Radial nerve mobilisation had bilateral sensory effects in people with thumb carpometacarpal osteoarthritis: a randomised trial

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Question: In people with thumb carpometacarpal osteoarthritis, does radial nerve mobilisation to the affected hand reduce pressure pain sensitivity in the contralateral hand? Design: Secondary analysis of data from a randomised trial with concealed allocation, assessor blinding, and intention-to-treat analysis. Participants: Sixty people with thumb CMC osteoarthritis in the dominant hand aged 70–90 years. Interventions: The experimental group received sliding mobilisation of the radial nerve and the control group received a non-therapeutic dose of intermittent ultrasound, on the affected side for six sessions over four weeks. Outcome measures: On the contralateral side, pressure pain thresholds at the lateral epicondyle, thumb CMC joint, tubercle of the scaphoid bone, and hamate bone were assessed before and after the intervention with follow-up at 1 and 2 months. Results: No important baseline differences were noted between groups. At the end of the intervention period, the experimental group had significantly a higher (ie, better) pressure pain threshold than the control group at the lateral epicondyle by 1.5 kg/cm² (95% CI 0.2 to 2.2), CMC joint by 1.2 kg/cm² (95% CI 0.2 to 2.1), scaphoid bone by 1.0 kg/cm² (95% CI 0.2 to 1.8) and hamate bone by 1.5 kg/cm² (95% CI 0.2 to 2.2). Although mean values in the experimental group remained better than the control group at all sites at both follow-up assessments, these differences were not statistically significant. Conclusion: Radial nerve gliding applied to the symptomatic hand induced hypoalgesic effects on the contralateral hand in people with CMC osteoarthritis, suggesting bilateral hypoalgesic effects of the intervention. Trial registration: ISRCTN81771317. [Villafañe JH, Bishop MD, Fernández-de-las-Peñas C, Langford D (2013) Radial nerve mobilisation had bilateral sensory effects in people with thumb carpometacarpal osteoarthritis: a randomised trial. Journal of Physiotherapy 59: 25–30]

Key words: Osteoarthritis, Hyperalgesia, Physiotherapy (techniques), Carpometacarpal joints, Hand

Introduction

Osteoarthritis is the most prevalent articular disorder worldwide (Bijlsma 2002), with thumb carpometacarpal osteoarthritis being a common manifestation in middle or older aged people (Pellegrini 2005). Thumb carpometacarpal osteoarthritis involves degeneration of the joint articular surfaces, with associated hyaline cartilage loss, ligament laxity, osteophyte formation, synovial inflammation, and muscle weakness (Pellegrini 2005). Advanced thumb carpometacarpal osteoarthritis is characterised by deterioration of the superficial surfaces of the joint and ectopic bone regeneration (Wajon and Ada 2005, Im et al 2010). The main symptom of this condition is pain at the base of the thumb, usually resulting in functional impairments in the performance of activities of daily living, and occupational and recreational tasks (Slatkowsky-Christensen et al 2007). In advanced disease, adduction contracture of the first web space with secondary thumb carpometacarpal hyperextension is also commonly seen (Wajon and Ada 2005). The pain of osteoarthritis is becoming recognised increasingly as being related not only to peripheral mechanisms, but also to central sensitisation at both spinal cord and brain levels (Im et al 2010, Mandl 2011, Mease et al 2011). For example, people with osteoarthritis are more sensitive to experimental noxious stimuli at body sites distant from their affected joints compared to people without arthritic pain (Farrell et al 2000, Imamura et al 2008, Lee et al 2011). Prolonged osteoarthritic pain is also associated with neurochemical, molecular and metabolic re-organisation in both the peripheral and central nervous systems (Farrell et al 2000, Bajaj et al 2001, Fernandez-de-las-Penas et al 2009, Imamura et al 2008, Gwilym et al 2009, Lee et al 2011). These profound changes help to explain the diverse clinical manifestations of osteoarthritis, such as discordances between the degree of...
joint damage and the subjective report of pain (McDougall 2006), as well as clinical features of hyperalgesia, allodynia and spread of pain from the affected joint to adjacent tissues (Graven-Nielsen 2006, Fernandez-de-las-Penas et al 2009). Interestingly, central sensitisation has been documented in people with knee and hand osteoarthritis (Creamer et al 1996, Bajaj et al 2001, Farrell et al 2000, Imamura et al 2008). Bilateral hyperalgesia has been reported in the tibialis anterior muscle in people with unilateral knee osteoarthritis (Bajaj et al 2001). Injection of local anesthetic in one knee was followed by pain relief in the contralateral, non-injected knee (Creamer et al 1996). Additionally, people with moderate to severe persistent knee pain have significantly lower pressure pain thresholds than controls (Imamura et al 2008). The role of central sensitisation mechanisms in maintenance and augmentation of upper extremity pain has been also studied in unilateral carpal tunnel (Fernandez-de-las-Penas et al 2009) and lateral epicondyalgia (Fernandez-Camero et al 2009), illustrating bilateral widespread pressure pain hypersensitivity, perhaps due to peripherally maintained central sensitisation. This sensitisation in both peripheral and central sensory neural pathways is believed to be relevant to the initiation and maintenance of persistent pain (Graven-Nielsen and Arendt-Nielsen 2002).

