Original Article

# Contralateral Sensory and Motor Effects of Unilateral Kaltenborn Mobilization in Patients with Thumb Carpometacarpal Osteoarthritis: A Secondary Analysis

Jorge H. Villafañe, PhD, MSc, PT<sup>1)\*</sup>, Cesar Fernandez-de-las-Peñas, PhD, MSc, PT<sup>2)</sup>, Guillermo B. Silva, PhD, MSc<sup>3)</sup>, Stefano Negrini, MD<sup>1, 4)</sup>

<sup>1)</sup> IRCCS Don Gnocchi Foundation: Milan, Italy

<sup>2)</sup> Department of Physical Therapy, Occupational Therapy, Rehabilitation and Physical Medicine, Universidad Rey Juan Carlos, Spain

<sup>3)</sup> School of Chemistry Sciences, Catholic University of Cordoba, Argentina

<sup>4)</sup> Department of Physical and Rehabilitation Medicine, University of Brescia, Italy

**Abstract.** [Purpose] The aim of this study was to determine changes in pressure sensitivity and pinch strength in patients with thumb carpometacarpal (CMC) osteoarthritis (OA) in the contralateral hand after unilateral Kaltenborn mobilization on the symptomatic hand. [Subjects and Methods] Twenty-nine females with dominant hand thumb CMC osteoarthritis participated (age 70–90), and were randomized into 2 groups. The experimental group received a Kaltenborn mobilization, and the placebo group received a nontherapeutic dose of intermittent ultrasound. Pressure pain thresholds (PPT) at the thumb CMC joint, scaphoid bone and hamate bone and tip and tripod pinch strength were assessed before and after the intervention and 1 week (1st follow-up) and 2 weeks (2nd follow-up) after the intervention. [Results] Significant increases in PPT in the experimental group at all follow-up periods as compared with baseline data were found. The post-intervention between-group mean differences for PPT were 1.1 (95%CI 0.4–1.8) for the CMC joint, 1.1 (95%CI 0.2–2.1) for the scaphoid, and 1.5 (95%CI 0.5–2.8) for the hamate. The post-intervention between-group mean differences were 0.5 (95%CI 0.2–0.9) for the tip pinch and 0.3 (95%CI 0.1–0.6) for the tripod pinch. [Conclusion] The current secondary analysis found that Kaltenborn mobilization for the symptomatic hand reduces pressure pain sensitivity (PPT increases) and also produces motor changes in the contralateral non-treated hand compared with a placebo group.

Key words: Carpometacarpal osteoarthritis, Kaltenborn mobilization, Pressure pain threshold

(This article was submitted Nov. 29, 2013, and was accepted Dec. 26, 2013)

## INTRODUCTION

Thumb carpometacarpal (CMC) osteoarthritis (OA) is a common condition after the age of 50, especially in females<sup>1)</sup>. The main cause of thumb CMC OA is a degenerative progressive alteration of the thumb CMC joint<sup>2)</sup>. This degeneration includes chronic deterioration of superficial surfaces of the joint and ectopic bone regeneration<sup>3–5)</sup>, which results in pain at the base of the thumb<sup>5, 6)</sup>.

Central sensitization is defined as an intensification of the responsiveness of central pain-signaling neurons from low-threshold mechanoreceptors<sup>7</sup>). Central sensitization includes changes in sensory processing and regulation down of descending pain-inhibitory mechanisms<sup>8</sup>). The importance of central sensitization processes underlies a mechanism of pain in OA, which has recently gained interest.

Some studies have investigated the involvement of central pain modulation in OA knee pain<sup>9-11</sup>). Imamura et al.<sup>9</sup>) found that patients with moderate to severe persistent knee pain and disability exhibited significantly lower pressure pain thresholds as compared with healthy controls. Similarly, Bajaj et al.<sup>10)</sup> described deep hyperalgesia and increased referred pain areas in the tibialis anterior muscle in patients with knee OA, observing bilateral effects as a sign of central sensitization. More importantly, these mechanisms appeared to respond to local analgesics. Creamer et al.<sup>11)</sup> reported that injection of local anesthetic into one knee relieves pain in the contralateral non-injected knee. These studies suggest a possible role of the central nervous system in the maintenance of chronic pain in individuals with unilateral knee OA, indicating sensitization mechanisms at the contralateral side of the symptoms.

