

Effects of Neurodynamic Mobilizations on Pain Hypersensitivity in Patients With Hand Osteoarthritis Compared to Robotic Assisted Mobilization: A Randomized Clinical Trial

Paolo Pedersini,¹ Kristin Valdes,² Raquel Cantero-Tellez,³ Joshua A. Cleland,⁴ Mark D. Bishop,⁵ and Jorge H. Villafañe¹ 

Objective. To evaluate the effectiveness of the neurodynamic mobilization techniques compared with passive robotic physiologic movement in patients with hand osteoarthritis (OA).

Methods. We conducted a randomized controlled trial. A total of 72 patients (mean \pm SD age 71 ± 11 years) with dominant symptomatic hand OA were randomized in 2 groups, and both received 12 treatment sessions over 4 weeks. The experimental group received neurodynamic mobilization of the median, radial, and ulnar nerves, and the control group received robotic-assisted passive movement treatment. Both groups also participated in a program of hand stability exercises. Outcome measures included pain intensity, pressure pain thresholds (PPTs), and strength measurements. Group-by-time effects were compared using mixed-model analyses of variance.

Results. After the intervention, the experimental group had statistically significant, higher PPTs than the control group at the thumb carpometacarpal joint by 0.7 kg/cm^2 (95% confidence interval [95% CI 0.6, 0.8]), the median nerve by 0.7 kg/cm^2 (95% CI 0.6, 0.7), and the radial nerve by 0.5 kg/cm^2 (95% CI 0.3, 0.6); however, the difference was not statistically significant at 3 months postintervention. Although mean values in the experimental group were higher than in the control group at all PPT sites at both assessments, these differences were not statistically significant. The experimental group experienced a statistically significant reduction in pain immediately postintervention, but this was not present at the 3-month follow-up. There were no statistically significant differences in pinch or grip strength between groups.

Conclusion. We found that neurodynamic mobilizations decreased hypersensitivity in patients with hand OA immediately after the intervention; however, differences were no longer present at 3 months. The results suggest that these techniques may have some limited value in the short term but do not have lasting effects.

INTRODUCTION

The prevalence of symptomatic osteoarthritis (OA) of the hand is ~67% in the general population (1). The carpometacarpal (CMC) joint of the thumb is most commonly affected by OA, followed by the interphalangeal (IP) joints (2,3). The magnitude of damage or inflammation present in OA is not directly correlated to the pain intensity reported by individuals with OA, particularly those with chronic pain. In individuals with chronic OA pain, the experience is more likely related to central nervous system (CNS)

involvement (4,5), and recent studies suggest that OA is a mixed pain state and that in some individuals, CNS factors play an important role (6,7).

For example, individuals with hand OA who underwent functional magnetic resonance imaging analysis showed increased activation in the thalamus, cingulate, and the frontal and somatosensory cortex, which are the brain's pain processing centers and have been implicated in central sensitization (8). Chronic OA pain may also lead to allodynia, in which nonpainful stimuli may produce the sensation of pain, or a painful stimulus may be perceived

⁴ ClinicalTrials.gov identifier: NCT02701335.

Supported by a grant from the Ministry of Health, Italy (project code GR-2013-02358472).

¹Paolo Pedersini, PT, Jorge H. Villafañe, PhD: IRCCS Fondazione Don Carlo Gnocchi, Milan, Italy; ²Kristin Valdes, OTD: Gannon University, Ruskin, Florida; ³Raquel Cantero-Tellez, PhD: University of Malaga, Malaga, Spain; ⁴Joshua A. Cleland, PhD: Franklin Pierce University, Manchester, New Hampshire; ⁵Mark D. Bishop, PhD: University of Florida, Gainesville.

No potential conflicts of interest relevant to this article were reported.

Address correspondence to Jorge H. Villafañe, PhD, ~~Clinical Research, Fondazione Don Carlo Gnocchi, Via Riccardo Galeazzi, 4 Milan Lombardia 20161, Italy~~. Email: mail@villafañe.it.

Submitted for publication May 3, 2019; accepted in revised form October 29, 2019.

SIGNIFICANCE & INNOVATIONS

- Neurodynamic mobilizations (sliding techniques) immediately decreased hypersensitivity in patients with hand osteoarthritis (OA). This effect was not maintained at the 3-month follow-up.
- The results suggest that these techniques may be useful in the short term for patients with hand OA.

as more intense compared to the experience in asymptomatic individuals (8,9). To examine the presence of this sensitivity, assessing pressure pain threshold (PPT) (i.e., tenderness to palpation) has been shown to be a reliable and valid method for identifying individuals with central sensitization (10).

The European League Against Rheumatism published a systematic literature review that summarized the current non-pharmacologic, pharmacologic, and surgical approaches for the management of hand OA (11). The review identified 28 studies that evaluated nonpharmacologic treatments of hand OA, including exercise, joint protection, splints, assisted devices, and combinations of the interventions (11). However, none of the reviewed studies considered interventions that specifically targeted reducing pain sensitivity (11). Identifying nonpharmacologic interventions to reduce local and widespread pain sensitivity in hand OA could address a missing component of management for individuals who present with signs and symptoms of nervous system sensitization.

