populations (Schmid et al., 2008).

It is particularly important to study osteopathic mobilization techniques which reduce neck pain, as it is suggested that between 30 and 50% of all individuals will suffer a clinically significant incidence of neck pain over a 12-month period (Fernandez-de-las-Penas et al., 2011; Hogg-Johnson et al., 2008). Of the patients who suffer an episode of neck pain, some will self-resolve within a number of weeks. However, over 50% of sufferers experience pain which lasts longer than six weeks, and progress into chronicity (Cohen, 2015).

Somatic pain is a subjective cortical response to injury (Merskey & Bogduk, 1994). Clinically, symptom presentation can appear non-specific due to the plasticity of the nervous system (Bogduk, 2011). This is particularly pertinent in the upper limb due to the close relationship and interaction between the anatomically connected nerve network of the brachial plexus (Drake et al., 2009; Kishner et al., 2013). Therefore, peripheral neuroanatomy plays an important role in how pain is perceived by patients.

Nociceptive pain is suggested to be generated by an influx of noxious stimulation, known as the nociceptive drive, which can be mechanical, thermal or chemical in nature. Persistent noxious stimulation can cause high-threshold responding A-delta and C-fibres to become disorganised inducing a maladaptive response known as maldynia which is involved

in the continued progression of the pain experience in the absence of the ongoing noxious stimulus (Woolf & Ma, 2007). As a result of the A-delta and C-fibres becoming altered, their mechanosensitivity (sensitivity to stimulation) is increased by disorganization of their synaptic connections and loss of the inhibitory neurons' modulatory function in the spinal cord. This causes the recurrent sense of nociceptive stimulation in the presence of no tissue injury (Butler, 1991; Ward, 2003).

Clinical Neurodynamic (CN) testing, or more specific to this study, the Median Nerve Upper Limb Neurodynamic Test (ULNT), has been used to assess the physical capabilities of a nerve and mechanosensitivity. Guidelines have been proposed which suggest this to be an aid in identifying the presence of neural mechanosensitivity (Butler, 1991; Nee & Butler, 2006; Shacklock, 1995). CN testing in these settings places tension on the nerves specifically hypothesized to be involved in this type of pain (Butler, 1991; Nee & Butler, 2006; Shacklock, 1995). Therefore, the ULNT is an ideally placed test for mechanosensitivity of the median nerve (and central connections), as the technique places tension on the major trunk of the median nerve, its nerve rootlets, cervicobrachial plexus and their central connections, which has been suggested to increase mechanosensitivity of this nerve and thus reduces movement in these associated areas as a result (McLellan and Swash, 1976; Elvey, 1979; Sunderland, 1978).

Reducing mechanosensitivity of the median nerve and its central connections through a mobilization technique is the focus of this paper, so the use of ULNT is appropriate. It will be conducted in conjunction with a passive (sham or control) or active (mobilization) intervention. The mobilization technique will be conducted through unilateral passive cervical mobilization of levels C2-T1 zygapophyseal joints for 30 seconds per joint level, during a neurodynamic test. It is expected that it will produce an immediate increase in upper limb range of motion (ROM). Several studies have focused on hypoalgesic effects of

mobilization, but few papers have explored the ROM of a participant after mobilization and none have specifically focused on mobilizing the C2-T1 areas specifically and within a neurodynamic test setting.

In terms of the use of ROM as an outcome measure, it has been argued that this is the most quantifiable and applicable outcome measure during a clinical setting i.e., tolerable stretch of the peripheral nervous system, as it can be used to differentiate between optimal and suboptimal neural responses (Butler, 1991).

The prediction of reduced mechanosensitivity measured through increased ROM is supported by previous evidence which has shown that non-noxious gliding, shearing or rotational components of passive cervical mobilization stretch the nerve rootlets exiting the spinal cord. As a result, the A-delta fibres within the peripheral nerve may be stimulated to produce relative hypoalgesia and reduced mechanosensitivity (Sterling, Jull, & Wright, 2001). Also, in addition to this, previous literature has acknowledged that passive cervical mobilization activates the sympathetic nervous system to produce local and extrasegmental hypoalgesia (Schmid et al., 2008; Vincenzino, Collins, & Wright, 1994; Vincenzino, Gutschlag, Collins, & Wright, 1995). Thus, because of this hypoalgestic effect and reduced neural mechanosensitivity caused by cervical mobilization, it is likely that ROM will be improved in this case.

The second component of this present study, as to ensure that mechanosensitivity was tested in the appropriate setting. The problem with mobilization research which uses neurodynamic testing, to date, is that it often has methodological flaws, which can contaminate the results through introducing confounding variables. Ellis and Hing (2008) used a PEDro scale to assess method quality of several of these studies and found most of them to be limited largely due to a lack of blinding, and lacking in the homogeneity of interventions used. Blinding within manual therapy can be problematic to implement.

However, it is critical to remove as much bias as possible in order to adequately test intervention effectiveness (Jadad & Enkin, 2007). Studies, to-date, which aim to improve the wealth of knowledge in CN have not effectively implemented blinding of therapists, subjects (e.g., Coppieters et al., 2003, Baysal et al., 2006) and even assessors (Akalin et al., 2002; Drechsler et al., 1997).

This is further exacerbated by the fact that in CN research, studies which implement an appropriate sham and a no-treatment control group seem to be very few. Studies which have used comparator groups, have often used shams which cause a therapeutic effect (e.g., Coppieters et al., 2003) while others have combined CN interventions with non-CN interventions (e.g., Allinson et al., 2002; Scrimshaw & Maher, 2001). This makes it incredibly difficult to ascertain the effect of the primary intervention itself during the CN test on a patient. With the rising evidence of placebo based effects, without an effective sham and control group it is impossible to say that the effects were solely intervention led.