In fact, the presence of contralateral sensitization mechanisms has been reported in unilateral local pain syndromes of the upper extremity. Fernández-de-las-Peñas et al.<sup>12)</sup> found a bilateral widespread pressure pain hypersensitivity

J. Phys. Ther. Sci. 26: 807–812, 2014

<sup>\*</sup>Corresponding author. Jorge H. Villafañe (E-mail: mail@ villafane.it)

<sup>©2014</sup> The Society of Physical Therapy Science. Published by IPEC Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-ncnd) License <a href="http://creativecommons.org/licenses/by-nc-nd/3.0/">http://creativecommons.org/licenses/by-nc-nd/3.0/</a>>.

in women with strictly unilateral carpal tunnel syndrome, whereas Fernández-Carnero et al.<sup>13)</sup> showed similar findings in individuals with unilateral lateral epicondylalgia. These studies suggest that unilateral local pain syndromes exhibit contralateral sensitization mechanisms.

It has been previously found that manual therapies induce mechanical hypoalgesia (which causes an increase in pressure pain thresholds; PPT) concurrent with sympathetic nervous system<sup>14)</sup> and motor<sup>15)</sup> excitation. Previous studies investigating hypoalgesic mechanical effects of manual therapies have focused on different passive mobilization techniques, i.e., lateral glide of the cervical spine<sup>16</sup>, posterior-anterior joint mobilization<sup>15)</sup> or mobilization-with-movement<sup>17)</sup>. These studies mainly investigated manual therapy targeted at the cervical spine, explaining that spinal joint interventions can exert bilateral effects. We have recently conducted a randomized controlled trial analyzing changes in pressure sensitivity after treatment with Kaltenborn mobilization in patients with thumb CMC OA<sup>18)</sup>. However, the data regarding the contralateral hand have not yet been analyzed.

Some studies have demonstrated that unilateral interventions exhibit bilateral effects, suggesting a central rather than peripheral effect of manual therapies<sup>19–21)</sup>. Nevertheless, it is unknown whether the use of a unilateral Kaltenborn mobilization on the symptomatic-affected side induces sensory and motor effects on the contralateral hand in individuals with thumb CMC OA. In the current work, we conducted a secondary exploration of our previous randomized controlled trial by analyzing changes occurring within the contralateral hand. We hypothesized that unilateral Kaltenborn mobilization applied on the symptomatic hand in individuals with thumb CMC OA would also induce contralateral mechanical hypoalgesia and motor effects.

# SUBJECTS AND METHODS

We conducted a secondary analysis of data previously reported in a randomized controlled clinical trial. The recruitment methods and a description of the trial have been previously described<sup>18</sup>. Here we have summarized the most relevant parts of the design (Fig. 1).

Patients with dominant hand thumb CMC OA were recruited from the "Residenze Sanitarie Assistenziali" (Avigliana and Sangano, Italy). The Inclusion criteria included patients who used their dominant hand on a regular basis (e.g., ex-factory workers and home workers), age between 70-90 years and those diagnosed with CMC OA in the dominant hand by X-ray detection of stage III-IV according to the Eaton-Littler-Burton Classification<sup>22)</sup>. The diagnosis of CMC OA was confirmed by a hand surgeon following X-ray examination. Patients with a medical history of carpal tunnel syndrome, prior surgical interventions to thumb CMC joint, or De Quervain's tenosynovitis were excluded, as well as those presenting degenerative or non-degenerative neurological conditions in which pain perception was altered<sup>5</sup>). This study was approved by the Local Ethics Committee (Azienda Sanitaria Locale 3, Collegno, Italy) and registered in the clinical trials database as ISRCTN06361999. All patients provided informed consent before enrollment in the

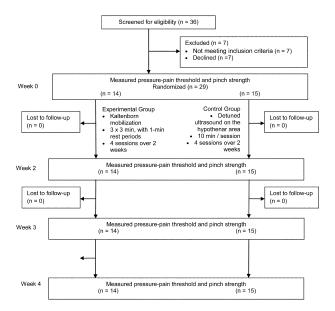


Fig. 1. Flow diagram of criteria in the study

study. They were randomly assigned to either the experimental or sham group by using a simple randomization with a random number generator. Blocked or stratified randomization was not used in this study<sup>18</sup>.