Neurodynamic mobilization techniques are a form of manual therapy aimed at influencing the neural structures through positioning and movement of multiple joints to reduce pain (12). Numerous studies by Wolney and Linek have shown that neurodynamic mobilization have been effective in reducing pain and improving functional status and nerve conduction velocity when compared to both a control group and a sham (13–15). However, a limited number of studies have examined the effects of neurodynamic techniques on individuals with joint pathology in the hand. Previous work (16) has shown that neurodynamic mobilization techniques may modify PPTs by potentially reducing pain sensitivity in individuals with hand OA and might potentially be an appropriate management strategy in the presence of central sensitization. Considering that neurodynamic techniques have been beneficial for individuals with carpal tunnel syndrome, and that preliminary evidence suggests that they may be beneficial for patients with OA of the CMC thumb joint, further research is warranted to determine the clinical effectiveness of these techniques compared to other interventions (13–15,17,18).

Additionally, robotic physiologic movements have recently been introduced as a method to assist with the completion of exercise (19,20). Recent technologies have developed robots to serve to assist patients in the rehabilitation process, thus maximizing patient outcomes (21). Actually, the focus of research using robotic devices has been on interventions to improve upper

extremity functionality in neurologic populations, particularly patients with a history of stroke (22). To our knowledge, robotic physiologic movement in orthopedic patients has not been well explored in clinical research beyond passive movement after joint arthroplasty, although it has already demonstrated beneficial effects on the CNS and sensorimotor deficits in neurologic patients (23,24). These robotic tools assist the patient with carrying out exercise protocols. Among these devices, the glove provides computer-controlled, repetitive and passive mobilization of the fingers with multisensory feedback (25). However, the effects of robotic physiologic movement have not been compared to neural mobilization in a patient population with hand OA. Therefore, the aim of the current study was to evaluate the effectiveness of the neurodynamic mobilization techniques compared with passive robotic physiologic movement in patients with hand OA.

SUBJECTS AND METHODS

Study design. We conducted a randomized clinical trial. Informed consent was obtained from all patients, and procedures were conducted according to the Declaration of Helsinki and approved by a local ethics committee. The study was registered at ClinicalTrials.gov (NCT02701335). The IRCCS Fondazione Don Carlo Gnocchi Ethics Committee approved the study on February 24, 2016. All participants gave written informed consent before data collection began.

Subjects. From July 2016 to April 2018, all patients presenting to the IRCCS Fondazione Don Carlo Gnocchi clinic in Italy and diagnosed with dominant hand OA were screened for eligibility. Inclusion criteria for the study were ages between 50 and 90 years and symptoms of OA in the dominant hand; only the dominant hand received the treatment intervention. OA was confirmed by the treating physician and by radiographic findings (OA severity of 3 to 4 on the Kellgren/Lawrence scale). Exclusion criteria were subjects scoring >6 points on the Beck Depression Inventory or >30 points in the State-Trait Anxiety Inventory. Patients with a medical history of carpal tunnel syndrome, surgical interventions to the hand, or DeQuervain's tenosynovitis, and those with degenerative or nondegenerative neurologic conditions in which pain perception could be altered, were also excluded.

Randomization. Participants were randomly assigned to either neurodynamic mobilization or passive robotic physiologic movements using simple randomization with a random number generator created by an individual not involved in subject recruitment. Randomization was conducted using a random sequence generator program (<http://www.random.org>).

An assessor blinded to the patients' allocated group obtained measurements at baseline, immediately after the 4-week treatment period, and at 3 months after the treatment. Interventions in both groups were applied by the same physical therapist, who

1 had 3 years of experience in manual therapy and the management
2 of musculoskeletal pain disorders. Both groups were provided with
3 the same instructions regarding effectiveness of the treatment.
4

5 **Interventions.** *Neurodynamic intervention group (NIG).*

6 The experimental group received a neurodynamic nerve slider
7 technique targeted to the median, radial, and ulnar nerves
8 of the symptomatic extremity for 12 sessions over a 4-week
9 timeframe (26). The technique was applied with the physio-
10 therapist standing and the patient positioned in supine. These
11 techniques aim to produce neural sliding in relation to adjacent
12 tissues (12). In order not to produce pain, speed and ampli-
13 tude of movements were adjusted. These movements were
14 alternated at a rate of ~2 seconds per cycle (1 second into
15 extension, and 1 second into flexion). At each session, the
16 techniques were applied 3 times for 3 minutes separated by
17 1-minute rest periods. These techniques originated from the
18 work of Shacklock and Butler (27).

19 Median nerve technique. The patient was placed in the fol-
20 lowing position prior to performing the median nerve slider tech-
21 nique: shoulder girdle depression; glenohumeral abduction and
22 external rotation; supination of the forearm; and wrist, thumb,
23 and finger extension. The neurodynamic technique for the medi-
24 an nerve consisted of the following alternating movements: the
25 combination of elbow extension (which increases tension) and
26 wrist flexion (which decreases tension) movement with the com-
27 bination of elbow flexion (decreasing tension) and wrist exten-
28 sion (increasing tension) movement (28).

29 Radial nerve technique. The patient was placed in the fol-
30 lowing position prior to the performance of the radial nerve slid-
31 er technique: shoulder girdle depression; glenohumeral internal
32 rotation; pronation of the forearm; elbow extension; and wrist,
33 thumb, and finger flexion. The neurodynamic technique for the
34 radial nerve involved alternating the following movements: the
35 combination of elbow flexion–wrist flexion (unloads the radial
36 nerve) with elbow extension–wrist extension (loading) (16,29).

