



Public University of Navarra,
Department of Health Sciences

**EFFECTS OF MANUAL THERAPY PROTOCOL IN
CHRONIC NECK PAIN, WITH A SPECIAL REFERENCE
TO A HIGH VELOCITY LOW AMPLITUDE
MANIPULATION TECHNIQUES**

Doctoral Thesis

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Supervisor

Mikel Izquierdo

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Ph.D. Thesis

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DECLARATION

I, Xabier Galindez Ibarbengoetxea, do hereby declare that the research presented in this dissertation is based on 4 articles that have been published, accepted or submitted for publication in international peer-reviewed journals. To meet the stylistic requirements of a thesis, the formats of the papers have been adjusted accordingly throughout. These edits did not substantially change the content of the published articles. The role which I fulfilled within each of the publications is presented below.

Study I

Effects of cervical high-velocity, low-amplitude techniques on range of motion, strength and cardiovascular performance: a review.

Xabier Galindez-Ibarbengoetxea, Igor Setuain, Miriam González-Izal, Andoni Jauregi, Robinson Ramírez-Velez, Lars L. Andersen and Mikel Izquierdo. Journal of Manipulative and Physiological Therapeutics. Submitted.

I conceived the research idea and designed the review under the supervision of Mikel Izquierdo. Mikel Izquierdo and I collected the articles; Miriam González-Izal, Igor Setuain, Andoni Jauregi, Robinson Ramírez-Velez and Lars L. Andersen critically reviewed and provided advices.

Study II

Randomised controlled pilot trial of high-velocity, low-amplitude manipulation on cervical and upper thoracic spine levels in asymptomatic subjects.

Xabier Galindez-Ibarbengoetxea, Igor Setuain, Miriam González-Izal, Andoni Jauregi, Robinson Ramírez-Velez, Lars L. Andersen and Mikel Izquierdo. International Journal of Osteopathic Medicine 2016. Published.

I conceived the research idea and designed the experiment under the supervision of Mikel Izquierdo. I collected all the subjects and data, also I assembled and analyzed all the data, and prepared the figures and tables. Miriam González-Izal analyzed and filtered EMG signals. Igor Setuain, Andoni Jauregi, Robinson Ramírez-Velez and Lars L. Andersen critically reviewed and provided advices.

Study III

Immediate effects of osteopathic treatment versus therapeutic exercise on patients with chronic cervical pain.

Xabier Galindez-Ibarbengoetxea, Igor Setuain, Miriam González-Izal, Andoni Jauregi, Robinson Ramírez-Velez, Lars L. Andersen and Mikel Izquierdo. Alternative Therapies in Health and Medicine. Submitted.

I conceived the research idea and designed the experiment under the supervision of Mikel Izquierdo. Igor Setuain and I collected all the subjects and data; I assembled and analyzed all the data, and prepared the figures and tables. Miriam González-Izal analyzed and filtered EMG signals. Igor Setuain, Andoni Jauregi, Robinson Ramírez-Velez and Lars L. Andersen critically reviewed and provided advices.

Study IV

Short-term effects of manipulative treatment versus a therapeutic home exercise protocol for chronic cervical pain: A randomized clinical trial.

Xabier Galindez-Ibarbengoetxea, Igor Setuain, Miriam González-Izal, Andoni Jauregi, Robinson Ramírez-Velez, Lars L. Andersen and Mikel Izquierdo. Journal of Back and Musculoskeletal Rehabilitation. Submitted.

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“La ignorancia afirma o niega rotundamente; la ciencia duda.” Voltaire.

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List of publications

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Galindez-Ibarbengoetxea X, Setuain I, González-Izal M, Jauregi A, Ramírez-Velez R, Andersen L, Izquierdo M. Randomised controlled pilot trial of high-velocity, low-amplitude manipulation on cervical and upper thoracic spine levels in asymptomatic subjects. International Journal of Osteopathic Medicine 2016. Article in press.

Galindez-Ibarbengoetxea X, Setuain I, González-Izal M, Jauregi A, Ramírez-Velez R, Andersen L, Izquierdo M. Immediate effects of osteopathic treatment versus

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Practical workshop by **Galindez-Ibarbengoetxea X**

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16 May 2013, Bilbao, Spain

LIST OF ABBREVIATIONS

Abbreviation	Meaning
AMC5 group	Indiscriminate manipulation on the C5 group
BP	Blood pressure
Bpm	Beats per minute
C0	Occiput
C1	First cervical vertebrae
C3	Third cervical vertebrae
C4	Fourth cervical vertebrae
C5	Fifth cervical vertebrae
C6	Sixth cervical vertebrae
C7	Seventh cervical vertebrae
CBRG	Cochrane back review group
CCF group	Cranio-cervical flexion group
CCFT	Cranio-cervical flexion test
CI	Confidence Interval
cm	Centimeters
CPT	Cold pain thresholds
CROM	Cervical range of motion
CSM	Cervical spine manipulation
e.g.	Exempli gratia
ECG	Electrocardiogram
EMG	Electromyography
HE group	Home exercise group

HE group	Home exercise group
HPT	Hot pain thresholds
HVLA	High-velocity low-amplitude
i.e.	Id est
ICC	Intraclass correlation coefficient
Kg	Kilogram
Kg/cm ²	Kilograms /centimeters ²
LE	Lateral epicondyle
Max	Maximum
MGF	Maximum handgrip strength
MI	Mikel Izquierdo
mm	Millimeters
mmHg	Millimeters of mercury
ms	milliseconds
MsC	Master of science
MT group	Manipulation treatment based on previous evaluation group
NDI	Neck disability index
NRS	Numerical rating scale
PFG	Pain handgrip strength
PhD	Doctor of Philosophy
PPT	Pressure pain threshold
PRISMA	Preferred reporting items for systematic reviews and Meta-Analyses
RCT	Randomized controlled trial
RMS	Root Mean Square
ROM	Range of motion

RR-V	Robinson Ramirez-Velez
SCM	Sternocleidmastoid
SD	Standard deviation
SE	Standard error
ST group	Sham intervention group
T1	First thoracic vertebrae
T3	Third thoracic vertebrae
T4	Fourth thoracic vertebrae
TMJ	Temporo-mandibular joint
TMS	Transcranial magnetic stimulation
USB	Universal Serial Bus
VAS	Visual analogue scale
VAS-ROM	Visual analogue scale during Range of motion
XG	Xabier Galindez

SUMMARY (English)

RESUMEN (Castellano)

SUMMARY

Neck pain is defined as pain experienced from the base of the skull (the occipital) to the upper part of the back and extending laterally to the outer and superior bounds of the shoulder blade (scapula) (1). This pathology is one of the most prevalent complaints in the general population and is a major cause of disability (2). In the general population, the prevalence has been reported to be greater than 70% (3) and it's higher among young female adults (4).

In the general working population, higher levels of neck-shoulder pain intensity have been found to gradually increase the odds of using pain medication for the treatment of musculoskeletal disorders (5). While these medications may offer immediate pain relief, long-term use of pain medication has been reported to often be associated with adverse effects (6). Thus, alternatives to medication for immediate and short term pain relief should be investigated, e.g. HVLA manipulation techniques.

The current Ph.D. dissertation revolves around the effects of a multi-segmental manual therapy protocol in chronic cervical pain, with special reference to the high-velocity, low-amplitude techniques. This doctoral thesis is based on 4 scientific studies that have been published, accepted or submitted for publication in scientific international journals.

The first study is a review of the effects of cervical high-velocity, low-amplitude techniques on range of motion, strength and cardiovascular performance. The aims were to describe the effects of cervical high-velocity, low-amplitude manipulation techniques

on range of motion, strength and cardiovascular performance. A computerized search was made using five databases PUBMED, Science Direct, Scopus, PeDro and Scielo, from January 2000 to August 2016. The review shows that CSM treatment results in a large effect size ($d > 0.80$) on increasing cervical ROM (range of motion) and mouth opening. In patients with lateral epicondylalgia, CSM resulted in increased pain free hand grip strength, with large effect sizes (1.44 and 0.78 respectively). Finally, in subjects with hypertension the blood pressure seems to decrease after CSM.

The second study is a control trial pilot study with the aim to evaluate the validity of a multi-segmental manipulation treatment. The effects of an indiscriminate manipulation on the C5 (AMC5) a manipulation treatment based on a previous evaluation (MT) and a sham intervention (ST) were analyzed on cervical spine range of motion (ROM); cervical flexion isometric peak force; EMG activation of sternocleidomastoid muscle (SCM) during the cranio-cervical flexion test (CCFT). The outcomes were measured pre and immediately post intervention. Significant changes ($p < 0.1$) were found in the cervical flexion isometric peak force (-13.15%), however, the effect size was considered moderate ($d = 0.52$). The extension (10.44%) and left rotation ROM (12.25%) showed significant improvement in MT group. During CCFT significant changes were not reported. In conclusion the pilot study suggested that a tendency toward a decrease in the isometric strength peak in the cervical flexion of the MT group may appear. In cervical ROM the MT group achieved significant effects in extension and left rotation movement.

The immediate effects of high-velocity, low-amplitude manipulation treatment with a craniocervical flexion exercise protocol on pain intensity assessed using the

visual analogue scale during ROM measurement (VAS-ROM), cervical spine range of motion (ROM), pressure-pain thresholds (PPT) and EMG activation of sternocleidomastoid muscle (SCM) during a craniocervical flexion test (CCFT) were analyzed in the third study. A total of 25 volunteers with chronic neck pain were randomly enrolled into 2 groups: the manipulation treatment group (MT) and the cranio-cervical flexion exercise protocol group (CCF). Following both interventions, significant differences were found in the VAS score during ROM measurement. In the MT group, flexion, right side-bending and left rotation differed significantly pre- and post-intervention; however, only the differences between pre- and post-intervention flexion and extension ROM were significant in the CCF group. Significant changes were observed in upper trapezius PPT following both interventions; in addition, significant post-intervention differences in C5 PPT were found in the CCF group. Between-group differences were significant for extension and right side-bending ROM, which were both greater in the MT group. In conclusion we could say that while both interventions improved ROM and pain immediately following treatment, MT was more effective than exercise in improving ROM, but none of the interventions led to changes in EMG.

Finally, the fourth study compare the short-term effects of high-velocity, low-amplitude manipulation techniques (MT) with those of home-exercise (HE) with stretching and low-intensity (10% of max) isometric contractions on visual analogue scale (VAS); neck disability index (NDI); pressure pain thresholds; cervical spine range of motion and electromyography during the cranio-cervical flexion test. After the intervention, both groups showed improved ($p < 0.05$) NDI and VAS scores and flexion in both rotation ranges compared with the pre-intervention values. For the NDI, pain

intensity, and neck flexion, the effects sizes were large; for the majority of the other measurements, the effect sizes were small to moderate. The MT group showed significantly better results than the HE group for 2 out of 17 tests. In summary both interventions improved function and pain after one week, with only marginal between-group differences in favour of MT.

RESUMEN

El dolor de cuello se define como el dolor experimentado desde la base del cráneo (occipital), hasta la parte superior de la espalda y se extiende lateralmente a los límites externo y superior del omóplato (escápula) (1). Esta patología es una de las afecciones más frecuentes en la población general y es una de las principales causas de discapacidad (2). En la población general, la prevalencia es mayor al 70% (3) e incluso es más alta entre las mujeres adultas jóvenes (4).

En la población activa, se ha observado una asociación entre los niveles más altos de intensidad de dolor en hombro y/o cuello y las probabilidades de usar analgésicos para el tratamiento de trastornos músculo-esqueléticos (5). Aunque estos medicamentos pueden ofrecer alivio inmediato del dolor, el uso a largo plazo de analgésicos suele estar asociado con efectos secundarios (6). Por lo tanto, se deben investigar alternativas a la medicación para el alivio del dolor inmediato y a corto plazo como las técnicas de manipulación HVLA.

La siguiente tesis doctoral gira en torno a los efectos de un protocolo de terapia manual multi-segmental en el dolor cervical crónico, con especial referencia a las técnicas de alta velocidad y baja amplitud. Esta tesis se basa en 4 estudios científicos que han sido publicados, aceptados o presentados para su publicación en revistas científicas internacionales.

El primer estudio es una revisión cuyo objetivo fue analizar los efectos de las técnicas cervicales de alta velocidad y baja amplitud en el rango de movimiento, la

fuerza y el sistema cardiovascular. Para ello se realizó una búsqueda informática utilizando cinco bases de datos PUBMED, Science Direct, Scopus, PeDro y Scielo, de Enero de 2000 a Agosto de 2016. La revisión mostró que el tratamiento con CSM logra un efecto importante ($d > 0,80$) en el rango de movimiento y la apertura de la boca. En los pacientes con epicondialgia lateral, la CSM dio lugar a un aumento de la fuerza de prensión libre de dolor, al igual que en el caso anterior los efectos fueron considerados largos (1,44 y 0,78, respectivamente). Por último, en los sujetos con hipertensión arterial la presión arterial parece disminuir después de la CSM.

El segundo estudio, es un ensayo piloto que se realizó con el objetivo de evaluar la validez de un tratamiento de manipulación multi-segmental. Se analizaron los efectos de una manipulación indiscriminada en C5 (AMC5), un tratamiento de manipulación multi-segmento basado en una evaluación previa (MT) y una manipulación placebo (ST) en el rango de movimiento de la columna cervical; la fuerza isométrica máxima de flexión cervical; la activación EMG del músculo esternocleidomastoideo (SCM) durante la prueba de flexión cráneo-cervical (CCFT). Los resultados se midieron antes e inmediatamente después de la intervención. Se encontraron cambios significativos ($p < 0,1$) en la fuerza isométrica máxima de flexión cervical (-13,15%), sin embargo, el tamaño del efecto fue moderado ($d = 0,52$). La movilidad en extensión (10,44%) y rotación izquierda (12,25%) mostraron una mejoría significativa en el grupo MT. Durante CCFT no se encontraron cambios significativos. En conclusión, el estudio piloto sugirió que puede aparecer una tendencia hacia una disminución en el pico de fuerza isométrica en la flexión cervical del grupo MT. Además el rango de movilidad cervical del grupo MT logró mejoras significativas en extensión y rotación izquierda.

En el tercer estudio de esta tesis, se han comparado los efectos inmediatos del tratamiento de manipulación de alta velocidad y baja amplitud, versus un protocolo de ejercicios de flexión cráneo-cervical. Se analizó la intensidad del dolor utilizando la escala visual analógica durante el movimiento (VAS-ROM), el rango de movimiento de la columna cervical, la algometría de presión sobre varios puntos (PPT) y la activación EMG del músculo esternocleidomastoideo (SCM) durante el test de flexión cráneo-cervical (CCFT). Se dividieron de forma aleatoria 25 voluntarios con dolor cervical crónico en 2 grupos: el grupo de tratamiento de manipulación (MT) y el grupo de ejercicio de flexión cráneo-cervical (CCF). Después de ambas intervenciones, se encontraron diferencias significativas en la puntuación de VAS-ROM. En el grupo MT, la flexión, la inclinación derecha y la rotación izquierda mejoraron significativamente después de la intervención; sin embargo, sólo las diferencias pre/post-intervención en la flexión y la extensión fueron significativas en el grupo CCF. También se observaron cambios significativos en el PPT del trapecio superior después de ambas intervenciones; además, se encontraron diferencias significativas después de la intervención del PPT en C5 en el grupo CCF. Entre grupos, las diferencias fueron significativas en el rango de extensión y de inclinación derecha. Estas diferencias fueron mayores en el grupo MT. En conclusión, podríamos decir que mientras ambas intervenciones mejoraron el rango de movimiento (ROM) cervical y el dolor inmediatamente después del tratamiento, el grupo MT fue más eficaz que el ejercicio en la mejora del ROM, pero ninguna de las intervenciones generó cambios significativos en la EMG durante el CCFT.

Por último, el cuarto estudio compara los efectos a corto plazo de las técnicas de manipulación de alta velocidad y baja amplitud (MT), con las de ejercicio en domicilio (HE). El protocolo de ejercicios incluyó estiramientos, movilizaciones, contracciones

isométricas de baja intensidad (10%) y ejercicio de estabilización. Se midieron la Escala Analógica Visual (VAS); el índice de discapacidad del cuello (NDI); el umbral de dolor de a la presión con algómetro; el rango de movimiento de la columna cervical y la electromiografía durante la prueba de flexión cráneo-cervical (CCFT). Después de la intervención, ambos grupos mostraron mejoras ($p < 0,05$) en la NDI y VAS, además el rango de flexión y ambas rotaciones también tuvieron mejoras significativas en comparación con los valores pre-intervención. Para el NDI, VAS y el rango de flexión del cuello, los tamaños de los efectos fueron grandes; Para la mayoría de las otras mediciones, los tamaños del efecto fueron de pequeños a moderados. El grupo MT mostró resultados significativamente mejores que el grupo HE para 2 de las 17 pruebas realizadas. En resumen, ambas intervenciones mejoraron la función y el dolor después de una semana, con sólo diferencias marginales entre grupos a favor del grupo MT.

1. Introduction

1. Introducción

1. INTRODUCTION

1.1 Effects of cervical high-velocity, low-amplitude techniques on range of motion, strength and cardiovascular performance: a review.

Spinal manipulative therapy is frequently used by osteopaths, physiotherapists, chiropractors and doctors. One of the most commonly used techniques involves high - velocity, low-amplitude (HVLA) manipulations. Tushin et al previously defined HVLA techniques as follows: “A HVLA technique uses a low-amplitude, high-velocity thrust in which vertebrae are carried beyond the normal physiological range of movement without exceeding the boundaries of anatomic integrity” (7). These techniques are applied with the intention to correct somatic dysfunctions that are associated with loss of movement, both qualitatively and quantitatively (8, 9).

Previous reviews of research from January 2000 to August 2016 have focused on the effects of CSM in relation to neck pain (10-12) and adverse effects after CSM treatments of the cervical spine (13, 14). Thus, a gap in the literature exists concerning reviews of CSM effects in relation to various other conditions.

Previous studies have investigated the effects of CSM at both local and remote sites. Local effects included a decrease of pain (15), an increase in mobility (16) or an improvement in posture (17). However, several articles described remote effects involving hand grip strength (18) or temporo-mandibular joint mobility (19). In addition to musculoskeletal effects, effects on the cardio-vascular (20), central nervous (21) and respiratory (22) systems have been described. Thus, rather than focusing on a single

condition, this review takes a broad approach and provides an overall review on the effects of CSM for various conditions. Indeed, several studies also show inconsistent results particularly with respect to adults, where data are scarce.

The aim of this review was to analyze the overall effects of CSM and compare them with control or placebo in randomized controlled study designs on spine and temporomandibular joint mobility, strength and cardiovascular system (15). Trials that used a combined treatment or that compared CSM with other techniques (23) were excluded to investigate the isolated effect of CSM (24).

1.2 Randomized controlled pilot trial of high-velocity, low-amplitude manipulation on cervical and upper thoracic spine levels in asymptomatic subjects.

Cervical spine pain is one of the most prevalent complaints and the largest causes of disability in industrialized countries (2). Spinal manipulative therapy is frequently used by osteopaths, physiotherapists, chiropractors and doctors. One of the used techniques involves high-velocity, low-amplitude (HVLA) manipulations. The HVLA manipulation technique is a traditional approach that has gained popularity during the past 50 years. These techniques are applied to correct somatic dysfunctions (8).

Multiple benefits have been attributed to HVLA manipulations such as, increase in sympathetic efferent activity at the level of the dermatome of the manipulated segment (25), short-term increase in biceps brachial bilaterally EMG at rest (26), increase in the oxytocin, neurotensin and cortisol blood levels (27), significant increases in the left (10.53%) and right (16.82%) handgrip strength (18) and significant changes on standing balance and postural sway (17, 28). On the contrary, controversial results after manipulation have been also reported such as, no significant EMG activity baseline changes in subjects with neck pain, (29), or the marginal improvement for maximum isometric handgrip strength (30) reported in asymptomatic athletes after a single C5/C6 HVLA manipulation.

In addition, contradictory results have been also reported in studying the relationship between mouth opening and cervical HVLA manipulation. After cervical HVLA, George and cols (31), observed no significant changes on normal mouth

opening in asymptomatic subjects between the control and CSM groups (31), whereas In the same line, Oliveira and cols (32), showed an immediate increase in mouth opening after cervical HVLA manipulation at the C1/C0 joint (1.5 mm) (32).

In regard to the relationship between cervical range of motion (ROM) a study reported immediate effects on cervical ROM after a single HVLA manipulation (16), whereas Passmore and cols (33) reported moderate effect on mobility improvement in asymptomatic subjects. In the same line recent reviews have also highlighted a small improvement in cervical spine range of motion (ROM) after the application of articular HVLA manipulation (34).

One of the main limitations of the different studies is the absence of previous evaluations to determine which parameters of ROM restriction were present before manipulation; therefore, these studies fail to adequately determine the proper technique to correct the dysfunction (8). In previous studies, the C5 was manipulated in an arbitrary way without taking into account whether it was actually affected in terms of joint motion reduction or alteration (26, 29). The C5 vertebral segment is not the only vertebral segment involved in possible cervical spine pathologies. Kayser and cols. (35) showed the importance of segments C1 to C3 in cervical pathology, while Cleland and cols. (36) showed that the upper dorsal spine is another spine level from which unspecific cervical pain can originate. Therefore, it has been hypothesized that a previous evaluation correctly attached to a protocol will improve the effects of the manipulations on the cervical spine to a greater extent than will an indiscriminate manipulation of a segment without a previous dysfunction assessment. For these reasons, it is necessary to clarify which type of spinal manipulative therapy, is more

effective to improve strength, ROM and EMG activation of muscle in asymptomatic subjects.

The aim of this pilot study was to compare the immediate effects of an indiscriminate manipulation on the C5 (AMC5) and a manipulation treatment based on a previous evaluation (MT) on cervical spine ROM; cervical flexion isometric peak force; surface cervical flexors EMG activation during cranio-cervical flexion tests; and an EMG signal on the right and left biceps. Also the effects of these two groups were researched using a sham group (ST).

1.3 Immediate effects of osteopathic treatment versus therapeutic exercise on patients with chronic cervical pain.

In the general working population, higher levels of neck-shoulder pain intensity have been found to gradually increase the odds of using pain medication for the treatment of musculoskeletal disorders (5). While these medications may offer immediate pain relief, long-term use of pain medication has been reported to often be associated with adverse effects (6). Thus, alternatives to medication for immediate pain relief should be investigated, e.g., manipulation or physical exercise.

Neck pain is defined as pain experienced from the base of the skull (occiput) to the upper part of the back and extending laterally to the outer and superior bounds of the shoulder blade (scapula) (1). Neck pain is one of the most prevalent complaints and a major cause of disability worldwide (2). In the United States of America, neck pain has been identified as the third most common chronic pain condition (37), and the prevalence of neck pain has been reported to be higher among young female adults (4). In the general population, the prevalence of neck pain has been reported to be greater than 70% (3, 38). In young adults, the prevalence of neck pain has been reported to be between 12 and 34%. Because data suggest that patients with neck pain use the healthcare system twice as often as the rest of the population, the public health and financial implications of neck pain are important considerations (1).

Chronic neck pain may result in physical dysfunctions, such as decreases in cervical mobility (39), alterations in motor control in association with impaired activation of deep cervical flexor muscles (40, 41) and widespread pain sensitivity (42).

A wide variety of treatment protocols for neck pain are available. However, the most effective type of management remains an area of debate. In this line, manipulation techniques and craniocervical flexion exercises have frequently been used by osteopaths, doctors, physiotherapists and chiropractors in the management of chronic neck pain (43, 44)(45). Several studies have investigated the immediate effects of isolated thoracic spine manipulation (42, 45), isolated cervical manipulation (46), and a combination of these treatments (47) on chronic neck pain subjects.

In our MT protocol, we included manipulation of the temporomandibular joint due to its relationship with the cervical spine (48-50). An exercise protocol used while comparing the effects of active and passive treatment was found to have analgesic effects in chronic neck pain patients (51). In an evaluation of an exercise protocol based on isometric craniocervical flexor muscle contractions, this protocol was found to be associated with immediate analgesic effects, especially in women (52).

In other studies, the effects of exercise and manipulation on chronic neck pain have been compared (24, 53); however, despite finding that both interventions showed significant improved effects, the authors of these studies never used a complete manipulation protocol, as was used in the present study.

There is a lack of sufficient evidence available to allow for conclusions to be derived regarding the effectiveness of MT relative to CCF exercise in relieving chronic cervical pain. Therefore, this study will add to the growing body of knowledge that if these two techniques yield comparable outcomes and if one technique is superior to the

other, which should be the alternative choice of therapy. Therefore, the study was conducted to compare the immediate effects of MT and CCF on VAS-ROM, cervical spine ROM, pressure pain thresholds (PPT), and EMG activation of the SCM during a craniocervical flexion test in young adult women with chronic neck pain.

1.4 Short-term effects of manipulative treatment versus a therapeutic home exercise protocol for chronic cervical pain: A randomized clinical trial.

Neck pain is defined as pain experienced from the base of the skull (the occiput) to the upper part of the back and extending laterally to the outer and superior bounds of the shoulder blade (scapula) (1). Neck pain is one of the most prevalent complaints in the general population and is a major cause of disability (2). In the United States of America, neck pain is the third most common chronic pain condition (37), and its prevalence is higher among young female adults (4). In the general population, the prevalence has been reported to be greater than 70% (3), while in young adults, the prevalence of neck pain is reported to be between 12 and 34% (38). It is important to consider the public health and financial implications of neck pain as neck pain patients use the health care system twice as often as the rest of the population (1).

A wide variety of treatment protocols for neck pain are available. However, the most effective management remains an area of debate. Manipulation techniques (MT) and home exercises are commonly used to manage neck pain, and spinal manipulative therapy plus home exercise and advice have yielded better clinical outcomes and lower total societal costs compared with other treatments (54). At least one study has found that a multi-segmental approach to spinal manipulation improved neck pain more than articular manipulation alone (47). In that study, manipulations were performed on the upper thoracic spine, the cervical spine and the temporomandibular joint (TMJ). The biomechanical relationship between the TMJ and the cervical complex and the most recent research findings recommend the inclusion of that segment in the management of neck pain (48, 49, 55, 56).

