



Original article

Heightened pain sensitivity in individuals with signs and symptoms of carpal tunnel syndrome and the relationship to clinical outcomes following a manual therapy intervention ☆☆☆

Joel E. Bialosky^{a,b,*}, Mark D. Bishop^{a,b}, Michael E. Robinson^{b,c}, Donald D. Price^{b,d}, Steven Z. George^{a,b}

^a University of Florida, Department of Physical Therapy, Gainesville, PO Box 100154, FL 32610-0154, USA

^b Center for Pain Research and Behavioral Health, University of Florida, Gainesville, FL 32610-0154, USA

^c University of Florida, Department of Clinical and Health Psychology, Gainesville, FL 32610-0154, USA

^d University of Florida, Department of Oral and Maxillofacial Surgery, Gainesville, FL 32610-0154, USA

ARTICLE INFO

Article history:

Received 5 January 2011

Received in revised form

25 May 2011

Accepted 6 June 2011

Keywords:

Carpal tunnel syndrome

Manual therapy

Pain

ABSTRACT

Neurophysiological responses related to lessening of pain sensitivity are a suggested mechanism of manual therapy. Prior studies have observed generalized lower pain thresholds associated with carpal tunnel syndrome (CTS) in comparison to healthy controls. The present study sought to determine whether similar findings were present in suprathreshold measures and measures specific to central integration of pain (temporal summation and after sensations). Additionally, we wished to determine whether measures of pain sensitivity were related to clinical outcomes in participants with signs and symptoms of CTS receiving a manual therapy intervention. Individuals with signs and symptoms of CTS reported greater pain sensitivity to suprathreshold measures of mechanical pain, temporal summation, and after sensation in comparison to healthy controls. Immediate lessening of mechanical pain sensitivity and after sensations in response to a manual therapy intervention and 3-week attenuation of temporal summation following a 3-week course of manual therapy were associated with 3-week changes in clinical pain intensity in participants with signs and symptoms of CTS. These findings suggest heightened pain sensitivity across several parameters may be associated with CTS. Furthermore, changes in mechanical pain, after sensation, and temporal summation may be related to improvements in clinical outcomes.

© 2011 Elsevier Ltd. All rights reserved.

1. Introduction

Neurodynamic interventions (NDI) result in force and motion along peripheral nerves (Coppieters and Alshami, 2007) and are often referred to as “neural mobilization” (Haddick, 2007; Sebastian, 2010) suggesting a mechanical mechanism. Carpal tunnel syndrome (CTS) is characterized by compression of the median nerve (Gelberman et al., 1988); adhesions and edema within the carpal

tunnel (Oh et al., 2006); and limited mobility of the median nerve (Hough et al., 2007). NDI are frequently included in the conservative management of individuals with CTS with evidence suggesting effectiveness (Medina McKeon and Yancosek, 2008) and improved mobility of the median nerve could represent one mechanism.

In addition to mechanical abnormalities, CTS is characterized by generalized pain sensitivity (de la Llave-Rincon et al., 2009; Fernandez-de-Las-Penas et al., 2009, 2010b) and altered central nervous system processing (Tecchio et al., 2002). For example, bilateral heightened pain sensitivity is observed in individuals presenting with unilateral CTS (de la Llave-Rincon et al., 2009; Fernandez-de-Las-Penas et al., 2010b). Furthermore, alterations in cortical hand somatotopy are associated with CTS (Tecchio et al., 2002). These findings suggest central nervous system alterations in pain processing accompany the peripheral dysfunction associated with CTS. Decreased pain sensitivity occurs in response to manual therapy (Vicenzino et al., 2001; Frey Law et al., 2008) suggesting favorable alteration of neuroplastic changes associated with central sensitization (Boal and Gillette, 2004). Subsequently,

☆ This study was supported by a grant (R21AT002796) awarded to SZG from The National Institutes of Health National Center for Complementary and Alternative Medicine (NCCAM), the same grant also provided supported for JEB and MDB.

☆☆ This manuscript was written while JEB received support from Rehabilitation Research Career Development Program (5K12HD055929-02) and MDB received support from the National Institute of Arthritis and Musculoskeletal and Skin Disorders (K01AR054331).

* Corresponding author. University of Florida, Department of Physical Therapy, PO Box 100154, Gainesville, FL 32610-0154, USA. Tel.: +1 352 273 8636; fax: +1 352 273 6109.

E-mail address: bialosky@php.ufl.edu (J.E. Bialosky).

one mechanism of NDI could be lessening of pain sensitivity corresponding to central sensitization.

The first purpose of the current study was to compare age- and sex-matched healthy participants to those with signs and symptoms of CTS to observe whether differences existed in pain sensitivity. Generalized heightened sensitivity to *threshold* measures of pain accompanies CTS (Fernandez-de-Las-Penas et al., 2009; de la Llave-Rincon et al., 2009). The present study sought to determine whether pain sensitivity was also heightened in response to *suprathreshold* measures. We hypothesized individuals with signs and symptoms of CTS would demonstrate increased pain sensitivity to both threshold and suprathreshold measures of pain sensitivity.