37 Ulnar nerve technique. For the ulnar nerve, the wrist was
38 placed in extension, the elbow was flexed, and the shoulder ab-
39 ducted. The slider neurodynamic technique for the ulnar nerve in-
40 volved alternating the following movements: elbow flexion (unloads
41 the ulnar nerve) and shoulder abduction (loads the ulnar nerve) was
42 alternated with elbow extension (loading) and shoulder adduction
43 (unloading) throughout the sliding technique; the wrist was main-
44 **13** tained in 60° extension and the forearm in supination (30).

45 *Passive physiologic movement group.* Participants re-
46 ceived half an hour of robotic passive movement treatment
47 using a Gloreha Workstation (Idrogenet) for 12 sessions over
48 4 weeks. The patients wore a glove, and every finger was
49 attached to individual thimbles connected through a nylon
50 thread to a device interfaced with a hybrid system (com-
51 pressed air and oil) that performed the passive movement of

52 **F1** flexion–extension of the fingers (Figure 1). Further details of

the intervention are available elsewhere (31). Patients in both
groups also received additional standardized exercises, as de-
scribed by Villafañe et al (32).

Outcome measures. Pain intensity was assessed using a
visual analog scale (VAS; 0 = no pain, 10 = maximum pain) for 3
separate pain status conditions: 1) level of pain while executing a
key pinch between the thumb and index finger; 2) average level of
pain over the last 24 hours; and 3) average level of pain over the
last week (31).

The PPT test is a quantitative sensory test of tissue sensi-
14 tivity, and it is defined as the minimal amount of pressure where
the sense of pressure changes to pain. An electronic algometer
(Algomed) was used to measure the PPTs (33). The validity and
reproducibility of algometry has been described, with higher PPTs
indicating lower pain sensitivity. PPTs near the pathologic site are
thought to represent the degree of peripheral nociception, whereas
decreased PPTs distal to the pathology are markers of hyperexcit-
15 ability of the CNS (34). An assessor blinded to the patient's group
assessed PPT bilaterally over the hand (thumb CMC at the center
of the anatomic snuffbox and unciform apophysis of the hamate
bone), the C5–C6 zygapophyseal joint, and the median, radial,
and ulnar nerves. We assessed widespread pain sensitivity given
the evidence for central sensitization in individuals with OA and
the recommendations for examining sensitivity at multiple sites.
The tested nerve sites were chosen based on the accessibility
of the nerve. The median nerve was palpated distally at the wrist
between the palmaris longus and flexor carpi radialis longus; the
nerve was accessed after moving the tendons laterally. The radial
nerve was palpated in the anatomic snuffbox, and the ulnar nerve
in the cubital tunnel at the elbow (35). Assessment of PPT in in-
dividuals with hand OA has been shown to be very reliable (36), with
scores for minimal detectable change (MDC) as follows: C5–C6
16 joint (95% confidence interval [95% CI] 0.3–0.5 kg/cm²), thumb
CMC joint (95% CI 0.3–0.5 kg/cm²), hamate bone (95% CI 0.2–0.4

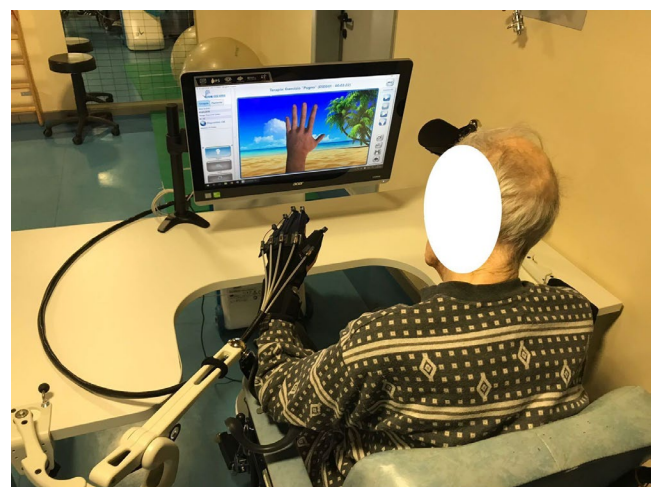


Figure 1. Robotic passive mobilization treatment.

1 kg/cm²), median nerve (95% CI 0.3–0.6 kg/cm²), radial nerve (95%
2 CI 0.2–0.8 kg/cm²), and ulnar nerve (95% CI 0.2–0.4 kg/cm²).

3 Grip strength measurements were obtained with a grip
4 dynamometer (Baseline), which has a precision of $\pm 3\%$. The grip
5 dynamometer has 5 settings representing grip spans; however,
6 position 2 was used during this study because it has been shown
7 to be the most reliable for reporting maximal grip strength for both
8 clinical and research purposes (37). Pinch strength was measured
9 with a mechanical pinch gauge (Baseline). The reliability of the pro-
10 cedure to measure pinch strength has been shown to be 0.93
11 (38). Patients, placed in a seated position, with elbow flexed to
12 90°, forearm in neutral resting on the arm of the chair, and wrist in
13 neutral, were instructed to compress the dynamometer with max-
14 imal isometric contractions for 3 seconds. The reported strength
15 value was the average of the 3 trials measured (with a 1-minute
16 rest period between each measurement).