Participants were randomly assigned to one of two groups: the experimental group received Kaltenborn mobilization therapy, whereas the control group received a placebo therapy. The treatment was performed unilaterally and only applied to the symptomatic (ipsilateral) hand. From all the possible treatments, we chose joint mobilization because of the improvement with respect to the limited ROM and therefore reduction in pain induced by traction and glide. As previously described<sup>18</sup>, the intervention group received unilateral Kaltenborn mobilization consisting of posterioranterior gliding with Grade 3 distraction in of the thumb CMC joint of the dominant hand. Grade 3 distraction was chosen to avoid contact between the articular surfaces and to stimulate hypoalgesic factors. The treatment duration was 6 sessions over a period of 2 weeks (3 sessions/ week). The mobilization was applied over the course of 3 minutes with a 1-minute pause; the action was repeated three times. The physiotherapist gripped the right thumb metacarpal bone of the subject with his right thumb and index finger and made a specific Kaltenborn mobilization of posterioranterior gliding with a short amplitude and distraction of the thumb CMC joint.

Participants in the placebo group received a sham dose of intermittent ultrasound therapy in the thumb region in 10 minutes for 6 sessions over 2 weeks<sup>23–25)</sup>. Interventions were applied by an experienced physical therapist with a 4 year Postgraduation Certificate in Manual Therapy and more than 11 years of experience in the management of musculoskeletal pain disorders.

In the first study, we analyzed the results from the symptomatic hand. The current secondary analysis was focused on the contralateral hand. The pressure pain threshold was measured bilaterally over the thumb CMC joint at the anatomical snuffbox, the tubercle of the scaphoid bone, and the unciform apophysis, of the hamate bone, to represent the spread of hyperalgesia in central sensitization. The pressure was applied approximately at 0.1 kg/cm<sup>2</sup>/s (until the onset of pain)<sup>2, 18, 26-28)</sup>. Participants were seated in a standardized position, and 2 trials of both tip and tripod pinch strength were taken using a pinch. Pinch strength measurements were taken bilaterally for each participant. The between-group differences in pain pressure threshold and pinch strength for the contralateral hand were analyzed in this study. PPT measurements were expressed in kg/cm<sup>2</sup>, and pinch strength was expressed in kg. For every outcome, three measurements was calculated and used for the main analysis. A 1-minute rest period was allowed between each measurement. The subjects were assessed at baseline, immediately after treatment, and 1 and 2 weeks after the treatment by an assessor blinded to their allocation group $^{18}$ .

Data were analyzed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). The results are expressed as means, standard deviations, and/or 95% confidence intervals. Normal distribution of the sample was analyzed using the Kolmogorov-Smirnov test (p>0.05). Baseline demographic and clinical variables were compared between the groups using independent Student t-tests for continuous data and  $\chi^2$ tests of independence for categorical data. A 2-way analysis of variance (ANOVA) was used to evaluate differences for PPT and strength measurements between sides (affected/ unaffected in patients) as the within-subjects factor and groups (experimental or sham) as the between-subject factor. A repeated measures ANOVA test was used to evaluate the differences in PPT at over time point and pinch strength levels with time as the within-subjects factor and group (experimental or placebo) as the between-subjects factor. The hypothesis of interest was group-by-time interaction. Post hoc comparisons were performed with the Bonferroni test. In those variables for which the baseline data were different, an analysis of covariance (ANVOCA) was conducted by including the baseline value as a covariate. Finally, between-group effect sizes were calculated using Cohen's d coefficient<sup>29)</sup>. An effect size greater than 0.8 was considered large, around 0.5 was considered moderate, and less than 0.2 was considered small<sup>29)</sup>. The statistical analysis was conducted at a 95% confidence level, and a p<0.05 was considered statistically significant.

## RESULTS

Twenty-nine women with thumb CMC OA, mean age 81  $\pm$ 7 years, met all the inclusion criteria and agreed to participate. No significant statistical differences were found in any outcome at baseline between groups, except for the scaphoid bone. Baseline data of the participants are summarized in Table 1.

The ANOVA revealed significant group-by-time interactions for PPT over the thumb CMC joint (F=9.591; p=0.005), scaphoid (F=9.083; p=0.006), and hamate (F=2.979; p=0.036) bones. The post hoc testing revealed significant increases in PPT within the experimental group for all follow-up periods as compared with the baseline data (p<0.01 for all groups). No differences between the post-

Characteristic	Randomiz	red (n = 29)
Characteristic	Exp $(n = 14)$	Con (n = 15)
Age (yr), mean (SD)	81 (8)	80 (7)
Gender, n females (%)	14 (100)	15 (100)

Exp = experimental group, Con = control group, CMC = carpometacarpal joint

intervention and follow-up periods were found (p>0.10). No significant changes were found within the control group. The post-intervention between-group mean differences for PPT were 1.1 (95%CI 0.4–1.8) for the CMC joint, 1.1 (95%CI 0.2–2.1) for the scaphoid bone, and 1.5 (95%CI 0.5–2.8) for the hamate bone. The data are summarized in Table 2.