There are different exercise protocols that can be performed to reduce one of stretching alone (57). A high-quality randomized clinical trial found that an intervention consisting of several elements, including strength training and stretching, produced results that were superior to those of an intervention that focused mostly on stretching (58). In another study, Ylinen and cols found that stretching and aerobic exercise alone were less effective than strength training for relieving chronic neck pain in women (59). The performance of specific cervical flexor exercises led to a decrease in the activation of superficial flexors and a decrease in pain and disability in patients with neck pain (60). A studied home exercise (HE) protocol included stretching, isometric exercises, general mobilizations and cranio-cervical flexion endurance exercises (61)(51, 60, 62, 63).

In our study, young adult women with chronic neck pain who volunteered to participate were included, both because they comprise the most common population with neck pain (4) and because compared with elderly people, young people have shown lower levels of sternocleidomastoid (SCM) activity in the cranio-cervical flexion test (CCFT) (64). This test relates the activation of superficial neck flexors during the CCFT with neck pain (65). In the present study, we did not include nonspecific aerobic exercise because although some authors have found an association between such exercise and a moderate decrease in pain (66), this improvement was not as important because it could be achieved through analytical strength exercise of the muscles involved in neck pain (67).

There is lack of evidence to support any conclusions regarding the effectiveness of MT versus HE for relieving mechanical neck pain. Therefore, this study will add to the growing body of knowledge regarding whether these two techniques yield comparable outcomes or one technique is superior to the other and which should be the therapy of choice. This study was performed to compare the short-term effects of an MT protocol and an HE protocol on the neck disability index (NDI), the visual analogue scale (VAS), pressure pain thresholds (PPT), cervical spine ROM and EMG activation of the sternocleidomastoid muscle (SCM) during the cranio-cervical flexion test (CCFT) in young adult women with chronic neck pain.

2. HYPOTHESIS

2. HIPÓTESIS

2. HYPOTHESIS

H-I: The study hypothesis posited that the high-velocity, low amplitude manipulation techniques improved the range of motion, strength and cardiovascular performance. Also the study hypothesized that the symptomatic patients achieved better effects than healthy subjects (Study I).

H-II: The present pilot trial hypothesis posited that the manipulation treatment based on a previous evaluation improved more than an indiscriminate manipulation on the C5 and a sham intervention on cervical spine range of motion; cervical flexion isometric peak force; EMG activation of sternocleidomastoid muscle during the cranio-cervical flexion test; and EMG signals of right and left biceps at rest were analyzed (Study II).

H-III: The present study protocol hypothesized that the manipulation treatment improved more than the craniocervical flexion exercise protocol on the studied variables: visual analogue scale during ROM measurement (VAS-ROM), cervical spine range of motion (ROM), pressure-pain thresholds (PPT) and EMG activation of sternocleidomastoid muscle (SCM) during a craniocervical flexion test (CCFT). Furthermore the study posited that both protocols obtained good effects immediately after interventions (Study III).

H-IV: The present trial hypothesis posited that the manipulation treatment protocol obtained better effects than the home exercise protocol on the neck disability index (NDI), the visual analogue scale (VAS), pressure pain thresholds (PPT), cervical

spine ROM and EMG activation of the sternocleidomastoid muscle (SCM) during the cranio-cervical flexion test (CCFT) in young adult women with chronic neck pain. Also the study hypothesized that both interventions achieved interesting short term effects in chronic pain management (Study IV).

3. OBJECTIVES

3. OBJETIVOS

3. OBJECTIVES

O-I: To clarify the effects cervical high velocity low amplitude effects on range of motion, strength and cardiovascular performance (Study I).

O-II: To evaluate effects of an indiscriminate manipulation on the C5 (AMC5) a manipulation treatment based on a previous evaluation (MT) and a sham intervention (ST) on cervical spine range of motion (ROM); cervical flexion isometric peak force; EMG activation of sternocleidomastoid muscle (SCM) during the cranio-cervical flexion test (CCFT); and EMG signals of right and left biceps at rest were analyzed (Study II).

O-III: To compare the immediate effects of high-velocity, low-amplitude manipulation treatment with a craniocervical flexion exercise protocol on pain intensity assessed using the visual analogue scale during ROM measurement (VAS-ROM), cervical spine range of motion (ROM), pressure-pain thresholds (PPT) and EMG activation of sternocleidomastoid muscle (SCM) during a craniocervical flexion test (CCFT) (Study III).

O-IV: To compare the short-term effects of an MT protocol and an HE protocol on the neck disability index (NDI), the visual analogue scale (VAS), pressure pain thresholds (PPT), cervical spine ROM and EMG activation of the sternocleidomastoid muscle (SCM) during the cranio-cervical flexion test (CCFT) in young adult women with chronic neck pain (Study IV).

4. METHODS

4. MÉTODOS

4. METHODS

4.1 Study I

The study was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (68) and the method used was based on the minimum criteria established by the Cochrane Back Review Group (CBRG)(69).

4.1.1 Literature search

Queries of the literature were performed using the electronic databases PUBMED, Science Direct, Scopus, PeDro, Scielo, from January 2000 to August 2016. The terms used were: [“Pain” and “chiropractic” OR], [“osteopathic” and “trust” and “manipulation” and “neck” and “cervical” OR]. All Medical Subject Headings terms were combined with pain*, adult*, controlled*, clinical trial*, experimental*, randomized*, strength* and spine* as limiters. Also, the reference lists were examined to detect studies potentially eligible for inclusion. Studies reported in languages other than English were not explored.

4.1.2 Eligibility criteria

4.1.2.1 Types of studies

Randomized-controlled trials (RCTs) that investigated the effects of cervical spine high-velocity, low-amplitude manipulation (CSM) were included. Studies included only English or Spanish language peer-reviewed scholarly journals. Designs included parallel and crossover trials. Case reports, case series, single-case studies, dissertations and conference proceedings were excluded. Authors were contacted to provide missing data or to clarify if data were duplicated in multiple publications. Incomplete data, or data from an already included study, were excluded.

4.1.2.2 Types of participants

The subjects included symptomatic or asymptomatic humans without any age or sex restrictions.

4.1.2.3 Types of interventions

The included interventions were high-velocity, low-amplitude (HVLA) manipulations targeting the cervical spine, regardless of whether cavitation occurred. CSM techniques involving the use of an instrument, such as an activator or other device, were excluded. Single or multiple CSM techniques were included, but only those that targeted the cervical spine region. To obtain maximum specificity regarding the CSM effects, studies that used multimodal treatments were excluded i.e., trials that used any type of co-interventions, such as electrotherapy, massage, manipulations that were not targeted to the cervical spine, exercise or other interventions, were excluded. Additionally, studies that used a preparatory soft massage were excluded.

4.1.2.4 Types of comparisons

The comparison group included inactive controls, sham techniques, manual contact, quiet rest or any form of placebo intervention. Exercise, manipulations not targeted to the cervical spine, medication, patient education and other interventions were excluded from the comparison group.

4.1.2.5 Types of outcome measures

Any type of physiological measurement, e.g., cervical range of motion (CROM) instrument readings, hand - held dynamometer readings or ECG, was accepted. Any device or questionnaire used in these techniques must have been validated previously.

4.1.2.6 Study selection

Two of the authors independently screened titles and abstracts of the studies identified by the search strategy. Potentially eligible studies were read in full text and independently evaluated for inclusion in the review.

4.1.3 Data extraction

Two authors (XG & MI) independently screened the titles and abstracts of potentially eligible studies identified by the search strategy. If necessary, a third researcher (RR-V) was consulted (69)

4.1.3.1 Dealing with missing data

If the article did not contain sufficient information, the authors of the article were contacted for additional information. Some authors were asked for more detail on investigation procedure and outcome data.

4.1.4 Risk of bias in individual studies

For the assessment of the risk of bias of individual studies, the Cochrane Back Review Group updated criteria were used (69). Discussion and consensus were used by the authors of the current review to resolve disagreements about the methodological quality of the studies assessed in the current review. For a study to be rated as having a low risk of bias, a score equal to or higher than 6 on a scale of 12 items must be obtained. Each assessed items can be scored as “yes”, “no” or “unclear”: “yes” if it is included in the article, “no” if is not included and if the article does not provide enough information allowing a yes/no score and the authors could not be contacted, the criteria were scored as unsure. Studies were not excluded from further analyses based on the results of risk of bias assessments.

4.1.5 Data analysis

The effect size was calculated using the mean difference to obtain the Cohen’s d with a 95% interval confidence. An effect size of 0.2 considered small, 0.5 considered medium and 0.8 considered large.

4.1.6 Clinical relevance

A small effect was defined as Cohen's d scores around 0.2. A moderate effect was defined as Cohen's d scores around 0.5 and finally scores around 0.8 was considered as a large effect.

4.2 Study II

4.2.1 Study design

This study was a prospective, randomized controlled pilot study. One research spinal physical therapy registered in Spain conducted patient recruitment and screening at osteopathic clinic. The study was performed in accordance with the Declaration of Helsinki (2000) and was approved by the local office for Medical Research Ethics Committee of The Public University of Navarra. Participants were required to sign a written, informed consent form. No formal sample size calculation was performed.

4.2.2 Participants

Social network and word of mouth were used to recruit 36 asymptomatic voluntary subjects. The participants were enrolled between February and June 2015. Participants were randomly allocated to either the AMC5 (n=12), MT (n=12), and ST group (n=12), (Fig II-1).

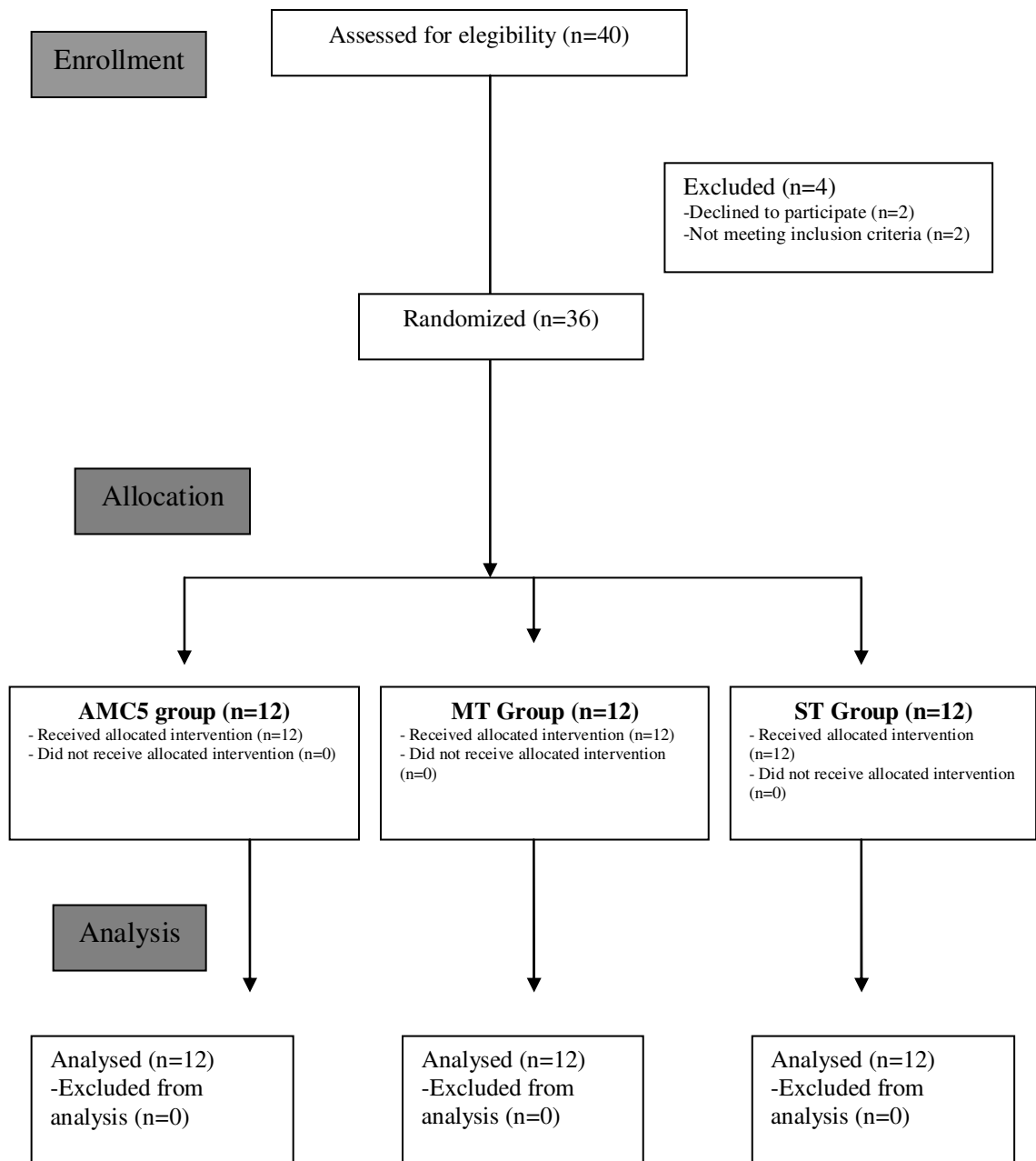


Figure II-1. *Flow of participants through the study.*

The inclusion criteria were being between 18 and 40 years old and asymptomatic in the time of the study. Exclusion criteria were any type of cranio-cervical trauma during the last two years, including whiplash; pain irradiation to the limbs; neurological

alterations in the upper limbs; neurological alterations of the central nervous system; diagnosed vertebral disc injury; degenerative, rheumatologic and/or inflammatory pathologies; pregnancy; previous cervical spine surgery; psychiatric pathologies; spine fractures; dislocation; or vertebral artery positive test (70). Risks was minimised by ruling out contraindications to the testing protocols via a health history and a thorough physical examination prior to the manipulation session.

4.2.3 Procedure

The randomization into the three study arms was performed by the osteopathic clinic, using a computer generated randomization (www.randomizer.org) and registered in an index card. The randomization sequence was not concealed from the investigator who was responsible for assigning participants to groups. The likelihood of bias introduced by unconcealed randomization was reduced by enrolment of consecutive participants. All participants and study personnel (including investigators, physical therapy, and statisticians) were blinded to treatment allocation throughout the trial protocol. Further, the investigators who performed the statistical analyses were not masked from group assignment. Once 12 individuals had been assigned to one group, the envelopes that contained said group was automatically retired. A baseline absence of significant differences among groups was established.

4.2.4 Data collection and outcome measures

The physical therapist that had five years of experience in osteopathic medicine and ten in manual therapies performed the measuring protocol. Every group followed the same measuring protocol.

4.2.4.1 Cervical spine ROM

All patients were evaluated with a cervical mobility exploration using a goniometer CROM (Performance Attainment Associates, St. Paul, MN, USA). This device has been validated in several studies and offers a moderate intra-examiner Intraclass Correlation Coefficient (ICC 0.69) and a good inter-examiner ICC (0.75) (71, 72). The CROM goniometer had three inclinometers, whose scales ranged from two to two degrees. These inclinometers are attached to a frame similar to glasses. The CROM device was mounted over the subjects nose bridge and ears and secured to head by a strap. The frontal and lateral gravity dependent inclinometers measured the side bending and flexion/extension respectively; instead, the third magnetic dependent inclinometer needed to put a magnetic necklace to measure the rotation. In the starting position the participants were seated relaxed with their feet flat on the floor, their knees and ankles at 90° of flexion, and their hands supported on their thighs. The researcher instructed each subject to move the head correctly before the test. The measuring protocol study includes, active cervical ROM flexion, extension, right side bending, left side bending, right rotation and left rotation. Three consecutive measurements were obtained and the mean of these 3 trials was used for data analysis.

4.2.4.2 Cervical flexion isometric peak force

Maximum voluntary isometric force was measured using a hand-held dynamometer Micro Fet 3 (Hoogan Health Industries, West Jordan UT). Hand-held dynamometers have excellent inter-examiner ICC s (0.94) (73) and excellent intra-examiner ICC (0.80) (74). The dynamometer is a good option if there is no access to more sophisticated and expensive equipment, such as an isokinetic machine (75). The subject was situated in supine position with straight legs; first of all, the participant was instructed to perform the correct movement. The test performed with the head supported and the dynamometer's load cell placed at the frontal bone, the patient was asked to lift his or her head off the table as much as possible, while the researcher maintained the device still obtaining an isometric contraction. Three consecutive measurements were obtained at intervals of 60 seconds; the mean of these 3 trials was used for data analysis.

4.2.4.3 Measurement of surface EMG

The surface electromyography (sEMG) activity of both sternocleidomastoid muscles (SCMs) during the cranio-cervical flexion test was measured. In addition, the sEMG activity from these two muscles, the cervical erector spinae muscles, and the biceps brachial muscles was measured during rest. An EMG-USB Multichannel Bioelectrical Amplifier (Bioelectronica, Torino, Italy) device, which displayed the information in real time and stored it on the disk of a personal computer, was used. The surface EMG was recorded with 24 mm diameter round adhesive bipolar connector electrodes (Spes Medica, Battipaglia, Italy). The skin was cleaned with water before electrode placement. The sEMG signals were recorded at a sample rate of 2048 Hz and

were post-processed offline using MATLAB (Mathworks, Inc). The sEMG signals were band -pass filtered between 10Hz and 500Hz, and the amplitude RMS value was obtained for each muscle.

4.2.4.4 Measurement of the efficiency of cervical deep flexor muscles

To measure of the efficiency of cervical deep flexor muscles, SCM activity was assessed by performing the cranio-cervical flexion test (65, 76). Both authors showed the relationship between neck pain, the inhibition of cervical deep flexor muscles (longus capitis and longus colli muscles), and increased EMG activity of the SCM. With the patient in the supine position, a pressure sensor was inflated to 20 mmHg and placed below the neck. The operator instructed the patient to perform five contractions of 10 seconds each. In the first contraction, the patient produced enough pressure to raise the pressure device to 22 mmHg; in the second, the device rose to 24 mmHg; in the third to 26 mmHg; in the fourth to 28 mmHg fourth; and in the fifth contraction the patient achieved maximum force. Between contractions, the patient rested for 30 seconds. During the test, the operator placed the electrodes in the sternal portion of the SCM (77) to assess its activity. To obtain the activation value of the SCM during the cranio-cervical flexion test, an average between the maximum and four sub-maximum values was determined.

4.2.4.5 Bilateral biceps brachial EMG signal at rest

The patient was seated relaxed with their feet flat on the floor, their knees and ankles at 90° of flexion, the arm was resting on the table with 90 ° elbow flexion and

supination, the wrist in neutral position and the fingers relaxed. The skin was cleaned with water swabs. The operator placed the 24 mm diameter round adhesive bipolar connector electrodes (Spes Medica, Battipaglia, Italy), on the belly of the long head of biceps in an imaginary line from the acromion to the biceps tendon (77). Prior to any data collection, subject was instructed not to move any part of the body and relax as much as possible. After the instruction training the test was performed and the operator monitored the biceps for 5 seconds during the rest period. The procedure was repeated with the other biceps brachial.

4.2.5 Interventions

4.2.5.1 AMC5 group

The overall goal for the AMC5 group is to perform HVLA manipulation technique on the C5 after completing the measurement protocol. With the patient in the supine position, the operator stood at the head of the table and made contact with the right C5 transverse process with his right hand's distal interphalangeal joint while cradling the patient's head with his left hand. During the manipulation, the patient maintained global flexion and analytical extension, right side bending, and left rotation until the C5-C6 segment reached the barrier, at which time the operator performed an HVLA left rotation movement, taking the glabella point as the direction (8, 9, 78) . The operator then returned the patient to a neutral position in a passive and slow way. After 30 seconds, the measurement protocol was performed again.

4.2.5.2 MT group

In the MT group, after the measurement protocol assessment, joint dysfunction was evaluated. The method chosen for the evaluation was exclusively manual, based on a study by G. Jull 1998 that showed high reliability in assessing dysfunctions using manual methods (79) . In our study, we used passive mobility tests and tests of anterior-posterior and lateral pressure. These tests have been validated by radiographic studies of the cervical spine and have shown high inter- and intra-examiner reliability, as well as a good relationship between manual diagnosis and hypomobility (80, 81). For the upper thoracic spine, operators used anterior-posterior pressure tests and passive mobility tests (78). The patient was evaluated in the neutral, flexion and extension positions. Also tenderness, tissue texture changes and asymmetry were assessed (8). After the diagnosis of dysfunctions, the operator proceeded perform the HVLA manipulation (8, 9, 78). After manipulation, the operator repeated the measurement protocol.

4.2.5.3 ST group

The ST group followed the same protocol as AMC5 group but with a modified sham technique (in the absence of drop) in place of the C5 technique (82). To perform the technique, the patient was placed in the supine position with the operator at the head of the table. The operator used the thumb of his right hand to make contact with the right C5 transverse process while his left hand cradled the patient's head. In this position, the operator performed right side bending and left rotation of the C5-C6 segment without reaching the barrier and performed three rotation movements in the direction of the glabella.

Additional outcomes of this study were participant adverse events (such as: pain, headache, dizziness or other symptoms) occurred in the next week after the study.

4.2.6 Statistical analysis

In order to retain data of all randomly allocated participants, an intention-to-treat analysis was performed. The statistical analysis was performed by a statistician blinded to the randomization, measuring and intervention protocol. An alpha level of 0.1 was used for all statistical analyses. Statistical analyses were conducted using SPSS Statistics 20 for Windows (SPSS, Inc., Chicago, Illinois). Numerical variables were summarized as means \pm SD, whereas categorical variables were given as frequencies and percentages. Prior to the planned statistical analyses, preliminary analysis was conducted (Levene test) to confirm data distribution normality. The Levene statistic showed a normal distribution ($P > 0.05$) in flexion, extension; right rotation; left and right side bending mobility increment; in cervical flexion isometric peak force increment; increment in the amplitude of the EMG rest signal of the left brachial biceps and an increment on both sides of the SCM muscle during the Cranio-cervical Flexion Test. On the contrary, the Levene statistic showed no normal distribution (heterogeneous) in left rotation mobility increment and in the EMG rest signal amplitude increment of the right brachial. When this normality assumption failed, non-parametric statistics were applied for means comparisons. For outcomes analysis, we used linear mixed-effects modeling for repeated measures over time using continuous outcome variables as the dependent variable and effects for time, group (AMC5, MT, and ST group), and time by group interaction. Within the mixed model, we calculated

95% CIs and P values for 3 pre-specified intergroup contrasts and for change in all variables within each group over time. Finally, to calculate the effect size the Cohen's d was used, a small effect was defined as Cohen's d scores around 0.2. A moderate effect was defined as Cohen's d scores around 0.5 and finally scores around 0.8 was considered as a large effect.

4.3 Study III

4.3.1 Study design

A single-blind randomized clinical trial was performed. One research spinal physical therapy registered in Spain conducted patient recruitment and screening at Osteopathic Clinic and at Sports Medicine Investigation Center of Pamplona. The study was performed in accordance with the Declaration of Helsinki (2000) and was approved by the local office for Medical Research Ethics Committee of The Public University of Navarra. A written consent form was taken from participants and the procedure was explained by the investigator. The study was registered in the Ethical Review Board of the Public University of Navarra.

4.3.2 Participants

Social network and word of mouth were used to recruit twenty-five volunteers with chronic idiopathic neck pain. The participants were enrolled between February and August 2016. Participants were randomly divided into 2 groups: group MT (n=12), and group CCF (n=13) (Fig III-1).

Patients were included if they were aged between 18 and 50 years with a history of neck pain 3 months during the last year, a pain intensity in the time of the study of 25/100 on a VAS during ROM, and somatic dysfunction in temporo -mandibular joint, cervical spine and upper thoracic spine. Exclusion criteria were any type of cranio-cervical trauma during the last two years, including whiplash; pain irradiation to the

limbs; neurological alterations in the upper limbs; neurological alterations of the central nervous system; diagnosed vertebral disc injury; degenerative, rheumatologic and/or inflammatory pathologies; pregnancy; previous cervical spine surgery; psychiatric pathologies; spine fractures; dislocation; or vertebral artery positive test(18). Risks were minimized by ruling out contraindications to the testing protocols via a health history and a thorough physical examination prior to the manipulation session.

4.3.3 Procedure

Individuals who met the inclusion criteria were randomly allocated to MT Group or CCF Group, using computer generated method (www.randomizer.org) without replacement. The allocation was conducted by the primary investigator prior to the baseline assessment. At each visit, after enter into an informed consent and prior to the start of data collection, an external researcher, blinded to study researchers, opened the two sealed envelopes and put inside the two index card, then the participants choose one of them. In this manner the risk of bias was reduced and randomization was ensured.

4.3.4 Data collection and outcome measures

The physical therapy that had five years of experience in osteopathic medicine and ten in manual therapies performed the measuring protocol. Every group followed the same measuring protocol. The order of assessments was VAS during ROM, cervical range of motion (CROM), PPT and EMG during CCFT before the intervention and 60 seconds after intervention

4.3.4.1 VAS during CROM

Neck pain during CROM measure was assessed with a VAS, both pre and postintervention. The patient placed a vertical mark on a continuous 100 mm line to indicate pain, ranging from no pain (0) to the worst pain could possibly feel (100). The reliability and validity of the VAS as a measure of pain has been established previously (83, 84).

4.3.4.2 Cervical spine ROM

The cervical mobility of included patients was evaluated using a CROM goniometer (Performance Attainment Associates, St. Paul, MN, USA). This device has been validated in several studies and has been found to have a moderate intra-examiner intraclass correlation coefficient (> 0.69) and good inter-examiner intraclass correlation coefficient (> 0.75) (71, 72). The CROM goniometer has three inclinometers with scales that range from two to two degrees. These inclinometers are attached to a frame that is similar in appearance to eyeglasses. The CROM device was mounted over each subject's nose bridge and ears and secured to the head by a strap. The frontal and lateral gravity-dependent inclinometers were used to measure side-bending and flexion/extension, respectively; in addition, the third inclinometer was attached to a magnetic necklace to measure rotation. In the starting position, the participants were seated in a relaxed position with their feet flat on the floor, their knees and ankles at 90° of flexion, and their hands supported on their thighs. The researcher instructed each subject on the head movement protocol before test initiation. The measuring protocol for this study included the testing of active cervical ROM flexion, extension, right side-bending, left

side-bending, right rotation and left rotation. Three consecutive measurements were obtained, and the mean value of measurements obtained during the 3 trials was used for data analysis.