17
18 **Sample size determination.** The sample size and power
19 calculations were performed with ENE 3.0 software (GlaxoSmith-
20 Kline, Universidad Autónoma). The calculations were based on
21 detecting the mean difference of a 2-cm, minimum clinically
22 important difference (MCID) (39) on a 10-cm VAS, assuming an
23 SD of 2 cm, a 2-tailed test, an α level of 0.05, and a desired power
24 of 90%. The estimated desired sample size was 30 individuals per
25 group. To accommodate expected dropouts before study com-
26 pletion, a total of 36 participants were included in each group.

Statistical analysis. Data were analyzed using SPSS for
Windows, version 24, conducted following an intent-to-treat
analysis using the last-value-forward method. The results are
expressed as means, SDs, and/or 95% confidence intervals
(95% CIs). A Kolmogorov-Smirnov test showed a normal dis-
tribution of the data. Separate $2 \times 2 \times 3$ mixed-model analyses
of variance (ANOVAs), with group (experimental, control) as the
between-subjects factor and side (ipsilateral, contralateral to the
hand with OA) and time (baseline, postintervention at 4 weeks, 20
and at 3-months follow-up) as within-subject factors, were con-
ducted to examine the effects of the intervention on VAS score,
PPT, and pinch and grip strength as the dependent variables.
The main hypothesis of interest was group \times time interaction.
Post hoc comparisons were conducted using Bonferroni cor-
rection. Between-groups effect sizes were calculated using
Cohen's d coefficient. We considered an effect size >0.8 large,
 ~ 0.5 moderate, and <0.2 small (40). The statistical analysis was
conducted at a 95% CI, and P values less than 0.05 were con-
sidered significant.

RESULTS

Demographic and clinical data on patients. A total of
74 consecutive patients were screened, and 72 patients (32 men
and 40 women, ages 74–90 years) were eligible and agreed
to participate. Figure 2 shows the recruitment and retention of 22

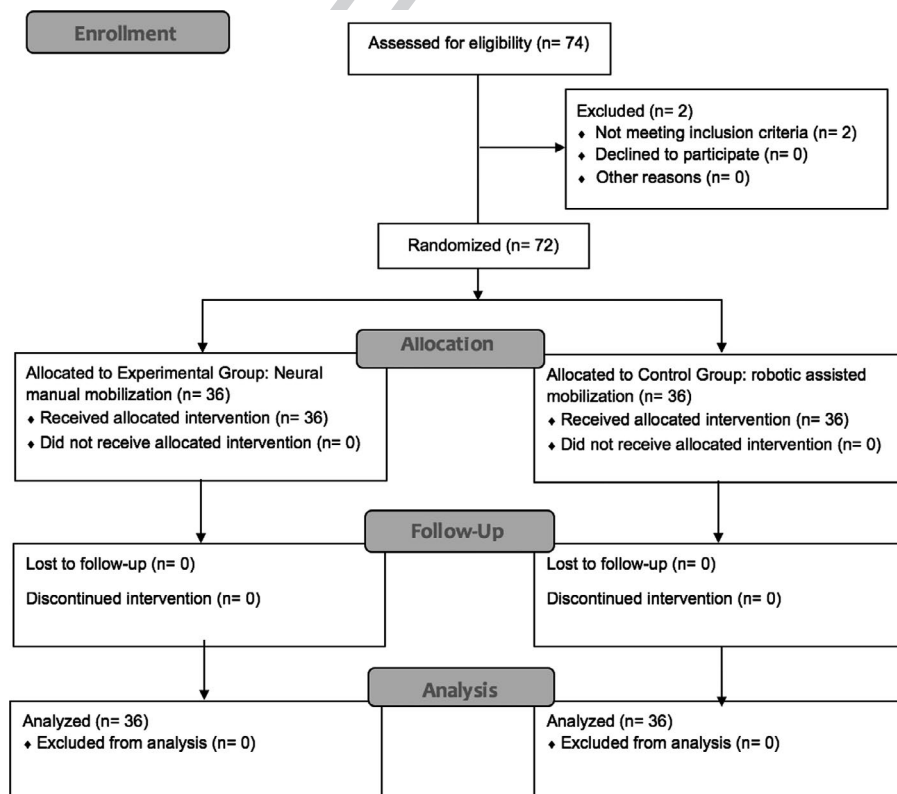


Figure 2. Consort flow chart.

1 patients through the trial. Baseline characteristics of the patients
2 T1 T2 in each group are presented in Tables 1 and 2.

3
4 **Response to treatment.** *Pain intensity of the hand.* For
5 average VAS during pinch strength testing, over the last 24
6 hours and over the last week, the ANOVA revealed no sig-
7 nificant group \times time \times side, group \times side, or side \times time (all
8 $P > 0.05$) interactions. There was also no significant main effect
9 23 for side. There was a significant main effect of group \times time for
10 pain intensity in VAS score over the last 24 hours ($F = 5.47$,
11 $P = 0.02$) but not in VAS score during pinch strength testing
12 ($F = 0.56$, $P = 0.46$) or VAS score over the last week ($F = 0.19$,
13 $P = 0.66$). Post hoc analysis indicated that patients with hand
14 24 OA receiving the NIG intervention experienced a significant
15 reduction in pain immediately postintervention (experimen-
16 tal group mean 1.4 [95% CI -1.8 , -0.9]; control group mean
17 0.6 [95% CI -1.1 , -0.1]; mean difference between groups
18 25 0.8 [95% CI -1.1 , -0.5]; all $P < 0.01$) but not at 3-months
19 follow-up for the dominant side (VAS score over the last 24
20 hours). Between-groups effect sizes were moderate at post-
21 treatment and follow-up periods ($d < 0.2$).