The ANOVA revealed a significant group-by-time interaction for tip pinch (F=5.343; p=0.029) and tripod pinch strength (F=7.834; p=0.009). The post hoc testing revealed significant increases in tip and tripod pinch strength in the experimental group for all follow-up periods compared with the baseline data (p<0.05 for all groups), with no differences between the post-intervention and follow-up periods (p>0.50). Again, no significant changes were observed within the control group. The post-intervention betweengroup mean differences for strength were 0.5 (95%CI 0.2– 0.9) for tip pinch, and 0.3 (95%CI 0.1–0.6) for the tripod pinch. Between-group effect sizes were small to moderate (d=0.35) for tip pinch and small to moderate (d=0.39) for tripod pinch strength (Table 2).

### DISCUSSION

The current secondary analysis found that application of a unilateral Kaltenborn mobilization to the symptomatic hand induces hypoalgesic effects, which can be monitored by increases in PPT in the contralateral hand in women with thumb CMC OA. Motor changes were also observed, as shown by increased tip and tripod pinch strength, in the contralateral hand. However, some of these changes were small, and their clinical relevance should be considered with caution particularly considering that they refer to the non-symptomatic side. Current and previous<sup>18)</sup> findings suggest a bilateral hypoalgesic and unilateral contralateral motor effect after the application of a unilateral manual mobilization in women with thumb CMC OA.

Historically, it was hypothesized that mechanisms by which manual therapies exert their effects were primarily biomechanical in nature; however, it has been recently proposed that these effects are neurophysiological origin<sup>30</sup>. Among the different theories, it is accepted that manual therapies affect central mechanisms by stimulating descending inhibitory pain mechanisms, particularly in the periaqueductal gray area<sup>30</sup>. This assumption is based on the premise that manual therapies result in a decrease in pressure pain sensitivity (by increasing PPT) and motor system excitation to a greater magnitude than in sham or control groups<sup>14, 21</sup>.

In the current secondary analysis, we found that a unilateral Kaltenborn mobilization applied to the symptom-