4.3.4.3 Pressure pain thresholds (PPT).

PPT is defined as the minimal amount of pressure where a sense of pressure first changes to pain (85). A mechanical pressure algometer (Force Dial FDK 20, Wagner Instruments, Greenwich CT) was used to measure PPT in this study. This device consists of a round metal disk (area, 1 cm²) attached to a pressure (force) gauge. The gauge displays values in kilograms. Because the surface of the device is 1 cm², the readings are expressed in kilograms per square centimeter. Algometers can measure pressures ranging from 0 to 10 kg with 0.1 kg divisions. Previous articles have reported algometer results to have good inter-examiner reliability and an average intra-class correlation coefficient (ICC) of 0.75; furthermore, the intra-examiner reproducibility of algometers has been reported to be excellent (mean ICC = 0.84) (86)(87, 88)

Before PPT measurement, patients were instructed to say, “Stop,” when the sensation changed from pressure to pain during the test. PPT was measured posterolaterally between the lower border of the occipital and the horizontal level of the spinous process of C2, over the C5/6 zygapophyseal joint, and over the upper trapezius (middle of the front edge of the upper trapezius fibers). We also used a trigger point within the gluteus medius muscle to act as a regional control point, given its segmental distance from the manipulated segment (89).

The PPT was assessed on the most painful side, as indicated by the patient. For cases reporting both sides to be equally painful, the right side was selected. Three measurements were recorded for each PPT, and the mean value of measurements obtained during the 3 trials was used in further statistical analyses.

4.3.4.4 Measurement of the efficiency of deep cervical flexor muscles.

An EMG-USB Multichannel Bioelectrical Amplifier (Bioelectronica, Torino, Italy) device, which displayed the information in real time and stored it on the disk of a personal computer, was used. Surface EMG was recorded using round, self-adhesive, bipolar connector electrodes with a diameter of 24 mm (Spes Medica, Battipaglia, Italy). The skin was cleaned with water before electrode placement. sEMG signals were recorded at a sample rate of 2048 Hz and were post-processed offline using MATLAB (MathWorks, Inc.). sEMG signals were band-pass filtered between 10 Hz and 500 Hz, and amplitude RMS values were obtained for each muscle. To measure of the efficiency of the deep cervical flexor muscles, SCM activity was assessed by performing the craniocervical flexion test according to the standard clinical protocol (65, 76)(90). Authors previously using this test have reported a relationship between neck pain, inhibition of the cervical deep flexor muscles (longus capitis and longus colli muscles) and increased EMG activity of the SCM. During the test, the patient was in the supine position with their neck in a neutral position and positioned so that the line of the face was horizontal and an imaginary line bisecting the neck longitudinally was horizontal to the testing surface. A pressure sensor was inflated to 20 mmHg and placed below the neck (Stabilizer, Chattanooga Group Inc. USA). First, the operator instructed the patient to perform a series of five incremental 10 second contractions. Subjects practiced

targeting the five test levels between 22 and 30 mmHg in two practice trials before the electrodes were applied. During the first contraction, the patient produced enough pressure to achieve a measurement of 22 mmHg. During the second, third, fourth and fifth contractions, pressures of 22 mmHg, 24 mmHg, 26 mmHg, 28 mmHg, and 30 mmHg were measured, respectively. Between contractions, the patient rested for 30 seconds. After training, the operator placed the electrodes on the sternal portion of the SCM (77) to assess its activity. To determine the activation value of the SCM during the craniocervical flexion test, the average of the maximum and five sub-maximum values was calculated. Following application of the electrodes, participants performed a standardized maneuver for EMG normalization (reference voluntary contraction). This reference voluntary contraction involved a head lift (cervical and cranio-cervical flexion) just clear of the bed, which was maintained for 10 s during which EMG data were recorded. A one minute rest period was given before participants performed the experimental CCFT condition during which EMG data were recorded.

4.3.4.5 Other outcomes

Additional outcomes evaluated in this study were participant adverse events (such as pain, headache, dizziness or other symptoms) occurring during treatment and within the week after study participation.

4.3.5 Interventions

4.3.5.1 Manipulation Group (MT)

In the MT group, the temporo-mandibular joint, cervical spine and upper thoracic spine dysfunctions were corrected. Passive mobility and anterior-posterior and lateral gliding tests were used to diagnose spinal dysfunctions. These tests have been validated by radiographic studies of the cervical spine and shown high inter- and intra-examiner reliability and strong association with manual diagnoses and hypomobility (80, 81). For the diagnosis of upper thoracic spine dysfunctions, operators used anterior-posterior pressure and passive mobility tests (78). The patient was evaluated in the neutral, flexion and extension positions. After the diagnosis of dysfunctions, the operator proceeded to correct them using HVLA manipulation (8, 9, 78). After manipulation, the operator repeated the measurement protocol. To correct temporomandibular joint (TMJ) dysfunctions, previously described articular techniques were used (91)(8). The participants were requested to contact with the principal investigator if adverse events, such as pain, headache, dizziness or other symptoms, occurred during the week following study participation.

4.3.5.2 Craniocervical Flexion (CCF) Exercise Group

While in the supine position, subjects performed a CCF exercise for 10 repetitions of 10 second duration, with a 10 second rest interval between each contraction (total contraction time: 100 seconds, total time of session: 190 seconds). Movements were guided by a physiotherapist to facilitate activation of the cervical deep

flexor muscles with a minimal activity of the superficial cervical flexors. To monitor the movement and contraction intensity, a pressure biofeedback device (Stabilizer; Chattanooga Group Inc., Chattanooga, TN) was used. During the exercise, the participants were instructed to maintain a pressure between 22 and 30 mmHg comfortably and without pain during the contraction (51).

4.3.6 Statistical Analysis

The statistical analysis was performed by a statistician who was blinded to the randomization, measurement and intervention protocol. Statistical analyses were conducted using SPSS Statistics 20 for Windows (SPSS, Inc., Chicago, IL, USA). The demographic data and initial assessment results were compared using t-tests. The statistical distribution of the data was analyzed using the Shapiro Wilks W test. For parametric data, the t-test for paired samples was used to compare the results of the assessment before and after treatment; for nonparametric data, the Wilcoxon signed-rank test was used. The independent t-test for parametric data or the Mann-Whitney U Test for non-parametric data was used to compare the difference (change score) from pre to post treatment between groups. Finally, to calculate the effect size, Cohen's d was used. A small effect was identified by a Cohen's d score of approximately 0.2, a moderate effect was defined as a Cohen's d score of approximately 0.5, and a score of approximately 0.8 identified a large effect. The alpha level was set at 0.05.

4.4 Study IV

4.4.1 Study design

A single-blind randomized clinical trial was performed. One research spinal physical therapist registered in Spain conducted patient recruitment and screening at the Osteopathic Clinic and the Sports Medicine Investigation Center of Pamplona. The study was performed in accordance with the Declaration of Helsinki (2000) and was approved by the local office for Medical Research Ethics Committee of The Public University of Navarra. A written consent form was signed by the participants, and the procedure was explained by the investigator. No formal sample size calculation was performed.

4.4.2 Participants

Social networks and word-of-mouth were used to recruit twenty-seven volunteers with chronic idiopathic neck pain. The participants were enrolled between April and August 2016 and were randomly allocated to either the manipulation group (MT, n=13) group or the home exercise group (HE, n=14) (Fig. IV-1).

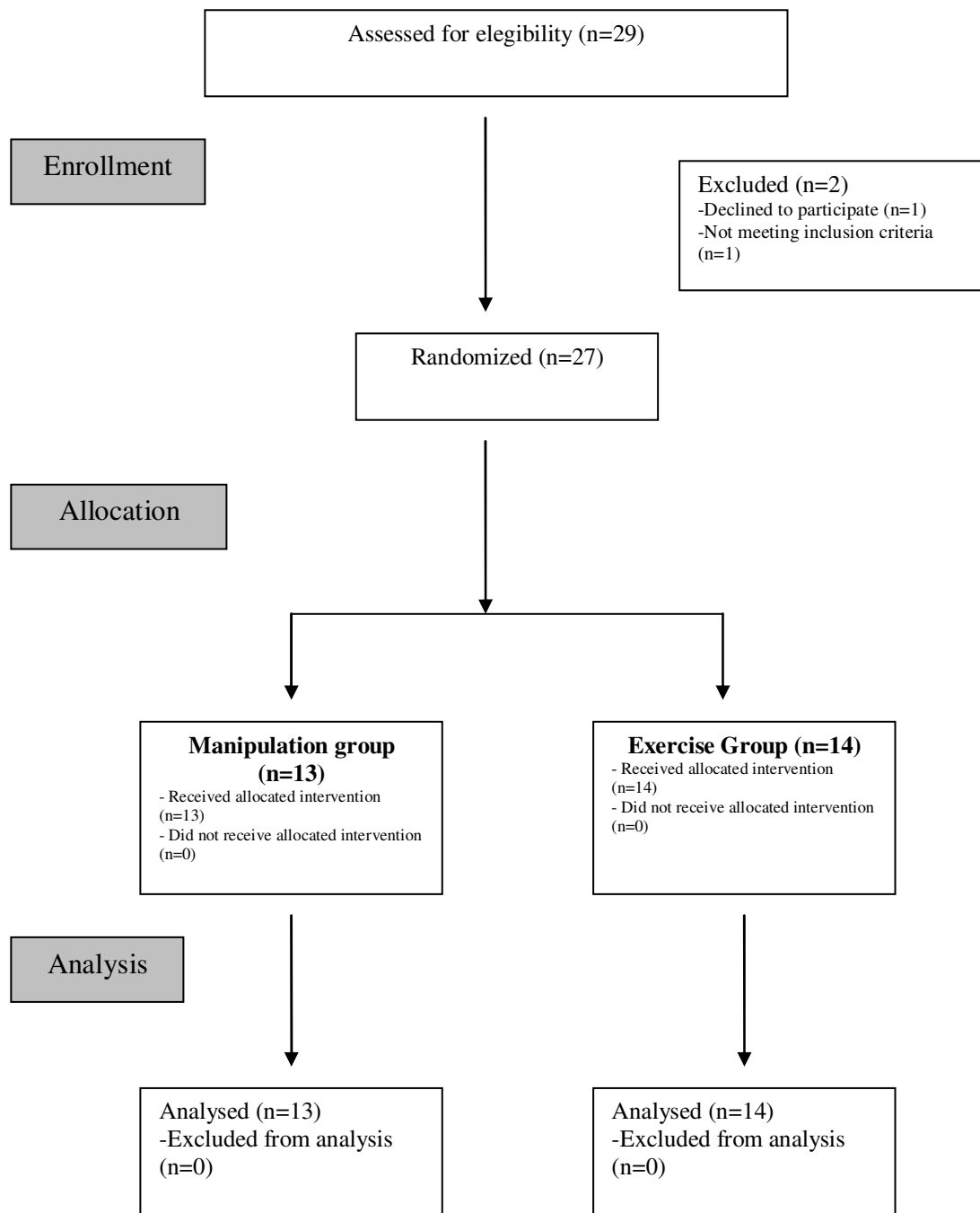


Figure IV-1. Flow of participants through the study.

Patients were included if they were between 18 and 50 years old with a history of neck pain for 3 months during the last year, a pain intensity at rest in the week before the study of 30/100 on a VAS and somatic dysfunction in temporo-mandibular joint, cervical spine and upper thoracic spine. The exclusion criteria were any type of cranio-cervical trauma during the last two years, including whiplash; pain radiating to the limbs; neurological alterations in the upper limbs; neurological alterations of the central nervous system; diagnosed vertebral disc injury; degenerative, rheumatologic and/or inflammatory pathologies; pregnancy; previous cervical spine surgery; psychiatric pathologies; spine fractures; dislocation; or positive vertebral artery test(18). The risks were minimized by ruling out contraindications to the testing protocols via a health history and a thorough physical examination prior to the manipulation session.

4.4.3 Procedure

The individuals who met the inclusion criteria were randomly allocated to the MT group or the HE group using a computer -generated method (www.randomizer.org) without replacement. The allocation was conducted by the primary investigator prior to the baseline assessment. At each visit, after entering informed consent was given and prior to the start of data collection, an external researcher who was blinded to the study researchers opened the two sealed envelopes and put two index cards inside them, and the participants choose one of them. In this manner, the risk of bias was reduced, and randomization was ensured.

4.4.4 Data collection and outcome measures

A physical therapist with five years of experience in osteopathic medicine and ten in manual therapies performed the measurement protocol. Each group followed the same measurement protocol. The order of assessments was NDI, VAS at rest, CROM, PPT and EMG during the CCFT before the intervention and one week later.

4.4.4.1 Neck disability index

This questionnaire evaluates pain intensity, personal care, lifting weights, reading, headache, concentration, hard work, driving, sleep and leisure activities (92). A Spanish version of the NDI validated by Andrade et al was used (93).

4.4.4.2 VAS at rest

Neck pain at rest was measured using a VAS both before and one week post intervention. The patient placed a vertical mark on a continuous 100 mm line to indicate her pain levels, ranging from no pain (0) to the worst pain possible (100). The reliability and validity of the VAS as a measure of pain has been established previously (83, 84).

4.4.4.3 Cervical spine ROM

All of the patients were evaluated for cervical mobility using a CROM goniometer (Performance Attainment Associates, St. Paul, MN, USA). This device has been validated in several studies and offers a moderate intra-examiner intraclass

correlation coefficient (> 0.69) and a good inter-examiner intraclass correlation coefficient (> 0.75) (71, 72). The CROM goniometer has three inclinometers whose scales range from two to two degrees. These inclinometers are attached to a frame similar to eyeglasses. The CROM device was mounted over the subject's nose bridge and ears and secured to the head with a strap. The frontal and lateral gravity-dependent inclinometers measured side bending and flexion/extension, respectively, while a third, magnetic-dependent inclinometer required the use of a magnetic necklace to measure rotation. At the start of the measurement, the participants were seated and relaxed with their feet flat on the floor, their knees and ankles at 90° of flexion, and their hands supported on their thighs. The researcher instructed each subject to move her head correctly before the test. The measurement protocol study included active cervical ROM flexion, extension, right side bending, left side bending, right rotation and left rotation. Three consecutive measurements were obtained, and the mean of these 3 trials was used for data analysis.

4.4.4.4 Pressure pain thresholds (PPT)

The pressure pain threshold is defined as the minimal amount of pressure at which the sensation of pressure changes to a sensation of pain (85). A mechanical pressure algometer (Force Dial FDK 20, Wagner Instruments, Greenwich, CT, USA) was used in this study. This device consists of a round metal disk (area, 1 cm^2) attached to a pressure (force) gauge. The gauge displays values in kilograms. Because the surface of the device is 1 cm^2 , the readings are expressed in kilograms per square centimeter. The range of the algometer is 0 to 10 kg in 0.1 kg increments. Previous articles have reported good inter-examiner reliability with a mean intra-class correlation coefficient

(ICC) of 0.75; furthermore, intra-examiner reproducibility was excellent (mean ICC = 0.84) (86)(87, 88).

Before the PPT measurement, the patients were instructed to say “stop” when the sensation changed from pressure to pain. The PPT was measured posterolaterally, between the lower border of the occiput and the horizontal level of the spinous process of C2, over the C5/6 zygapophyseal joint, and the middle of the front edge of the upper trapezius fibers). We also used a trigger point within the gluteus medius muscle as a regional control point, given its segmental distance from the manipulated segment (89). The PPT was assessed on the most painful side indicated by the patient. When both sides were reported as equally painful, the right side was selected. Three measurements were recorded for each PPT, and the mean was used for the statistical analyses.

4.4.4.5 Measurement of the efficiency of the cervical deep flexor muscles (cranio-cervical flexion test)

An EMG-USB Multichannel Bioelectrical Amplifier (Bioelecttronica, Torino, Italy) device, which displayed information in real time and stored it on a personal computer, was used. The surface EMG was recorded with 24- mm-diameter round adhesive bipolar connector electrodes (Spes Medica, Battipaglia, Italy). The participant’s skin was cleaned with water before electrode placement.

The sEMG signals were recorded at a sample rate of 2048 Hz and were post-processed offline using MATLAB (Mathworks, Inc.). The sEMG signals were band-

pass filtered between 10 Hz and 500 Hz, and the amplitude RMS value was obtained for each muscle.

To measure of the efficiency of the cervical deep flexor muscles, SCM activity was assessed by performing the cranio-cervical flexion standard clinical protocol described in previous studies (65, 76)(90). These studies showed the relationship between neck pain, the inhibition of cervical deep flexor muscles (the longus capitis and longus colli muscles) and the increased EMG activity of the SCM. During this protocol, the patient was in the supine position with the neck in a neutral position, such that the line of the face was horizontal and a line bisecting the neck longitudinally was horizontal to the testing surface. The layers of a pressure sensor were inflated to 20 mmHg and placed below the neck (Stabilizer, Chattanooga Group Inc., USA). First, the operator instructed the patient to perform five incremental contractions of 10 seconds each. The participants practiced targeting the five test levels between 22 and 30 mmHg in two practice trials before the electrodes were applied. During the first contraction, the patient was asked to produce enough pressure to raise the pressure device to 22 mmHg; in the second, the device was to reach 24 mmHg; in the third, the target was 26 mmHg; in the fourth, it was 28 mmHg; and in the fifth, the target was 30 mmHg. Between contractions, the patient rested for 30 seconds. After training, the operator placed the electrodes on the sternal portion of the SCM (77) to assess its activity. To obtain the activation value of the SCM during the cranio-cervical flexion test, an average between the maximum and the five sub-maximum values was determined. Following the application of the electrodes, the participants performed a standardized maneuver for EMG normalization (reference voluntary contraction). This reference voluntary contraction involved a head lift (cervical and cranio-cervical flexion) just clear of the

bed that was maintained for 10 s, during which EMG data were recorded. A one-minute rest period was allowed before the participants performed the experimental CCFT measurement during which the EMG data were recorded.

4.4.5 Interventions

4.4.5.1 Manipulation group (MT)

In the MT group, after the measurement protocol assessment, joint dysfunction was evaluated. The method chosen for the evaluation was exclusively manual, based on a study by G. Jull in 1998 that showed high reliability for assessing dysfunctions using manual methods (79). In our study, we used passive mobility tests and tests of anterior-posterior and lateral pressure. These tests have been validated with radiographic studies of the cervical spine and have shown high inter- and intra-examiner reliability as well as a good relationship between manual diagnosis and hypomobility (80, 81). For the upper thoracic spine, the operators used anterior-posterior pressure tests and passive mobility tests (78). The patient was evaluated in the neutral, flexion and extension positions. After the diagnosis of dysfunctions, the operator proceeded to the correction with HVLA manipulation (8, 9, 78). After manipulation, the operator repeated the measurement protocol.

To correct the TMJ dysfunctions, previously described articular techniques were used (91)(8).

The participants were instructed to contact the principal researcher if adverse events such as pain, headache, dizziness or other symptoms occurred in the week after the study.

4.4.5.2 Home exercise group (HE)

On the first day, the patients in the HE group received personal instruction and supervision by an experienced physiotherapist to ensure that they performed the exercises correctly. All of the subjects were given an exercise diary and a telephone and email contact. The exercise lasted no longer than 10–20 minutes once per day. The exercises were to be performed without provoking neck pain.

The HE protocol consisted of a general range of motion movements, specific stretching of the bilateral upper trapezius and cervical extensor muscles, CCF and submaximal isometric exercises (Appendix 1).

First, while the participant was in a sitting position, general range of motion movements of the neck (flexion, rotation and side bending) were achieved 10 times in each direction. The movements were performed gently, with the goal of trying to go a little further during each repetition.

The stretching exercises were performed with the participant in a sitting position. To stretch the right upper trapezius, the subjects fixed the right shoulder with the left hand and then performed a left lateral flexion, right rotation and slight anterior flexion of the head and neck. The left trapezius was then stretched in the same manner.

The cervical extensor muscles were stretched using neck and head flexion; to aid the stretch, the hands were placed at the occipital bone. The stretch position was maintained for 30 seconds. Each exercise was repeated 3 times (62)(63).

In the supine position, the subjects performed a CCF exercise for 10 repetitions of 10 seconds' duration, with a 10-second rest interval between each contraction (total contraction time: 100 seconds, total time of session: 190 seconds). The correct movement was first guided by a physical therapist to activate the deep cervical flexor muscles with minimal activity of the superficial cervical flexors. To monitor the correct movement and contraction intensity, a pressure biofeedback device (Stabilizer; Chattanooga Group, Inc., Chattanooga, TN, USA) was used. The participants were instructed to maintain pressure sensor levels between 22 and 30 mmHg comfortably and with no pain during contraction (51)(60). When performing the exercises at home, the patients placed a towel under the neck and then placed one hand gently on the front of the neck to feel the superficial muscles during the cranio- cervical flexion movement. The patients were instructed to stop the contraction if they felt that the muscles were beginning to harden.

Finally, submaximal isometric contractions were performed. In sitting position, the patients achieved a five-second contraction using only 10% effort. The contractions were performed 5 times in each direction (rotation, flexion, extension and lateral flexion in both directions) (61) .

Additional outcomes of this study were participant adverse events (such as: pain, headache, dizziness or other symptoms) occurred in the next week after the study.

4.4.6. Statistical Analysis

The statistical analysis was performed by a statistician who was blinded to the randomization, measurement and intervention protocol. Statistical analyses were conducted using SPSS Statistics 20 for Windows (SPSS, Inc., Chicago, IL, USA). The demographic data and initial assessment results were compared using t-tests. The statistical distribution of the data was analyzed using the Shapiro Wilks W test. For parametric data, the t-test for paired samples was used to compare the results of the assessment before and after treatment; for nonparametric data, the Wilcoxon signed-rank test was used. The independent t-test for parametric data or the Mann-Whitney U Test for non-parametric data was used to compare the difference (change score) from pre to post treatment between groups. Finally, to calculate the effect size, Cohen's d was used. A small effect was identified by a Cohen's d score of approximately 0.2, a moderate effect was defined as a Cohen's d score of approximately 0.5, and a score of approximately 0.8 identified a large effect. The alpha level was set at 0.05.

5. RESULTS & DISCUSSION

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5. RESULTS AND DISCUSSION

5.1 Study 1

5.1.1 Study selection

In our preliminary search, the titles of 2,145 manuscripts were read; of these, 183 were eligible for the next step, which included reading the abstracts. Based on the 183 abstract, 42 were eligible for full-text screening. From the 42 full-text articles, 11 original research studies that investigated the effects of CSM were included (Figure I-1).

Other studies that investigated the effects of CSM combined with other treatment techniques were excluded. Studies that did not include a control or sham group were excluded. Case report studies were excluded.

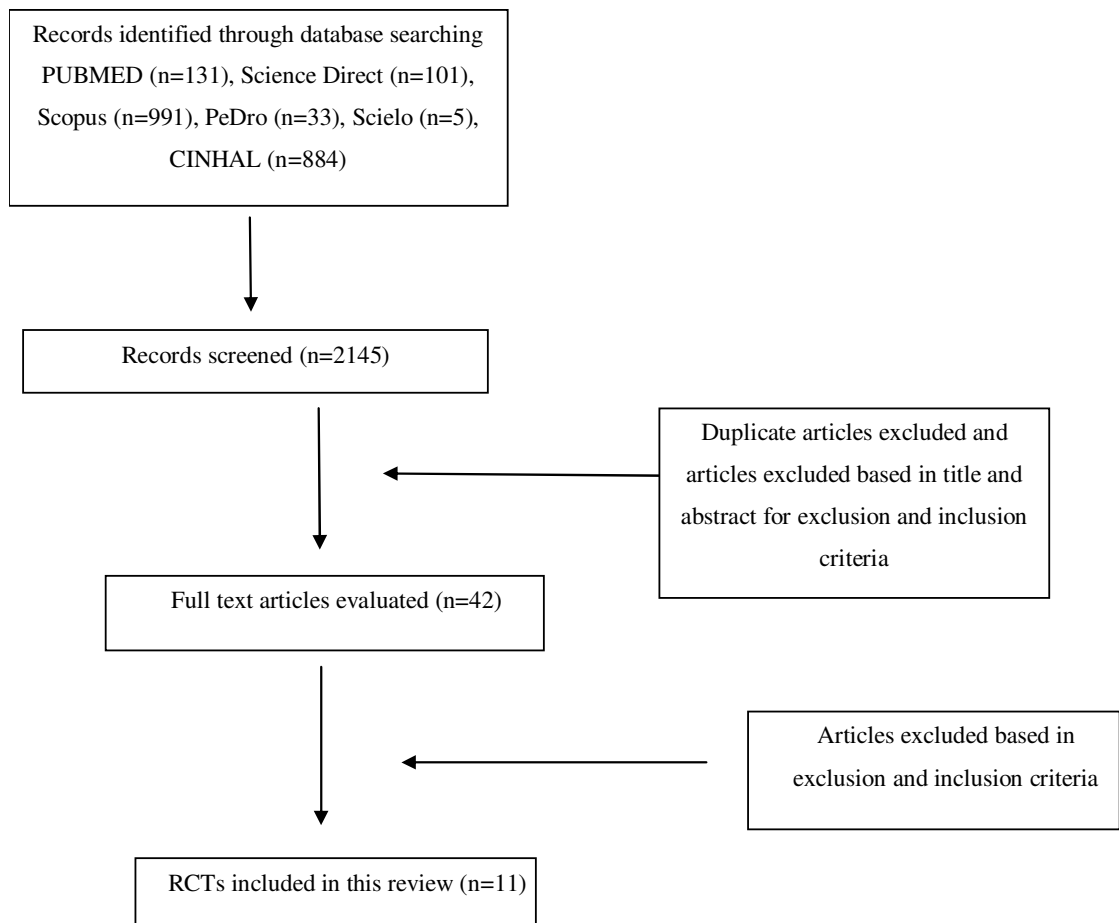


Figure I-1. *Study selection flow diagram.*

5.1.2 Study characteristics

Among the 11 eligible studies, most reported on CSM and mobility; in the remaining cases, the relationships between CSM and strength and cardiovascular system were investigated. (table I-1).

Data	Type	Units
Cervical mobility	Outcome	degrees
Temporo-mandibular joint mobility	Outcome	mm

Strength	Outcome	kg
Systolic blood pressure	Outcome	mmHg
Diastolic blood pressure	Outcome	mmHg
ECG	Outcome	ms
Hearth rate	Outcome	bpm
Programme duration	Covariate	Weeks
Session frequency	Covariate	Sessions per week
Year	Year of publication	Year

Table I-1. List of outcome measures and other data extracted from included studies.

5.1.3 Risk of bias within studies

Table I-2 reports the methodological score by each criteria developed by CBRG. Out of a total of 11 articles all of them have low risk of bias.