22 *PPTs.* PPT data for the 5 sites are presented in Table 2.
23 The ANOVA revealed no statistically significant group \times time \times
24 side, side \times time, or group \times side (all $P > 0.05$) interactions.
25 The ANOVA did reveal significant group \times time interactions for
26 PPT over the ipsilateral thumb CMC joint ($P = 0.044$), median
27 ($P < 0.001$), and radial ($P = 0.005$) nerves for the experimental
28 group, and group \times side interactions for PPT of the median nerve
29 ($P = 0.001$) for the experimental group.

30 The post hoc testing revealed increases in PPT at the thumb
31 CMC joint and the median and radial nerves in the experimental
32 group immediately after intervention as compared with baseline

33
34
35 **Table 1.** Characteristics of patients at baseline*

Characteristics	Exp. (n = 36)	Con. (n = 36)
Age, years	71 \pm 11	69 \pm 12
Female sex, no. (%)	21 (58)	19 (52)
BDI score	2.7 \pm 1.2	3.0 \pm 1.7
STAI score	22.9 \pm 3.4	23.8 \pm 3.1
Q-DASH score	22 \pm 15	19 \pm 12
Right hand		
VAS score, strength†	2.4 \pm 1.5	2.5 \pm 1.4
VAS score, 24 hours‡	3.0 \pm 2.2	3.0 \pm 1.6
VAS score, 1 week§	2.5 \pm 1.5	2.8 \pm 1.4
Left hand		
VAS score, strength†	1.2 \pm 0.6	1.0 \pm 0.1
VAS score, 24 hours‡	1.6 \pm 1.3	1.2 \pm 0.5
VAS score, 1 week§	1.5 \pm 1.1	1.2 \pm 0.5

36
37
38
39
40
41
42
43
44
45
46
47
48 * Values are the mean \pm SD unless indicated otherwise. BDI = Beck
49 Depression Inventory; Con. = control group; Exp. = experimental
50 group; Q-DASH = Quick Disabilities of the Arm, Shoulder, and Hand;
51 STAI = State-Trait Anxiety Inventory; VAS = visual analog scale.

51 † VAS score while executing a grip strength.

52 ‡ VAS score over the last 24 hours.

§ VAS score over the last week.

data (experimental group mean 0.7 [95% CI 0.6, 0.8]; control
group mean 0.2 [95% CI 0.1, 0.4], experimental group mean
0.7 [95% CI 0.6, 0.7]; control group mean 0.1 [95% CI 0.2,
0.4] and experimental group mean 0.5 [95% CI 0.3, 0.6]; con-
control group mean 0.2 [95% CI 0.1, 0.4], respectively; all $P < 0.02$)
but not at 3-month follow-up. The post hoc testing also revealed
a significant difference between groups in PPT on the median
nerve on both sides (dominant side mean 1.5 [95% CI 2.2, 0.9];
nondominant side mean 1.1 [95% CI 1.8, 0.4]; $P = 0.01$) but not
at 3-month follow-up. Between-groups effect sizes were small
to moderate (between $d = 0.09$ and $d = 0.25$) and small ($d < 0.2$)
at between-sides after the intervention. 26

26 *Pinch and grip strength.* For key pinch strength, the ANOVA
revealed no significant group \times time \times side ($F = 1.49$, $P = 0.23$),
group \times time ($F = 0.01$, $P = 0.99$), side \times time ($F = 0.06$, $P = 0.81$),
or group \times side ($F = 0.46$, $P = 0.50$) interactions. For grip strength,
the ANOVA revealed no significant group \times time \times side ($F = 2.71$,
 $P = 0.11$), group \times time ($F = 0.02$, $P = 0.89$), side \times time ($F = 3.35$,
 $P = 0.07$), or group \times side ($F = 0.33$, $P = 0.57$) interactions (Table 2).

DISCUSSION

Our results showed significantly heightened PPTs (indicat-
ing lower pain sensitivity) over the thumb CMC joint and median
and radial nerves immediately after neurodynamic mobilizations
but not after passive movement. There was also a significant 27
decrease in pain intensity over the past 24 hours in the dominant
hand of the NIG intervention group. However, these effects were
not maintained at 3 months postintervention.

These results are similar to those of previous work investigat-
ing the effects of neurodynamic mobilization on individuals with
OA of the CMC thumb joint. For example, Villafañe et al (28) found
in a series of 15 patients with OA of the CMC thumb joint receiv-
ing neurodynamic mobilizations changes in PPT over the carpal
bones immediately following the techniques. In a follow-up clinical
trial, the same group found radial nerve mobilizations to be supe-
rior to placebo for improving PPT and pinch strength (29). Further-
more, a clinical trial examining the effects of radial mobilization also
found that nerve techniques were superior to placebo for improv-
ing sensory deficits (16). However, those studies only examined
the effects of a single intervention, radial nerve-biased mobiliza-
tion. The current study is the first to examine effects of median and
ulnar nerve-biased techniques in individuals with hand OA.