Therefore, in addition to its methodological novelty, this present study aimed to improve on the rigour implemented in CN studies by adding a no-treatment control, and an appropriate non-neural loading sham. Furthermore, it aimed to increase this validity by improving the levels of blinding previously used, by blinding the participants and neurodynamic tester to intervention procedures and outcomes, the outcome assessor to the interventions, and finally the intervention practitioner to all outcome readings.

In summary, the main purpose of this study was to investigate the therapeutic application of cervical mobilization on upper limb mechanosensitivity (i.e., during a neurodynamic test) and to compare this against a sham intervention, and control, with appropriate blinding and reliability testing to limit confounding variables. It is specifically predicted that the mobilization intervention will significantly increase ROM more than the sham and control conditions, which will indicate a reduction in mechanosensitivity during the

neurodynamic test. In addition to this, psychological influences are explored in the form of potential placebo effects.

Methods

Participants

A purposive sample of 34 healthy, asymptomatic subjects were obtained from Swansea University, who were all first and second year osteopathic students. The respondents were then screened for eligibility. Four were removed due to refusing to participate (see Consort flow diagram, figure 1). Please see Table 1 for the participant demographics of age, height, weight and body mass index.

Inclusion criteria for participation were ages 18 – 45 to minimize inherent risk of spondylitic changes. Participants were excluded if they were suffering from symptoms of paraesthesia, dysesthesia or radiculopathy lasting for longer than one week or had previously been diagnosed with an entrapment syndrome such as carpal tunnel or thoracic outlet syndrome. None of the participants reported these symptoms.

In addition to this, if participants elicited positive symptoms following Spurling's test (Spurling & Scoville, 1944) for intervertebral foramen (IVF) compression or if they were experiencing symptoms which indicated the presence of adverse neural tension according to Shacklock's criteria (Shacklock; 2005) they were also omitted. Each participant was required to speak and comprehend English in order to fully consent and understand the assessment process. Participants were allocated a number and assigned to one of three randomised intervention groups.

-----PLACE FIGURE 1 HERE-----

Research Design

This experimental design method consisted of a triple-blind, randomized, sham-controlled, between subjects design.

Ethical approval

Ethical approval was obtained through Swansea University College of Human and Health Science.

Examiner Repeatability

To ensure a high level of examiner reliability and repeatability, intra-rater reliability tests were conducted in the form of intraclass correlation coefficients (ICC). This was conducted comparing ROM recordings for pre and post as described by Fless (1987). Reliability of this was determined through the classification system described by Shrout and Fleiss (1979), where: >0.75 was determined as excellent; $0.6-0.75$ as good; $0.4-0.59$ as fair; and <0.04 as poor. An analysis of variance using a two-way mixed model (i.e., fixed raters and random participants) was used on the ROM data. Measurements of ROM were taken using an inclinometer.

Internal validity

Blinding

In this triple-blind, randomized, placebo-controlled trial, there were the participants, and three examiners. Examiner 1 (E1) was tasked with performing the neurodynamic testing, Examiner 2 (E2) performed each therapeutic intervention, and Examiner 3 (E3) took the ROM readings. The participants were blinded to the condition they were in and ROM readings, the neurodynamic tester (E1) was blinded to the condition and the ROM

measurements made; E2 was blinded to the measurements made by the assessor, and the ROM assessor (E3) was blinded to the study intervention. This meets the correct blinding criteria identified by Ellis and Hing (2008) for manual therapy studies of this nature.

Randomization

Random allocation of the student participants was applied through a simple sealed envelope method (Schulz, 1995) before testing sessions began. This method has been validated as an effective randomization technique by Suresh (2011). It involved sealing in an envelope, an intervention code (i.e., control, 1; sham, 2; experimental, 3). Only E2 (the intervention therapist) was able to see the condition group sealed in the envelope. There was no communication between the change-over of examiners, and complete blinding of technique and data readings was ensured throughout (i.e. where appropriate, the blinded assessor would leave the room).

External validity of experimental design

External validity is important to the significance and generalizability of findings. It is the degree to which the research findings can generalize to clinical populations in this setting. It is always best to obtain clinical populations, however, a systematic review by Schmid et al. (2008) has demonstrated that cervical spine mobilization techniques have been successfully employed to increase ROM in both asymptomatic and clinical populations with similar outcomes being found in both populations. This suggests high generalizability when using asymptomatic participants in a study of this kind, and therefore high external validity of this study. As such, the use of asymptomatic participants, is both justified, and methodologically valid, as it is important to develop the therapeutic interventions as a proof-of-concept, in a

safe as possible environment, before committing patients to these often, novel intervention applications.

Experimental Conditions

Cervical Mobilization

Osteopathic rotational mobilization was applied on six segments from C2-T1 zygapophyseal joints for 30 seconds per joint of the left side of each participant's cervical spine totalling three minutes of therapeutic interaction. Due to the known interconnectedness of the spinal nerves and synapses within Substantia Gelatinosa and tract of Lissauer, it seemed appropriate to target levels outside of the median nerves typical spinal roots to optimally exploit the nerve's relationship with all cervical rootlets. Furthermore, the upper limb tension test may also tension other branches of the brachial plexus thus supporting application of extrasegmental mobilization. See Figure 2 for an illustration of the mobilization technique.

Sham Intervention

Each participant was told they would receive a gentle, cranial osteopathic technique. The examiner (E2) cradled the participants' cervical spine for three minutes while their head lay on a pillow. The sham chosen was deemed appropriate due to the participant's unawareness and reduced understanding of the technique. The examiner ensured to disengage from any cranial rhythm while performing the sham technique (see Figure 2).

-----PLACE FIGURE 2 HERE-----

Control

Each participant lay supine on the plinth with their head on a single pillow for a total of three minutes.