Article	1	2	3	4	5	6	7	8	9	10	11	12	Score
Martinez Segura et al 2006	Y	N	Y	N	Y	N	Y	Y	Y	Y	Y	Y	9/12
Passmore et al 2010	U	N	N	N	Y	N	Y	Y	Y	Y	Y	Y	7/12
George et al 2007	U	N	N	N	Y	N	Y	Y	Y	Y	Y	Y	7/12
Mansilla Ferragut et al 2009	Y	N	N	N	N	N	Y	Y	Y	Y	Y	Y	7/12
Fernandez Carnero et al 2008	Y	N	Y	N	Y	N	Y	Y	Y	Y	Y	Y	9/12
Oliveira et al 2010	Y	N	N	N	N	N	Y	Y	Y	Y	Y	Y	7/12
Humpries et al 2013	U	N	Y	N	Y	N	Y	Y	Y	Y	Y	Y	8/12
Botelho et al 2012	Y	N	N	N	U	N	Y	Y	Y	Y	Y	Y	7/12
Bakris et al 2007	Y	N	Y	N	U	Y	Y	Y	Y	Y	Y	Y	9/12
Knutson et al 2001	U	N	N	N	N	N	U	Y	Y	Y	Y	Y	5/12
Ward et al 2012	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	9/12

Table I-2. Summary of methodological quality Criteria items: 1 Was the method of randomization adequate? 2 Was the treatment allocation concealed? 3 Was the patient blinded to the intervention? 4 Was the care provider blinded to the intervention?

5 Was the outcome assessor blinded to the intervention? 6 Was the drop-out rate described and acceptable? 7 Were all randomized participants analysed in the group to which they were allocated? 8 Are reports of the study free of suggestion of selective outcome reporting? 9 Were the groups similar at baseline regarding the most important prognostic indicators? 10 Were co-interventions avoided or similar? 11 Was the compliance acceptable in all groups? 12 Was the timing of the outcome assessment similar in all groups?. Unsure (U), Yes (Y), No (N)

5.1.4. Synthesis of results and discussion

5.1.4.1 CSM and mobility

5.1.4.1.1 CSM and cervical spine mobility

Cervical spine ROM recovery is one of the main goals of many treatments to alleviate musculoskeletal pain in the neck (94, 95). Additionally, the aim of CSM is to correct the quality and quantity of movement loss and to achieve this, CSM attempts to correct the somatic dysfunction (8). (Table I-3)

Two studies have examined the relationship between CSM and cervical spine mobility. Martinez – Segura et al (16) investigated the immediate effects on cervical ROM after a single high-velocity low-amplitude (HVLA) manipulation at the middle cervical spine level in seventy subjects with neck pain. Immediately after treatment, CSM increased neck flexion by 7°, extension by 8°, left side bending by 5°, right side bending by 5°, left rotation by 9° and right rotation by 10°. All the cervical ROM the effect size was considered large (>0.80) except in right side bending ROM which the effect size was considered moderate (0.71) (16). However, Passmore et al investigated mobility improvement after CSM in the upper cervical spine. In this case, the

dysfunctional level manipulated was C1/C2, and the subjects were asymptomatic with palpable intervertebral motion restriction at the C1-C2 level. The results were different; the only significant improvement found was for right rotation (by 3.75°) with a moderate effect size (0.50) (33)

The difference between these results can be explained in that Martinez–Segura studied patients with neck pain and possibly with important cervical spine ROM limitations, whereas Passmore studied healthy volunteers with dysfunction but with less cervical spine ROM alterations. In the author’s opinion, these results might show that the effect of CSM is to recover lost mobility, not only to improve mobility.

<u>Study</u>	<u>Subjects (n) /</u>	<u>Groups</u>	<u>Groups size</u>	<u>Intervention</u>	<u>Intervention Duration</u>	<u>Frequency (days/week)</u>	<u>Outcomes</u>	<u>Effect Size of CSM*</u>
MOBILITY (CERVICAL)								
Martinez-Segura et al 2006	48 (16 male, 32 women, 18-48 years of age) /	CSM Control	34 37	CSM C3/C4 or C4/C5 (experimental) Placebo mobilization (control)	One session	0	↑flexion 7° ↑extension 8° ↑left side bending 5° ↑right side bending 5° ↑left rotation 9° ↑right rotation 10°	Flexion 1 (0.49,1.49) Extension 0.89 (0.38,1.38) Left side bending 0.83(0.33,1.32) Right side bending 0.71(0.22,1.20) Left rotation 0.95(0.43,1.44) Right rotation 1.17(0.65,1.67)
Passmore et al 2010	n=15 Age 29.1±6.5 (experimental) and 26.5±5.7(control) Men and women asymptomatic but with dysfunction in C1/C2	CSM Control	8 7	CSM C1/C2 (experimental) NO-intervention (control)	One session	0	↑right rotation 3.75° No significant changes in flexion, extension, left rotation, right side bending and left side bending	Right rotation 0.50(-0.52,1.47)
MOBILITY (TEMPOROMANDIBULAR)								
George et al 2007	n=101 Age 24.6±2.6 Men and women asymptomatic	CSM Control	34 33	CSM C1/C2 (experimental) No-intervention (control)	One session	0	No significant changes in PFMO	PFMO 0.01(-0.46,0.49)
Mansilla-Ferragut et al 2009	n=37 Age 36±7 (experimental) and	CSM Control	18 19	CSM C0/C1 (experimental) Manual contact	One session	0	↑ 3.5 mm PFMO	PFMO>1.5

	34±8(control) Women with neck pain			(control)				
Oliveira-Campelo et al 2010	n=122 Age 35±10 (experimental) and 39±10(control) Men and women asymptomatic with trigger point in masseter muscle	CSM Control	41 40	CSM C0/C1 (experimental) No-intervention (control)	One session	0	↑ 1.5 mm PFMO	PFMO 0.22(- 0.22,0.65)
HAND GRIP STRENGTH								
Humphries et al. 2013	n=24 Age 26.3±8.5 (experimental) and 26.3±10(control) Men asymptomatic	CSM Control	12 12	CSM C5/C6 (experimental) Placebo activator (control)	One session	0	No significant changes in HGS	HGS 0.07(- 0.73,0.87)
Botelho et al. 2012	n=18 Men and women asymptomatic elite athletes.	CSM Control	9 9	CSM at dysfunction levels once a week during 3weeks (experimental) Sham technique (control)	3 sessions	1	↑left 10.53% in HGS ↑right 16.82% in HGS	Not found – no SD
Fernandez-Carnero et al 2008	n=10 Age 42±6 Men and women with lateral epicondylalgia	CSM Control	10 10 (crossov er)	CSM C5/C6 (experimental) Manual contact (control)	One session	0	No changes in HGS ↑ 37.8% in PFG	HGS 0.05(- 0.93,0.82) PFG 0.78 (- 0.16,1.66)
CARDIOVASCULAR SYSTEM								
Bakris et al 2007	n=50 Age 53.6±8.6 (experimental) and 51.8±10.9(control) Men and women with hypertension stage 1	CSM Control	50 50	CSM C1/C2 (experimental) once a week during 8 weeks Sham technique (control)	8 sessions	1	↓17.2mmHg SBP ↓10.3 mmHg DBP No significant changes in HR	Not found-no SD

		and dysfunction at C1							
Knutson et al 2001	n=80			CSM C1/C2			↓10.3 mmHg DBP No significant changes in SBP and HR	One session	0
	Age 53 (21-83 range) (experimental) and 54 (20-83 range) (control)	CSM	40	(experimental) Sham mobilization (control)					
	Men and women with and without hypertension but with dysfunction in C1/C2	Control	40						
Ward et al 2012	n=48			CSM C1/C2 Right			No significant changes in SBP, DBP, ECG, BPO.	One session	0
	Age 27±4.5 (experimental 1) 25.5±2.9 (experimental 2) 25.1±2.1 (control 1) 26.5±2.6 (control 2) Men and women asymptomatic	CSM	12/12	(experimental 1) CSM C1/C2 Left (experimental 2) No Neck contact (control 1) sham mobilization (control 2)					
		Control	12						

Table I-3. Summary of studies that investigated the effects of CSM on cervical and temporomandibular range of motion, strength and the cardiovascular system. Cervical spine manipulation (CSM). Pain free mouth opening (PFMO). Hand grip strength (HGS), pain free grip (PFG). Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (PR), Electrocardiogram (ECG), bilateral pulse oximetry (BPO). Effect sizes were calculated using Cohen's d coefficient, an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small. *Calculated by the authors of this review

5.1.4.1.2 CSM and temporo-mandibular joint mobility

Many studies have investigated the effects of treatments that target the neck to modulate pain in craniofacial regions (96). The application of treatments directed at the cervical spine may be beneficial in decreasing pain intensity, in increasing pressure pain thresholds (PPT) over the mastication muscles, and in increasing pain-free mouth opening (97). (Table I-3)

The relationship between mouth opening and CSM was studied in three articles. In the first article, George et al investigated the effect of CSM and manual therapy on normal mouth opening in asymptomatic subjects. The intervention applied to the CSM group comprised an upper cervical HVLA manipulation at the fixated side. No significant changes were found between the control and CSM groups (31). In contrast, Mansilla – Ferragut et al found a significant increase in active mouth opening after CSM. In this case, the authors investigated the effects of an upper cervical CSM on active mouth opening in women with mechanical neck pain; mouth opening was assessed pre-treatment and 5 minutes post-treatment, and a 3.5 mm difference between pre and post measurement was found. Large effect size was considered $d > 1.5$ (19). Oliveira et al, in healthy subjects, also found an immediate increase in mouth opening after CSM at the C1/C0 joint (1.5 mm), but the effect size was considered small (0.22). (32).

The results obtained in the studies analyzed here are controversial. The most significant increase of mouth opening was found in a study of symptomatic subjects

(19). Considering that the neck pain can decrease mouth opening, treatment with CSM in those subjects might improve mouth opening more significantly (97).

5.1.4.2 CSM and strength

Continuing with the possible effects of CSM on innervated related tissues, several authors investigated whether CSM can improve motor control of the upper limb. Three articles reported the effects of CSM on hand grip strength with different conclusions (Table I-3).

Humphries et al investigated the immediate effects of a single C5/C6 HVLA manipulation on right maximum handgrip in recreational basketball players. A marginal improvement (mean, 0.7 kg) was observed for maximum isometric handgrip strength, but this difference was not significant (effect size small (0.07) (30).

On the other hand, Botelho et al studied elite judo athletes; all cervical levels with dysfunction were manipulated three times in a three-week period. The authors found a significant increase in the left (10.53%) and right (16.82%) handgrip strengths (18).

In relation to symptomatic subjects, Fernandez Carnero et al, in a crossover study, investigated the effect of C5/C6 HVLA in patients with lateral epicondylalgia (LE) (98). The authors studied the maximum free pain handgrip strength (PFG) on the affected side and the maximum hand-grip strength on the other side (MGF). The application of HVLA manipulation at C5/C6 produced an immediate increase of PFG

on the affected side 37.8% [with a large effect size (0.78)]; on the unaffected side, the results obtained were similar to those obtained by Humphries et al and were not significant [(small effect size (0.05)] (30).

5.1.4.3 CSM and cardiovascular system

Bakris et al in their pilot study concluded that restoration of the atlas alignment using a HVLA technique once a week during 8 weeks in patients with hypertension stage 1, blood pressure (BP) descended more than placebo technique; the results obtained were similar to those obtained in studies using drug therapy. In contrast, heart rate was not reduced (99). Consistently, Knuston et al found a significant decrease in systolic BP of 10.3 mmHg (Effect size moderate (0.42)). However, the authors did not observe significant changes in heart rate or diastolic BP (20).

In contrast, Ward et al studied forty-eight healthy subjects; the CSM group intervention involved a C1 rotation technique. No statistically significant differences were shown for Electrocardiogram (ECG), bilateral pulse oximetry, and bilateral blood pressure any between-group comparisons of cardiovascular-dependent variables (100).

These different findings might be explained as follows: in the studies of Knutson et al (20) and Bakris et al (99) the dysfunction of the subjects was diagnosed; however, in the study of Ward et al (100), the subjects were randomized into four groups. In this last case, the CSM technique used might not have been the most appropriate. Perhaps if the study were conducted in hypertensive patients with real dysfunction and adequate

correction at C1 the results might have been different to those observed by Bakris et al (Table I-3).

5.2 Study II

5.2.1 Subjects

Figure II-1 shows the flowchart of this randomized clinical trial. A total of 40 potential subjects were assessed for eligibility, of which 4 persons were excluded for not meeting inclusion criteria. Thirty-six participants were enrolled and randomly into 3 groups: AMC5 (n=12), group MT (n=12), and group ST (n=12). The comparative test indicated no statistically significant differences ($p > 0.05$) in baseline characteristics between groups. (Table II-1).

	AMC5 Group	MT Group	ST Group	P value
Sex (% males)	50% (6/12)	41.66% (5/12)	58.33% (7/12)	AMC5-MT: 0.696 AMC5-ST: 0.696 MT-ST: 0.436
Age (years) (mean \pm SD)	30.50 \pm 3.11	30.75 \pm 3.98	31.16 \pm 2.24	AMC5-MT: 0.849 AMC5-ST: 0.613 MT-ST: 0.751
Weight (kg) (mean \pm SD)	66.22 \pm 14.36	62.18 \pm 7.89	67.66 \pm 7.19	AMC5-MT: 0.385 AMC5-ST: 0.766 MT-ST: 0.241
Height (cm) (Mean \pm SD)	170 \pm 7.52	168 \pm 8.04	172 \pm 3.65	AMC5-MT: 0.376 AMC5-ST: 0.584 MT-ST: 0.159
BMI (Mean \pm SD)	22.56 \pm 4.01	21.93 \pm 1.56	22.26 \pm 2.14	AMC5-MT: 0.610 AMC5-ST: 0.817

				MT-ST: 0.788
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Table II-1. *Baseline characteristics of the subjects included in the study. Pre and post values were expressed as mean (SD) three groups and all variables. Significant group interaction ($P < 0.05$). .*

5.2.2 Cervical flexion isometric peak force data

The changes in the isometric peak force of the cervical flexion in the MT group were significantly greater (-13.15%; $P=0.09$) than those observed in the C5 articular manipulation and sham technique groups (-7.8% and -1.7 %, respectively), but the effect size was considered moderate ($d=0.52$) (figure II-2) (table II-2).

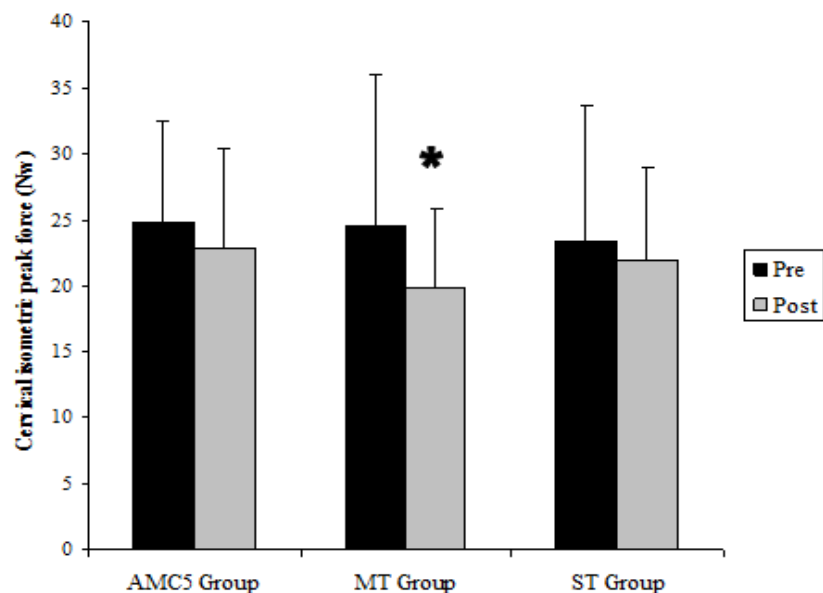


Figure II-2. *Cervical flexion isometric peak force results. Pre and post values are expressed as mean (Newtons) (SD) in three groups and all variables. * denotes p value < 0.1 with respect to other groups*

	n	Mean (SD)		From baseline to post intervention, Mean (95%CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Cervical flexion isometric peak force					
AMC5 Group	12	24.87 (7.54)	22.90 (7.48)	-7.81 (-15.05 to -0.55)	NA
MT Group	12	24.53 (11.47)	19.80 (6.08)	-13.15 (-25.73 to -0.57)	NA
ST Group	12	23.43 (10.22)	21.93 (7.08)	-1.74 (-11.58 to 8.10)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.41
ST Group vs MT Group	NA	NA	NA	NA	0.09
AMC5 Group vs ST Group	NA	NA	NA	NA	0.36

Table II-2. Cervical Flexion Isometric Peak Force results. Pre and post values are expressed as mean (Newtons) (SD) in three groups and all variables.

5.2.3 Biceps Brachial at rest EMG Data

No significant differences were observed in the changes in SCM in the left biceps brachial at rest among the three intervention groups. However, the changes in the RMS of the right biceps brachial at rest showed a tendency (P=0.14) to increase in the AMC5 group compared with the ST and MT groups, the effect size was considered large (d=0.91) (table II-3).

	n	Mean (SD)		From baseline to post intervention, Mean (95%CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Right Biceps Brachial					
AMC5 Group	12	91.95 (43.57)	146.96 (73.56)	54.08 (9.34 to 98.82)	NA
MT Group	12	115.40 (74.10)	135.34 (100.37)	23.45(-10.49 to 57.39)	NA
ST Group	12	108.13±95.73	126.24 (128.13)	11.21(-3.12 to 25.55)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.21*
ST Group vs MT Group	NA	NA	NA	NA	0.95*
AMC5 Group vs ST Group	NA	NA	NA	NA	0.14*
Left Biceps Brachial					
AMC5 Group	12	115.40 (93.79)	131.82 (56.66)	23.99 (-7.69 to 55.69)	NA
MT Group	12	136.33 (85.27)	148.99 (96.87)	5.67 (-16.37 to 27.72)	NA
ST Group	12	11.92 (64.01)	150.02 (135.20)	23.02 (-0.74 to 46.79)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.27

ST Group vs MT Group	NA	NA	NA	NA	0.30
AMC5 Group vs ST Group	NA	NA	NA	NA	0.95

Table II-3. *Biceps Brachial EMG RMS at rest results. Pre and post values are expressed as mean (mV) (SD) three groups and all variables. Significant group interaction ($P < 0.01$). * p -values were drawn from nonparametrical tests.*

5.2.4 Cervical Range of Motion Data

Immediately after all manipulations, no significance differences were observed in flexion, right rotation, or left and right side bending range changes in the three intervention groups. However, the changes in extension range in the MT and AMC5 groups were significantly greater (10.4% and 6.9%, respectively; $p=0.01$) than those observed in the ST group (-3.37 %), furthermore the effect size for the MT group was considered large ($d=0.88$). In the left rotation range, the MT group effect size was considered large (1.07). The changes in the MT group were significantly greater (12.2%; $p=0.01$) than those observed in the AMC5 and ST groups (4.03% and 5.8%, respectively) (Table II-4).

	n	Mean (SD)		From baseline to post intervention, Mean (95%CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Flexion					
AMC5 Group	12	60.75 (11.96)	63.50 (10.02)	3.40 (-2.56 to 9.36)	NA
MT Group	12	61.66 (11.11)	64.50 (11.18)	5.16 (-1.19 to 11.52)	NA
ST Group	12	60.66 (11.79)	61.00 (11.29)	1.59 (-6.74 to 9.91)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.70
ST Group vs MT Group	NA	NA	NA	NA	0.43
AMC5 Group vs ST Group	NA	NA	NA	NA	0.69
Extension					
AMC5 Group	12	73.83 (14.95)	78.33 (13.15)	6.98 (1.35 to 12.60)	NA
MT Group	12	68.83 (6.52)	75.83 (9.24)	10.44 (3.11 to 17.77)	NA
ST Group	12	70.80 (7.55)	68.00 (8.79)	-3.37 (-13.14 to 6.39)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.46
ST Group vs MT Group	NA	NA	NA	NA	0.08

AMC5 Group vs ST Group	NA	NA	NA	NA	0.04
Right Side Bending					
AMC5 Group	12	45.41 (12.10)	47.50 (8.82)	3.62 (-3.30 to 10.54)	NA
MT Group	12	43.16 (6.11)	46.50 (7.48)	7.65 (3.14 to 12.15)	NA
ST Group	12	45.00 (7.74)	48.00 (11.56)	5.98 (-1.67 to 13.62)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.34
ST Group vs MT Group	NA	NA	NA	NA	0.68
AMC5 Group vs ST Group	NA	NA	NA	NA	0.57
Left Side Bending					
AMC5 Group	12	44.16 (11.70)	46.50 (9.42)	6.90 (1.55 to 12.25)	NA
MT Group	12	44.16 (7.83)	48.33 (7.66)	10.05 (4.66 to 15.44)	NA
ST Group	12	45.83 (6.68)	50.00 (10.23)	5.85 (-0.56 to 12.27)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.39
ST Group vs MT Group	NA	NA	NA	NA	0.26
AMC5 Group vs ST Group	NA	NA	NA	NA	0.78
Right Rotation					
AMC5 Group	12	68.67 (13.62)	77.50 (10.48)	8.70 (3.60 to 13.78)	NA
MT Group	12	71.16 (10.17)	77.16 (6.05)	7.66 (1.40 to 13.92)	NA
ST Group	12	71.83 (7.30)	76.66 (7.30)	7.09 (1.42 to 12.74)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.78
ST Group vs MT Group	NA	NA	NA	NA	0.87
AMC5 Group vs ST Group	NA	NA	NA	NA	0.66
Left Rotation					
AMC5 Group	12	72.33 (12.38)	76.50 (12.56)	4.03 (1.91 to 6.14)	NA
MT Group	12	68.00 (8.35)	75.83 (6.17)	12.25 (6.51 to 17.98)	NA
ST Group	12	70.16 (6.17)	74.33 (10.12)	5.81 (-0.67 to 12.28)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.009*
ST Group vs MT Group	NA	NA	NA	NA	0.10*
AMC5 Group vs ST Group	NA	NA	NA	NA	0.32*

Table II-4. Summary Cervical Range of Motion Results. Pre and post values are expressed as the mean (degrees) (SD) of the three groups and all variables. Significant group interaction ($P < 0.01$). * p -values were drawn from non-parametrical tests.

5.2.5 Cranio-cervical Flexion Test

After all manipulations, no significant differences were observed in the RMS of the both sides of SCM during the cranio-cervical flexion test changes in the three intervention groups (Figure II-3). Also, large effect size was not found in any group (Range from $d = 0.16$ to $d = 0.54$) (Table II-5).

Finally, no adverse events were reported over the course of this investigation.

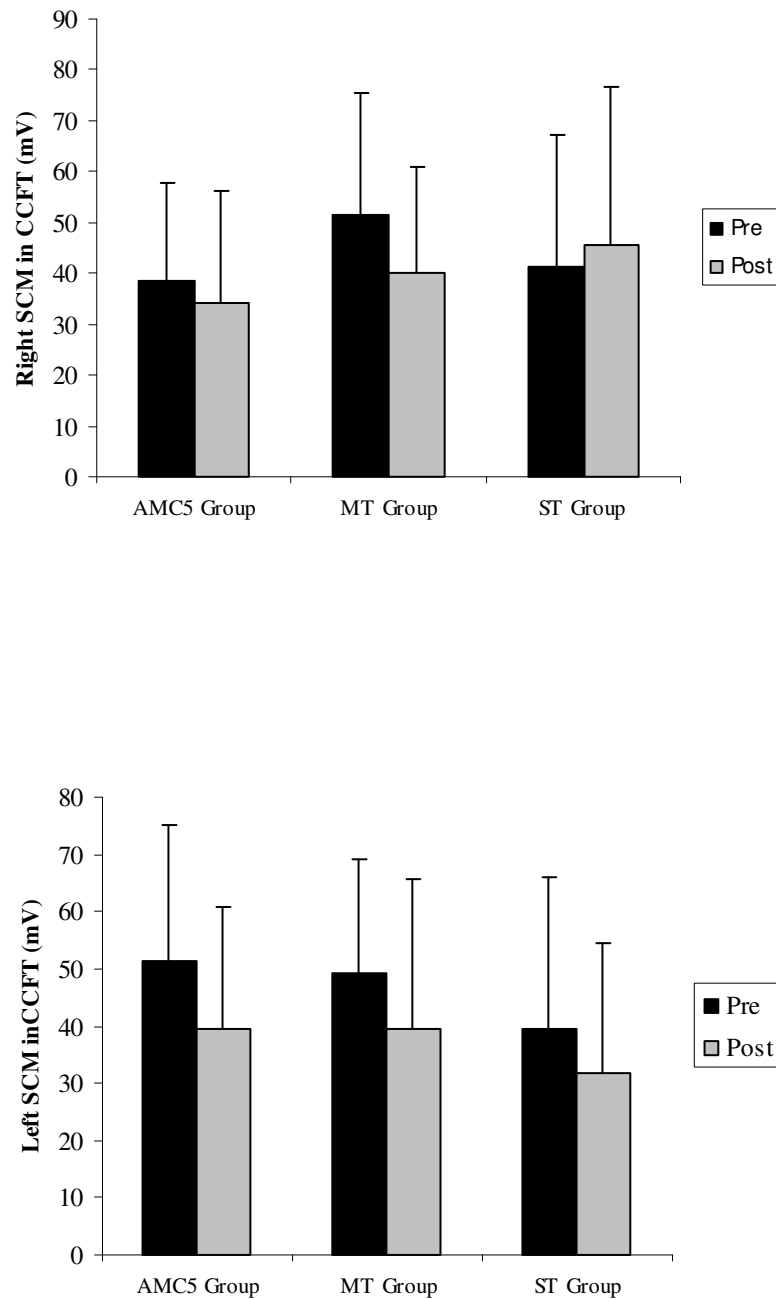


Figure II-3. *Cranio-cervical flexion test results of both sides. Pre and post values are expressed as the mean (mV) (SD) of the three groups and all variables.*

Cranio-cervical Flexion Test	n	Mean (SD)		From baseline to post intervention, Mean (95%CI)	
		Baseline	Post intervention	Within-Group Change	Between-Group Difference in Change
Right SCM					
AMC5 Group	12	38.57 (19.11)	34.34 (21.79)	-7.30 (-33.64 to 19.04)	NA
MT Group	12	51.51 (23.92)	40.08 (20.88)	-19.20 (-48.99 to 10.59)	NA
ST Group	12	41.27 (25.88)	45.73 (30.93)	8.23 (-26.53 to 42.99)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.53
ST Group vs MT Group	NA	NA	NA	NA	0.17
AMC5 Group vs ST Group	NA	NA	NA	NA	0.41
Left SCM					
AMC5 Group	12	51.51 (23.50)	39.46 (21.50)	-16.90 (-44.04 to 10.23)	NA
MT Group	12	49.18 (19.98)	39.60 (26.05)	-12.75 (-54.37 to 28.86)	NA
ST Group	12	39.50 (26.52)	31.80 (22.66)	-3.70 (-43.44 to 36.04)	NA
AMC5 Group vs MT Group	NA	NA	NA	NA	0.85
ST Group vs MT Group	NA	NA	NA	NA	0.69
AMC5 Group vs ST Group	NA	NA	NA	NA	0.55

Table II-5. Summary Cranio-cervical Flexion Test Results. Pre and post values are expressed as the mean (mV) (SD) of the three groups and all variables.