Outcome				Groups	sdr					Diffe	Difference within groups	thin grou	tps		Diff	Difference between groups	sdno.
	Week 0	k 0	Week 2	k 2	Week 3	k 3	Week 4	٤4	Week 2 minus Week 0	minus c 0	Week 3 minus Week 0	minus c 0	Week 4 minus Week 0	minus - 0	Week 2 minus Week 0	Week 3 minus Week 0	Week 4 minus Week 0
	Exn	Con	Exn	Exn Con	Fxn	Con	Exn	Con	Fxn	Con	Exn	Con	Exn	4	Exn minus Con	Exp minus Con Exp minus Con Exp minus Con	Exn minus Con
	dvr	100	dvr -		der		der		dva	2011	dva		dvr				
	(n=14)	(n=15)	(n=14)	(n=15)	(n=14) (n=15) (n=14) (n=15) (n=14) (n	=15)	(n=14)	(n=15)									
CMC joint PPT,	3.0	3.2	3.9	3.0	3.6	3.1	3.6	3.1	0.9	-0.2	0.6	-0.1	0.6	-0.1	1.1	0.7	0.7
$(kg/cm^2)$	(1.2)	(1.0)	(1.5)	(1.2)	(1.3)	(1.0)	(1.5)	(1.1)	(0.9)	(0.0)	(0.7)	(1.0)	(1.0)	(0.7)	(0.4 to 1.8)	(0.3 to 1.3)	(0.3 to 1.4)
Scaphoid PPT,	3.6	4.8	4.9	4.8	4.5	4.9	4.5	4.0	1.3	0.0	0.9	0.1	0.9	-0.8	1.1	0.8	1.7
$(kg/cm^2)$	(1.1)	(1.7)	(2.0)	(1.1)	(1.1)	(1.4)	(1.7)	(1.4)	(1.0)	(1.6)	(1.0)	(1.4)	(1.6)	(1.2)	(0.2 to 2.1)	(0.2 to 1.6)	(0.8 to 2.6)
Hamate PPT,	4.6	5.8	6.0	5.7	5.6	5.7	5.6	5.5	1.4	-0.1	1.0	-0.1	1.0	-0.3	1.5	1.1	1.3
$(kg/cm^2)$	(1.6)	(2.0)	(1.3)	(2.2)	(1.3)	(1.6)	(1.8)	(1.9)	(1.8)	(1.5)	(2.1)	(2.0)	(2.3)	(2.1)	(0.5 to 2.8)	(0.4 to 2.5)	(0.3 to 2.6)
Tip pinch strength,	2.1	2.3	2.2	2.5	2.6	2.1	2.3	2.0	0.1	0.2	0.5	-0.2	0.2	-0.3	0.5	0.7	0.6
(kg)	(0.6)	(0.8)	(1.1)	(0.8)	(1.1)	(6.0)	(1.0)	(0.0)	(1.9)	(1.3)	(1.9)	(1.7)	(2.2)	(1.0)	(0.2 to 0.9)	(0.2 to 1.0)	(0.1 to 0.6)
Tripod pinch	2.7	2.8	3.1	2.9	3.4	2.9	3.0	2.5	0.4	0.1	0.7	0.1	0.3	-0.2	0.3	0.6	0.6
strength, (kg)	(1.2)	(0.0)	(1.6)	(1.1)	(2.0)	(0.0)	(1.4)	(1.0)	(0.6)	(0.0)	(0.6)	(0.7)	(0.8)	(0.7)	(0.1  to  0.6)	(0.3 to 1.3)	(0.1 to 0.9)
Exp: experimental group; Con: control group; CMC: carpo-meta carpal joint; PPT: pressure-pain threshold	oup; Con: rpal joint;	control £ PPT: pre	group; ssure-pa	in thresh	old												

Table 2. Mean (SD) for outcomes at all study visits for each group, mean (SD) difference within groups, and mean (95% CI) difference between groups

810 J. Phys. Ther. Sci. Vol. 26, No. 6, 2014

atic hand in patients with thumb CMC OA increased PPT levels in the thumb CMC joint and scaphoid and hamate bones on the contralateral hand a greater magnitude than the placebo intervention. In fact, PPT increased by around 35% at all the points analyzed, showing large effect sizes. Regarding these magnitudes, it is important to note that different structures may or may not exhibit similar values. Prushansky et al.<sup>31)</sup> established that differences ranging from 20% to 25% are required to indicate a relevant clinical interpretation. However, we should consider that this study investigated changes in pressure pain sensitivity over the cervical spine and in healthy people, so extrapolation of the percentage improvement in this specific group cannot be directly transferred to other body parts in subjects in a totally different age group with a particular disease, and therefore, the results should be considered with caution at this stage. Therefore, our records are greater than this preestablished cutoff value, emphasizing the calidity of the changes we found. Nevertheless, we should recognize that this study was focused on PPT in the cervical spine, where decreases in pain are more difficult to achieve. Additionally, previous studies analyzing changes in PPT after the use of different manual interventions reported changes between 15–25%<sup>14</sup>, <sup>21)</sup>. Again, the PPT changes obtained in the current study on the contralateral hand were similar, or sometimes, greater than these values since they were greater than 20% of preintervention scores at all points; however, the current results should not be compared with the ones from other studies, since the features of the present protocol were different.

The findings obtained in the present study along with previous results<sup>18)</sup> suggest a bilateral hypoalgesic effect of unilateral Kaltenborn mobilization, supporting that manual mobilization may exert a central effect, at least an effect referred to the contralateral side. In fact, it has been suggested that manual therapies, e.g., manipulative therapy, may provide counter-inflammatory effects mediated by inhibition of neuroplastic changes associated with central sensitization at the dorsal horn of the spinal cord<sup>32)</sup>. However, this theory is based on studies investigating spinal manipulative therapy but not manipulations applied to peripheral joints. The results of our study would support the idea that use of unilateral mobilization for a local peripheral joint (CMC) induces bilateral and mirror-type changes in PPT in related areas at the contralateral side. However, the mediators and mechanism of these effects remain unknown.