Median Nerve Upper Limb Neurodynamic Test (ULNT)

There were four stages to the ULNT (Butler, 1991) which E1 performed. (1) A gentle depressive force was applied to the shoulder which was maintained throughout the procedure to prevent scapula elevation. The glenohumeral joint was abducted to 110 degrees in line with the goniometer while maintaining elbow flexion perpendicular to the humerus. (2) In the next step, the therapist induced wrist extension then forearm supination in sequence. (3) The glenohumeral joint was then externally rotated to the available range, up to the maximum of 50 degrees. The therapist then placed an inclinometer on the distal, posterior shaft of the ulna just superior to the olecranon. (4) Finally, elbow extension, with the wrist extended was induced up to the point in which the patient reported discomfort in the upper limb (see Figure 3).

Dependent Variable Outcome Measure: Range of Motion (ROM) During Median Nerve ULNT

Readings of ROM were taken using the iHandy application on an iPhone® 5S model (see Figure 3), utilizing the iOS 8.1 software and an in-built inclinometer which has been shown to be equal or superior to more commonly used methods (Charlton et al., 2015; Kolber et al., 2012; Kolber et al., 2013). To ensure the repeatability of the used application see the ICC results in Table 2.

In order to account for baseline ROM differences which could affect the intervention outcome readings, change data was calculated, where post data was subtracted from pre-intervention data. As such, change of ROM between pre-and post-interventions across both

left and right sites were recorded and used as the dependent variable (DV) in the analysis. This, therefore, accounts for the baseline pre-intervention ROM and thus controls for any baseline differences.

-----PLACE FIGURE 3 HERE-----

Testing Procedure

Each participant was invited to a separate pre-testing session prior to the actual testing session to ensure they met the inclusion criteria. A trial run was performed on each arm of every participant in their initial session to ensure a degree of familiarity to outcome responses. After the trial run, the testing procedure began, where participants lay supine on a plinth with their heads on a single pillow. The room was a quiet, well ventilated laboratory with no clock. The four stages of the neurodynamic testing (ULNT) were then performed by E1 (see section on ULNT).

At this point elbow extension (ROM) was recorded by E3 and concealed from the testing examiner (E1). Then, the participant's position was reset and the procedure was completed on the contralateral arm. Following this, both examiners (E1 and E3) left the room and the intervention session was performed for three minutes by E2 (e.g., control, sham or mobilization), who ensured randomization through the envelope approach. After completion of the intervention, the four stages of ULNT was completed again by E1 for both the left and right arms with ROM being recorded once again by E3. Appropriate blinding was ensured throughout (see the section on blinding).

Data Analysis

First, a Shapiro-Wilk test was conducted on the data, to test for a normal distribution, and this was identified ($p > 0.05$), which justifies the use of parametric tests. Thus, a general linear model, consisting of a one-way between measures Analysis of Variance (ANOVA) was used to analyse the differences between the three interventions of the change data using pre-post differences (where post ROM scores were subtracted from pre) to represent change.

Following this, t -tests were performed comparing pre-post ROM for each of the conditions, which were simply to identify any placebo effects across conditions. In addition to this, an Intraclass Correlation Coefficient (ICC) was conducted to test for reliability of the single ROM assessor (one-way Analysis of Variance using a two-way mixed model).

Results

Demographic results

See Table 1 for the participant demographics of age, height, weight and body mass index. In addition to this, a Levene's test of equality was used to assess the homogeneity of the basic demographics between conditions. They did not differ significantly in age ($F(2, 27) = 1.574$, $p = 0.266$), or height ($F(2, 27) = 0.080$, $p = 0.924$). However, they did differ in weight ($F(2, 27) = 5.544$, $p = 0.010$) and BMI ($F(2, 27) = 4.116$, $p = 0.028$).

-----PLACE TABLE 1 HERE-----

ICC results

Table 2 displays the intra-rater reliability of the ROM measures at test sites pre-and post-testing phases in the form of an ICC. This is an important test as there was a single ROM

examiner. It was hypothesised that for both pre and post phases there would be a significant intraclass correlation coefficient, indicating high intra-rater reliability (the p values of an ICC are expressed as the probability of observing the ICC when the null, no interclass correlation, is assumed to be true). The ICCs ranged from 0.698 to 0.736, $p < 0.001$.

-----PLACE TABLE 2 HERE-----

Mechanosensitivity: Range of Motion (ROM)

Table 3 shows the mean, standard deviation, standard error and range of both the right-left site locations and at both pre-and post-intervention. As can be seen by this, post-right and left mobilization ROM scores are higher than the post-sham and post-control left -right ROM scores. This indicates that the mobilization intervention was more successful at increasing ROM, however, these results do not take into account the baseline data. In order to take this into consideration, difference (change) results of pre-and post-data was used in the following inferential statistics (see Table 3).

-----PLACE TABLE 3 HERE-----

Two separate one-way between measures ANOVAs was conducted comparing pre-post change in ROM for the control, sham, and mobilization conditions for the left site (the first one-way ANOVA), and right side (the second one-way ANOVA). See Table 4 for a full break down of the inferential statistics.

For the first one-way between measures ANOVA, which compared pre-post change in ROM for control, sham, and mobilization for the left site, this showed a significant difference across these three conditions ($F(2) = 3.44$, $\eta_p^2 = 0.203$, $p < 0.5$) indicating a large effect size

according to Cohen's (1988) classification. In addition to this, post-hoc Bonferoni pairwise comparisons were made between conditions Mobilization-Left vs. Control-Left ($p < 0.05$), Mobilization-Left vs. Sham-Left ($p < 0.001$) and Sham-Left vs. Control-Left ($p = 0.372$). This indicated that the mobilization condition was significantly different when compared to the sham and control groups for the left side. There was no difference between the sham and control, as expected.