Our second purpose was a planned secondary analysis of previously published data (Bialosky et al., 2009). The original study compared NDI to a sham intervention for outcomes related to clinical pain intensity and thermal and mechanical pain sensitivity in participants presenting with signs and symptoms of CTS. Significant improvements, not differing by group, were observed in measures of mechanical pain sensitivity, clinical pain, and function over 3 weeks. Additionally, immediate reductions in thermal pain sensitivity were observed in response to a 3-week trial of the studied NDI and not in response to the sham (Bialosky et al., 2009). This secondary analysis sought to study the relationship between changes in thermal and mechanical pain sensitivity and 3-week changes in clinical pain intensity in participants with signs and symptoms of CTS who received NDI. A recent study observed *threshold* measures of pain sensitivity which were not predictive of treatment success in response to a single session of physical therapy including NDI and soft tissue intervention in individuals with CTS (Fernandez-de-Las-Penas et al., 2010a). We wished to determine the relationship between *suprathreshold* measures of pain sensitivity and clinical outcomes. *Suprathreshold* measures of pain sensitivity are highly related to clinical pain (Staud et al., 2003b) and are potentially more predictive of clinical pain than *threshold* measures (Granot et al., 2003; Staud et al., 2003b; Werner et al., 2004). Accordingly, we hypothesized changes in *suprathreshold* measures of pain sensitivity would correlate to 3-week changes in clinical pain intensity.

2. Methods

2.1. Participants

The Institutional Review Board of the University of Florida approved this study. Participants with CTS were recruited from the clinics of orthopedic surgeons at the University of Florida and from the general public through posted flyers and electronic distribution. Participants were included if between the ages of 18 and 70 with signs and symptoms consistent with CTS as defined by pain or paresthesia in the median nerve distribution and at least one of the following clinical signs: 1) a positive Phalen sign, 2) a positive Tinel sign over the carpal tunnel, or 3) a positive carpal compression test. Participants were required to have CTS symptoms present for greater than twelve weeks and to rate their pain or symptom intensity at least a 4/10 on a numeric rating scale over the past 24 h. Exclusion criteria included non-English speaking; prior surgery for CTS; prior treatment with the studied NDI; pregnancy, other systemic disease known to cause peripheral neuropathy; current or history of chronic pain conditions. Healthy participants were recruited from the general public through posted flyers and electronic distribution and age and sex matched to those with signs and symptoms of CTS. Exclusion criteria for healthy participants included current or history of CTS in either extremity; systemic disease known to cause peripheral neuropathy; current or history of chronic pain condition; and pregnancy.

2.2. Measures

2.2.1. Identification of CTS signs and symptoms

We based inclusion on a clinical presentation of CTS rather than electrodiagnostic studies. The utility of electrodiagnostic testing in diagnosing CTS is not established (Graham, 2008; Taylor-Gjevrev et al., 2010). In fact, recent guidelines necessitate their use only when considering surgical intervention (Keith et al., 2009). We did not base inclusion in this study on electrodiagnostic findings due to 1) our participants were managed conservatively, and 2) our belief the clinical diagnosis was consistent with the typical patient presentation commonly treated conservatively with NDI. Inclusion for this study was based upon patient report of pain and paresthesia in the median nerve distribution in conjunction with positive findings on clinical tests for CTS. These tests are commonly included in isolation or in combination (Boland and Kiernan, 2009; Fernandez-de-Las-Penas et al., 2010a) and are common in the clinical diagnosis of CTS. Subsequently, we felt the combination of median nerve symptom distribution along with at least one positive clinical sign was representative of a patient likely to be given a clinical diagnosis of CTS and treated with NDI.

2.2.2. Demographic

Participants completed a demographic questionnaire for age, sex, ethnicity, racial group, employment status, marital status, education level, and household income.

2.2.3. Mechanical pain sensitivity (*suprathreshold*)

Mechanical pain sensitivity was obtained with a pressure algometer (Pain Diagnostics & Treatment, Great Neck, NY) through the application of 2.3 kg of force at a rate of 1 kg/s through a 1 cm² application tip over the carpal tunnel and the brachioradialis. We chose 2.3 kg of force as we desired a *suprathreshold* measure of mechanical pain sensitivity and have previously observed average mechanical pain thresholds of 2.0 kg in pilot studies from healthy participants (unpublished data). Subsequently, we expected 2.3 kg to produce pain in our healthy participants and those with signs and symptoms of CTS. Sites were chosen as specific to the carpal tunnel and a remote site indicative of general pain sensitivity (brachioradialis). Participants rated associated pain at each region on separate 100 mm mechanical visual analog scales (MVAS) anchored at one end with “no pain at all” and at the other with “worst pain imaginable”.

2.2.4. Thermal pain sensitivity

Participants underwent thermal pain assessment using the Medoc Neurosensory Analyzer (TSA-2001, Ramat Yishai, Israel) with a hand-held, peltier-element-based stimulator including the following:

2.2.5. Threshold

Thermal pain threshold was assessed at the thenar surface of the involved/more involved palm of participants with CTS and the dominant palm of healthy participants. The stimulator was applied at a baseline temperature of 35 °C and increased at a rate of 0.5 °C. Participants were instructed to verbally indicate when “the sensation changed from warm to painful”. The temperature at which the participant first indicated pain was recorded. A threshold measure was repeated 2 times and the average calculated.