We also found that a unilateral Kaltenborn mobilization exerted motor effects on the contralateral hand by increasing the tip and tripod pinch strength in women with thumb CMC OA. In fact, the tip and tripod pinch strength increased 22% and 26% respectively, supporting a motor effect after the intervention. However, some of these changes were small, and their clinical relevance should be considered with caution particularly considering that they refer to the non-symptomatic side. When the findings obtained in the current study along with previous results<sup>18)</sup> are taken together, it seems that an unilateral mobilization of the thumb CMC joint may be able to elicit contralateral motor responses in patients with thumb CMC OA. It is interesting to note that the application of unilateral mobilization of the thumb for the symptomatic joint only induces a contralateral motor effect, which was unexpected. This may be related to the fact that the symptomatic joint exhibited degenerative changes on X-ray and pain, and it is possible that a single mobilization session is not able to induce motor changes.

The presence of contralateral motor responses after unilateral manual mobilization would support the idea of, at least, centrally-mediated responses. Animal studies have shown that stimulation of the dorsal periaqueductal gray matter provokes increased activity of alpha motor neurons in rodents<sup>33)</sup>. Similarly, in humans, manual mobilization enhances motor activity in combination with mechanical hypoalgesic effects by stimulating the dorsal periaqueductal gray matter<sup>34)</sup>. The current secondary analysis found an hypoalgesic effect concurrent with a motor effect in the contralateral hand, supporting findings from previous studies conducted on the cervical spine<sup>14, 15, 35)</sup>. It is possible that structures such as the mesencephalon coordinate motor effects through a direct link involving neuronal networks and projections to the motor  $cortex^{36-39}$ . Therefore, we can hypothesize that peripheral unilateral stimulation of the affected joint (CMC in this case) via central structures may increase motor activity. However this hypothesis remains to be tested for the CMC since we only found contralateral motor responses after a single session of mobilization of the CMC joint.

Although the results of this study are promising, we recognize several limitations. First, we only applied a localized intervention for the symptomatic peripheral joint, which does not represent the common clinical practice for these patients. It would be of great interest to investigate sensory and motor changes after the inclusion of interventions targeted at the thoracic and cervical innervated areas, which may serve as nodes for sharing information. In fact, it is possible that the application of a single joint intervention explains the motor effects found just in the contralateral side. Second, the advanced age of the patients may present concomitant pathologies that could affect the results. Third, we had only evaluated sensory and motor changes in segment-related areas. In addition, we only assessed PPT. It would be interesting to determine changes in other sensory modalities, such as thermal, electrical or cutaneous thresholds, to determine more relevant changes. To finally confirm a central effect of manual interventions, future studies should analyze widespread hypoalgesic and motor changes. In fact, we did not evaluate activation of cortical brain areas after intervention. Therefore, we cannot confirm that the hypoalgesic and motor changes observed in the current study are directly associated with activation of central structures. Finally, the analyses reported in the present study were exploratory and hypothesis-generating rather than confirmatory. Further studies are now needed to investigate the mechanisms underling our findings and fully investigate the nervous system mediators involved.

The current secondary analysis found that a unilateral Kaltenborn mobilization for the symptomatic hand reduced pressure pain sensitivity by increasing PPTs in the CMC joint and the scaphoid and hamate bones of the contralateral hand in patients with CMC OA. Furthermore, we also observed positive motor changes including an increase in tip and tripod pinch strength of the contralateral hand. Future

studies with larger sample sizes are needed to further examine the effects of joint mobilization on motor and sensory effects.