An important feature of central sensitisation in osteoarthritis pain is hyperalgesia, often radiating far from the painful joint (Nisj et al 2009). Several studies indicate that manual therapies can induce mechanical hypoalgesia (Vicenzino et al 1996, Sterling et al 2001, Vicenzino et al 2001, Villafañe et al 2011a, Villafañe et al 2012a, Villafañe et al 2012b). This effect may be concurrent with sympathetic nervous system (Vicenzino et al 1996) and motor (Sterling et al 2001) excitation. The manual therapies demonstrating these effects include neurodynamic gliding (Villafañe et al 2011b), passive accessory joint mobilisation (Villafañe 2012b), posterior-anterior joint mobilisation (Sterling et al 2001) and mobilisation with movement of the elbow (Vicenzino et al 2001). Two recent randomised trials of Kaltenborn mobilisation (Villafañe et al 2011a) and radial nerve gliding (Villafañe et al 2012a) in people with thumb carpometacarpal osteoarthritis found that these interventions applied over the symptomatic hand exerted unilateral hypoalgesic effects. However, hypoalgesia induced by manual therapies may be bilateral (Mansilla-Ferragut et al 2009).

Given this emerging evidence of widespread hyperalgesia in osteoarthritis related-pain, we hypothesised that a neurodynamic radial nerve slider intervention applied to the affected hand in people with carpometacarpal osteoarthritis would induce bilateral mechanical hypoalgesia. Therefore, we conducted a secondary analysis of our randomised trial of nerve sliding in people with thumb carpometacarpal osteoarthritis, which has already shown ipsilateral hypoalgesic effects (Villafañe et al 2012a), to examine contralateral hypoalgesic effects. Therefore, the specific research question for this study was:

In people with thumb carpometacarpal osteoarthritis, does radial nerve mobilisation on the affected side reduce pressure pain sensitivity on the contralateral side?

Method

Design

Full details of the trial design and primary analysis are available elsewhere (Villafañe et al 2012a), with relevant parts of the design summarised here. Participants with thumb carpometacarpal osteoarthritis of the dominant hand were randomly assigned to an experimental or control group using simple randomisation with a random number generator. Allocation was concealed by generating each allocation after enrolment. The experimental group received a radial nerve slider technique and the control group received a sham intervention of sub-therapeutic ultrasound. Both interventions were applied only to the symptomatic hand. Pressure pain sensitivity was measured contralaterally at the carpometacarpal joint, the lateral epicondyle, and the hamate and scaphoid bones. Measurements were made at baseline, immediately after the 4-week treatment period, and at one month and two months after the treatment by an assessor blinded to the participants’ allocated group.

Participants and therapists

People with a diagnosis of carpometacarpal osteoarthritis of the dominant hand referred to a physiotherapy outpatient clinic at ‘Residenze Sanitarie Assistenziali’ (Avigiana and Sangano), Azienda Sanitaria Locale 3, Collegno, Italy were screened consecutively for eligibility. Inclusion criteria for this study were age between 70 and 90 years, intact cognitive abilities, and unilateral dominant hand thumb carpometacarpal osteoarthritis confirmed by the treating physician and by radiographic confirmation of Stage III–IV thumb carpometacarpal osteoarthritis according to the Eaton-Littler-Burton Classification (Eaton and Littler 1969). Exclusion criteria were other neuromuscular pathology in the hand (eg, De Quervain’s tenosynovitis, trigger finger), surgical interventions on the carpometacarpal joint, a Beck Depression Inventory score of more than 4 (Wang et al 2005), a State Trait Anxiety Inventory score of 30 or more (Antunes et al 2005), or any neurological condition in which pain perception was altered (Wajon and Ada 2005).

Both interventions were applied by an experienced physiotherapist with a 4-year post-graduate certificate in manual therapy and 11 years of experience in the management of musculoskeletal pain disorders.