The second one-way between measures ANOVA, which compared pre-post change in ROM for control, sham, and mobilization for the right site, also showed a significant difference across the three conditions ($F(2) = 307.233$, $\eta_p^2 = 0.143$, $p < 0.05$), again, according to Cohen's (1988) classification system, this is considered a large effect size. In addition to this, post-hoc Bonferoni pairwise comparisons were made between conditions Mobilization-Right vs. Control-Right ($p < 0.05$), Mobilization Right vs. Sham Right ($p < 0.05$) and Sham Right vs. Control-Right ($p = 0.381$). Again, this indicated that mobilization was significant when compared against the sham and control conditions for the right-hand side. Also, there was no significance between the sham and control, as expected.

Paired samples t -tests were conducted to compare Change-Left vs. Change-Right for each condition, to see if there was any significant difference, between sites. None of the conditions differed significantly in terms of changes left and right.

Finally, pre-post comparisons were made for each condition at both sites using paired sample t -test. All of these were significant except for Pre-Left Control vs Post Left Control, and Pre-Right Sham vs. Post-Right Sham.

-----PLACE TABLE 4 HERE-----

Discussion

This present study sought to identify whether a mobilization technique was more effective at increasing the ROM, when compared to a sham and control, and during a neurodynamic test setting. This was done in a way where there was adequate blinding and suitable control and sham conditions were utilized. The appropriate methodology was important, so that the clinical results were not confounded (or at least confounds were limited) by inappropriate methodology such as multiple interventions in a single condition and without blinding, as what has been found in other studies (Coppieters et al., 2003, Baysal et al., 2006; Akalin et al., 2002; Drechsler et al., 1997).

The results found suggest that the mobilization technique was more effective than the sham and control in increasing ROM for both Change-Left and Change-Right through the one-way ANOVAs. In addition to this, the *t*-tests indicated that there was no difference between the control and sham for Change-Left and Change-Right.

More generally, the present study's findings may support work which has demonstrated that passive cervical mobilization reduces mechanosensitivity, where A-delta fibres within the peripheral nerve are stimulated by the mobilization technique resulting in a hypoalgestic effect thus reducing mechanosensitivity (Sterling, Jull, & Wright, 2001). It may also be possible that the mobilization technique activates the sympathetic nervous system (SNS) to produce local and extrasegmental hypoalgesia (Schmid et al., 2008; Vincenzino, Collins, & Wright, 1994; Vincenzino, Gutschlag, Collins, & Wright, 1995). The activation of the SNS through mobilization is generally associated with increased ROM, and increased hypoalgestic effects, e.g., see the review by Schmid et al. (2008).

A third possible explanation for the reduction in mechanosensitivity, is that there is evidence, that following mobilization it induces a reduction in local hypoxia and thus increases venous circulation. Therefore, ROM can be increased by changes in epineural

circulation and axoplasmic flow (Butler, 2000; Nee et al., 2006). Evidence suggests that the axon is typically sensitive to hypoxia (Okabe & Hirokawa, 1989). When an axon is mechanically sensitized it is suggested to suffer from venous congestion, predisposing it to reduced venous and axoplasmic flow (Kobayashi et al., 2000; Parke et al., 2002). The mobilization procedure produces pressure to the surrounding tissue, and it has been found that as little as 30mm/Hg can reduce axoplasmic flow (Ang & Foo, 2014). This in turn is suggested to increase action potentials to sympathetic nerve fibres and produce short term hypoalgesia and increased ROM (Shacklock, 1995; Slater, Vincenzino, & Wright, 1994).

In terms of methodological design, this study did implement the appropriate blinding of the participants, ROM assessor and neurodynamic tester to the intervention conditions, as well as the intervention therapist and neurodynamic tester to the ROM results as suggested by Ellis and Hing (2008).

In addition to this, this study ensured that an appropriate sham and control were used which had no therapeutic effect, unlike in previous studies such as Coppieters et al. (2003) who included a sham which induced a therapeutic effect. The present investigation, through rigorous methodology, ensured that the mobilization intervention showed a genuine increase in ROM.

Another area which is commonly ignored by previous research, is potential psychological placebo effects in the form of expectation bias (e.g., Benecuik et al., 2010). The advantage of appropriate blinding is that it reduces this placebo effect. In manual therapy, expectation bias may be powerful with the combined patient (participant) beliefs in combination with the oxytocin and serotonin which can be stimulated through touch alone (e.g., Gallace & Spence, 2010; Mendell, 2014; Morhenn, Beavin & Zac 2012). To control for this, the appropriate sham and control groups (both touch based) were presented along with baseline testing of ROM, to highlight any placebo effects present.

There was indeed an increase in ROM from baseline for all of the conditions except for Left-Control and Right-Sham when comparing post-intervention against baseline pre-intervention. This indicates that there was possibly a placebo effect, which increased ROM, however, due to the appropriate sham and control conditions, it was identified that the increase in ROM was significantly greater for the mobilization condition when compared against the sham and control conditions. This indicates that the mobilization intervention was genuinely effective.

In terms of recommendations for future research, there are clearly both physiological and psychological elements to neurodynamic testing and treatment modalities which need to be explored in more detail. More research into different treatment areas could aid in understanding how the tests effect neural tissue, and how psychological interpretation can alter outcomes in all of these individual cases.

Applying psychological theories can be particularly useful for this. For example, studies into categorical interoceptive representations of the cognitive system have been shown to bias bodily sensation perceptions (Peterson et al., 2014). This theory of categorization bias may go some way in explaining the observed placebo effects. Categorization research is a large subject area in cognitive science, and may be useful in exploring perceptual biases in manual therapy research such as by explaining contextual biases (e.g., Edwards, 2017; Edwards & Wood, 2016; Edwards et al., 2012a; Edwards et al., 2012b), as well as contextual behavioural psychology through Relational Frame Theory (RFT) (Edwards et al., 2017).