#### REFERENCES

- Stahl S, Shapira D: Trapeziometacarpal joint osteoarthritis and carpal tunnel syndrome: a new surgical approach for concomitant treatment. J Hand Surg [Br], 2003, 28: 246–250. [Medline] [CrossRef]
- Villafañe JH, Silva GB, Bishop MD, et al.: Radial nerve mobilization decreases pain sensitivity and improves motor performance in patients with thumb carpometacarpal osteoarthritis: a randomized controlled trial. Arch Phys Med Rehabil, 2012, 93: 396–403. [Medline] [CrossRef]
- Rogers MW, Wilder FV: Exercise and hand osteoarthritis symptomatology: a controlled crossover trial. J Hand Ther, 2009, 22: 10–17, discussion 19–20, quiz 18. [Medline] [CrossRef]
- Bagis S, Sahin G, Yapici Y, et al.: The effect of hand osteoarthritis on grip and pinch strength and hand function in postmenopausal women. Clin Rheumatol, 2003, 22: 420–424. [Medline] [CrossRef]
- Wajon A, Ada L: No difference between two splint and exercise regimens for people with osteoarthritis of the thumb: a randomised controlled trial. Aust J Physiother, 2005, 51: 245–249. [Medline] [CrossRef]
- 6) Weilby A: Tendon interposition arthroplasty of the first carpo-metacarpal joint. J Hand Surg [Br], 1988, 13: 421–425. [Medline] [CrossRef]
- Beckwée D, De Hertogh W, Lievens P, et al.: Effect of tens on pain in relation to central sensitization in patients with osteoarthritis of the knee: study protocol of a randomized controlled trial. Trials, 2012, 13: 21. [Medline] [CrossRef]
- Nijs J, Van Oosterwijck J, De Hertogh W: Rehabilitation of chronic whiplash: treatment of cervical dysfunctions or chronic pain syndrome? Clin Rheumatol, 2009, 28: 243–251. [Medline] [CrossRef]
- Imamura M, Imamura ST, Kaziyama HH, et al.: Impact of nervous system hyperalgesia on pain, disability, and quality of life in patients with knee osteoarthritis: a controlled analysis. Arthritis Rheum, 2008, 59: 1424–1431. [Medline] [CrossRef]
- Bajaj P, Bajaj P, Graven-Nielsen T, et al.: Osteoarthritis and its association with muscle hyperalgesia: an experimental controlled study. Pain, 2001, 93: 107–114. [Medline] [CrossRef]
- Creamer P, Hunt M, Dieppe P: Pain mechanisms in osteoarthritis of the knee: effect of intraarticular anesthetic. J Rheumatol, 1996, 23: 1031–1036. [Medline]
- 12) Fernández-de-las-Peñas C, de la Llave-Rincón AI, Fernández-Carnero J, et al.: Bilateral widespread mechanical pain sensitivity in carpal tunnel syndrome: evidence of central processing in unilateral neuropathy. Brain, 2009, 132: 1472–1479. [Medline] [CrossRef]
- 13) Fernández-Carnero J, Fernández-de-Las-Peñas C, de la Llave-Rincón AI, et al.: Widespread mechanical pain hypersensitivity as sign of central sensitization in unilateral epicondylalgia: a blinded, controlled study. Clin J Pain, 2009, 25: 555–561. [Medline] [CrossRef]
- 14) Vicenzino B, Collins D, Wright A: The initial effects of a cervical spine manipulative physiotherapy treatment on the pain and dysfunction of lateral epicondylalgia. Pain, 1996, 68: 69–74. [Medline] [CrossRef]
- Sterling M, Jull G, Wright A: Cervical mobilisation: concurrent effects on pain, sympathetic nervous system activity and motor activity. Man Ther, 2001, 6: 72–81. [Medline] [CrossRef]
- 16) Vicenzino B, Collins D, Benson H, et al.: An investigation of the interrelationship between manipulative therapy-induced hypoalgesia and sympathoexcitation. J Manipulative Physiol Ther, 1998, 21: 448–453. [Medline]
- Vicenzino B, Paungmali A, Buratowski S, et al.: Specific manipulative therapy treatment for chronic lateral epicondylalgia produces uniquely characteristic hypoalgesia. Man Ther, 2001, 6: 205–212. [Medline] [CrossRef]
- 18) Villafañe JH, Silva GB, Diaz-Parreño SA, et al.: Hypoalgesic and motor effects of kaltenborn mobilization on elderly patients with secondary thumb carpometacarpal osteoarthritis: a randomized controlled trial. J Manipulative Physiol Ther, 2011, 34: 547–556. [Medline] [CrossRef]
- Fernández-de-las-Peñas C, Pérez-de-Heredia M, Brea-Rivero M, et al.: Immediate effects on pressure pain threshold following a single cervical spine manipulation in healthy subjects. J Orthop Sports Phys Ther, 2007,

37: 325-329. [Medline] [CrossRef]