Interventions

The experimental group received a neurodynamic nerve slider technique targeted to the radial nerve over the symptomatic hand for 6 sessions over 4 weeks. The technique was applied with the patient positioned in supine and the physiotherapist seated. The technique involved alternating the following two movements: shoulder depression applied simultaneously with elbow flexion and wrist extension; and shoulder elevation simultaneously with elbow extension, wrist flexion, and ulnar deviation. These movements were alternated at a rate of approximately 2 seconds per cycle (1 second into extension and 1 second into flexion). This technique is intended to produce a sliding movement of neural structures in relation to their adjacent tissues. Speed and amplitude of movement were adjusted such that no pain was produced. At each session, the technique was applied 3 times for 3 min separated by 1-min rest periods. Participants in the control group received a sham dose of intermittent ultrasound therapy to the thumb region for 10
Screened for eligibility (n = 68)

Excluded (n = 8)
- Not meeting inclusion criteria (n = 8)

Measured pressure-pain threshold
Randomised (n = 60)

Experimental Group
- Radial nerve sliding technique
- 3 x 3 min, with 1-min rest periods
- 6 sessions over 4 weeks

Control Group
- Detuned ultrasound to the hypothenar area
- 10 min/session
- 6 sessions over 4 weeks

Week 0
(n = 30)

Week 4
(n = 30)

Week 8
(n = 30)

Week 12
(n = 30)

Figure 1. Design and flow of participants through the trial.

minutes for 6 sessions over 4 weeks. Further detail of each intervention is available in the primary report of this trial (Villafañe et al 2012a).

Outcome measures
Pressure pain threshold is a quantitative sensory test of tissue sensitivity and it is defined as the minimal amount of pressure that produces pain, measured via a pressure algometer (Ylinen 2007). Pressure pain thresholds near to the pathological site are thought to represent the degree of peripheral nociception, whereas pressure pain thresholds distant to the pathology are a marker of central nervous system hyper-excitability (Kamper et al 2011). The validity and reproducibility of algometry has been described, with higher pressure pain thresholds indicating lower pain sensitivity (Fischer 1987). Pressure pain threshold was measured contralaterally over the lateral epicondyle, thumb carpometacarpal joint at the anatomical snuffbox, the tubercle of the scaphoid bone, and the unciform apophysis of the hamate bone. The pressure applied was increased by approximately 0.1 kg/cm² each second until the onset of pain. Three measurements were obtained from each point and the mean was used for statistical analysis. A 1-min rest period was allowed between each measurement. Pressure pain thresholds were measured in kg/cm² at baseline, immediately after treatment, and 1 and 2 months after the treatment period by an assessor blinded to the subject’s allocated group.

Data analysis
Group data were summarised using means and standard deviations. The Kolmogorov-Smirnov test confirmed the normality of the distribution of the data, so a repeated measures analysis of variance (ANOVA) was used to
Results

Screening identified 60 participants (6 men and 54 women) who met the eligibility criteria and agreed to participate. Between-group differences were observed (p < 0.05) at both follow-up periods. No important changes in any characteristic were found at baseline between the first two columns of Table 2. No important differences between post intervention and follow up periods (all p > 0.10). Between-groups effect sizes were large (between 0.5 and 0.8). The main hypothesis of interest was Group × Time interaction. Between-group differences were expressed as mean differences in kg/m² with 95% CIs. Between-groups effect sizes were calculated using Cohen's d coefficients (1988). An effect size greater than 0.8 was considered large, around 0.5 moderate, and less than 0.2 small (Cohen 1988). All analyses, p < 0.05 was considered statistically significant.

Table 1. Characteristics of participants at baseline.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exp</th>
<th>Con</th>
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<tbody>
<tr>
<td>Gender, n female (%)</td>
<td>28 (93)</td>
<td>26 (87)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>81 (7)</td>
<td>82 (7)</td>
</tr>
<tr>
<td>State Trait Anxiety Inventory score</td>
<td>24 (3)</td>
<td>23 (3)</td>
</tr>
<tr>
<td>Beck Depression Inventory score</td>
<td>24 (3)</td>
<td>23 (3)</td>
</tr>
<tr>
<td>Pain scores</td>
<td>24 (3)</td>
<td>23 (3)</td>
</tr>
<tr>
<td>PPT (EP)</td>
<td>5.3 (2.1)</td>
<td>5.1 (1.9)</td>
</tr>
<tr>
<td>PPT (CMC joint)</td>
<td>3.6 (1.5)</td>
<td>3.3 (1.3)</td>
</tr>
<tr>
<td>PPT (Scaphoid)</td>
<td>4.8 (2.3)</td>
<td>4.6 (1.7)</td>
</tr>
<tr>
<td>PPT (Hamate)</td>
<td>5.4 (2.4)</td>
<td>6.0 (2.1)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Groups</th>
<th>Difference within groups</th>
<th>Difference between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 4</td>
<td>Week 8</td>
</tr>
<tr>
<td></td>
<td>Exp</td>
<td>Con</td>
<td>Exp</td>
</tr>
<tr>
<td>Epicondyle PPT, (kg/cm²)</td>
<td>5.3 (2.1)</td>
<td>5.1 (1.9)</td>
<td>6.6 (1.9)</td>
</tr>
<tr>
<td>CMC joint PPT, (kg/cm²)</td>
<td>3.6 (1.5)</td>
<td>3.3 (1.3)</td>
<td>4.6 (1.9)</td>
</tr>
<tr>
<td>Scaphoid PPT, (kg/cm²)</td>
<td>4.8 (2.3)</td>
<td>4.6 (1.7)</td>
<td>5.9 (2.2)</td>
</tr>
<tr>
<td>Hamate PPT, (kg/cm²)</td>
<td>5.4 (2.4)</td>
<td>6.0 (2.1)</td>
<td>7.4 (2.1)</td>
</tr>
</tbody>
</table>