In addition to this, other cognitive models can be applied to support these assumptions, such as Melzack's (1999) Neuromatrix. This describes an individual's pain as purely subjective with somatosensory, limbic and cognitive components. The Neuromatrix concept suggests that a person's pain experience will be affected by the combination of the

sensory input given, their perceptions and their previous experiences and expectations. These expectations may have caused the global increase in ROM observed, in the form of placebo effects.

Another aspect of placebo inducing effects which has not been explored in depth is how touch (whether sham or osteopathic) can affect the oxytocin and serotonin levels in these specific types of tests. This may also account for some of the placebo effects presented, as oxytocin can provide a hypoalgesic effect (Gallace & Spence 2010; Mendell, 2014; Morhenn, Beavin & Zac 2012). Additional research could explore oxytocin levels increase with sham and mobilization conditions.

Finally, not all previous studies have found an increase change in ROM following interventions. So, studies may implement psychological questionnaires such as the Visual Analogue Scale (VAS) (Crichton, 2001), the Pain Catastrophizing Scale (PCS) (Sullivan, Bishop, & Pivik, 1995), or Pain Pressure Thresholds (PPT) (McCoss et al., 2016) to further assess the effectiveness of these techniques and to present a wider range of outcome measures in neurodynamic testing for different interventions.

Limitations

In this study it has been recognized that the first and second year osteopathic students who were used as participants in this study may have known that laying supine on a plinth, for instance, was not an active intervention, so this may have enhanced any placebo effect. Great efforts were made to ensure adequate blinding, but as in many disciplines of human science, student cohorts are often used of the same discipline, for the convenience in the recruitment that they provide. In future studies, post questionnaires could be used, asking whether they were aware of what the study was investigating, and how effective was the blinding. Or, more ideally, a non-student population would be used.

Conclusion

The findings of this study indicate that unilateral passive cervical mobilization of levels C2-T1 zygapophyseal joints for 30 seconds per joint level produces an immediate increase in ROM during a median nerve specific neurodynamic test. The treatment outcome was significant to both left and right sides, indicating a reduction in mechanosensitivity of the peripheral nervous system following mobilization of the axial skeleton and related neuraxis. Additionally, there was an overall increase in ROM during control and sham groups of varying degrees. Future studies should consider the effect of placebo, cognitive and other psycho-physiological changes that may be as a result of the provocative nature of the neurodynamic test.

Acknowledgments

None.

References

- Akalin, E., El, Ö., Peker, Ö., Senocak, Ö., Tamci, S., Gülbahar, S., ... & Öncel, S. (2002). Treatment of carpal tunnel syndrome with nerve and tendon gliding exercises. *American journal of physical medicine & rehabilitation*, *81*(2), 108-113.
- Allison, G. T., Nagy, B. M., & Hall, T. (2002). A randomized clinical trial of manual therapy for cervico-brachial pain syndrome—a pilot study. *Manual Therapy*, *7*(2), 95-102.
- Ang, C. L., & Foo, L. S. S. (2014). Multiple Locations of Nerve Compression: An Unusual Cause of Persistent Lower Limb Parasthesia. *The Journal of Foot & Ankle Surgery*, *53*(6), 763-767.
- Baysal, O., Altay, Z., Ozcan, C., Ertem, K., Yologlu, S., & Kayhan, A. (2006). Comparison of three conservative treatment protocols in carpal tunnel syndrome. *International journal of clinical practice*, *60*(7), 820-828.
- Beneciuk, J. M., Bishop, M. D., & George, S. Z. (2009). Effects of Upper Extremity Neural Mobilisation on Thermal Pain Sensitivity: A Sham-Controlled Study in Asymptomatic Participants. *Journal of Orthopaedic & Sports Physical Therapy*, *39*(6).
- Beneciuk, J. M., Bishop, M. D., & George, S. Z. (2010). Pain catastrophizing predicts pain intensity during a neurodynamics test for the median nerve in healthy participants. *Manual Therapy*, *15*(4), 370-375.
- Bogduk, N. (2011). The anatomy and pathophysiology of neck pain. *Physical Medicine and rehabilitation clinics of North America*, *22*(3), 367-382.
- Bove, G. M., Ransil, B. J., Lin, H. C., & Leem, J. G. (2003). Inflammation induces ectopic

- mechanical sensitivity in axons of nociceptors innervating deep tissues. *Journal of Neurophysiology*, 90(3), 1949-1955.
- Butler, D. (1991). *Mobilisation of the Nervous System*. Melbourne: Churchill Livingstone.
- Butler, D. S. (2000). *The sensitive nervous system*. Noigroup publications.
- Charlton, P. C., Mentiplay, B. F., Pua, Y. H., & Clark, R. A. (2015). Reliability and concurrent validity of a Smartphone, bubble inclinometer and motion analysis system for measurement of hip joint range of motion. *Journal of Science and Medicine in Sport*, 18(3), 262-267.
- Cohen, J. (1988). *Statistical power analysis for the behavior sciences*. (2nd ed.). Hillsdale, NJ: Erlbaum
- Cohen, S. P. (2015, February). Epidemiology, diagnosis, and treatment of neck pain. In *Mayo Clinic Proceedings* (Vol. 90, No. 2, pp. 284-299). Elsevier.
- Coppieters, M. W., Stappaerts, K. H., Wouters, L. L., & Janssens, K. (2003). Aberrant protective force generation during neural provocation testing and the effect of treatment in patients with neurogenic cervicobrachial pain. *Journal of Manipulative and Physiological Therapeutics*, 26(2), 99-106. doi:10.1067/mmt.2003.16.
- Crichton, N. (2001). Visual analogue scale (VAS). *J Clin Nurs*, 10(5), 706-6.
- Drake, R., Vogl, W. A., & Mitchell, A. (2009). *Gray's Anatomy for Students* (2nd ed., p. 918-929). Philadelphia: Elsevier/ Churchill Livingstone.
- Drechsler, W. I., Knarr, J. F., & Snyder-Mackler, L. (1997). A comparison of two treatment regimens for lateral epicondylitis: a randomized trial of clinical interventions. *Journal of Sport Rehabilitation*, 6(3), 226-234.