5.2.6 Discussion

The findings of the present study suggest that MT manipulation immediately induces a decrease in the isometric strength peak in the cervical flexion as well as a meaningful increase of cervical spine extension and left rotation range of motion. These results show the importance of a previous evaluation of vertebral dysfunction and suggest that a manipulation treatment based on a previous evaluation enhances the effects of an articular manipulation on the C5 compared to a sham technique. There are few studies comparing the effects of a treatment based on a previous standardized diagnostic screening to both an isolated manipulation of the C5 and a control group that used a previously studied sham technique (82, 101).

Maximal voluntary isometric strength performance during cervical flexion provides information on the activity of the superficial flexor SCM and scalene muscles (63). In the present study, the manipulation group suffered more inhibition than the other groups. Although this result might at first seem questionable, it could be related to an activation of the deep flexors muscles and therefore, to a manipulation-induced decrease in the surface flexors activation (65, 76).

Immediate effects on extension and left rotation range of motion in the manipulation group were noticeably greater than those observed in the C5 and placebo groups. The extension ROM showed significant changes, and improvements in the C5 group were also significant compared to the placebo group. These results are within our expectations because the correction technique of C5 is focused on improving extension. However, the effect size of MT group in extension was considered large ($d=1.07$), while the AMC5 group was considered moderate ($d=0.32$).

There were movements that did not improve with the manipulation group, including right and left side bending, right rotation and flexion. Regarding both side bendings, the non-improvement may be due to the measures in the pre-treatment intervention, which showed 44.52° right side bending and 44.72° left side bending. These measurements are already similar to normal (102), and therefore, any gain would be minimal and insignificant. If symptomatic subjects had been studied, the results may have been similar to those of Martinez - Segura and cols. (16). These authors found mobility improvement after middle cervical spine manipulation in symptomatic patients, who showed significant improvements in flexion, extension, and both side bendings but not in rotation. This last result could be explained by the absence of

limitation in rotation movement of the subjects or by not having included the manipulations of the C1, C2, C7 and upper thoracic segments in the examination protocol.

In terms of right rotation and flexion, we suggest that the results of our study can be explained by the absence of treatment of the temporomandibular joint (TMJ). Von Piekartz and cols. (50) emphasized the relationship between TMJ dysfunction and upper cervical spine dysfunctions in terms of decreased flexion and particularly rotation movements. On the other hand, Kayser and cols. (35), showed the importance of segment C0, which we did not take into account, and this may have caused the mobility correction to be incomplete. However, we did take into account upper thoracic dysfunction because this area is considered to be the seat of dysfunction affecting cervical mobility (78, 103).

In a study of symptomatic patients suffering from headaches, Whittingham and cols. (104) reported improvements in both rotation and side bending. In that study, the authors did not considering flexion or extension because they related those to the weight of the head.

In the EMG at rest of the studied muscles, there was not significant change in any of the groups before and after the interventions and only an increase in the signal in the right brachial biceps after manipulation of the C5, this increase was not significant but had a large effect size (0.91). These data could be related to those reflected in a study by Dunning and Rushton that studied the effects of a manipulation technique at the C5-C6 level. The authors demonstrate an increased signal of RMS at rest in both

biceps after applying an HVLA manipulation in asymptomatic patients (26). These results can be explained because after spine manipulation, the alpha motor neuron can facilitate increased muscle activity at rest or decrease inhibition (105). In addition, in that study, the C5 was manipulated to the right and the defect was in the ipsilateral biceps. This result was in agreement with Symons et al., who analyzed the response after mechanical manipulation using an activator device and found responses only at the ipsilateral level, in this case C2-C3, and they analyzed the splenius capitis and the upper trapezius in asymptomatic male subjects (106). This is important because patients with chronic neck pain usually show an inhibition of the brachial biceps, and manipulation techniques on the C5 may minimize the inhibition, as noted by Suter et al (107).

On the other hand, there were not significant changes in the SCM EMG signal during the cranio-cervical flexion test in three groups. This test is very important for its clinical application because the efficiency of cervical deep flexor muscles is related to cervical spine pathology (65, 76). Sterling and cols. (108) referred to a significant effect after the application of an HVLA technique at the C5-C6 level, this phenomenon could be explained by the reflex facilitation of the deep flexor of the neck which can prevent surface musculature from contracting during the test. However, we not achieved any significant results, this difference may be related to the fact that Sterling et al. used symptomatic subjects and our study used asymptomatic ones. Maybe it is possible that the manipulation of the segments in dysfunction improved the cervical proprioception more than an isolated manipulation would have, particularly because the origins of cervical deep muscles do not focus only on the C5-C6 level but further investigation is needed in symptomatic subjects.

More studies comparing the immediate effects of an isolated manipulation and a manipulation treatment based on a previous evaluation (MT) are needed, especially on symptomatic subjects. Also more research is needed to investigate the immediate effects of cervical HVLA manipulations.

However, our findings from the present study are limited but support the feasibility for a future definitive trial. The study was performed on asymptomatic subjects, and this type of subject will be less influenced by possible limitations in mobility or strength. The results may not be as significant as expected. Given the high cut-off we chose for our significance level ($p < 0.1$) and the important number of tests that were done, we cannot exclude that some of our results are solely due to random error. This study is exploratory and therefore will need replication before conclusions can be drawn on true effects of manipulation.

The relatively small sample size of the present study is a further limitation which increases the risk of statistical type 2 errors, i.e. we may have failed to detect true changes that would have been statistically significant with a larger sample size. Having many different outcomes measures (about 10 in the present study) increases the risk of statistical type 1 errors, i.e. significant findings due to chance. However, adjusting for multiple outcomes – e.g. by Bonferroni correction – causes overly conservative P-values (43). Thus, the results of the present study should be interpreted with limitations in mind and can therefore be considered exploratory in nature. Future large scale studies should confirm the present findings before solid recommendations can be provided. The future well-designed, adequately powered trial will require a larger sample size and long-term follow-up periods to confirm the effect of HVLA manipulations.

We cannot say with certainty that results observed after manipulation at the C5-C6 level are unique to this segment, and there are studies that suggest a low specificity of the technique in question (109). In addition, the strength and speed of the impulse during the procedure is not reproducible, and these variations may alter the effects (105).

Fine wire EMG and transcranial magnetic stimulation (TMS) might make it easier to detect subtle changes in motor function within deeper muscles. TMS would make it possible to provide a controlled impulse from the motor region and the muscular response read by the fine wire would be more specific.

5.3 Study III

5.3.1 Subjects

Of the 27 patients assessed for eligibility, 92% (25 of 27) were eligible for inclusion, enrolled in the study, and randomly divided into 2 groups: MT (n=12) and CCF (n=13) (Fig. III-1). There were no significant differences in baseline characteristics (Table III-1) between the two groups of participants. In both groups, all the participants had temporo-mandibular joint, cervical spine and upper thoracic spine dysfunctions. No adverse events were reported, and all participants who were randomly assigned to a group completed the study.

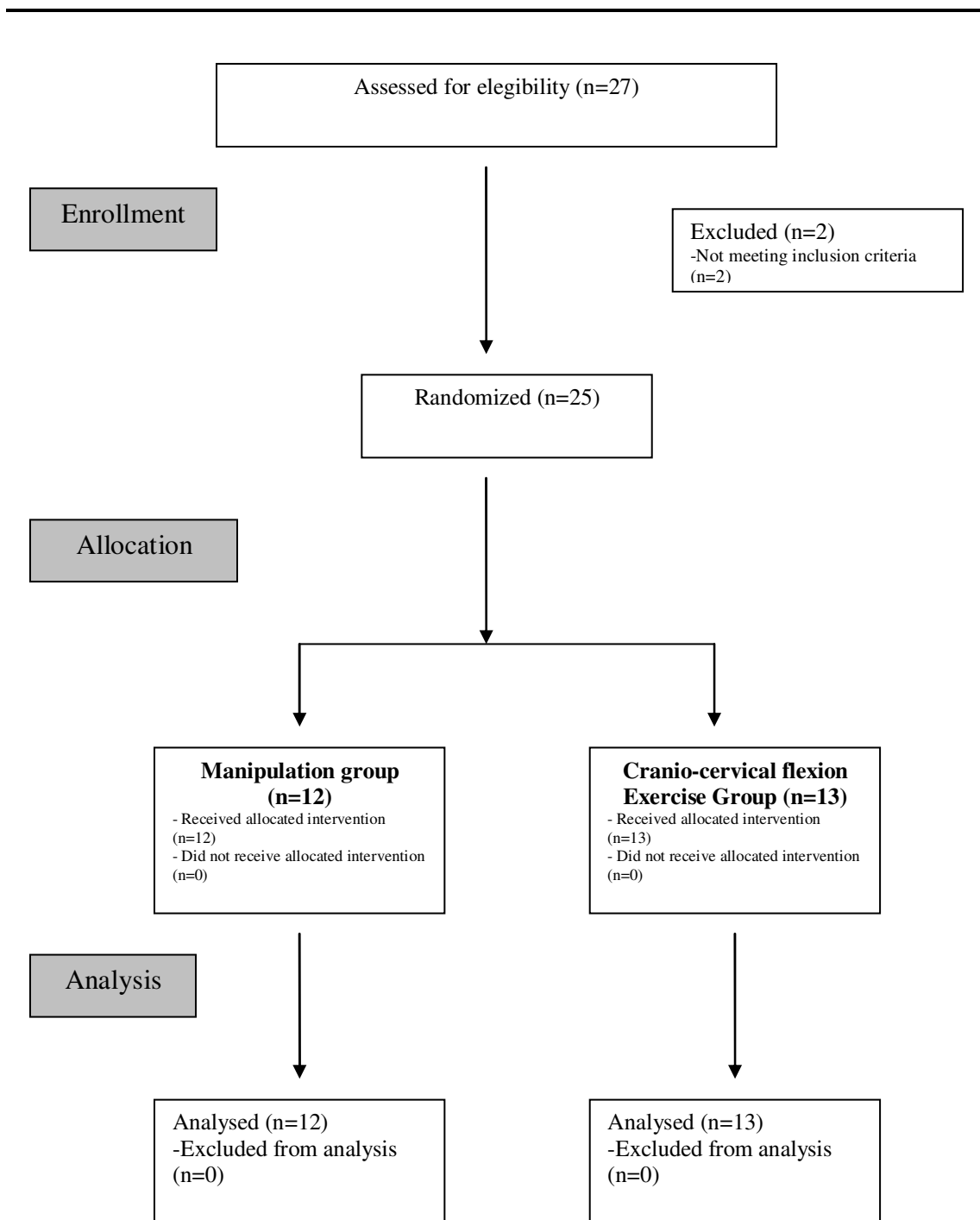


Figure III-1. Flow of participants through the study.

	MT Group	CCF Group	P value
Sex (% females)	100% (12/12)	100% (13/13)	XXX
Age (years) (mean \pm SD)	31.33 (1.83)	34.00 (1.80)	0.311
Weight (kg) (mean \pm SD)	58.83 (1.40)	65.11 (4.79)	0.318
Height (cm) (Mean \pm SD)	1.63 (0.22)	1.64 (0.14)	0.780
BMI (Mean \pm SD)	21.99 (0.86)	24.04 (1.71)	0.376

Table III-1. Baseline characteristics of the subjects included in the study. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P < 0.05$).).

5.3.2 VAS during ROM measurement

Immediately following both interventions, significant differences in VAS scores during ROM measurement were found within the manipulation and craniocervical flexion protocol groups ($p=0.004$ and $p=0.015$, respectively); however, while the effect size was considered large in the MT group ($d=1.17$; 0.37-1.88), in the CCF group the effect size was considered moderate ($d=0.64$; -0.07-1.31). No significant differences were observed between groups ($p=0.196$) (Table III-2) (Figure III-2).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
VAS ROM					
MT Group (n=12)	61.18(5.65)	40.27(5.11)	1.17(0.37 to 1.88)	0.004	0.196
CCF Group (n=13)	52.25(5.72)	40.58(4.71)	0.64(-0.07 to 1.31)	0.015	XXX

Table III-2. Summary VAS at ROM Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P < 0.05$).). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small.

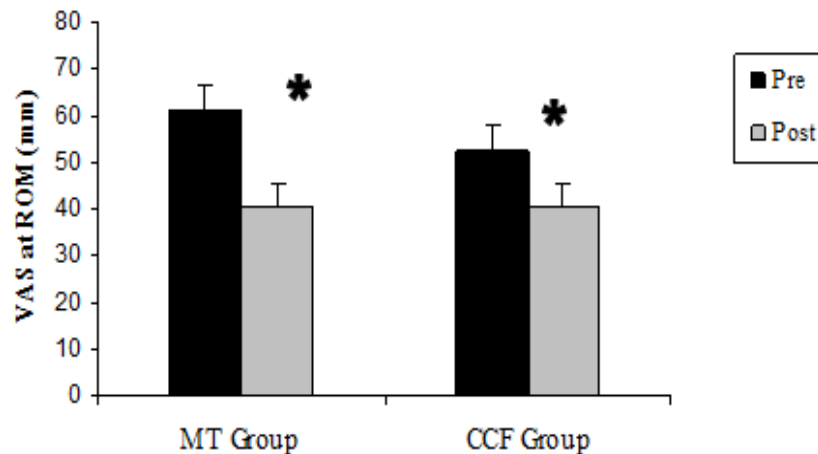


Figure III-2. VAS at ROM Results. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

5.3.3 Cervical Range of Motion Data

In the MT group, pre- and post- intervention flexion ($p=0.001$), right side-bending ($p=0.002$) and left rotation ($p=0.005$) differed significantly; additionally, the effect sizes were considered large for flexion ($d=1.69$; 0.82-2.44) and left rotation ($d=0.78$; 0.08-1.44). However, only flexion ($p=0.026$) and extension ($p=0.040$) changed significantly post-intervention in the CCF group, and only the flexion effect size was considered large ($d=0.94$; 0.23-1.59). The between-group differences in extension and right side-bending range of motion were found to be significant ($p=0.019$ and $p=0.012$, respectively) (Table III-3) (Figure III-3 and III-4).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
Flexion					
MT Group (n=12)	32.90(2.50)	50.91(3.77)	1.69(0.82 to 2.44)	0.001	0.106
CCF Group (n=13)	35.79(2.63)	44.76(2.64)	0.94(0.23 to 1.59)	0.026	XXX
Extension					

MT Group (n=12)	55.55(3.54)	60.77(3.42)	0.43(-0.26 to 1.10)	0.063	0.019
CCF Group (n=13)	63.94(3.25)	62.18(6.16)	0.16(-0.54 to 0.86)	0.040	XXX
Right Side Bending					
MT Group (n=12)	39.21(1.95)	43.09(2.43)	0.53(-0.20 to 1.22)	0.002	0.012
CCF Group (n=13)	40.06(1.65)	40.91(1.55)	0.16 (-0.55 to 0.86)	0.211	XXX
Left Side Bending					
MT Group (n=12)	37.94(2.06)	40.44(1.73)	0.38(-0.31 to 1.04)	0.126	0.263
CCF Group (n=13)	38.91(1.94)	39.39(1.98)	0.07(-0.63 to 0.77)	0.556	XXX
Right Rotation					
MT Group (n=12)	56.44(1.99)	61.44(2.38)	0.66(-0.06 to 1.32)	0.063	0.136
CCF Group (n=13)	59.02(3.52)	59.95(3.76)	0.07(-0.58 to 0.71)	0.463	XXX
Left Rotation					
MT Group (n=12)	54.44(2.45)	61.94(3.07)	0.78(0.08 to 1.44)	0.005	0.028
CCF Group (n=13)	55.23(2.28)	57.02(2.55)	0.21(-0.46 to 0.86)	0.184	XXX

Table III-3. Summary Cervical Range of Motion Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P < 0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small.

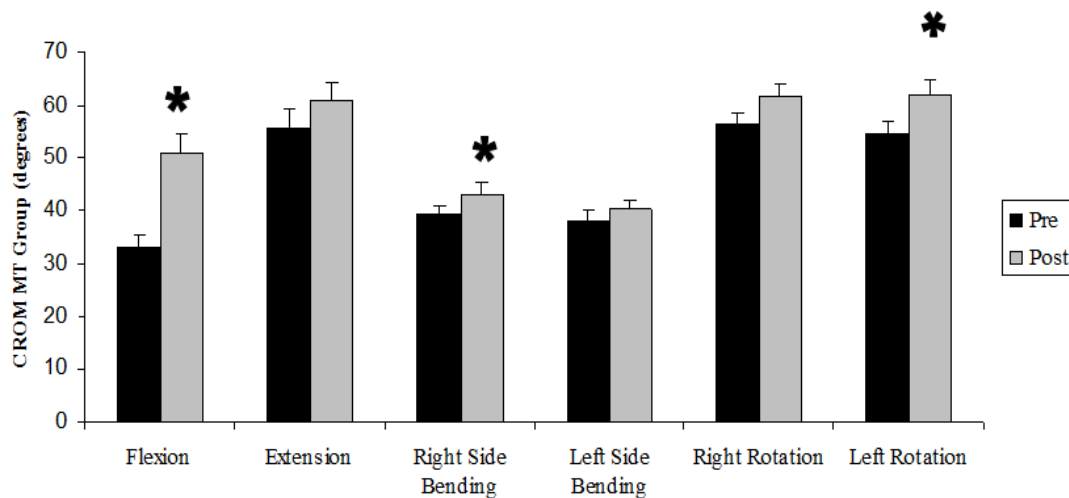


Figure III-3. Cervical Range of Motion Results MT Group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

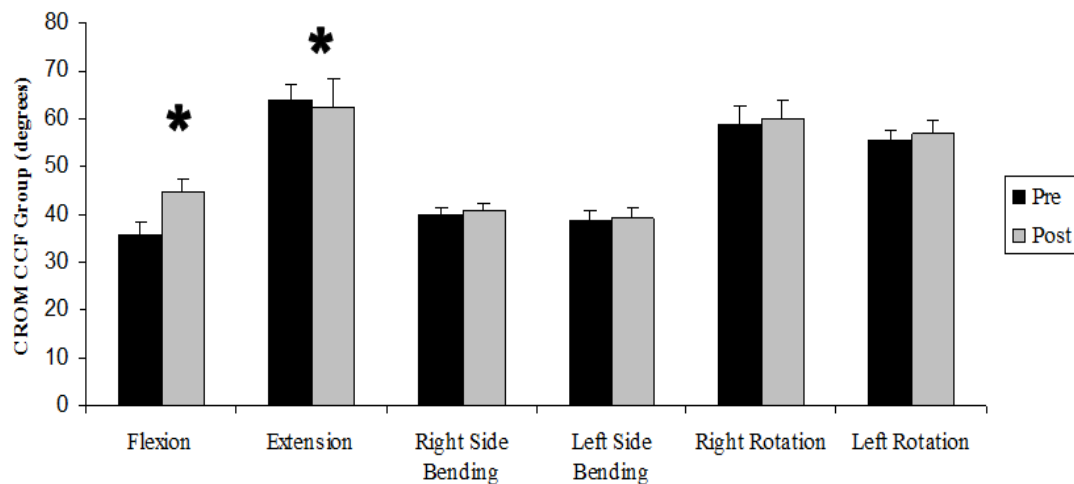


Figure III-4. Cervical Range of Motion Results CCF Group. *Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.*

5.3.4 Pressure pain thresholds

Significant changes were observed in upper trapezius PPT following both interventions (MT group $p=0.043$ and CCF group $p=0.005$); in addition, significant post-intervention differences were identified in C5 PPT in the exercise group ($p=0.020$). For these three findings, the effect sizes were considered moderate ($d=0.62$ (-0.09-1.28), $d=0.65$ (-0.03-1.29) and $d=0.54$ (-0.13-1.18), respectively). No differences were identified between groups. No significant changes were observed in the C1 and gluteus medius PPT after accounting for time and group interactions (Table III-4) (Figure III-5 and III-6).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
PPT C1					
MT Group (n=12)	1.31(0.04)	1.35(0.05)	0.26(-0.42 to 0.92)	0.456	0.788
CCF Group (n=13)	1.25(0.06)	1.27(0.09)	0.09(-0.56 to 0.73)	0.640	XXX
PPT C5					

MT Group (n=12)	1.30(0.07)	1.45(0.07)	0.58(-0.12 to 1.25)	0.076	0.991
CCF Group (n=13)	1.27(0.06)	1.42(0.08)	0.54(-0.13 to 1.18)	0.020	XXX
PPT Upper Trapezius					
MT Group (n=12)	1.23(0.06)	1.36(0.06)	0.62(-0.09 to 1.28)	0.043	0.554
CCF Group (n=13)	1.25(0.06)	1.43(0.08)	0.65(-0.03 to 1.29)	0.005	XXX
PPT Gluteus Medius					
MT Group (n=12)	2.15(0.15)	2.15(0.14)	0.00 (-0.74 to 0.74)	1.000	0.994
CCF Group (n=13)	2.30(0.17)	2.30(0.17)	0.00(-0.65 to 0.64)	0.993	XXX

Table III-4. Summary Pressure Pain Thresholds Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P < 0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small.

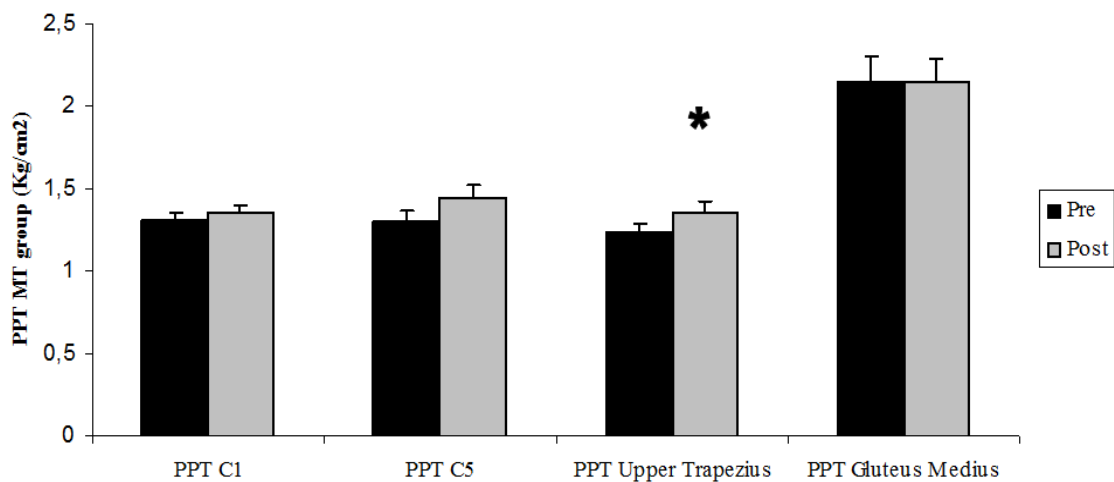


Figure III-5. Pressure Pain Thresholds Results MT Group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

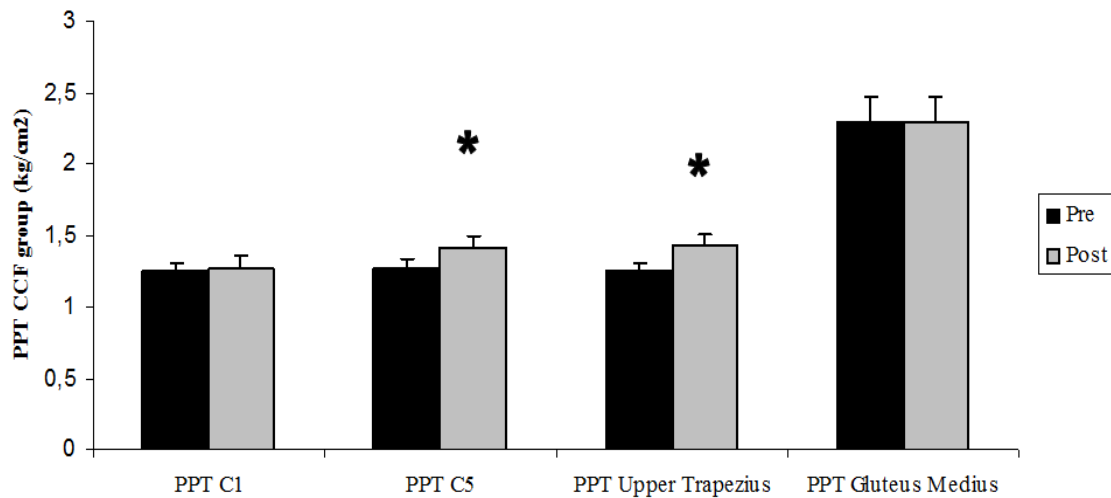


Figure III-6. Pressure Pain Thresholds Results CCF Group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

5.3.5 Craniocervical Flexion Test

No significant pre-post differences were observed in the RMS value of the EMG signal detected at the SCM during the five stages of the craniocervical flexion test in either group. However, statistical analysis indicated a moderate effect size ($d=0.60$; -0.14 - 1.30) during the second stage of the CCFT exercise in the MT group. No significant differences were observed between groups (Table III-5) (Figure III-7 and III-8).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
First stage					
MT Group (n=12)	7.13(2.28)	10.70(4.36)	0.32(-0.43 to 1.05)	0.372	0.187
CCF Group (n=13)	12.35(3.82)	8.95(4.24)	0.24(-0.44 to 0.91)	0.340	XXX
Second stage					
MT Group (n=12)	20.39(6.23)	10.01(3.89)	0.60(-0.14 to 1.30)	0.227	0.151
CCF Group (n=13)	10.54(2.93)	12.00(2.94)	0.14(-0.53 to 0.81)	0.434	XXX

Third stage					
MT Group (n=12)	17.94(6.85)	20.52(5.15)	0.13(-0.61 to 0.87)	0.602	0.950
CCF Group (n=13)	19.97(2.77)	23.07(4.46)	0.28(-0.51 to 1.04)	0.660	XXX
Fourth stage					
MT Group (n=12)	27.02(7.83)	21.55(5.20)	0.24(-0.44 to 0.90)	0.471	0.364
CCF Group (n=13)	21.24(3.37)	25.34(6.44)	0.23(-0.45 to 0.90)	0.585	XXX
Fifth stage					
MT Group (n=12)	32.07(6.73)	26.89(7.57)	0.22(-0.49 to 0.91)	0.444	0.420
CCF Group (n=13)	26.82(4.97)	28.37(3.92)	0.10 (-0.60 to 0.80)	0.761	XXX

Table III-5. Summary SCM activation during TFCC Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P < 0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small.