2.2.6. Tolerance (*suprathreshold*)

Thermal pain threshold was assessed at the thenar surface of the involved/more involved palm of participants with CTS and the dominant palm of healthy participants. The stimulator was applied at a baseline temperature of 35 °C and increased at a rate of 0.5 °C. Participants were instructed to indicate “when the temperature

becomes so painful you can no longer stand it” and this temperature recorded. A thermal tolerance measure was repeated 2 times and the average temperature calculated.

2.2.7. Ramp and hold (suprathreshold)

Ramp and hold was assessed on the volar forearm of each participant. The thermode was applied with a baseline temperature of 35 °C rising rapidly (10 °C/s) to a peak of 49 °C. Participants rated the associated pain using a 100 mm MVAS anchored at one end with “no pain” and at the other with “worst pain imaginable” indicating A-delta fiber mediated pain sensitivity (Price et al., 2002). The protocol was performed two times with the average rating analyzed.

2.2.8. Temporal summation (suprathreshold)

Temporal summation was assessed on the palmar surface of the hand using ten consecutive heat pulses of less than 1 s duration at an inter-stimulus frequently of 0.33 Hz. The baseline temperature of each pulse was 35 °C and peaked at 51 °C. Participants rated their delayed (s) pain for each of the ten pulses using a 101 point numeric rating scale (NRS) anchored with “0 = no pain” and “100 = worst pain imaginable”. Temporal summation was quantified as a measure of the 5th pulse minus the 2nd pulse (Price et al., 2002).

2.2.9. After sensation (suprathreshold)

Participants quantified any pain they continued to feel 15 s following the tenth pulse in the temporal summation protocol using the same NRS. After sensation was defined as the rating of any pain persisting at 15 s following the last thermal pulse (Staud et al., 2007).

Temporal summation and after sensations are considered primarily mediated by C-fiber afferents (Price et al., 1977).

2.2.10. Clinical pain intensity

Clinical pain intensity was assessed using an NRS (0 = “none” to 100 = “worst imaginable”) for “usual pain” over the past week. The NRS is reliable and valid (Jensen et al., 1999) measure of pain intensity.

2.3. Procedures

All individuals agreeing to participate signed an informed consent form approved by the University of Florida Institutional Review Board and completed a demographic form. Participants with signs and symptoms of CTS provided an NRS for “usual pain over the previous week”. Next, all participants underwent baseline standardized quantitative sensory assessment of mechanical and thermal pain sensitivity. Healthy participants were then finished with the study.

Participants with signs and symptoms of CTS were randomly assigned to receive either an NDI known to cause specific force and movement across the median nerve (Coppieters and Alshami, 2007) or a sham NDI. Description of the studied and sham NDI and related outcomes has been previously reported (Bialosky et al., 2009). We included only individuals who received the NDI in the current analysis to assess relationships between clinical pain and changes in thermal and mechanical pain sensitivity in response to a common manual therapy intervention. Following randomization, participants underwent the first session of their assigned intervention followed immediately by reassessment of pain sensitivity to observe for an immediate within session treatment effect. Participants with signs and symptoms of CTS were seen 2 times per week over the next 3 weeks for a maximum of 6 treatment sessions. The final treatment session included follow-up questionnaires, pre-

and post-intervention pain sensitivity testing, and measurement of clinical pain intensity. Assessment at the 3-week follow-up session was performed by an examiner blinded to group assignment.

2.4. Data analysis

Twenty participants with signs and symptoms of CTS and 20 age- and sex-matched healthy participants were included in the analysis for the first purpose of the study. Each participant was assessed unilaterally. The involved side was used for analysis in participants with unilateral CTS. The more involved side was used for analysis in participants with bilateral CTS. The dominant side was used for analysis in participants with bilateral CTS unable to identify a “more involved” side. The dominant arm was used for analysis in the healthy participants. Significance was set at $p \leq 0.05$ for all outcomes.

2.4.1. Differences in pain sensitivity

Baseline group differences in pain sensitivity were assessed through independent *t*-tests. After sensation was categorized as present or absent based upon whether the participant reported persistent pain 15 s following the temporal summation protocol. The incidence of after sensation between healthy participants and those with CTS was assessed using a chi-square test.

2.4.2. Relationship between pain sensitivity and clinical pain intensity

Measures of pain sensitivity difference between groups were included in these analyses. Bivariate associations were calculated for baseline measures of pain sensitivity and clinical pain intensity in participants with CTS. Next, bivariate associations were calculated for baseline within session changes in pain sensitivity in response to manual therapy and 3-week change in “usual” clinical pain. This analysis indicated the relationship between immediate hypoalgesia in response to manual therapy and clinical outcome. Finally, bivariate associations were calculated for 3 weeks changes in measures of both pain sensitivity and usual clinical pain to examine whether observed change was associated with clinical outcomes.

Cohen’s *d* was calculated where appropriate as a parallel measure of magnitude.