- Edwards, D. J. (2017). Unsupervised categorization with a child sample: category cohesion development. *European Journal of Developmental Psychology, 14*(1), 75-86.
- Edwards, D. J., Pothos, E. M., & Perlman, A. (2012). Relational Vs. absolute representation in categorization. *American Journal of Psychology, 125*, 4, 481- 497.
- Edwards, D. J., Perlman, A., & Reed, P. (2012). Unsupervised Categorization in a sample of children with autism spectrum disorders. *Research in Developmental Disabilities, 33*, 4, 1264-1269.
- Edwards, D. J., & Wood, R. (2016). Unsupervised categorization with individuals diagnosed as having moderate traumatic brain injury: over-selective responding. *Brain injury, 30*(13-14), 1576-1580.
- Edwards, D. J., McEntegart, C., Barnes-Holmes, Y., Lowe, R., Evans, N., & Vilaradaga, R. (2017). The impact of mindfulness and perspective-taking on implicit associations towards the elderly: a Relational Frame Theory account. To be published in *Mindfulness*/[Preprint] 2017 [cited 4 May 2017]. Available from: <http://link.springer.com/article/10.1007/s12671-017-0734-x>
- Ellis, R. F., & Hing, W. A. (2008). Neural Mobilization: A Systematic Review of Randomised Controlled Trials with an Analysis of Therapeutic Effects. *Journal of Manual & Manipulative Therapy, 16*(1), 8-22.
- Elvey R., L. (1979). Brachial plexus tension tests and the pathoanatomical origin of arm pain. In: Idczak R, editor. *Aspects of manipulative therapy*. Melbourne: Lincoln Institute of Health Sciences
- Fernández-de-las-Peñas, C., Hernández-Barrera, V., Alonso-Blanco, C., Palacios-Ceña, D.,

- Carrasco-Garrido, P., Jiménez-Sánchez, S., & Jiménez- Garcia, R. (2011). Prevalence of neck and low back pain I community-dwelling adults in Spain: a population-based national study. *Spine*, 36, E213-E219.
- Fleiss, J.L., 1987. In: *The Design and Analysis of Clinical Experiments. Computers & Mathematics with Applications*, vol. 14. Wiley Classics Library, New York.
- Gallace, A., & Spence, C. (2010). The science of interpersonal touch: An overview. *Neuroscience and Biobehavioural Reviews*, 34, 246-259.
- Hogg-Johnson, S., van der Velde, G., Carroll, L. J., Holm, L. W., Cassidy, J. D., Guzman, J., Côté, P., Haldeman, S., Ammendolia, C., Carragee, E., Hurwitz, E., Nordin, M., & Peloso, P. (2008). The Burden and Determinants of Neck Pain in the General Population: results of- the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated /sDisorders. *European Spine Journal*, 17(1), S39-S51.
- Jadad, A. R., & Enkin, M. W. (2007). *Bias in Randomised Controlled Trials: Questions, Answers, and Musings*. 2nd Ed, Blackwell Publishings Ltd, Oxford, UK.
- Kishner, S., Ventre, J. M., Loffe, J., & Lorenzo, C. T. (2013). *Brachial Plexus Anatomy*. Retrieved 27 December 2014, from <http://emedicine.medscape.com/article/1877731-overview>.
- Kobayashi, S., Yoshizawa, H., & Nakai, S. (2000). Experimental study on the dynamics of lumbosacral nerve root circulation. *Spine*, 25, 298-305.
- Kolber, M. J., & Hanney, W. J. (2012). The reliability and concurrent validity of shoulder mobility measurements using a digital inclinometer and goniometer: a technical report. *International journal of sports physical therapy*, 7(3), 306.

- Kolber, M. J., Pizzini, M., Robinson, A., Yanez, D., & Hanney, W. J. (2013). The reliability and concurrent validity of measurements used to quantify lumbar spine mobility: an analysis of an iPhone® application and gravity based inclinometry. *International journal of sports physical therapy*, 8(2), 129.
- McLellan D, Swash M. (1976). Longitudinal sliding of the median nerve during movements of the upper limb. *J Neurol Neurosurg Psychiatr*; 39:556–70.
- McCoss, C. A., Johnston, R., Edwards, D. J. & Millward, C. (in press). Preliminary evidence of Regional Interdependent Inhibition, using a ‘Diaphragm Release’ to specifically induce an immediate hypoalgesic effect in the cervical spine. To be published in *Journal of Bodywork & Movement Therapies*/[Preprint] 2016 [cited 8 January 2017]. Available from: <http://dx.doi.org/10.1016/j.jbmt.2016.08.015>
- Melzack, R. (1999). From the gate to the neuromatrix. *Pain*, 81(1), S121-S126.
- Mendell, L. M. (2014). Constructing and deconstructing the gate theory of pain. *Pain*, 155, 210-216.
- Merskey H., & Bogduk, N. (1994). *Classification of Chronic Pain: Descriptions of chronic pain syndromes and definitions of pain terms* (2nd ed), Seattle: IASP Press.
- Morhenn, V., Beavin, L. E., & Zak, P. J. (2012). Massage Increases Oxytocin and Reduces Adrenocorticotropin Hormone in Humans. *Alternative Therapies in Health and Medicine*, 18(6), 11-18.
- Nee, R., & Butler, D. (2006). Management of peripheral neuropathic pain: Integrating neurobiology, neurodynamics and clinical evidence. *Physical Therapy in Sport*, 7(1), 36-49.