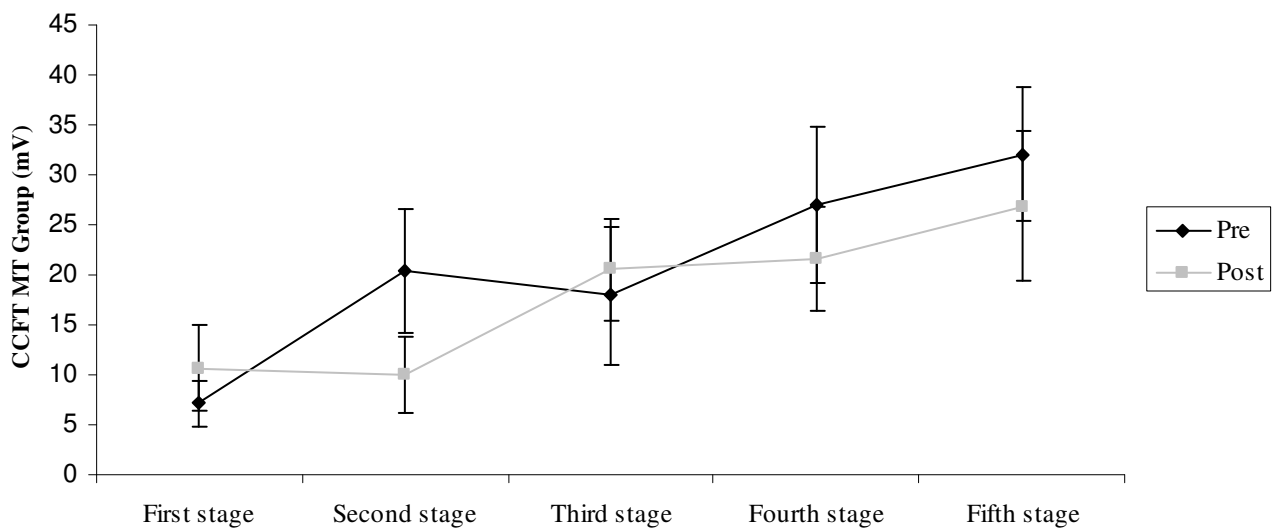


Figure III-7. SCM activation during TFCC Results MT Group. Pre and post values were expressed as mean (SE) two groups and all variables.

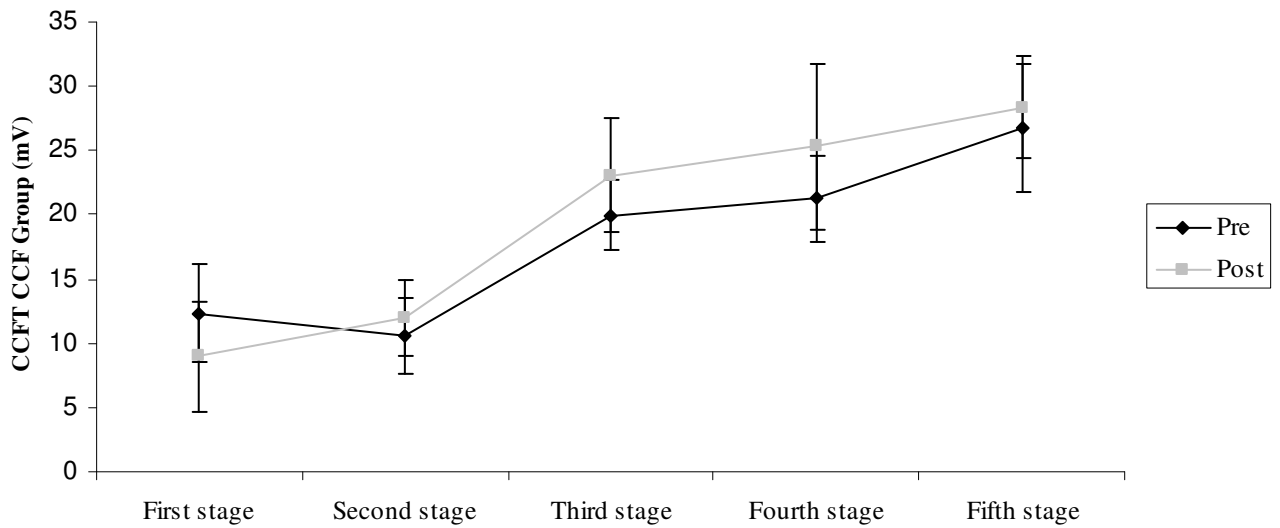


Figure III-8. SCM activation during TFCC Results CCF Group. *Pre and post values were expressed as mean (SE) two groups and all variables.*

Finally, no adverse events were reported over the course of this investigation.

5.3.6 Discussion

The main purpose of this study was to compare the immediate effects of manipulation and exercise on pain and range of motion on chronic neck pain patients. Immediately following both interventions, significant differences were identified within the manipulation and craniocervical flexion exercise groups. Similar to our results, studies using similar protocols (53) have reported significant changes in pain upon movement in patients enrolled in CCF groups but not in patients enrolled in mobilization groups. This difference could be explained by the fact that the approach used in manipulation groups has previously only included manipulation of the upper cervical spine, while our approach was multi-segmental. Saavedra and colleagues (47)

reported that in chronic mechanical neck pain patients, a greater reduction in NDI was observed when both the cervical and thoracic spine were manipulated compared to manipulation of the cervical spine alone. While the manual interventions have differed between studies, the effects of both interventions (manipulation or mobilization) on pain have usually been similar (110). The differences between groups were not significant in this study; however, while the effect size for VAS score during ROM measurement was considered large in the MT group ($d=1.17$), in the CCF group, the effect size for this indicator was considered moderate ($d=0.64$). Furthermore, some authors have reported identifying a large effect size ($d>0.8$) using the CCF protocol employed in this study (51). Isometric contractions of higher intensity (40-50% of max) may yield better results (52).

The mechanism of analgesia following MT remains unclear (105). Spinal manipulation may alter sensorimotor integration (21, 111), activating descending inhibitory pathways in the dorsal periaqueductal gray area of the midbrain, (108), which has been reported to be associated with endogen analgesic modulation in humans (112), or activating the large diameter motor neurons that block the nociceptive stimulus (gate control theory) (113). Given the evidence in the literature that was previously discussed in the introduction and our results, the analgesic effect observed in association with the MT protocol was strong. However, further research is needed to confirm these mechanisms, especially in subjects with chronic mechanical neck pain during and after participating in MT protocols.

Regarding cervical ROM, in the MT group, significant pre-post differences were observed in flexion, right side-bending and left rotation. These results were similar to

those of other studies identified in the literature (39)(114). However, it is difficult to compare improvement in CROM between various studies because the improvement observed could be associated with the limitations of movement studied.

In the CCF group, only the flexion effect size was considered large ($d=0.94$). This finding may have been identified because the biomechanics of the CCF exercise specifically involve upper cervical spine flexion action, and therefore, this movement could be facilitated (51). The between -group differences observed in extension and right side-bending range of motion were considered significant, and the effect size was considered large for flexion and left rotation ($d=0.78$ (0.08-1.44)); these findings clearly indicated that the manipulation intervention was more effective than CCF exercises in improving CROM.

Significant post-intervention differences were identified in C5 PPT in the CCF group. This finding is in accordance with the results of the study conducted by Lluch and colleagues (115), which also identified significant post-intervention changes in C5 PPT in their MT group. In our study, the post-intervention C5 PPT differences observed in the MT group were not significant but exhibited a tendency to increase after the intervention ($p=0.076$). Similar tendencies have also reported following manual intervention by other authors (42)(116). Unlike in our study, Lluch and colleagues (117) also identified significant changes in suboccipital PPT following manual and exercise interventions. This finding may be explained by the evaluation of PPT at different suboccipital sites, as O'Leary and colleagues reported that the C2/3 segment was identified as the most symptomatic cervical segment in their study of chronic pain (51). However, significant differences were observed in upper trapezius PPT following both

interventions. In our study, greater improvements in PPT were found in the most painful (upper trapezius) area, suggesting that it may be possible that a relationship exists between the level of pain and pain improvement. In future studies, we suggest that only the painful segments should be evaluated instead of all of the segments included in the full PPT protocol (51).

No significant pre-post differences were observed in the RMS value of the EMG signal detected at the SCM during the five stages of the craniocervical flexion test in the MT group. However, statistical analysis indicated a moderate effect size ($d=0.60$) during the second stage of the CCFT in the MT group. This result was in the line with that of the study conducted by Sterling and colleagues (108), who reported observing a decrease in SCM signals after C5/6 mobilization during the lower stages of the CCFT (22-24-26 mmHg). That study reported a post-intervention effect on motor control in the cervical region. Regarding this finding, it must be emphasized that the neck pain of the subjects included in the study conducted by Sterling and colleagues primarily originated from the C5/6 segment, and it is possible that within a population with more widespread neck pain, these results may be different. In our opinion, the specificity of neck pain treatment may be low; for that reason, it is recommended that the temporomandibular joint be included in MT protocols because TMJ dysfunction may be associated with increased SCM signals during the CCFT (56, 118). Additionally, it is possible that rhythmic mobilization was associated with a greater increase in the activity of alpha motor neurons than were manipulation techniques, facilitating the motor activity of deep flexor muscles and improving CCFT results.

Furthermore, no significant pre-post changes were observed in the CCF exercise intervention group. The results were in opposition with those reported by Lluch and colleagues (117). These findings reveal that although the exercise protocol used was effective in reducing pain, it may have been less effective at activating the deep flexors muscles during the CCFT. However, Jull and colleagues identified significant changes in their CCFT group after 6 weeks of using this exercise protocol two times a day (60).

There are several limitations to this study. A primary limitation of this study was the lack of a true control group. The absence of a defined control group may result in difficulties deriving precise conclusions regarding the effects of both interventions. Furthermore, the statistical analyses in this study were not adjusted for multiple comparisons. Additionally, the significance level was set at 5%, which could promote the identification of false positive results (statistical type I error). Third, false negatives could have arisen because the sample size was small (statistical type II error). More studies with larger sample sizes comparing the immediate effects of HVLA manipulation and exercise are needed.

5.4 Study IV

5.4.1 Subjects

Of the 28 patients deemed eligible for inclusion, 96% (27 of 28) were enrolled and randomly divided into 2 groups: the MT group (n=13) and the HE group (n=14; Fig. IV-1). There were no significant differences in the subjects' baseline characteristics (Table IV-1) between the two groups. No adverse events were reported, and all of the participants who were randomly assigned to a group completed the study.

	MT Group	HE Group	P value
Sex (% females)	100% (13/13)	100% (14/14)	XXX
Age (years) (mean \pm SD)	32.15 (1.87)	34.35 (1.71)	0.393
Weight (kg) (mean \pm SD)	64.71 (5.99)	67.10 (4.72)	0.756
Height (cm) (Mean \pm SD)	1.64 (0.01)	1.65 (0.01)	0.779
BMI (Mean \pm SD)	23.91 (2.05)	24.58 (1.62)	0.802

Table IV-1. *Baseline characteristics of the subjects included in the study. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P < 0.05$).).*

5.4.2 Neck Disability Index

After one week, both interventions (manipulation and home exercises), showed significant ant differences ($p=0.000$ in both cases), and the changes were not significantly better in the manipulation group ($-43.4\% \pm 21.82$) than in the home exercise group (-39.72 ± 22.68). Additionally, the Cohen's d showed large effects ($d=1.36$; $0.61-2.03$) in both the manipulation and the exercise group ($d=1.43$; $0.70-$

2.09); however, no differences were observed between the groups ($p=0.909$) (Table IV-2) (Figure IV-2 and IV-3).

5.4.3 Visual analogue scale

Significant changes were observed in both groups between the pre- and post-intervention measurements ($p=0.001$ in both cases), and the effect size was large ($d=1.11$; 0.39-1.77 in the manipulation group and 1.52; 0.77-2.17 in the home exercise group), but no differences were observed between the groups ($p=0.908$) (Table IV-2) (Figure IV-2 and IV-3).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
NDI					
MT Group (n=13)	13.07(1.09)	7.46(1.19)	1.36(0.61 to 2.03)	0.000	0.909
HE Group (n=14)	14.14(1.15)	8.35(0.99)	1.43(0.70 to 2.09)	0.000	XXX
VAS					
MT Group (n=13)	48.23(4.30)	25.84(6.61)	1.11(0.39 to 1.77)	0.001	0.958
HE Group (n=14)	53.85(3.64)	31.85(4.10)	1.52(0.77 to 2.17)	0.001	XXX

Table IV-2. Summary Neck Disability and VAS Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P<0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small.

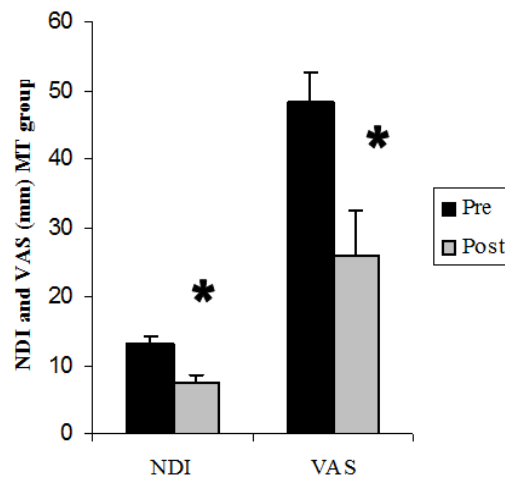


Figure IV-2. NDI and VAS results, MT group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

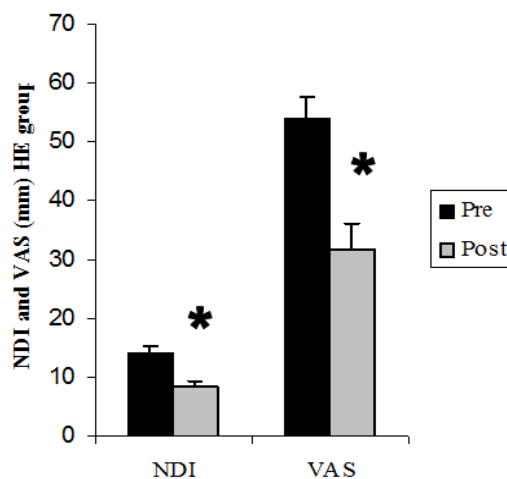


Figure IV-3. NDI and VAS results, HE group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

5.4.4 Cervical Range of Motion Data

One week after the interventions, no significance differences were observed in extension or left and right side bending range between the two intervention groups. However, the changes in flexion, right rotation and left rotation range in the MT and HE

groups were significant ($p=0.004$, $p=0.006$ and $p=0.000$, respectively, in the MT group and $p=0.016$, $p=0.016$ and $p=0.006$, respectively, in the HE group). Furthermore, in the MT group, the effect size was considered large for flexion ($d=1.25$; 0.51-1.91), right rotation ($d=0.94$; 0.25-1.58) and left rotation ($d=0.99$; 0.27-1.64); however, in the HE group, only the flexion effect size was large ($d=1.25$; 0.51-1.91). Regarding the between-group interaction, only the extension range differences were considered significant ($p=0.037$) (Table IV-3) (Figure IV-4 and IV-5).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
Flexion					
MT Group (n=13)	34.02(3.47)	47.69(2.53)	1.25(0.51 to 1.91)	0.004	0.700
HE Group (n=14)	35.07(2.54)	46.52(3.31)	1.04(0.35 to 1.66)	0.016	XXX
Extension					
MT Group (n=13)	56.46(3.38)	60.30(2.65)	0.35(-0.31 to 0.99)	0.092	0.037
HE Group (n=14)	64.66(3.60)	61.85(2.41)	0.24(-0.39 to 0.86)	0.214	XXX
Right Side Bending					
MT Group (n=13)	39.38(1.79)	40.50(1.94)	0.17(-0.51 to 0.84)	0.324	0.965
HE Group (n=14)	39.71(1.64)	40.80(2.06)	0.16(-0.47 to 0.77)	0.463*	XXX
Left Side Bending					
MT Group (n=13)	37.84(1.90)	38.10(1.72)	0.04(-0.61 to 0.68)	0.899	0.974
HE Group (n=14)	39.38(1.90)	39.57(1.71)	0.03(-0.59 to 0.65)	0.789*	XXX
Right Rotation					
MT Group (n=13)	56.30(1.84)	63.02(2.11)	0.94(0.25 to 1.58)	0.006	0.488*
HE Group (n=14)	59.90(3.37)	65.80(2.04)	0.57(-0.09 to 1.20)	0.016*	XXX
Left Rotation					
MT Group (n=13)	53.89(2.31)	62.25(2.38)	0.99(0.27 to 1.64)	0.000	0.189
HE Group (n=14)	56.38(2.40)	61.66(1.90)	0.65(0.00 to 1.27)	0.006	XXX

Table IV-3. Summary Cervical Range of Motion Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P<0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small. * p-values were drawn from nonparametrical tests.

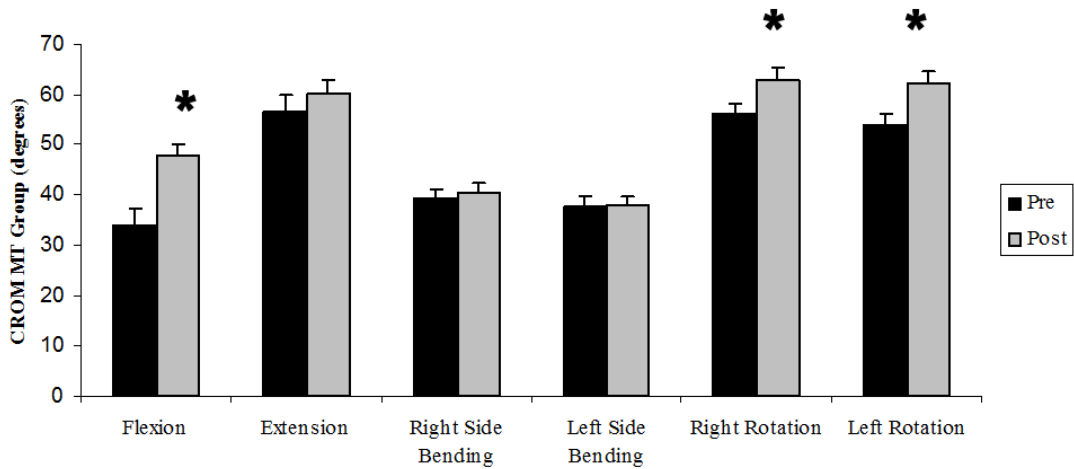


Figure IV-4. CROM results, MT Group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

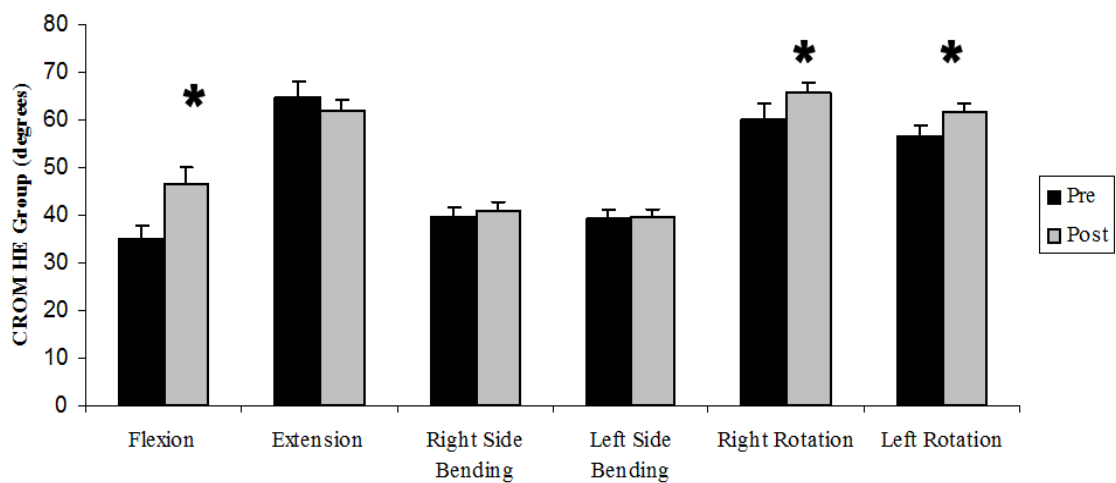


Figure IV-5. CROM results, HE Group. Pre and post values were expressed as mean (SE) two groups and all variables. * denotes p value < 0.05 within – group interaction.

5.4.5 Pressure pain thresholds

No significant changes were observed in any of the measured PPTs from pre to post intervention or between groups; however, the effect size in the MT group was

considered moderate for the upper trapezius PPT ($d=0.48$; $-0.19-1.12$), which had a decrease of 11.24%. No differences were observed between the two groups (Table IV-4) (Figure IV-6 and IV-7).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
PPT C1					
MT Group (n=13)	1.33(0.04)	1.30(0.06)	0.11(-0.54 to 0.75)	0.759	0.863
HE Group (n=14)	1.24(0.06)	1.23(0.07)	0.03(-0.60 to 0.65)	0.885	XXX
PPT C5					
MT Group (n=13)	1.30(0.06)	1.43(0.12)	0.38(-0.29 to 1.01)	0.231	0.818
HE Group (n=14)	1.28(0.06)	1.38(0.10)	0.31(-0.32 to 0.93)	0.236	XXX
PPT Upper Trapezius					
MT Group (n=13)	1.24(0.05)	1.34(0.05)	0.48(-0.19 to 1.12)	0.162	0.737
HE Group (n=14)	1.23(0.06)	1.30(0.05)	0.28(-0.35 to 0.90)	0.315	XXX
PPT Gluteus Medius					
MT Group (n=13)	2.22(0.16)	2.27(0.16)	0.08(-0.60 to 0.75)	0.937*	0.487
HE Group (n=14)	2.25(0.17)	2.40(0.13)	0.26(-0.37 to 0.88)	0.150	XXX

Table IV-4. Summary Pressure Pain Thresholds Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P<0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small. * p-values were drawn from nonparametrical tests.

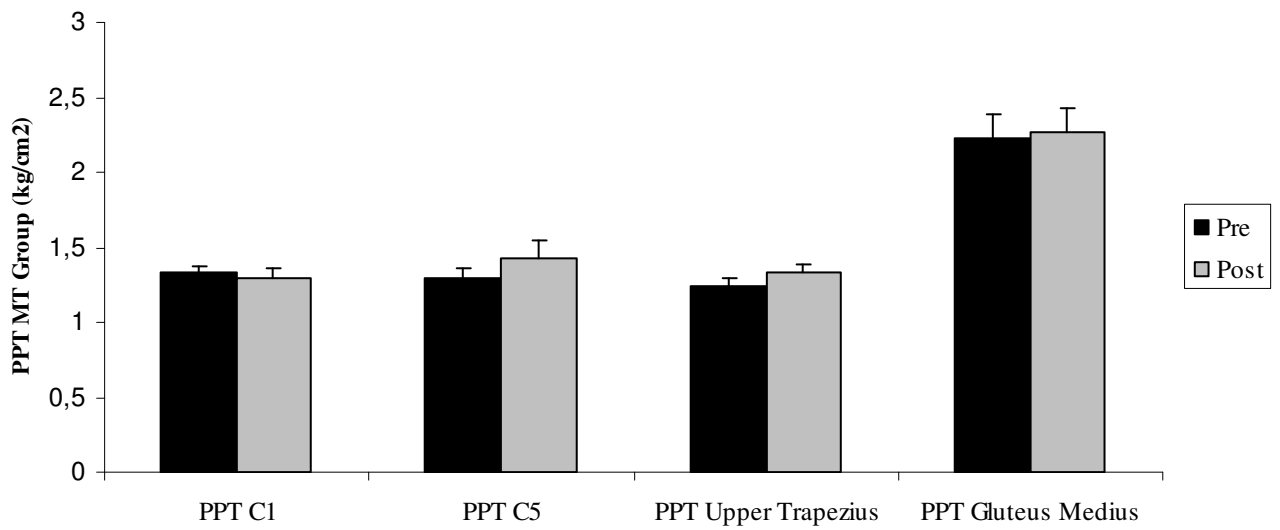


Figure IV-6. Pressure Pain Thresholds Results MT Group. Pre and post values were expressed as mean (SE) two groups and all variables.