3. Results

3.1. Group-related differences in pain sensitivity

Twenty female participants with CTS were age matched to 20 female healthy participants. Clinical examination findings for the participants with CTS included a positive Tinnel sign in 17/20 (85%), Phalen sign in 15/20 (75%), and carpal compression test in 14/20 (70%). Furthermore, 17/20 (85%) of the participants were positive on 2 of 3 clinical tests and 10/20 (50%) were positive on 3 of 3 clinical tests. Mean age for participants experiencing CTS was 40.75 (sd = 10.38) years old and for healthy participants 38.25 (sd = 12.32). The groups did not differ significantly on age ($p = 0.49$) and Levene’s test for equality of variance indicated no difference ($F = 2.50$, $p = 0.12$). Duration of symptoms for the participants with CTS ranged from 12 weeks to 936 weeks with a median value of 156 weeks. Duration of symptoms had large variability however was not associated with any of the outcome measures ($p > 0.05$) so we did not include it as a covariate in any of the analyses. Demographic information is reported in Table 1. Education differed significantly between the groups, however was not considered a covariate as a significant association was not observed with any of the studied outcome variables ($p > 0.05$).

Table 1
Demographic information for sample.

	Signs and symptoms of CTS	Healthy	<i>p</i> -value
Age (weeks (sd))	40.75 (10.38)	38.25 (12.32)	0.49
Ethnicity			
Hispanic/Latino	3	2	
Not Hispanic/Latino	17	18	0.63
Race			
Asian	1	2	
African American	3	0	
Caucasian	16	18	0.18
Employment			
Full time	13	13	
Part time	3	5	
Unemployed	3	1	
Retired	1	0	0.48
Marital status			
Single	7	10	
Married	5	9	
Living with significant other	2	0	
Divorced	5	0	
Widowed	1	1	0.07
Education			
High school	4	1	
Some college	6	2	
Graduated college	5	1	
Some postgraduate work	3	5	
Postgraduate degree	2	11	0.01*
Income			
<20,000	6	9	
20,000–35,000	7	2	
35,001–50,000	1	4	
50,001–70,000	3	0	
>70,000	3	5	0.07

Demographic information for individuals with signs and symptoms of carpal tunnel syndrome (CTS) and healthy controls. * $p < 0.05$.

Significant ($p < 0.05$) differences in pain sensitivity were observed in measures of mechanical pain sensitivity at the carpal tunnel and brachioradialis, and temporal summation (Table 2). A greater prevalence of after sensation was also observed in participants with CTS ($\chi_{(1)}^2 = 3.96, p = 0.05$).

Table 2
Pain sensitivity comparison between individuals with signs and symptoms of carpal tunnel syndrome and healthy controls.

	s/s CTS	Healthy	Mean difference (SE)	<i>p</i> -value	Cohen's <i>d</i>
Thermal threshold	43.70 (2.40)	44.88 (2.22)	1.18 (0.73)	0.12	0.51
Thermal tolerance	48.70 (1.39)	49.06 (1.02)	0.36 (0.38)	0.36	0.30
Ramp and hold	39.05 (24.46)	27.10 (24.37)	1.20 (0.77)	0.13	0.49
Temporal summation	8.10 (16.86)	-2.35 (8.13)	10.45 (4.19)	0.02*	0.79
After sensation	25.70 (23.86)	10.50 (6.66)	15.2 (12.4)	0.24	0.87
MP flexor retinaculum	11.80 (16.31)	3.60 (6.79)	0.82 (0.40)	0.05*	0.66
MP brachioradialis	28.80 (31.67)	10.75 (14.87)	1.81 (0.78)	0.03*	0.73

Presented in means (standard deviation). Thermal threshold and tolerance are provided as the temperatures at which the participant first indicated pain perception (threshold) and reported the inability to tolerate any greater temperature (tolerance). SE = standard error of difference. MP = mechanical pain sensitivity to 2.2 kg of force. χ^2 was used to determine between group differences in after sensation with a significantly greater proportion of individuals with signs and symptoms of carpal tunnel syndrome (s/s CTS) reporting after sensation (10/20) than healthy participants (4/20). Ratings for after sensation reported in the table are only for the participants who reported persistent pain 15 s following the final pulse in the temporal summation protocol ($n = 12$). * Significant at $p < 0.05$.

3.2. Changes in clinical pain and pain sensitivity in response to NDI

Changes in clinical pain and measures of pain sensitivity observed to differ between participants with and without CTS are displayed in Table 3.

3.3. Correlates of pain sensitivity and clinical pain intensity

We further assessed the variables found to significantly differ by group for a relationship with ratings of clinical pain in participants with CTS. A small to moderate association was observed between baseline measures of both after sensation and temporal summation and baseline clinical pain intensity (Table 4). Immediate changes following the manual therapy intervention in both mechanical pain sensitivity at the brachioradialis and after sensation were moderately associated with 3-week changes in usual clinical pain (Table 5). A small to moderate relationship was observed between 3-week changes in temporal summation and 3-week changes in usual clinical pain (Table 6).

4. Discussion

We observed increased pain sensitivity to suprathreshold measures in individuals with signs and symptoms of CTS. Furthermore, we observed a relationship between both immediate and 3-week changes in measures of pain sensitivity and clinical outcomes. These findings provide preliminary evidence for a prognostic value for immediate changes in pain sensitivity and a potential mechanism through which NDI may alter pain associated with CTS.