- Okabe, S., & Hirokawa, N. (1989). Incorporation and turnover of biotin-labeled actin microinjected into fibroblastic cells: an immunoelectron microscopic study. *The Journal of cell biology*, 109(4), 1581-1595.
- Parke, W. W., & Whalen, J.L. (2002). The vascular pattern of the human dorsal root ganglion and its probable bearing on a compartment syndrome. *Spine*, 27, 347-352.
- Petersen, S., Schroyen, M., Mölders, C., Zenker, S., & Van den Bergh, O. (2014). Categorical interoception perceptual organization of sensations from inside. *Psychological science*, 25(5), 1059-1066.
- Schmid, A. B., Brunner, F., Wright, A., & Bachmann, L. M. (2008). Paradigm shift in manual therapy? Evidence for a central nervous system component in the response to passive cervical joint mobilisation. *Manual Therapy*, 13(5), 387-396.
- Schulz, K. F. (1995). Subverting randomisation in controlled trials. *JAMA*, 274, 1456-1458.
- Scrimshaw, S. V., & Maher, C. G. (2001). Randomized controlled trial of neural mobilization after spinal surgery. *Spine*, 26(24), 2647-2652.
- Shacklock, M. (1995). Neurodynamics. *Physiotherapy*, 81(1), 1-8.
- Shacklock, M. (2005). *Clinical Neurodynamics*. Edinburgh: Elsevier Butterworth-Heinemann.
- Slater, H., Vincenzino, B., & Wright, A. (1994). "Sympathetic slump". The effects of a novel manual therapy technique on peripheral sympathetic function. *Journal of Manual & Manipulative Therapy*, 2(4), 156-162.
- Sperling, R. S., Scoville, W. B. (1944). Lateral rupture of the cervical intervertebral discs: a

- common cause of shoulder and arm pain. *Surg Gynecol Obstet*. 78:350-358.
- Sterling, M, Jull, G., & Wright, A. (2001). Cervical mobilisation: concurrent effects on pain, sympathetic nervous system activity and motor activity. *Manual Therapy*, 6(2), 72-81.
- Shrout, P.E., Fleiss, J.L., 1979. Intraclass correlations: uses in assessing rater reliability. *Psychol. Bull.* 86, 420e428.
- Sullivan, M. J. L., Bishop, S. R., & Pivik, J. (1995). The pain catastrophizing scale: development and validation. *Psychological Assessment*, 7, 524-532.
- Sunderland, S. (1978). Nerve and Nerve Injuries, edn. *Churchill Livingstone, Edinburgh*
- Suresh, K. (2011). An overview of randomization techniques: an unbiased assessment of outcome in clinical research. *Journal of human reproductive sciences*, 4(1), 8.
- Vicenzino, B., Collins, D., & Wright, A. (1994). Sudomotor changes induced by neural mobilisation techniques in asymptomatic subjects. *The Journal of Manual and Manipulative Therapy*, 2(2), 66-74.
- Vicenzino, B., Gutschlag, F., Collins, D., & Wright, A. (1995). An investigation of the pain thresholds and sympathetic nervous system activity in asymptomatic subjects: a preliminary report. In M. Shacklock, *Moving in on pain* (1st ed., pp.185-193). Australia: Butterworth-Heinemann.
- Ward, R. (2003). *Foundations for Osteopathic Medicine* (2nd ed). Philadelphia: Lippincott Williams & Wilkins.
- Woolf, C. J., & Ma, Q. (2007). Nociceptors – noxious stimulus detectors. *Neuron*, 55(3), 353-364.

Figure 1. Consort Flow Diagram with three conditions and with immediate effects recorded.