The presence of widespread hyperalgesia to pressure in indi-
viduals with OA of the CMC thumb joint has been reported previ-
ously (41). Clinically, a reliable way to assess pain sensitivity in the
hands and arms of patients with OA is by applying firm pressure
over several IP joints of each hand and over the adjacent phalan-
ges, and then proximally to include firm palpation of the muscles
of the forearm, including the lateral epicondyle region, to assess
overall pain threshold (4). If the individual is tender in many of these 28
areas, or in just the muscles of the forearm, he or she is likely

21 Table 2. Mean \pm SD for outcomes at all study visits for each group (n = 36), mean \pm SD difference within groups (n = 36), and mean (95% confidence interval) difference between groups (n = 72)*

Outcome	Pre-group dominant		Pre-group nondominant		Post-group dominant		Post-group nondominant		Within-group difference, post minus pre, dominant†		Within-group difference, post minus pre, nondominant		Between-group difference, dominant†	Between-group difference, nondominant†
	Exp.	Con.	Exp.	Con.	Exp.	Con.	Exp.	Con.	Exp.	Con.	Exp.	Con.		
VAS score, strength	2.4 \pm 1.5	2.5 \pm 2.5	1.4 \pm 1.3	1.1 \pm 0.3	1.4 \pm 0.6	1.7 \pm 0.8	1.2 \pm 0.7	1.0 \pm 0.1	-1.0 \pm 0.2	-0.8 \pm 0.2	-0.2 \pm 0.1	-0.1 \pm 0.1	-0.3 (-0.8, 0.1)	0.2 (-0.1, 0.5)
VAS score, 24 hours	3.0 \pm 2.2	3.0 \pm 1.6	1.6 \pm 1.3	1.2 \pm 0.5	1.6 \pm 0.9	2.4 \pm 1.3	1.4 \pm 0.8	1.1 \pm 0.3	-1.4 \pm 0.2†	-0.6 \pm 0.2	-0.2 \pm 0.1	-0.1 \pm 0.1	-0.8 (-1.4, -0.2)	0.3 (-0.1, 0.6)
VAS score, 1 week	2.5 \pm 1.5	2.8 \pm 1.4	1.5 \pm 1.1	1.2 \pm 0.5	1.2 \pm 0.5	1.2 \pm 0.5	1.7 \pm 0.8	2.0 \pm 1.0	-1.3 \pm 0.3	-1.6 \pm 0.3	0.2 \pm 0.2	0.8 \pm 0.3	0.1 (-0.2, 0.4)	-0.3 (-0.8, 0.2)
Thumb CMC joint PPT, kg/cm ²	4.0 \pm 1.6	4.0 \pm 1.3	4.3 \pm 1.3	4.3 \pm 1.2	4.7 \pm 1.4	4.3 \pm 1.3	4.5 \pm 1.3	4.3 \pm 1.2	0.7 \pm 0.1†	-0.3 \pm 0.1	0.2 \pm 0.1	0.0 \pm 0.1	0.4 (-0.6, 1.0)	0.2 (-0.6, 0.9)
Hamate PPT, kg/cm ²	4.3 \pm 1.6	3.9 \pm 1.4	4.6 \pm 1.5	4.2 \pm 1.1	4.6 \pm 1.5	4.2 \pm 1.2	4.6 \pm 1.4	4.3 \pm 1.2	0.3 \pm 0.1	0.3 \pm 0.1	0.0 \pm 0.1	0.1 \pm 0.1	0.4 (-0.4, 1.2)	0.3 (-0.4, 1.1)
Median nerve PPT, kg/cm ²	5.2 \pm 1.4	4.0 \pm 1.1	5.5 \pm 1.2	4.4 \pm 1.0	5.9 \pm 1.3	4.3 \pm 1.1	5.6 \pm 1.3	4.5 \pm 1.1	0.7 \pm 0.1†	0.3 \pm 0.1	0.1 \pm 0.1	0.1 \pm 0.1	1.5 (0.9, 2.2)‡	1.1 (0.4, 1.8)‡
Radial nerve PPT, kg/cm ²	4.4 \pm 1.2	4.6 \pm 1.3	4.7 \pm 0.9	4.8 \pm 1.0	4.9 \pm 1.1	4.8 \pm 1.0	4.8 \pm 0.9	4.7 \pm 1.0	0.5 \pm 0.1†	0.2 \pm 0.1	0.1 \pm 0.1	-0.1 \pm 0.1	0.1 (-0.5, 0.7)	0.1 (-0.4, 0.7)
Ulnar nerve PPT, kg/cm ²	5.0 \pm 1.3	4.7 \pm 1.0	5.4 \pm 1.3	5.2 \pm 1.0	5.2 \pm 1.3	5.0 \pm 1.0	5.5 \pm 1.3	5.3 \pm 1.0	0.2 \pm 0.1	0.3 \pm 0.1	0.1 \pm 0.1	0.1 \pm 0.1	0.2 (-0.4, 0.9)	0.2 (-0.4, 0.9)
Key pinch strength, kg	6.7 \pm 3.2	5.4 \pm 2.2	7.1 \pm 3.0	6.0 \pm 2.0	7.5 \pm 2.9	6.0 \pm 1.8	7.6 \pm 3.0	6.7 \pm 2.0	0.8 \pm 0.4	0.6 \pm 0.2	0.5 \pm 0.2	0.7 \pm 0.4	1.5 (0.2, 2.9)	0.9 (-0.4, 2.4)
Grip strength, kg	7.4 \pm 3.1	7.0 \pm 2.8	8.0 \pm 2.3	7.6 \pm 2.3	8.2 \pm 2.7	7.6 \pm 2.5	8.2 \pm 2.3	8.2 \pm 2.5	0.8 \pm 0.3	0.6 \pm 0.3	0.2 \pm 0.2	0.6 \pm 0.2	0.6 (-0.8, 2.1)	0.0 (-1.4, 1.4)