4.1. Group-related differences in pain sensitivity

Prior studies suggest heightened pain sensitivity is associated with CTS (de la Llave-Rincon et al., 2009; Fernandez-de-Las-Penas et al., 2009, 2010b). We have extended this finding to suprathreshold stimuli including temporal summation and after sensation. Temporal summation and after sensation differentiate individuals with other chronic pain conditions from healthy controls (Staud et al., 2003a). Similarly, we observed temporal summation and after sensation to differentiate participants with signs and symptoms of CTS from healthy individuals. Prior studies of CTS suggest a central pain mechanism (Zanette et al., 2006; Fernandez-de-Las-Penas et al., 2009). Specifically, CTS is associated with generalized pain sensitivity, (Fernandez-de-Las-Penas et al., 2009) complaints beyond the median nerve distribution, (Zanette et al., 2006) and cortical changes (Tecchio et al., 2002). Collectively these studies suggest a central pain mechanism in addition to peripheral dysfunction at the carpal tunnel. Temporal summation and after sensation reflect afferent pain processing at the dorsal horn of the spinal cord (Price et al., 2002) and increased sensitivity to these measures likely represents a change in central nervous system response or processing of afferent pain inputs. Our findings converge with previous studies suggesting a centrally mediated pain mechanism of CTS and identify temporal summation and after sensation as additional indicators of this process.

Interventions for CTS frequently target peripheral dysfunction such as braces to minimize pressure and surgery. Our findings suggest, in addition to a peripheral process, pain associated with CTS is reflective of a central process with a potential role in both the progression of acute pain to chronic pain and the maintenance of chronic pain (Rygh et al., 2005). NDI provides a peripheral stimulus (Coppieters and Alshami, 2007) and may inhibit musculoskeletal pain centrally through a reduction of central sensitization of pain (Boal and Gillette, 2004). Furthermore, a peripheral process may

Table 3
Changes in outcome measures associated with neurodynamic intervention.

	Baseline pre-NDI	Baseline post-NDI	Change in baseline	<i>p</i> -value	3-week	3-week change	<i>p</i> -value
Clinical pain	51.3 (28.7)	NA	NA	NA	37.9 (29.5)	–13.4 (31.2)	0.08
MP brachioradialis	30.8 (26.7)	26.5 (29.4)	–4.3 (18.2)	0.32	23.9 (25.5)	–6.9 (16.4)	0.14
MP flexor retinaculum	14.0 (20.9)	14.5 (21.2)	0.05 (13.5)	0.87	8.1(13.8)	–5.9 (17.6)	0.09
Temporal summation	8.1 (19.0)	1.2 (13.4)	–6.9 (23.9)	0.21	2.5 (16.0)	–5.6 (21.4)	0.23
After-sensation	25.4 (21.2)	22.9 (26.1)	–2.5 (16.9)	0.62	30.2 (31.5)	4.8 (24.8)	0.43

Immediate and 3-week changes in pain sensitivity and clinical pain intensity in response to a neurodynamic intervention (NDI). MP = mechanical pain sensitivity to 2.3 kg of force as indicated along a 100 mm mechanical visual analog scale (mvas). Clinical pain, temporal summation, and after-sensation were all measured by a 0 to 100 numeric rating scale anchored with 0 = no pain to 100 = the worst pain imaginable.

Table 4
Baseline relationship between clinical pain and pain sensitivity in participants with signs and symptoms of carpal tunnel syndrome (CTS).

	Usual pain	Temporal summation	After sensation	MP flexor retinaculum	MP brachioradialis
Usual pain	1				
Temporal summation	0.39 (<i>p</i> = 0.09)	1			
After sensation	0.39 (<i>p</i> = 0.21)	0.37 (<i>p</i> = 0.24)	1		
MP flexor retinaculum	0.13 (<i>p</i> = 0.21)	0.15 (<i>p</i> = 0.53)	0.88* (<i>p</i> < 0.01)	1	
MP brachioradialis	0.27 (<i>p</i> = 0.24)	0.23 (<i>p</i> = 0.34)	0.08 (<i>p</i> = 0.81)	0.38 (<i>p</i> = 0.10)	1

Associations between baseline measures of pain sensitivity and clinical pain intensity. Usual pain obtained with a 101-point numeric rating scale anchored with 0 = “no pain at all” to 100 = “the worst pain imaginable”. Participants were instructed to indicate their usual level of pain related to carpal tunnel syndrome during the past week. Measures of after sensation are provided only for participants who reported pain at 15 s following the final thermal pulse in the temporal summation protocol (*n* = 12). MP = mechanical pain sensitivity to 2.3 kg of force. * Significant at *p* < 0.05.

Table 5
Relationship between immediate changes in pain sensitivity and 3-week changes in clinical pain in participants with signs and symptoms of carpal tunnel syndrome (CTS).