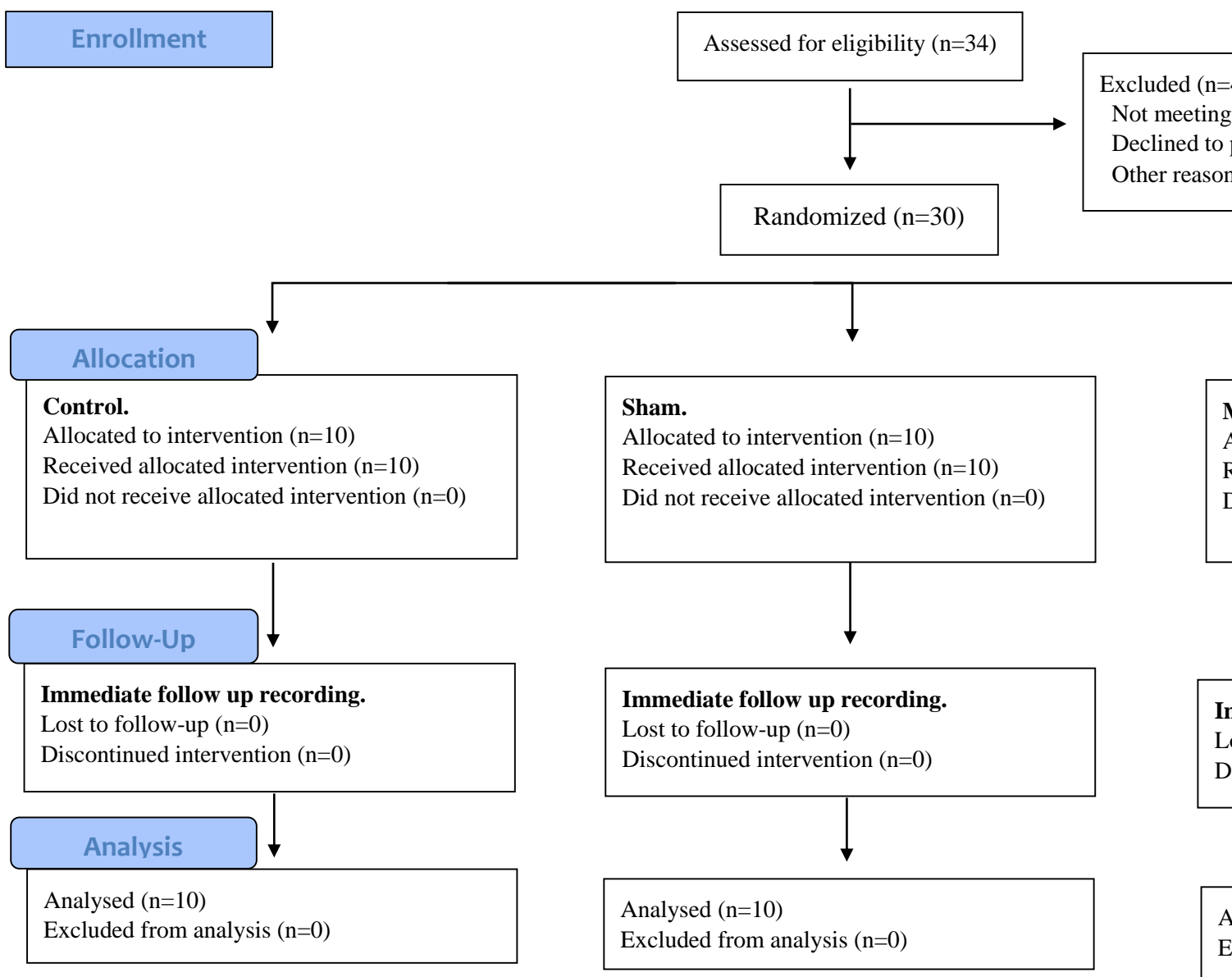


Figure 2. The mobilization procedure (left), and sham procedure (right)



Figure 3. Taking the ROM measure during the ULNT, with the starting point measure (left), and fully extended measure (right)



Table 1. Demographic data.

Measurement Means (SD)	Total subjects	Control group	Sham group	Mobilization group	Homogeneity (Levene's test) between groups
Age (SD)	20.53 (4.02)	20.50 (4.12)	20.00 (2.54)	21.10 (5.28)	$p = 0.266$
Weight (SD)	67.50 (12.22)	62.30 (5.29)	65.70 (11.07)	74.50 (15.57)	$p = 0.010$
Height (SD)	169.50 (7.56)	169.40 (7.734)	170.00 (7.49)	169.10 (8.23)	$p = 0.924$
BMI (SD)	23.49 (3.80)	36.86 (3.77)	38.51 (5.10)	43.97 (8.34)	$p = 0.028$

SD=Standard Deviation; Age=years; Weight=kilograms; Height=Centimetres; BMI= Body Mass Index.
Male (N=11), Female (N=19). Total N = 30

Table 2. Intra-rater reliability.

	Interclass Correlation	95% Confidence interval		Level of reliability	<i>p</i>
		Lower bound	Upper bound		
Pre-Left-Right All conditions	0.698	0.374	0.855	Good	<0.001
Post-Left-Right All conditions	0.736	0.440	0.875	Good	<0.001

Note: Shrout and Fleiss (1979) classification reliability >0.75, excellent; 0.6-0.75, good; 0.4-0.59, fair; and <0.4, poor.

Table 3. Mean, standard deviation (SD) and standard error (SE) of the Range of Motion scores and participa

Study condition	N	Mean	SD	SE	Range	
Pre-Left Control	10	48.67	30.43	9.62	0-84	
Post-Left Control	10	53.20	29.84	9.43	0-88	
Pre-Left Sham	10	61.40	17.87	5.65	27-84	} **
Post-Left Sham	10	53.20	29.84	9.44	40-90	
Pre-Left Mobilization	10	42.40	27.16	8.59	0-83	} **
Post-Left Mobilization	10	69.10	23.41	7.40	20-105	
Pre-Right Control	10	51.00	27.77	8.79	5-90	} *
Post-Right Control	10	57.30	25.72	8.13	16-90	
Pre-Right Sham	10	61.30	20.93	6.62	24-85	
Post-Right Sham	10	68.50	16.37	5.18	40-89	
Pre-Right Mobilization	10	56.60	26.39	8.34	0-90	} *
Post-Right Mobilization	10	70.20	26.18	8.28	5-90	
Change-Left Control	10	13.20	13.42	4.25	0-39	} **] *
Change-Left Sham	10	11.10	7.13	2.25	2-24	
Change-Left Mobilization	10	26.50	19.40	6.14	3-55	
Change-Right Control	10	11.00	7.23	2.29	0-22	} *] *
Change-Right Sham	10	9.40	11.36	3.59	1-37	
Change-Right Mobilization	10	19.70	15.06	4.76	5-45	

Note: * = $p < 0.05$, ** = $p < 0.01$, between conditions post-hoc pairwise comparisons and t -tests

Table 4. Analysis summary: One-way ANOVA comparisons with post hoc pairwise comparisons for the RO

Study condition	F value	df	p value	Partial Eta Squared
Change Left (CL)	3.44	(2)	<0.05*	0.203
Change Right (CR)	307.233	(2)	<0.05*	0.143
Pairwise comparisons	Mean difference	SE	p value	95% CI for difference
				Low bound
CL Mobilization vs. Control	13.300	6.364	< 0.05*	0.23
CL Mobilization vs. Sham	15.400	6.364	< 0.01**	2.34
CL Control vs. Sham	2.100	6.364	= 0.372	-10.9
CR Mobilization vs. Control	8.700	5.214	<0.05*	-1.99
CR Mobilization vs. Sham	10.300	5.214	<0.05*	-.039
CR Control vs. Sham	1.600	5.214	=0.381	-9.09

Note: * = between conditions comparisons, $p < 0.05$, ** = between condition comparisons, $p < 0.01$