- 20) Fernández-de-Las-Peñas C, Alonso-Blanco C, Cleland JA, et al.: Changes in pressure pain thresholds over C5-C6 zygapophyseal joint after a cervicothoracic junction manipulation in healthy subjects. J Manipulative Physiol Ther, 2008, 31: 332–337. [Medline] [CrossRef]
- 21) Mansilla-Ferragut P, Fernández-de-Las Peñas C, Alburquerque-Sendín F, et al.: 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, 32: 101–106. [Medline] [CrossRef]
- 22) Jaggi R, Morris S: Practice tips. Rule of thumb: update on first carpometacarpal joint osteoarthritis. Can Fam Physician, 2007, 53: 1309–1310. [Medline]
- 23) Celik D, Atalar AC, Sahinkaya S, et al.: [The value of intermittent ultrasound treatment in subacromial impingement syndrome]. Acta Orthop Traumatol Turc, 2009, 43: 243–247. [Medline] [CrossRef]
- 24) Hancock MJ, Maher CG, Latimer J, et al.: Independent evaluation of a clinical prediction rule for spinal manipulative therapy: a randomised controlled trial. Eur Spine J, 2008, 17: 936–943. [Medline] [CrossRef]
- 25) Bennell K, Wee E, Coburn S, et al.: Efficacy of standardised manual therapy and home exercise programme for chronic rotator cuff disease: randomised placebo controlled trial. BMJ, 2010, 340: c2756. [Medline] [CrossRef]
- 26) Villafañe JH, Silva GB, Fernandez-Carnero J: Short-term effects of the neurodynamic mobilization in patients with secondary thumb carpometacarpal osteoarthritis: a Cases Series study. J Manipulative Physiol Ther, 2011, 34: 449–456. [Medline] [CrossRef]
- Villafañe JH, Silva GB, Fernandez-Carnero J: Effect of thumb joint mobilization on pressure pain threshold in elderly patients with thumb carpometacarpal osteoarthritis. J Manipulative Physiol Ther, 2012, 35: 110–120. [Medline] [CrossRef]
- 28) Villafañe JH, Silva GB, Chiarotto A: Effects of passive upper extremity joint mobilization on pain sensitivity and function in participants with secondary carpometacarpal osteoarthritis: a case series. J Manipulative Physiol Ther, 2012, 35: 735–742. [Medline] [CrossRef]
- Cohen J: Statistical power analysis for the behavioural sciences. Hillsdale: Lawrence Erlbaum Associates, 1988.
- Bialosky JE, Bishop MD, Price DD, et al.: The mechanisms of manual therapy in the treatment of musculoskeletal pain: a comprehensive model. Man Ther, 2009, 14: 531–538. [Medline] [CrossRef]
- Prushansky T, Dvir Z, Defrin-Assa R: Reproducibility indices applied to cervical pressure pain threshold measurements in healthy subjects. Clin J Pain, 2004, 20: 341–347. [Medline] [CrossRef]
- 32) Boal RW, Gillette RG: Central neuronal plasticity, low back pain and spinal manipulative therapy. J Manipulative Physiol Ther, 2004, 27: 314–326. [Medline] [CrossRef]
- 33) Fields H, Basbaum A: Central nervous system mechainisms of pain modulation. In: Wall PD, Melzack R, Textbook of pain. 4th ed. Edinburgh: Churchill Livingstone, 1999, pp 309–329.
- Wright A: Hypoalgesia post-manipulative therapy: a review of a potential neurophysiological mechanism. Man Ther, 1995, 1: 11–16. [Medline] [CrossRef]
- 35) Fernández-Carnero J, Fernández-de-las-Peñas C, Cleland JA: Immediate hypoalgesic and motor effects after a single cervical spine manipulation in subjects with lateral epicondylalgia. J Manipulative Physiol Ther, 2008, 31: 675–681. [Medline] [CrossRef]
- 36) Boyd BS, Wanek L, Gray AT, et al.: Mechanosensitivity of the lower extremity nervous system during straight-leg raise neurodynamic testing in healthy individuals. J Orthop Sports Phys Ther, 2009, 39: 780–790. [Medline] [CrossRef]
- Balster SM, Jull GA: Upper trapezius muscle activity during the brachial plexus tension test in asymptomatic subjects. Man Ther, 1997, 2: 144–149. [Medline] [CrossRef]
- 38) van der Heide B, Allison GT, Zusman M: Pain and muscular responses to a neural tissue provocation test in the upper limb. Man Ther, 2001, 6: 154–162. [Medline] [CrossRef]
- 39) Coppieters MW, Stappaerts KH, Wouters LL, et al.: Aberrant protective force generation during neural provocation testing and the effect of treatment in patients with neurogenic cervicobrachial pain. J Manipulative Physiol Ther, 2003, 26: 99–106. [Medline] [CrossRef]