	Change in usual pain over 3 weeks	Temporal summation	After sensation	MP flexor retinaculum	MP brachioradialis
Change in usual pain over 3 weeks	1				
Temporal summation	0.35 (<i>p</i> = 0.14)	1			
After sensation	0.54 (<i>p</i> = 0.07)	0.24 (<i>p</i> = 0.45)	1		
MP flexor retinaculum	–0.11 (<i>p</i> = 0.68)	–0.57* (<i>p</i> = 0.05)	–0.55* (<i>p</i> = 0.01)	1	
MP brachioradialis	0.52* (<i>p</i> = 0.03)	0.34 (<i>p</i> = 0.16)	0.53 (<i>p</i> = 0.08)	–0.16 (<i>p</i> = 0.51)	1

Pain sensitivity changes assessed during the initial research session prior to and immediately following a neurodynamic intervention (NDI). Baseline clinical pain was assessed at the first visit when participants with signs and symptoms of CTS were asked to indicate their “usual” pain over the past week using a 101-point numeric rating scale anchored with 0 = no pain and 100 = the worst pain imaginable. Participants were seen up to 6 sessions over the next 3 weeks to receive the NDI. A measure of “usual” pain was again taken at the final session in 3 weeks. After sensation includes only participants (*n* = 12) reporting pain at 15 s following conclusion of the temporal summation protocol. MP = mechanical pain sensitivity to 2.3 kg of force. * Significant at *p* < 0.05.

drive or maintain central sensitization (Fernandez-de-Las-Penas et al., 2009; Staud et al., 2009) and NDI may interrupt this process through a peripheral effect. The current study suggests a potential central pain process beyond peripheral impairments through which NDI may inhibit pain in individuals with CTS.

4.2. Correlates of changes in pain sensitivity and changes in clinical pain intensity

We did not observe mean changes in measures of pain sensitivity; however, changes were observed at the individual level (Figs. 1 and 2). Treatment effects of conservative interventions for pain conditions are often small leading to the

suggestion subgroups of individuals may respond to specific interventions (Stanton et al., 2011). Similar findings are reported in CTS in response to NDI leading to similar suggestions (Medina McKeon and Yancosek, 2008). The results of the current study suggest changes in pain sensitivity that may be a prognostic and mechanistic consideration for a subgroup of individuals with CTS.

Prior studies of manual therapy have reported within session changes in clinical pain intensity predict between session changes (Tuttle, 2005). Our findings suggest immediate changes in mechanical pain sensitivity and after sensation may be prognostic for clinical pain relief following a 3-week course of NDI. Temporal summation is a behavioral measure of wind up at the dorsal horn of

Table 6
Relationship between 3-week changes in pain sensitivity and 3-week changes in clinical pain.

	Change in usual pain over 3 weeks	Temporal summation	After sensation	MP flexor retinaculum	MP brachioradialis
Change in usual pain over 3 weeks	1				
Temporal summation	0.41 (<i>p</i> = 0.08)	1			
After sensation	0.09 (<i>p</i> = 0.79)	0.33 (<i>p</i> = 0.32)	1		
MP flexor retinaculum	–0.19 (<i>p</i> = 0.45)	0.21 (<i>p</i> = 0.40)	0.49 (<i>p</i> = 0.13)	1	
MP brachioradialis	0.03 (<i>p</i> = 0.91)	–0.06 (<i>p</i> = 0.80)	–0.39 (<i>p</i> = 0.24)	–0.09 (<i>p</i> = 0.73)	1

Pain sensitivity and clinical pain changes occurring over 3 weeks. Clinical pain was assessed with a 101-point numeric rating scale anchored with 0 = no pain and 100 = the worst pain imaginable for “usual” pain over the past week. Participants were seen up to 6 sessions over the next 3 weeks to receive the NDI. After sensation includes only participants (*n* = 12) reporting pain at 15 s following conclusion of the temporal summation protocol during baseline assessment. Measures of pain sensitivity and “usual” pain were again taken at the final session in 3 weeks. MP = mechanical pain sensitivity to 2.3 kg of force. * Significant at *p* < 0.05.

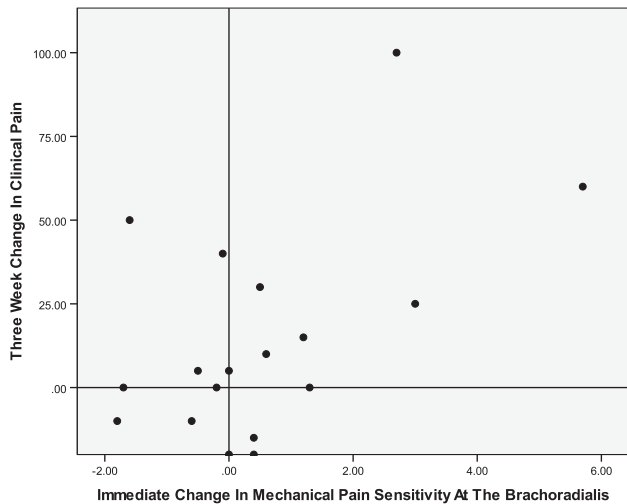


Fig. 1. Association between immediate change in mechanical pain sensitivity at the brachioradialis and 3-week change in clinical pain ($r = 0.52$). Positive numbers on the y-axis indicate greater improvement in clinical pain related to carpal tunnel syndrome over a 3-week period. Positive numbers on the x-axis indicate lessening of mechanical pain sensitivity at the brachioradialis over a 3-week period. Individuals in the top right quadrant and lower left quadrant demonstrated a positive association between immediate changes in mechanical pain sensitivity at the brachioradialis and 3-week changes in clinical pain.

the spinal cord (Price et al., 2002) and immediate hypoalgesia of temporal summation corresponds to the studied NDI (Beneciuk et al., 2009; Bialosky et al., 2009). The findings from the current study also provide preliminary support for attenuation of temporal summation as a potential mechanism through which NDI inhibits pain related to CTS.