Exp = experimental group, Con = control group, CMC = carpometacarpal, PPT = pressure-pain threshold.
Discussion

This secondary analysis found that the application of a nerve slider neurodynamic intervention targeted to the radial nerve on the affected limb in participants with thumb carpometacarpal osteoarthritis exerted contralateral hypoalgesic effects, monitored by increases in pressure pain thresholds on the contralateral hand. The primary report of this trial identified ipsilateral hypoalgesia, indicating bilateral hypoalgesia from this unilateral technique.

These findings are consistent with emerging evidence suggesting that pain in osteoarthritis cannot be attributed solely to peripheral nociception, and that modulation by nociceptive processing contributes to the pain experience (Imamura et al 2008, Hochman et al 2010). Mechanisms of osteoarthritis-related pain are complex, involving local nociceptive signal generators (eg, synovium, bone marrow, and soft tissue inflammation), which release pro-inflammatory molecular mediators such as nerve growth factor, nitric oxide and prostanoids. These chemical mediators provoke neuroplastic sensitisation in the dorsal horn (Gwilym et al 2009) and central pain processing pathways (Ji et al 2002). For a comprehensive review of pain mechanisms in osteoarthritis, readers are referred to recent reviews (eg, Mease et al 2011). Clinically, radiation of pain proximally and distally from the affected joint, with descriptors such as burning, tingling, pins and needles, as well as hyperalgesia and allodynia indicate that central sensitisation mechanisms are present (Hochman et al 2010).

Mechanisms explaining a bilateral hypoalgesic effect of manual therapies remain hypothetical, although some theories exist. One potential mechanism is that spinal segmental sensitivity is enhanced bilaterally in osteoarthritis (Imamura et al 2008), and that neurodynamic intervention over the affected area would be able to decrease this sensitivity. Osteoarthritis is associated with enhanced excitability of dorsal horn neurons (Gwilym et al 2009), and this study tends to support the presence of peripheral sensitisation at the spinal cord level. An alternate mechanism may be that peripheral nerve nociceptive modulation influences endogenous cortical descending inhibitory pain pathways (Ossipov et al 2010). Modifying central sensitisation via the peripheral nervous system, including nerve slider neurodynamic techniques (de-la-Llave-Rincon et al 2012), may be a promising finding for improving pain management via decreasing dorsal horn sensitivity (Bialosky et al 2009), particularly in the subset of people who exhibit hyperalgesia and allodynia responses to persistent thumb carpometacarpal osteoarthritis pain.

A lack of blinding of the participants and therapists may have been a source of bias in this study. A second limitation is that we did not assess the participants’ preferences or expectations for treatment of their painful hand. Patient- and investigator-related factors are interrelated (eg, therapists’ beliefs can influence patients’ expectations of benefit) and have been shown to be influential in clinical trials of interventions for pain (Bishop et al 2011). Future studies are needed to confirm current findings, and to further investigate pain mechanisms in osteoarthritis-related pain.

In conclusion, this secondary analysis found that the application of a unilateral nerve slider neurodynamic intervention targeting the radial nerve on the symptomatic hand induced bilateral hypoalgesic effects in people with carpometacarpal osteoarthritis. This finding has important implications for therapy targets, as it suggests that peripherally directed therapies may modulate pain perception bilaterally. This preliminary finding opens avenues for future research in the modulation of pain pathways, perhaps offering targets to optimise peripheral manual and physical therapies for pain management in osteoarthritis. Future work could examine the extent to which application of manual therapies to the unaffected limb modulates pain on the affected extremity.

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References