* CMC = carpometacarpal (joint); Con. = control group; Exp. = experimental group; PPT = pressure pain threshold; VAS = visual analog scale.

† Exp. minus Con.

‡ Significant difference between group (P < 0.05).

22

1 diffusely tender (i.e., has a low central pain threshold) (4), whereas
2 patients who exhibit sharp local tenderness or pain distal to the
3 joint with OA may exhibit CNS hypersensitivity (34).

4 We agree with previous recommendations that clinicians
5 should take into account the presence of central sensitization and
6 widespread pressure pain hypersensitivity in patients with hand
7 OA by not limiting their intervention to the affected area (18). We
8 used the neurodynamic sliding techniques in our study. Alterna-
9 tive neurodynamic methods (e.g., tensioning techniques) exist
10 that are proposed to affect intraneural pressure, thereby affecting
11 function (12). However, we specifically used sliding techniques to
12 allow large amplitude movements to be performed. This may pres-
13 ent the movement in a novel way to the brain, uncoupling pre-
14 viously learned expectations of pain with movement (12). It has
15 also been suggested that the larger-range sliding movements may
16 decrease the fear of movement, assisting in cortical remapping (12)
17 and decreasing sensitivity, as generally seen in the current study.
18 Specifically, we identified improvements in PPT at the median and
19 radial nerves; however, we didn't see the same effect at the ulnar
20 nerve. Therefore, the true physiologic mechanisms by which slid-
21 ing techniques alter PPT at the median and radial nerves require
22 further scientific investigation.

23 In our prior work (36), we identified MDC values for PPT in
24 individuals with hand OA across many of the regions tested in
25 the current study. Changes in PPT that exceeded the MDC were
26 identified for the thumb CMC joint and over the radial and median
27 nerves in this study. What is not known is the MCID for individuals
28 with hand OA. The MCID has been established in patients with
29 hip and knee OA, with a status of "much better" as a reduction
30 of 33%, while 15% reduction was considered "slightly better" (42)
31 for changes in sensitivity measures (i.e., PPT). Our study found
32 that changes in the PPTs of the thumb CMC joint and median
33 and radial nerves ranged from 11% to 13% in the arthritic hand.
34 Although not reaching the benchmark of 15–33% for lower
35 extremity OA, the changes found in the current study surpassed
36 10% and may potentially be clinically relevant.

37 Our study did have some limitations. We only used 1 test-
38 ing measure to determine the presence of pain sensitivity (i.e., PPT).
39 It would be useful to use multiple testing measures to adequately
40 assess pain-processing alterations in hand OA. Also, we assessed
41 outcomes at 4 weeks and then again at 3 months. It would be
42 useful to have a longer follow-up period. Despite the conflicting
43 evidence for the effect of neurodynamic mobilization on nerve con-
44 duction velocity, performing such testing bilaterally might also have
45 provided insight into any changes in central and peripheral neural
46 function. Also, it was impossible to blind the patients to the treat-
47 ment that they received, although all patients received the same
48 information regarding the efficacy of the treatment. Both groups
49 received a program of hand stability exercises as well. This may be
50 a confounding variable if the combination of treatments (i.e., NIR
51 and exercise) was more important for outcome than the treatments
52 without exercise. Additionally, 1 physical therapist performed all

treatment techniques, which may limit the generalizability. Another
limitation is that we did not assess all outcome domains recom-
mended in the Outcome Measures in Rheumatology–Osteoarthritis
Research Society International core sets for outcome measurement
in hand OA trials (43); specifically, physical function and health-
related quality of life. Consequently, we are unable to comment on
the impact of observed changes in the proxy measures of sensi-
tization (i.e., PPT) in these areas. Future studies should also con-
sider incorporating a graded motor imagery program, which may
provide better insight into the role of peripheral versus central input
in the maintenance of sensitization in this disorder.

In conclusion, we found that neurodynamic mobilizations
(sliding techniques) and exercise decreased hypersensitivity in
patients with hand OA to a greater extent than passive movement
combined with exercise immediately after the intervention. We are
unable to calculate the effect of the neurodynamic mobilization
without the influence of the exercise program. These results were
not maintained at the 3-month follow-up. Therefore, future studies
should continue to examine the effects of neural mobilization in
individuals with hand OA to determine if any true benefits exist. **30**

ACKNOWLEDGMENTS

The authors thank B. P. for her contributions to this study. **31**

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically
for important intellectual content, and all authors approved the final version
to be submitted for publication. Dr. Villafañe had full access to all of the
data in the study and takes responsibility for the integrity of the data and
the accuracy of the data analysis.

Study conception and design. Villafañe.

Acquisition of data. Pedersini, Villafañe.