4.3. Limitations

Limitations of the current study are we included only women and our findings may not translate to men. Additionally, the individuals in our study were followed for only 3 weeks. We cannot say

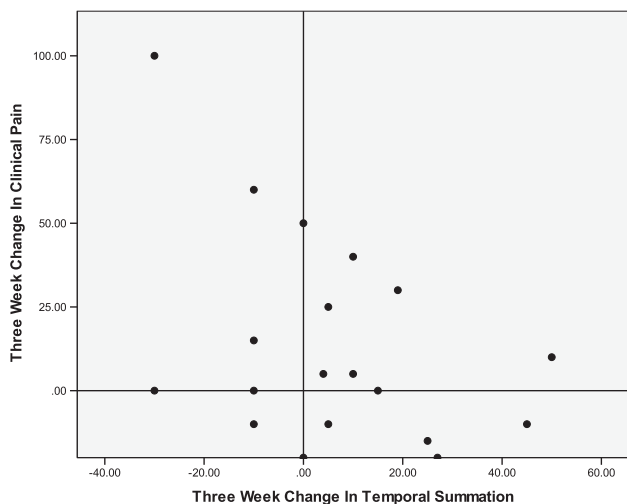


Fig. 2. Association between 3-week change in temporal summation and 3-week change in clinical pain ($r = 0.41$). Positive numbers on the y-axis indicate greater improvement in clinical pain related to carpal tunnel syndrome over a 3-week period. Positive numbers on the x-axis indicate lessening of temporal summation of thermal pain over a 3-week period. Individuals in the top right quadrant and lower left quadrant demonstrated a positive association between 3-week changes in temporal summation and clinical pain.

with certainty the relationships observed between changes in pain sensitivity and clinical pain would persist over a longer time period. Our sample size was a further limitation. A larger sample size may have resulted in additional findings or allowed for multivariate analyses.

5. Conclusion

Participants with signs and symptoms of CTS differed from healthy age- and sex-matched controls in suprathreshold measures of pain sensitivity suggesting a central mechanism of pain. Immediate change in mechanical pain sensitivity and after sensation and 3-week change in temporal summation were associated with improvements in clinical pain intensity suggesting prognostic factors and a potential mechanism for improvement respectively.

References

Beneciuk J, Bishop M, George S. Effects of upper extremity neural mobilization on thermal pain sensitivity: a Sham controlled study in asymptomatic participants. *J Orthop Sports Phys Ther* 2009;39(6):428–38.

Bialosky JE, Bishop MD, Price DD, Robinson ME, Vincent KR, George SZ. A randomized Sham-controlled trial of a neurodynamic technique in the treatment of carpal tunnel syndrome. *J Orthop Sports Phys Ther* 2009;39(10):709–23.

Boal RW, Gillette RG. Central neuronal plasticity, low back pain and spinal manipulative therapy. *J Manipulative Physiol Ther* 2004;27(5):314–26.

Boland RA, Kiernan MC. Assessing the accuracy of a combination of clinical tests for identifying carpal tunnel syndrome. *J Clin Neurosci* 2009;16(7):929–33.

Coppieters MW, Alshami AM. Longitudinal excursion and strain in the median nerve during novel nerve gliding exercises for carpal tunnel syndrome. *J Orthop Res* 2007;25(7):972–80.

Fernandez-de-Las-Penas C, de la Llave-Rincon AI, Fernandez-Carnero J, Cuadrado ML, rendt-Nielsen L, Pareja JA. Bilateral widespread mechanical pain sensitivity in carpal tunnel syndrome: evidence of central processing in unilateral neuropathy. *Brain* 2009;132:1472–9.

Fernandez-de-Las-Penas C, Cleland JA, Ortega-Santiago R, de-la-Llave-Rincon AI, Martinez-Perez A, Pareja JA. Central sensitization does not identify patients with carpal tunnel syndrome who are likely to achieve short-term success with physical therapy. *Exp Brain Res* 2010a;207(1–2):85–94.

Fernandez-de-Las-Penas C, Madeleine P, Martinez-Perez A, Arendt-Nielsen L, Jimenez-Garcia R, Pareja JA. Pressure pain sensitivity topographical maps reveal bilateral hyperalgesia of the hands in patients with unilateral carpal tunnel syndrome. *Arthritis Care Res (Hoboken)* 2010b;62(8):1055–64.

Frey Law LA, Evans S, Knudtson J, Nus S, Scholl K, Sluka KA. Massage reduces pain perception and hyperalgesia in experimental muscle pain: a randomized, controlled trial. *J Pain* 2008;9(8):714–21.

Gelberman RH, Rydevik BL, Pess GM, Szabo RM, Lundborg G. Carpal tunnel syndrome. A scientific basis for clinical care. *Orthop Clin North Am* 1988;19(1):115–24.