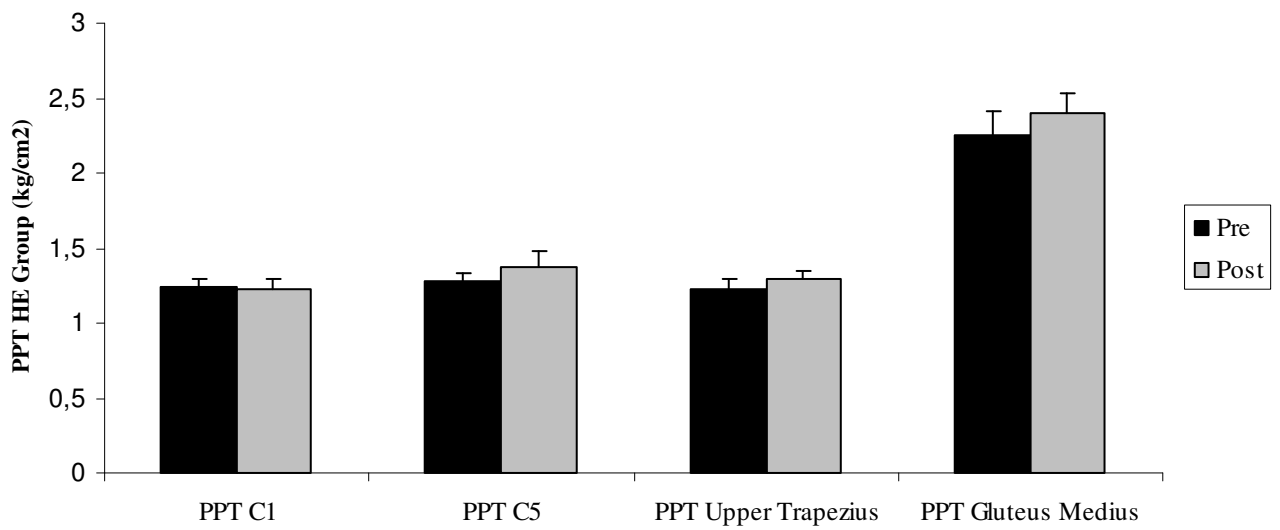


Figure IV-7. Pressure Pain Thresholds Results HE Group. Pre and post values were expressed as mean (SE) two groups and all variables.

5.4.6 Cranio-cervical Flexion Test

No significant differences were observed between the pre- and post-intervention RMS of the SCM during the five stages of the cranio-cervical flexion test for the two groups. However, the statistical analysis showed a tendency toward a decreased SCM signal in the first stage of CCFT in the exercise-group interaction ($p=0.062$), with a moderate effect size ($d=0.57$, $-0.12-1.22$). Additionally, in the MT group, the SCM signal decreased 29% and 34% in the first and fifth stage, respectively, showing a moderate effect size in both stages ($d=0.40$, $-0.31-1.08$ and 0.46 ; $-0.23-1.13$, respectively). No significant differences were observed between the groups (Table IV-5) (Figure IV-8 and IV-9).

	Baseline	Post intervention	Cohen's d Effect size 95%CI	Within-Group p value	Between-Group p value
First stage					
MT Group (n=13)	11.59(2.78)	10.30(3.15)	0.12(-0.57 to 0.78)	0.935	0.376
HE Group (n=14)	15.38(3.58)	9.49(2.20)	0.57(-0.12 to 1.22)	0.62	XXX
Second stage					
MT Group (n=13)	22.61(6.01)	14.33(6.22)	0.40(-0.31 to 1.08)	0.488	0.346
HE Group (n=14)	12.36(2.56)	13.21(3.84)	0.07(-0.60 to 0.74)	0.848	XXX
Third stage					
MT Group (n=13)	24.96(6.56)	20.63(6.66)	0.18 (-0.82 to 0.47)	0.461	0.583*
HE Group (n=14)	19.00(2.23)	23.75(5.89)	0.29(-0.35 to 0.90)	0.380	XXX
Fourth stage					
MT Group (n=13)	30.64(7.57)	25.29(7.97)	0.20(-0.48 to 0.87)	0.379	0.566
HE Group (n=14)	21.94(3.18)	19.20(4.69)	0.18(-0.46 to 0.81)	0.299	XXX
Fifth stage					
MT Group (n=13)	36.91(5.14)	25.00(9.12)	0.46(-0.23 to 1.13)	0.151	0.362
HE Group (n=14)	28.35(3.98)	24.93(7.08)	0.17(-0.49 to 0.81)	0.508	XXX

Table IV-5. Summary SCM activation during TFCC Results. Pre and post values were expressed as mean (SE) two groups and all variables. Significant group interaction ($P<0.05$). Effect sizes were expressed as Cohen's d (95% Confidence Interval), and an effect size greater than 0.8 was considered large, an effect size of approximately 0.5 was considered moderate, and an effect size of less than 0.2 was considered small. * p-values were drawn from nonparametrical tests.

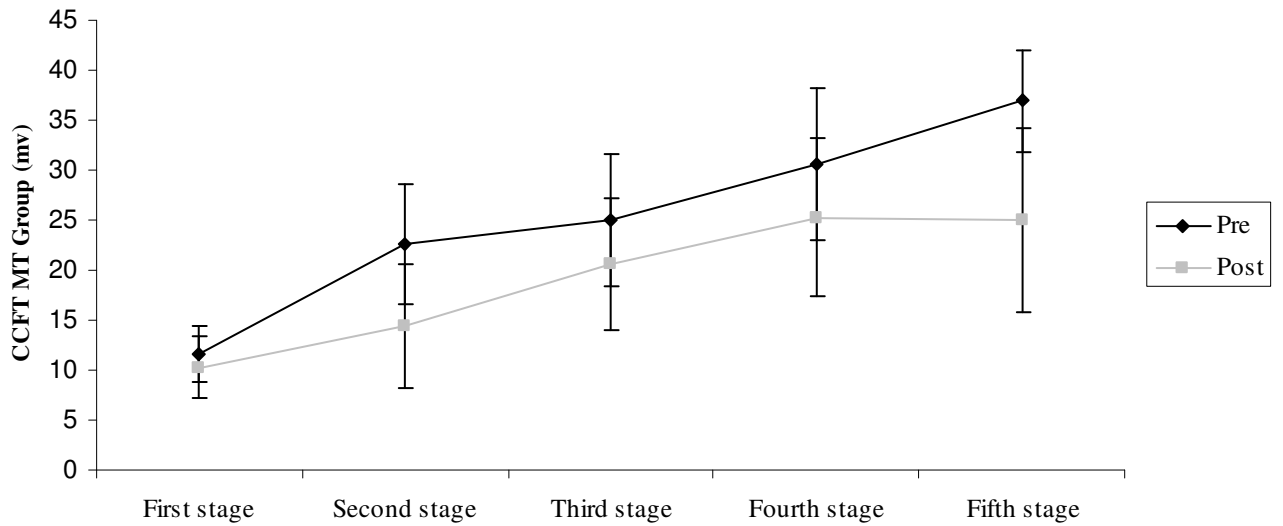


Figure IV-8. *SCM activation during CCFT MT group. Pre and post values were expressed as mean (SE) two groups and all variables.*

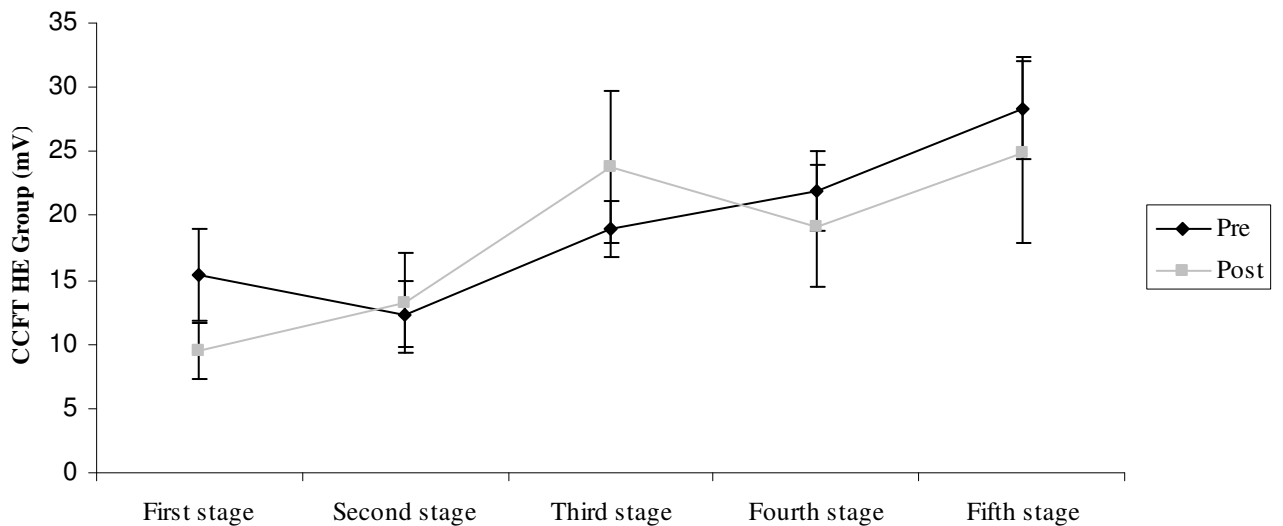


Figure IV-9. *SCM activation during CCFT HE group. Pre and post values were expressed as mean (SE) two groups and all variables.*

5.4.7 Discussion

To our knowledge, our study is the first to compare the short-term effects of an MT protocol with those of an HE protocol in women with chronic neck pain. The main finding was that both interventions improved function and pain, with only marginal between-group differences in favor of MT group, manipulation was more effective than exercise for only 2 out of 17 measures.

After one week, both interventions showed an important decrease in NDI and VAS scores. The manipulation protocol decreased the NDI 43.48% (6.05) and the VAS 50% (6.06). The NDI changes in the MT group may be similar to those found in previous studies. For example, Saavedra and cols (47) found patients with chronic mechanical neck pain showed greater reduction in NDI scores after manipulations of the cervical and thoracic spine than after manipulation of the cervical spine alone. The short-term effects on pain could be different if, like Pires and cols (45), these authors did not find significant differences in VAS scores 48-72 hours before manipulating T1. These conclusions seem to reinforce the belief that multisegment manipulation treatment improves the effects on neck pain more than isolated manipulation. Our protocol also included the temporo-mandibular joint; because of its relationships with the neck and cervical pain and biomechanics (49, 50, 119), including the TMJ in treatment yields more effective results. The physiological mechanism by which CSM produces analgesic effects is still unknown. Some authors studied a chemical response, while others examined biomechanical effects or neurophysiological relationships (105, 120, 121). More studies investigating the mechanism behind these effects are needed.

In our study, the HE group showed decreases of 39.72% (6.06) in the NDI value and 37.37% (10.72) in the VAS score. These results are similar to those of other authors, such as Karlsson (122)(51); however, our study differs in that it investigated the short-term effects of the treatments and that our HE protocol was a combined strength and stretching program. The analgesic effect of the home exercise protocol studied seems to be related to various aspects; on the one hand, the motor unit recruitment during isometric contractions elicits a significant hypoalgesic response (66), while on the other hand, cranio-cervical flexion exercise improves the motor control activation of the deep flexors (60).

Regarding ROM, significant changes were found in flexion and in both directions of rotations in the MT group. The HE group also showed similar changes, but only the flexion effect size was considered large in this group ($d=1.25$; 0.51-0.91). The results in the MT group were similar to other studies (116)(123). A study by Saavedra and cols of a manipulation protocol also concluded that MT resulted in significant improvement in ROM and functional status. For the HE group, our results are in accordance with the Freimann and cols study (124). While no significant changes were observed in either group in side-bending range, the non-improvement may be due to the pre-intervention measures (39.38 (1.79) and 37.84 (1.90) for right and left, respectively, in the MT group and 39.71 (1.64) and 39.38 (1.90) for right and left, respectively, in the HE group), which were already similar to normal (102). At any rate, the between-groups differences observed in these movements were not significant.

Regarding the PPT investigation, no significant differences between the pre- and post-intervention results were found in any of the measured PPTs between groups. In the MT group, these results differ from those of another study of the short-term effects of manipulation (116); however, in that study, the short-term effect was measured 20 minutes post intervention. Similarly, for the HE group, Lluch and cols (117)(51) found immediate effects on the suboccipital and C5/6 PPTs, but it is possible that in that study the immediate effects did not persist over time because the last home exercise protocol repetition was performed several hours before assessment. Regardless, although the performance of cranio-cervical flexion exercise for 6 weeks demonstrated reductions in pain and the NDI, no changes in the PPTs over the upper trapezius and at other locations were found (44).

Among the studied subjects, only those in the MT group showed a moderate effect size ($d=0.48$; $-0.19-1.12$) for the upper trapezius PPT was found. This is consistent with the findings of Camargo and cols (29), who also found a moderate effect size for upper trapezius PPT change after C5/6 manipulation. No differences were observed between the two groups.

Patients with chronic cervical pain often present a significant correlation between pain intensity and superficial muscle activity during cranio-cervical flexion tests, a finding that could explain altered neuromuscular function (51). In the exercise group, after one week, statistical analysis showed a decreasing trend in the SCM signal during the first stage of the CCFT with a moderate effect size ($d=0.57$; $-0.12-1.22$). This result was not consistent with those of previous studies (117), which showed immediate, significant changes during the third and fifth stage; however, our findings were in the

same line as those of Gallego and cols (125), who found significant changes in the long term but not immediately or one month after the intervention. In the MT group, at the first and fifth stages, the SCM signals decreased by 29% and 34%, respectively, showing moderate effect sizes for both stages ($d=0.40$; $-0.31-1.08$ and 0.46 ; $-0.23-1.13$, respectively). These findings were in with those of other studies (108)(126), but while Sterling and cols found significant changes in the first, second and third stage after grade III C5/6 mobilization, Moraleida and cols only found significant differences in the first stage based on ultrasonography results. Other authors, such as Pires and cols (45), did not find significant short-term changes in motor control of the neck; however, a different motor control test was used. In the authors' opinion, the SCM signal decrease in the fifth stage could be explained because the temporomandibular joint manipulation had an effect on cranio-cervical biomechanics (49)(48, 56); however, this conclusion should be affirmed by an exhaustive investigation.

These findings did not explain the excellent results on the NDI and VAS; however, in the authors' opinion and in agreement with other investigators, multiple factors could contribute to altered motor function in individuals with chronic mechanical neck pain (51).

Some limitations of this study should be considered. First, the investigator who performed the measurement protocol was not blinded to the intervention. Second, although we attempted to control for adherence to the home exercises through telephone contact, it was impossible to determine whether the exercises were being performed correctly. Third, the VAS and NDI are self-reported measures of pain, not objective measures. Fourth, the study did not have a control group. Fifth, there may have been an

interaction between the treatment effects of the HE and MT protocols; therefore, the results may have demonstrated only the relative effectiveness of the two protocols. Another limitation is that the present HE protocol did not include strength training, only stretching and low-intensity isometric contractions. Additionally, the statistical analyses were not adjusted for multiple comparisons; because the significance level was set at 5%, some of the significant differences may have occurred by chance (statistical type I error). Conversely, a number of potentially significant differences may not have been significant because the sample size was small (statistical type II error). Lastly, the outcome assessor was not blinded, which might have led to measurement bias. More studies with larger sample sizes comparing the short-term effects of an HVLA manipulation protocol and a home exercise protocol are needed. We suggest a longer duration of treatment with more sessions to maximize the treatment effect.

6. CONCLUSIONS, PRACTICAL APPLICATIONS AND FUTURE PERSPECTIVES

6. CONCLUSIONES, APLICACIONES PRÁCTICAS Y PERSPECTIVAS FUTURAS

6.1 Study I

Conclusions

A large effect size was found in cervical ROM improvement, especially for patients with neck pain. Rotation was the most clearly improved movement.

Mouth opening without pain was improved after upper CSM, mainly in patients with neck pain.

Free hand grip improved after CSM in patients with lateral epicondylalgia pain.

A decrease in diastolic blood pressure was found; however, for other studied variables, such as heart rate, systolic blood pressure, electrocardiogram and bilateral pulse oximetry, the changes were not significant.

Studies that examined symptomatic subjects and real dysfunctions showed better improvement than others; this might indicate that the effects of CSM were related more to the recovery of limitations than to improvements in mobility, strength and other parameters.

Practical applications

The CSM improves the mobility in patients with neck pain.

CSM decrease diastolic blood pressure in subjects with hypertension.

CSM improve the pain free hand grip strength in patients with lateral epicondylalgia.

Future perspectives

All the assumptions effects of CSM should be reviewed to apply them to patients.

6.2 Study II

Conclusion

The manipulation treatment based on a previous evaluation achieved better effects compared to the sham group and C5 manipulation group in extension movement and left rotation movement.

Practical applications

The evaluation of the dysfunctions is necessary to obtain the best mobility improvements in asymptomatic subjects.

Future perspectives

The manipulation treatment based on a previous evaluation approach is necessary to study in patients with neck pain.

6.3 Study III

Conclusion

While both interventions were associated with immediately improved ROM and pain after treatment, MT was more effective than exercise in improving ROM.

None of the interventions led to changes in EMG.

Practical applications

MT is a good option in the management of women chronic cervical pain.

Future perspectives

New trials with more subjects are needed to obtain more consistent conclusions.

Is necessary to compare the MT protocol with other options of treatment of chronic neck pain.

6.4 Study IV

Conclusions

Both interventions decreased the NDI and VAS in patients with chronic neck pain.

Both interventions increased the cervical ROM.

Practical applications

MT and HE are good options in the short term management of women chronic cervical pain.

Future perspectives

New trials with more subjects are needed to obtain more consistent conclusions.

Is necessary to compare the MT protocol with other options of treatment of chronic neck pain.

Is suitable to study the long term effects of MT protocol in chronic neck pain.

APPENDIX 1**PROTOCOLO DE EJERCICIOS****Cuestiones previas**

Si antes de realizar le surge cualquier duda, pónganse en contacto con el centro investigador en el número de teléfono 94 413 08 63 o en la dirección email: xabiergi@hotmail.com

Cualquier ejercicio que le cause dolor debe ponerlo en conocimiento de los investigadores en el teléfono y email anteriormente señalados.

Los ejercicios debe realizarlos suave y lentamente, sintiendo cada matiz que previamente se le ha explicado, solo así conseguirá que sus efectos repercutan sobre el dolor.

Siga el orden propuesto de los ejercicios.

1.Ejercicios de movilidad**Rotación**

Gire la cabeza suavemente hacia la izquierda hasta llegar al límite, vuelva a la posición inicial y descanse 5 segundos, a continuación gire la cabeza hacia la derecha hasta llegar al final del movimiento, después vuelva a la posición inicial y descanse, repita la secuencia 10 veces intentando llegar un poco más en el final de movimiento pero sin provocarnos dolor.

**Inclinación**

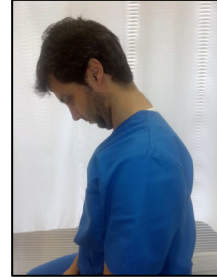
Incline la cabeza suavemente hacia la izquierda hasta llegar al límite, vuelva a la posición inicial y descanse 5 segundos, a continuación incline la cabeza hacia la derecha hasta llegar al



final del movimiento, después vuelva a la posición inicial y descanse, repita la secuencia 10 veces intentando llegar un poco más en el final de movimiento pero sin provocarnos dolor, asegurarnos que los hombros no ascienden hacia las orejas.

Flexión

Mire hacia abajo y vaya llevando la barbilla hacia el pecho suavemente, vuelva a la posición inicial. Repita 10 veces descansando 5 segundos entre cada repetición.



2.Ejercicios de estiramiento

Trapezio superior

Colóquese sentado, sitúe su mano derecha sobre su hombro izquierdo, coloque su mano izquierda sobre su muñeca derecha, ambas manos tiran del hombro izquierdo hacia el suelo suavemente sin llevar la espalda hacia delante, la cabeza realiza una inclinación derecha y rotación izquierda hasta sentir estiramiento en la zona del hombro izquierdo, mantenemos la posición 30 segundos y volvemos a la posición inicial suavemente, repetimos el ejercicio 3 veces cada lado.



Paravertebrales cervicales

Colóquese sentado, sitúe sus manos entrelazadas en la nuca, junte los codos y lleve la nuca hacia el suelo ayudándose con las manos hasta sentir estiramiento en la zona posterior del cuello, mantenemos la posición 30 segundos y volvemos a la posición inicial suavemente, repetimos el ejercicio 3 veces.



3.Ejercicio de fortalecimiento de los flexores profundos

Colóquese boca arriba con las rodillas flexionadas y los pies apoyados en el suelo, sitúe una almohada o una toalla doblada sobre su nuca, no sobre su cuello, coloque una mano sobre la musculatura anterior del cuello (a nivel del ECOM) para sentir la tensión muscular a este nivel como ya le han explicado, es importante que la musculatura que palpa la mano debe permanecer relajada. Busque un punto en el techo con la mirada, imagine que ese punto empieza a descender hasta colocarse entre sus rodillas y usted debe seguirlo, sienta como su nuca empieza a rodar encima de la toalla que hemos colocado anteriormente, descienda la barbilla un poco más hacia el pecho asta que note que la musculatura que usted palpa empieza a tensarse, manténgase en esa posición 10 segundos, vuelva suavemente a la posición inicial y descanse lo que necesite. Repita 10 veces.



4.Ejercicios de contracción isométrica (Contracción sin movimiento)

Rotación

Colóquese en posición neutra y sitúe una mano en la zona lateral izquierda de su cabeza, intente realizar un giro hacia la izquierda mientras su mano evita el movimiento, de esta manera lograremos una contracción sin movimiento, utilice solamente un 10 % de su fuerza máxima, mantenga la contracción durante cinco segundos y



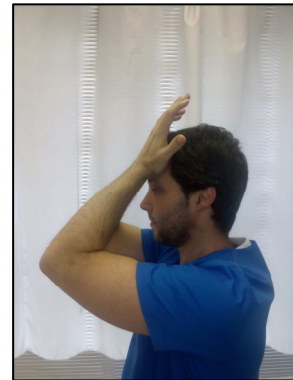
descanse el tiempo que necesite. Realice el ejercicio cinco veces a cada lado.

Inclinación

Colóquese en posición neutra y sitúe una mano en la zona lateral izquierda de su cabeza, intente realizar una inclinación hacia la izquierda mientras su mano evita el movimiento, de esta manera lograremos una contracción sin movimiento, utilice solamente un 10 % de su fuerza máxima, mantenga la contracción durante cinco segundos y descanse el tiempo que necesite. Realice el ejercicio cinco veces a cada lado.

Flexión

Colóquese en posición neutra y sitúe una mano en su frente, intente llevar su frente hacia abajo mientras su mano evita el movimiento, de esta manera lograremos una contracción sin movimiento, utilice solamente un 10 % de su fuerza máxima, mantenga la contracción durante cinco segundos y descanse el tiempo que necesite. Realice el ejercicio cinco veces.



Extensión

Colóquese en posición neutra y sitúe una mano en su nuca, intente llevar su frente hacia arriba mientras su mano evita el movimiento, de esta manera lograremos una contracción sin movimiento, utilice solamente un 10 % de su fuerza máxima, mantenga la contracción durante cinco segundos y descanse el tiempo que necesite. Realice el ejercicio cinco veces.



7. REFERENCES

7. BIBLIOGRAFÍA

7. REFERENCES

1. Green BN. A literature review of neck pain associated with computer use: public health implications. *J Can Chiropr Assoc.* 2008 Aug;52(3):161-7.
2. Hoy DG, Protani M, De R, Buchbinder R. The epidemiology of neck pain. *Best Pract Res Clin Rheumatol.* 2010 Dec;24(6):783-92.
3. Tsauo JY, Jang Y, Du CL, Liang HW. Incidence and risk factors of neck discomfort: a 6-month sedentary-worker cohort study. *J Occup Rehabil.* 2007 Jun;17(2):171-9.
4. Cote P, Cassidy JD, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain.* 2004 Dec;112(3):267-73.
5. Sundstrup E, Jakobsen MD, Brandt M, Jay K, Ajslev JZ, Andersen LL. Regular use of pain medication due to musculoskeletal disorders in the general working population: Cross-sectional study among 10,000 workers. *Am J Ind Med.* 2016 Jun 1.
6. Sehgal N, Manchikanti L, Smith HS. Prescription opioid abuse in chronic pain: a review of opioid abuse predictors and strategies to curb opioid abuse. *Pain Physician.* 2012 Jul;15(3 Suppl):ES67-92.
7. Tuchin PJ, Pollard H, Bonello R. A randomized controlled trial of chiropractic spinal manipulative therapy for migraine. *J Manipulative Physiol Ther.* 2000 Feb;23(2):91-5.
8. Ward R. *Fundamentos de Medicina Osteopática.* Buenos aires - Argentina: Médica Panamericana; 2006.
9. Gibbons P, Tehan P. *Manipulación de la columna, el torax y la pelvis. Una perspectiva osteopatica.* 2002nd ed. Edinburgh: Mc Graw-Hill.

-
10. Gross AR, Hoving JL, Haines TA, Goldsmith CH, Kay T, Aker P, et al. Manipulation and mobilisation for mechanical neck disorders. *Cochrane Database Syst Rev.* 2004;(1)(1):CD004249.
 11. Gross AR, Kay TM, Kennedy C, Gasner D, Hurley L, Yardley K, et al. Clinical practice guideline on the use of manipulation or mobilization in the treatment of adults with mechanical neck disorders. *Man Ther.* 2002 Nov;7(4):193-205.
 12. Haneline MT. Chiropractic manipulation and acute neck pain: a review of the evidence. *J Manipulative Physiol Ther.* 2005 Sep;28(7):520-5.
 13. Ernst E. Adverse effects of spinal manipulation: a systematic review. *J R Soc Med.* 2007 Jul;100(7):330-8.
 14. Haynes MJ, Vincent K, Fischhoff C, Bremner AP, Lanlo O, Hankey GJ. Assessing the risk of stroke from neck manipulation: a systematic review. *Int J Clin Pract.* 2012 Oct;66(10):940-7.
 15. Ruiz-Saez M, Fernandez-de-las-Penas C, Blanco CR, Martinez-Segura R, Garcia-Leon R. Changes in pressure pain sensitivity in latent myofascial trigger points in the upper trapezius muscle after a cervical spine manipulation in pain-free subjects. *J Manipulative Physiol Ther.* 2007 Oct;30(8):578-83.
 16. Martinez-Segura R, Fernandez-de-las-Penas C, Ruiz-Saez M, Lopez-Jimenez C, Rodriguez-Blanco C. Immediate effects on neck pain and active range of motion after a single cervical high-velocity low-amplitude manipulation in subjects presenting with mechanical neck pain: a randomized controlled trial. *J Manipulative Physiol Ther.* 2006 Sep;29(7):511-7.
 17. Smith L, Mehta M. The effects of upper cervical complex high velocity low amplitude thrust technique and sub-occipital muscle group inhibition techniques on standing balance. *Int J Osteopath Med.* 2008 12;11(4):162,162 1p.