Graham B. The value added by electrodiagnostic testing in the diagnosis of carpal tunnel syndrome. *J Bone Joint Surg Am* 2008;90(12):2587–93.

Granot M, Lowenstein L, Yarnitsky D, Tamir A, Zimmer EZ. Postcesarean section pain prediction by preoperative experimental pain assessment. *Anesthesiology* 2003;98(6):1422–6.

Haddick E. Management of a patient with shoulder pain and disability: a manual physical therapy approach addressing impairments of the cervical spine and upper limb neural tissue. *J Orthop Sports Phys Ther* 2007;37(6):342–50.

Hough AD, Moore AP, Jones MP. Reduced longitudinal excursion of the median nerve in carpal tunnel syndrome. *Arch Phys Med Rehabil* 2007;88(5):569–76.

Jensen MP, Turner JA, Romano JM, Fisher LD. Comparative reliability and validity of chronic pain intensity measures. *Pain* 1999;83(2):157–62.

Keith MW, Masear V, Chung K, Maupin K, Andary M, Amadio PC, et al. Diagnosis of carpal tunnel syndrome. *J Am Acad Orthop Surg* 2009;17(6):389–96.

de la Llave-Rincon AI, Fernandez-de-Las-Penas C, Fernandez-Carnero J, Padua L, Arendt-Nielsen L, Pareja JA. Bilateral hand/wrist heat and cold hyperalgesia, but not hypoesthesia, in unilateral carpal tunnel syndrome. *Exp Brain Res* 2009;198(4):455–63.

Medina McKeon JM, Yancosek KE. Neural gliding techniques for the treatment of carpal tunnel syndrome: a systematic review. *J Sport Rehabil* 2008;17(3):324–41.

Oh J, Zhao C, Zobitz ME, Wold LE, An KN, Amadio PC. Morphological changes of collagen fibrils in the subsynovial connective tissue in carpal tunnel syndrome. *J Bone Jt Surg Am* 2006;88(4):824–31.

Price DD, Hu JW, Dubner R, Gracely RH. Peripheral suppression of first pain and central summation of second pain evoked by noxious heat pulses. *Pain* 1977;3(1):57–68.

- Price DD, Staud R, Robinson ME, Mauderli AP, Cannon R, Vierck CJ. Enhanced temporal summation of second pain and its central modulation in fibromyalgia patients. *Pain* 2002;99(1–2):49–59.
- Rygh LJ, Svendsen F, Fiska A, Haugan F, Hole K, Tjolsen A. Long-term potentiation in spinal nociceptive systems – how acute pain may become chronic. *Psychoneuroendocrinology* 2005;30(10):959–64.
- Sebastian D. Triangular interval syndrome: a differential diagnosis for upper extremity radicular pain. *Physiother Theory Pract* 2010;26(2):113–9.
- Stanton TR, Fritz JM, Hancock MJ, Latimer J, Maher CG, Wand BM, et al. Evaluation of a treatment-based classification algorithm for low back pain: a cross-sectional study. *Phys Ther* 2011;91(4):496–509.
- Staud R, Cannon RC, Mauderli AP, Robinson ME, Price DD, Vierck Jr CJ. Temporal summation of pain from mechanical stimulation of muscle tissue in normal controls and subjects with fibromyalgia syndrome. *Pain* 2003a;102(1–2):87–95.
- Staud R, Robinson ME, Vierck Jr CJ, Cannon RC, Mauderli AP, Price DD. Ratings of experimental pain and pain-related negative affect predict clinical pain in patients with fibromyalgia syndrome. *Pain* 2003b;105(1–2):215–22.
- Staud R, Robinson ME, Price DD. Temporal summation of second pain and its maintenance are useful for characterizing widespread central sensitization of fibromyalgia patients. *J Pain* 2007;8(11):893–901.
- Staud R, Nagel S, Robinson ME, Price DD. Enhanced central pain processing of fibromyalgia patients is maintained by muscle afferent input: a randomized, double-blind, placebo-controlled study. *Pain* 2009;145(1–2):96–104.
- Taylor-Gjevrev RM, Gjevrev JA, Nair B. Suspected carpal tunnel syndrome: do nerve conduction study results and symptoms match? *Can Fam Physician* 2010;56(7):e250–4.
- Tecchio F, Padua L, Aprile I, Rossini PM. Carpal tunnel syndrome modifies sensory hand cortical somatotopy: a MEG study. *Hum Brain Mapp* 2002;17(1):28–36.
- Tuttle N. Do changes within a manual therapy treatment session predict between-session changes for patients with cervical spine pain? *Aust J Physiother* 2005;51(1):43–8.
- Vicenzino B, Paungmali A, Buratowski S, Wright A. Specific manipulative therapy treatment for chronic lateral epicondylalgia produces uniquely characteristic hypoalgesia. *Man Ther* 2001;6(4):205–12.
- Werner MU, Duun P, Kehlet H. Prediction of postoperative pain by preoperative nociceptive responses to heat stimulation. *Anesthesiology* 2004;100(1):115–9.
- Zanette G, Marani S, Tamburin S. Extra-median spread of sensory symptoms in carpal tunnel syndrome suggests the presence of pain-related mechanisms. *Pain* 2006;122(3):264–70.