-
18. Botelho MB, Andrade BB. Effect of cervical spine manipulative therapy on judo athletes' grip strength. *J Manipulative Physiol Ther.* 2012 Jan;35(1):38-44.
 19. Mansilla-Ferragut P, Fernandez-de-Las Penas C, Albuquerque-Sendin F, Cleland JA, Bosca-Gandia JJ. Immediate effects of atlanto-occipital joint manipulation on active mouth opening and pressure pain sensitivity in women with mechanical neck pain. *J Manipulative Physiol Ther.* 2009 Feb;32(2):101-6.
 20. Knutson GA. Significant changes in systolic blood pressure post vectored upper cervical adjustment vs resting control groups: a possible effect of the cervicosympathetic and/or pressor reflex. *J Manipulative Physiol Ther.* 2001 Feb;24(2):101-9.
 21. Taylor HH, Murphy B. Altered sensorimotor integration with cervical spine manipulation. *J Manipulative Physiol Ther.* 2008 02;31(2):115,126 12p.
 22. Da Silva PHL, De Ré D, Behne GR, Vazatta MP, De Carvalho AR. Maximum respiratory pressure alterations after spinal manipulation. *European Journal of Physiotherapy.* 2013;15(2):64-9.
 23. Bronfort G, Evans R, Anderson AV, Svendsen KH, Bracha Y, Grimm RH. Spinal manipulation, medication, or home exercise with advice for acute and subacute neck pain: a randomized trial. *Ann Intern Med.* 2012 Jan 3;156(1 Pt 1):1-10.
 24. Evans R, Bronfort G, Schulz C, Maiers M, Bracha Y, Svendsen K, et al. Supervised exercise with and without spinal manipulation performs similarly and better than home exercise for chronic neck pain: a randomized controlled trial. *Spine (Phila Pa 1976).* 2012 May 15;37(11):903-14.
 25. Chiu TW, Wright A. To compare the effects of different rates of application of a cervical mobilisation technique on sympathetic outflow to the upper limb in normal subjects. *Man Ther.* 1996 Sep;1(4):198-203.

-
26. Dunning J, Rushton A. The effects of cervical high-velocity low-amplitude thrust manipulation on resting electromyographic activity of the biceps brachii muscle. *Man Ther.* 2009 Oct;14(5):508-13.
27. Plaza-Manzano G, Molina-Ortega F, Lomas-Vega R, Martinez-Amat A, Achalandabaso A, Hita-Contreras F. Changes in biochemical markers of pain perception and stress response after spinal manipulation. *J Orthop Sports Phys Ther.* 2014 Apr;44(4):231-9.
28. Fisher AR, Bacon CJ, Mannion JVH. The Effect of Cervical Spine Manipulation on Postural Sway in Patients with Nonspecific Neck Pain. *J Manipulative Physiol Ther.* 2015 01;38(1):65,73 9p.
29. de Camargo VM, Albuquerque-Sendin F, Berzin F, Stefanelli VC, de Souza DP, Fernandez-de-las-Penas C. Immediate effects on electromyographic activity and pressure pain thresholds after a cervical manipulation in mechanical neck pain: a randomized controlled trial. *J Manipulative Physiol Ther.* 2011 May;34(4):211-20.
30. Humphries KM, Ward J, Coats J, Nobert J, Amonette W, Dyess S. Immediate effects of lower cervical spine manipulation on handgrip strength and free-throw accuracy of asymptomatic basketball players: a pilot study. *J Chiropr Med.* 2013 Sep;12(3):153-9.
31. George JW, Fennema J, Maddox A, Nessler M, Skaggs CD. The effect of cervical spine manual therapy on normal mouth opening in asymptomatic subjects. *J Chiropract Med.* 2007 2007;6(4):141,145 5p.
32. Oliveira-Campelo NM, Rubens-Rebelatto J, Marti N-Vallejo FJ, Albuquerque-Sendi NF, Fernandez-de-Las-Penas C. The immediate effects of atlanto-occipital joint manipulation and suboccipital muscle inhibition technique on active

mouth opening and pressure pain sensitivity over latent myofascial trigger points in the masticatory muscles. *J Orthop Sports Phys Ther.* 2010 May;40(5):310-7.

33. Passmore SR, Burke JR, Good C, Lyons JL, Dunn AS. Spinal manipulation impacts cervical spine movement and fitts' task performance: a single-blind randomized before-after trial. *J Manipulative Physiol Ther.* 2010 Mar-Apr;33(3):189-92.

34. Millan M, Leboeuf-Yde C, Budgell B, Descarreaux M, Amorim MA. The effect of spinal manipulative therapy on spinal range of motion: a systematic literature review. *Chiropr Man Therap.* 2012 Aug 6;20(1):23,709X-20-23.

35. Kayser R, Heyde CE. Functional disorders and functional diseases in the region of the upper cervical spine particularly regarding the cervical joints. Current status and clinical relevance. *Orthopade.* 2006 Mar;35(3):306-18.

36. Cleland JA, Glynn P, Whitman JM, Eberhart SL, MacDonald C, Childs JD. Short-term effects of thrust versus nonthrust mobilization/manipulation directed at the thoracic spine in patients with neck pain: a randomized clinical trial. *Phys Ther.* 2007 Apr;87(4):431-40.

37. Johannes CB, Le TK, Zhou X, Johnston JA, Dworkin RH. The prevalence of chronic pain in United States adults: results of an Internet-based survey. *J Pain.* 2010 Nov;11(11):1230-9.

38. Cagnie B, Danneels L, Van Tiggelen D, De Loose V, Cambier D. Individual and work related risk factors for neck pain among office workers: a cross sectional study. *Eur Spine J.* 2007 May;16(5):679-86.

39. Martinez-Segura R, De-la-Llave-Rincon AI, Ortega-Santiago R, Cleland JA, Fernandez-de-Las-Penas C. Immediate changes in widespread pressure pain sensitivity, neck pain, and cervical range of motion after cervical or thoracic thrust manipulation in

patients with bilateral chronic mechanical neck pain: a randomized clinical trial. *J Orthop Sports Phys Ther.* 2012 Sep;42(9):806-14.

40. Falla DL, Jull GA, Hodges PW. Patients with neck pain demonstrate reduced electromyographic activity of the deep cervical flexor muscles during performance of the craniocervical flexion test. *Spine (Phila Pa 1976).* 2004 Oct 1;29(19):2108-14.

41. Jull G, Falla D. Does increased superficial neck flexor activity in the craniocervical flexion test reflect reduced deep flexor activity in people with neck pain? *Man Ther.* 2016 Sep;25:43-7.

42. Salom-Moreno J, Ortega-Santiago R, Cleland JA, Palacios-Cena M, Truyols-Dominguez S, Fernandez-de-las-Penas C. Immediate changes in neck pain intensity and widespread pressure pain sensitivity in patients with bilateral chronic mechanical neck pain: a randomized controlled trial of thoracic thrust manipulation vs non-thrust mobilization. *J Manipulative Physiol Ther.* 2014 Jun;37(5):312-9.

43. Lluch E, Schomacher J, Gizzi L, Petzke F, Seegar D, Falla D. Immediate effects of active cranio-cervical flexion exercise versus passive mobilisation of the upper cervical spine on pain and performance on the cranio-cervical flexion test. *Man Ther.* 2014 Feb;19(1):25-31.

44. Lluch E, Arguisuelas MD, Coloma PS, Palma F, Rey A, Falla D. Effects of deep cervical flexor training on pressure pain thresholds over myofascial trigger points in patients with chronic neck pain. *J Manipulative Physiol Ther.* 2013 Nov-Dec;36(9):604-11.

45. Pires PF, Packer AC, Dibai-Filho AV, Rodrigues-Bigaton D. Immediate and Short-Term Effects of Upper Thoracic Manipulation on Myoelectric Activity of Sternocleidomastoid Muscles in Young Women With Chronic Neck Pain: A Randomized Blind Clinical Trial. *J Manipulative Physiol Ther.* 2015 Oct;38(8):555-63.

-
46. Martinez-Segura R, De-la-Llave-Rincon AI, Ortega-Santiago R, Cleland JA, Fernandez-de-Las-Penas C. Immediate changes in widespread pressure pain sensitivity, neck pain, and cervical range of motion after cervical or thoracic thrust manipulation in patients with bilateral chronic mechanical neck pain: a randomized clinical trial. *J Orthop Sports Phys Ther.* 2012 Sep;42(9):806-14.
47. Saavedra-Hernandez M, Arroyo-Morales M, Cantarero-Villanueva I, Fernandez-Lao C, Castro-Sanchez AM, Puenteadura EJ, et al. Short-term effects of spinal thrust joint manipulation in patients with chronic neck pain: a randomized clinical trial. *Clin Rehabil.* 2013 Jun;27(6):504-12.
48. Armijo-Olivo S, Silvestre R, Fuentes J, da Costa BR, Gadotti IC, Warren S, et al. Electromyographic activity of the cervical flexor muscles in patients with temporomandibular disorders while performing the craniocervical flexion test: a cross-sectional study. *Phys Ther.* 2011 Aug;91(8):1184-97.
49. Rocabado M. Biomechanical relationship of the cranial, cervical, and hyoid regions. *J Craniomandibular Pract.* 1983 Jun-Aug;1(3):61-6.
50. von Piekartz H, Hall T. Orofacial manual therapy improves cervical movement impairment associated with headache and features of temporomandibular dysfunction: a randomized controlled trial. *Man Ther.* 2013 Aug;18(4):345-50.
51. O'Leary S, Falla D, Hodges PW, Jull G, Vicenzino B. Specific therapeutic exercise of the neck induces immediate local hypoalgesia. *J Pain.* 2007 Nov;8(11):832-9.
52. Koltyn KF, Trine MR, Stegner AJ, Tobar DA. Effect of isometric exercise on pain perception and blood pressure in men and women. *Med Sci Sports Exerc.* 2001 Feb;33(2):282-90.
-

-
53. Lluch E, Schomacher J, Gizzi L, Petzke F, Seegar D, Falla D. Immediate effects of active cranio-cervical flexion exercise versus passive mobilisation of the upper cervical spine on pain and performance on the cranio-cervical flexion test. *Man Ther.* 2014 Feb;19(1):25-31.
54. Leininger B, McDonough C, Evans R, Tosteson T, Tosteson AN, Bronfort G. Cost-effectiveness of spinal manipulative therapy, supervised exercise, and home exercise for older adults with chronic neck pain. *Spine J.* 2016 Jun 23.
55. von Piekartz H, Hall T. Orofacial manual therapy improves cervical movement impairment associated with headache and features of temporomandibular dysfunction: a randomized controlled trial. *Man Ther.* 2013 Aug;18(4):345-50.
56. Armijo-Olivo S, Fuentes JP, da Costa BR, Major PW, Warren S, Thie NM, et al. Reduced endurance of the cervical flexor muscles in patients with concurrent temporomandibular disorders and neck disability. *Man Ther.* 2010 Dec;15(6):586-92.
57. Hakkinen A, Kautiainen H, Hannonen P, Ylinen J. Strength training and stretching versus stretching only in the treatment of patients with chronic neck pain: a randomized one-year follow-up study. *Clin Rehabil.* 2008 Jul;22(7):592-600.
58. Ylinen JJ, Takala EP, Nykanen MJ, Kautiainen HJ, Hakkinen AH, Airaksinen OV. Effects of twelve-month strength training subsequent to twelve-month stretching exercise in treatment of chronic neck pain. *J Strength Cond Res.* 2006 May;20(2):304-8.
59. Ylinen J, Takala EP, Nykanen M, Hakkinen A, Malkia E, Pohjolainen T, et al. Active neck muscle training in the treatment of chronic neck pain in women: a randomized controlled trial. *JAMA.* 2003 May 21;289(19):2509-16.

-
60. Jull GA, Falla D, Vicenzino B, Hodges PW. The effect of therapeutic exercise on activation of the deep cervical flexor muscles in people with chronic neck pain. *Man Ther.* 2009 Dec;14(6):696-701.
61. Jull G. SM. Whiplash injury recovery booklet. 2011.
62. Ylinen J, Kautiainen H, Wiren K, Hakkinen A. Stretching exercises vs manual therapy in treatment of chronic neck pain: a randomized, controlled cross-over trial. *J Rehabil Med.* 2007 Mar;39(2):126-32.
63. Peterson F, Kendall E, Geise P, McIntyre M, Anthony W, editors. *Múscles, testing and function, with posture and pain.* 5 th ed. Lippincot Williams & Wilkins; 2007.
64. Uthairkhu S, Jull G. Performance in the cranio-cervical flexion test is altered in elderly subjects. *Man Ther.* 2009 Oct;14(5):475-9.
65. Falla DL, Jull GA, Hodges PW. Patients with neck pain demonstrate reduced electromyographic activity of the deep cervical flexor muscles during performance of the craniocervical flexion test. *Spine (Phila Pa 1976).* 2004 Oct 1;29(19):2108-14.
66. Naugle KM, Fillingim RB, Riley JL,3rd. A meta-analytic review of the hypoalgesic effects of exercise. *J Pain.* 2012 Dec;13(12):1139-50.
67. Andersen LL, Kjaer M, Sogaard K, Hansen L, Kryger AI, Sjogaard G. Effect of two contrasting types of physical exercise on chronic neck muscle pain. *Arthritis Rheum.* 2008 Jan 15;59(1):84-91.
68. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ.* 2009 Jul 21;339:b2700.

-
69. Furlan AD, Pennick V, Bombardier C, van Tulder M, Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)*. 2009 Aug 15;34(18):1929-41.
70. Arnold C, Bourassa R, Langer T, Stoneham G. Doppler studies evaluating the effect of a physical therapy screening protocol on vertebral artery blood flow. *Man Ther*. 2004 Feb;9(1):13-21.
71. Youdas JW, Carey JR, Garrett TR. Reliability of measurements of cervical spine range of motion--comparison of three methods. *Phys Ther*. 1991 Feb;71(2):98,104; discussion 105-6.
72. Florencio LL, Pereira PA, Silva ER, Pegoretti KS, Goncalves MC, Bevilaqua-Grossi D. Agreement and reliability of two non-invasive methods for assessing cervical range of motion among young adults. *Rev Bras Fisioter*. 2010 Mar-Apr;14(2):175-81.
73. Kwok CK, Petrick MA, Munin MC. Inter-rater reliability for function and strength measurements in the acute care hospital after elective hip and knee arthroplasty. *Arthritis Care Res*. 1997 Apr;10(2):128-34.
74. Douma RK, Soer R, Krijnen WP, Reneman M, van der Schans CP. Reference values for isometric muscle force among workers for the Netherlands: a comparison of reference values. *BMC Sports Sci Med Rehabil*. 2014 Feb 25;6(1):10,1847-6-10.
75. Hayes KW, Falconer J. Reliability of hand-held dynamometry and its relationship with manual muscle testing in patients with osteoarthritis in the knee. *J Orthop Sports Phys Ther*. 1992;16(3):145-9.

-
76. Chiu TT, Law EY, Chiu TH. Performance of the craniocervical flexion test in subjects with and without chronic neck pain. *J Orthop Sports Phys Ther.* 2005 Sep;35(9):567-71.
77. Barbero M, Merletti R, Rainoldi A. *Atlas of Muscle Innervation Zones.* Italy: Springer-Verlag; 2012.
78. Greenman P. *Principios y Práctica de la Medicina Manual.* 3ª Edición ed. Buenos Aires: Médica Panamericana; 2005.
79. Jull G, Bogduk N, Marsland A. The accuracy of manual diagnosis for cervical zygapophysial joint pain syndromes. *Med J Aust.* 1988 Mar 7;148(5):233-6.
80. Fernandez-de-las-Penas C, Downey C, Miangolarra-Page JC. Validity of the lateral gliding test as tool for the diagnosis of intervertebral joint dysfunction in the lower cervical spine. *J Manipulative Physiol Ther.* 2005 Oct;28(8):610-6.
81. Rey-Eiriz G, Albuquerque-Sendin F, Barrera-Mellado I, Martin-Vallejo FJ, Fernandez-de-las-Penas C. Validity of the posterior-anterior middle cervical spine gliding test for the examination of intervertebral joint hypomobility in mechanical neck pain. *J Manipulative Physiol Ther.* 2010 May;33(4):279-85.
82. Vernon H, MacAdam K, Marshall V, Pion M, Sadowska M. Validation of a sham manipulative procedure for the cervical spine for use in clinical trials. *J Manipulative Physiol Ther.* 2005 Nov-Dec;28(9):662-6.
83. Price DD, McGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain.* 1983 Sep;17(1):45-56.
84. Sriwatanakul K, Kelvie W, Lasagna L, Calimlim JF, Weis OF, Mehta G. Studies with different types of visual analog scales for measurement of pain. *Clin Pharmacol Ther.* 1983 Aug;34(2):234-9.
-

-
85. Fischer AA. Pressure algometry over normal muscles. Standard values, validity and reproducibility of pressure threshold. *Pain*. 1987 Jul;30(1):115-26.
86. Antonaci F, Sand T, Lucas GA. Pressure algometry in healthy subjects: inter-examiner variability. *Scand J Rehabil Med*. 1998 Mar;30(1):3-8.
87. Kinser AM, Sands WA, Stone MH. Reliability and validity of a pressure algometer. *J Strength Cond Res*. 2009 Jan;23(1):312-4.
88. Sciotti VM, Mittak VL, DiMarco L, Ford LM, Plezbert J, Santipadri E, et al. Clinical precision of myofascial trigger point location in the trapezius muscle. *Pain*. 2001 Sep;93(3):259-66.
89. Srbely JZ, Vernon H, Lee D, Polgar M. Immediate Effects of Spinal Manipulative Therapy on Regional Antinociceptive Effects in Myofascial Tissues in Healthy Young Adults. *J Manipulative Physiol Ther*. 2013 07;36(6):333,341 9p.
90. Jull GA, O'Leary SP, Falla DL. Clinical assessment of the deep cervical flexor muscles: the craniocervical flexion test. *J Manipulative Physiol Ther*. 2008 Sep;31(7):525-33.
91. Ricard F. Terapia manual en las disfunciones de la articulacion temporomandibular. . 2004;7(2):65-82.
92. Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. *J Manipulative Physiol Ther*. 1991 Sep;14(7):409-15.
93. Andrade J, Damián A, Almécija R. Validación de una versión española del Índice de Discapacidad Cervical. *Med Clin*. 2007;130(3):85.
94. Kim JH, Lee HS, Park SW. Effects of the active release technique on pain and range of motion of patients with chronic neck pain. *J Phys Ther Sci*. 2015 Aug;27(8):2461-4.

-
95. Field T, Diego M, Gonzalez G, Funk CG. Neck arthritis pain is reduced and range of motion is increased by massage therapy. *Complement Ther Clin Pract*. 2014 Nov;20(4):219-23.
96. La Touche R, París-Alemaný A, Mannheimer JS, Angulo-Díaz-Parreño S, Bishop MD, López-Valverde-Centeno A, et al. Does mobilization of the upper cervical spine affect pain sensitivity and autonomic nervous system function in patients with cervico-craniofacial pain?: A randomized-controlled trial. *Clin J Pain*. 2013;29(3):205-15.
97. La Touche R, Fernandez-de-las-Penas C, Fernandez-Carnero J, Escalante K, Angulo-Diaz-Parreno S, Paris-Alemaný A, et al. The effects of manual therapy and exercise directed at the cervical spine on pain and pressure pain sensitivity in patients with myofascial temporomandibular disorders. *J Oral Rehabil*. 2009 Sep;36(9):644-52.
98. Fernandez-Carnero J, Fernandez-de-las-Penas C, Cleland JA. Immediate hypoalgesic and motor effects after a single cervical spine manipulation in subjects with lateral epicondylalgia. *J Manipulative Physiol Ther*. 2008 Nov-Dec;31(9):675-81.
99. Bakris GL, Dickholtz M, Sr, Meyer P, Kravitz G, Avery E, Miller M, et al. Atlas vertebra realignment and achievement of arterial pressure goal in hypertensive patients: a pilot study. *J Vertebral Subluxation Res*. 2007 10/29:1,9 9p.
100. Ward J, Tyer K, Coats J, Williams G, Weigand S, Cockburn D. Immediate effects of atlas manipulation on cardiovascular physiology. *Clin Chiropract*. 2012 12;15(3):147,157 11p.
101. Vernon HT, Triano JJ, Ross JK, Tran SK, Soave DM, Dinulos MD. Validation of a novel sham cervical manipulation procedure. *Spine J*. 2012 Nov;22(11):1021-8.
-

-
102. Youdas JW, Garrett TR, Suman VJ, Bogard CL, Hallman HO, Carey JR. Normal range of motion of the cervical spine: an initial goniometric study. *Phys Ther.* 1992 Nov;72(11):770-80.
103. Krauss J, Creighton D, Ely JD, Podlowska-Ely J. The immediate effects of upper thoracic translatoric spinal manipulation on cervical pain and range of motion: a randomized clinical trial. *J Man Manip Ther.* 2008;16(2):93-9.
104. Whittingham W, Nilsson N. Active range of motion in the cervical spine increases after spinal manipulation (toggle recoil). *J Manipulative Physiol Ther.* 2001 Nov;24(9):552,555 4p.
105. Pickar JG. Neurophysiological effects of spinal manipulation. *Spine J.* 2002 Sep-Oct;2(5):357-71.
106. Symons BP, Herzog W, Leonard T, Nguyen H. Reflex responses associated with activator treatment. *J Manipulative Physiol Ther.* 2000 Mar-Apr;23(3):155-9.
107. Suter E, McMorland G. Decrease in elbow flexor inhibition after cervical spine manipulation in patients with chronic neck pain. *Clin Biomech (Bristol, Avon).* 2002 Aug;17(7):541-4.
108. Sterling M, Jull G, Wright A. Cervical mobilisation: concurrent effects on pain, sympathetic nervous system activity and motor activity. *Man Ther.* 2001 May;6(2):72-81.
109. Ross JK, Bereznick DE, McGill SM. Determining cavitation location during lumbar and thoracic spinal manipulation: is spinal manipulation accurate and specific? *Spine (Phila Pa 1976).* 2004 Jul 1;29(13):1452-7.
110. Suvarnnato T, Puntumetakul R, Kaber D, Boucaut R, Boonphakob Y, Arayawichanon P, et al. The effects of thoracic manipulation versus mobilization for

chronic neck pain: a randomized controlled trial pilot study. *J Phys Ther Sci.* 2013 Jul;25(7):865-71.

111. Haavik-Taylor H, Murphy B. Cervical spine manipulation alters sensorimotor integration: a somatosensory evoked potential study. *Clin Neurophysiol.* 2007 Feb;118(2):391-402.

112. Hemington KS, Coulombe MA. The periaqueductal gray and descending pain modulation: why should we study them and what role do they play in chronic pain? *J Neurophysiol.* 2015 Oct;114(4):2080-3.

113. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science.* 1965 Nov 19;150(3699):971-9.

114. Lau HM, Wing Chiu TT, Lam TH. The effectiveness of thoracic manipulation on patients with chronic mechanical neck pain - a randomized controlled trial. *Man Ther.* 2011 Apr;16(2):141-7.

115. Lluch E, Arguisuelas MD, Calvente Quesada O, Martinez Noguera E, Peiro Puchades M, Perez Rodriguez JA, et al. Immediate effects of active versus passive scapular correction on pain and pressure pain threshold in patients with chronic neck pain. *J Manipulative Physiol Ther.* 2014 Nov-Dec;37(9):660-6.

116. Casanova-Mendez A, Oliva-Pascual-Vaca A, Rodriguez-Blanco C, Heredia-Rizo AM, Gogorza-Arroitaonandia K, Almazan-Campos G. Comparative short-term effects of two thoracic spinal manipulation techniques in subjects with chronic mechanical neck pain: a randomized controlled trial. *Man Ther.* 2014 Aug;19(4):331-7.

117. Lluch E, Schomacher J, Gizzi L, Petzke F, Seegar D, Falla D. Immediate effects of active cranio-cervical flexion exercise versus passive mobilisation of the

upper cervical spine on pain and performance on the cranio-cervical flexion test. *Man Ther.* 2014;19(1):25-31.

118. Armijo-Olivo S, Silvestre R, Fuentes J, da Costa BR, Gadotti IC, Warren S, et al. Electromyographic activity of the cervical flexor muscles in patients with temporomandibular disorders while performing the craniocervical flexion test: a cross-sectional study. *Phys Ther.* 2011 Aug;91(8):1184-97.

119. Ciancaglini R, Testa M, Radaelli G. Association of neck pain with symptoms of temporomandibular dysfunction in the general adult population. *Scand J Rehabil Med.* 1999 Mar;31(1):17-22.

120. Pickar JG, Bolton PS. Spinal manipulative therapy and somatosensory activation. *Journal of Electromyography and Kinesiology.* 2012 10;22(5):785-94.

121. Molina-Ortega F, Lomas-Vega R, Hita-Contreras F, Plaza Manzano G, Achalandabaso A, Ramos-Morcillo AJ, et al. Immediate effects of spinal manipulation on nitric oxide, substance P and pain perception. *Man Ther.* 2014 Oct;19(5):411-7.

122. Karlsson L, Takala EP, Gerdle B, Larsson B. Evaluation of pain and function after two home exercise programs in a clinical trial on women with chronic neck pain - with special emphasises on completers and responders. *BMC Musculoskeletal Disord.* 2014 Jan 8;15:6,2474-15-6.

123. Saavedra-Hernandez M, Castro-Sanchez AM, Arroyo-Morales M, Cleland JA, Lara-Palomo IC, Fernandez-de-Las-Penas C. Short-term effects of kinesio taping versus cervical thrust manipulation in patients with mechanical neck pain: a randomized clinical trial. *J Orthop Sports Phys Ther.* 2012 Aug;42(8):724-30.

124. Freimann T, Merisalu E, Paasuke M. Effects of a home-exercise therapy programme on cervical and lumbar range of motion among nurses with neck and lower

back pain: a quasi-experimental study. *BMC Sports Sci Med Rehabil.* 2015 Dec 4;7:31,015-0025-6. eCollection 2015.

125. Gallego Izquierdo T, Pecos-Martin D, Lluch Girbes E, Plaza-Manzano G, Rodriguez Caldentey R, Mayor Melus R, et al. Comparison of cranio-cervical flexion training versus cervical proprioception training in patients with chronic neck pain: A randomized controlled clinical trial. *J Rehabil Med.* 2016 Jan;48(1):48-55.

126. Jesus-Moraleida FR, Ferreira PH, Pereira LS, Vasconcelos CM, Ferreira ML. Ultrasonographic analysis of the neck flexor muscles in patients with chronic neck pain and changes after cervical spine mobilization. *J Manipulative Physiol Ther.* 2011 Oct;34(8):514-24.