Analysis and interpretation of data. Pedersini, Valdes, Cantero-Tellez,
Cleland, Bishop, Villafañe.

REFERENCES

1. Zhang Y, Niu J, Kelly-Hayes M, Chaisson CE, Aliabadi P, Felson DT. Prevalence of symptomatic hand osteoarthritis and its impact on functional status among the elderly: the Framingham Study. *Am J Epidemiol* 2002;156:1021–7.
2. Wilder FV, Barrett JP, Farina EJ. Joint-specific prevalence of osteoarthritis of the hand. *Osteoarthritis Cartilage* 2006;14:953–7.
3. Kroon FB, van Beest S, Ermurat S, Kortekaas MC, Bloem JL, Reijnen M, et al. In thumb base osteoarthritis structural damage is more strongly associated with pain than synovitis. *Osteoarthritis Cartilage* 2018;26:1196–202.
4. Clauw DJ, Hassett AL. The role of centralised pain in osteoarthritis. *Clin Exp Rheumatol* 2017;35 Suppl 107:79–84.
5. Villafañe JH, Valdes K, Pedersini P, Berjano P. Osteoarthritis: a call for research on central pain mechanism and personalized prevention strategies. *Clin Rheumatol* 2019;38:583–4.
6. Fingleton C, Smart KM, Moloney NA, Fullen BM, Doody CM. Pain sensitization in people with knee osteoarthritis: a systematic review and meta-analysis. *Osteoarthritis Cartilage* 2015;23:1043–56.
7. O'Leary H, Smart KM, Moloney NA, Blake C, Doody CM. Pain sensitization associated with nonresponse after physiotherapy in people with knee osteoarthritis. *Pain* 2018;159:1877–86.

- 1 8. Sofat N, Smee C, Hermansson M, Howard M, Baker EH, Howe FA,
2 et al. Functional MRI demonstrates pain perception in hand osteo-
3 arthrosis has features of central pain processing. *J Biomed Graph*
4 *Comput* 2013;3:10.5430.
- 5 9. He BH, Christin M, Mouchbahani-Constance S, Davidova A,
6 Sharif-Naeini R. Mechanosensitive ion channels in articular nocicep-
7 tors drive mechanical allodynia in osteoarthritis. *Osteoarthritis*
8 *Cartilage* 2017;25:2091–9.
- 9 10. Greenspan JD, Slade GD, Bair E, Dubner R, Fillingim RB, Ohrbach
10 R, et al. Pain sensitivity risk factors for chronic TMD: descriptive data
11 and empirically identified domains from the OPPERA case control
12 study. *J Pain* 2011;12 Suppl:T61–74.
- 13 11. Kroon FP, Carmona L, Schoones JW, Kloppenburg M. Efficacy and
14 safety of non-pharmacological, pharmacological and surgical treat-
15 ment for hand osteoarthritis: a systematic literature review informing
16 the 2018 update of the EULAR recommendations for the manage-
17 ment of hand osteoarthritis. *RMD Open* 2018;4:e000734.
- 18 12. Coppieters MW, Butler DS. Do ‘sliders’ slide and ‘tensioners’ ten-
19 sion? An analysis of neurodynamic techniques and considerations
20 regarding their application. *Man Ther* 2008;13:213–21.
- 21 13. Wolny T, Linek P. The effect of manual therapy including neurody-
22 namic techniques on the overall health status of people with car-
23 pal tunnel syndrome: a randomized controlled trial. *J Manipulative*
24 *Physiol Ther* 2018;41:641–9.
- 25 14. Wolny T, Linek P. Neurodynamic techniques versus “sham” therapy
26 in the treatment of carpal tunnel syndrome: a randomized placebo-
27 controlled trial. *Arch Phys Med Rehabil* 2018;99:843–54.
- 28 15. Wolny T, Linek P. Is manual therapy based on neurodynamic tech-
29 niques effective in the treatment of carpal tunnel syndrome? A ran-
30 domized controlled trial. *Clin Rehabil* 2019;33:408–17.
- 31 16. Villafañe JH, Bishop MD, Fernandez-de-Las-Penas C, Langford
32 D. Radial nerve mobilisation had bilateral sensory effects in people
33 with thumb carpometacarpal osteoarthritis: a randomised trial. *J*
34 *Physiother* 2013;59:25–30.
- 35 17. Bertozzi L, Valdes K, Vanti C, Negrini S, Pillastrini P, Villafane JH.
36 Investigation of the effect of conservative interventions in thumb car-
37 pometacarpal osteoarthritis: systematic review and meta-analysis.
38 *Disabil Rehabil* 2015;37:2025–43.
- 39 18. Villafañe JH, Valdes K, Berjano P, Wajon A. Clinical update: con-
40 servative management of carpometacarpal joint osteoarthritis. *J*
41 *Rheumatol* 2015;42:1728–9.
- 42 19. Borboni A, Villafañe JH, Mulle C, Valdes K, Faglia R, Taveggia G, et al.
43 Robot-assisted rehabilitation of hand paralysis after stroke reduces
44 wrist edema and pain: a prospective clinical trial. *J Manipulative*
45 *Physiol Ther* 2017;40:21–30.
- 46 20. Bissolotti L, Villafañe JH, Gaffurini P, Orizio C, Valdes K, Negrini S.
47 Changes in skeletal muscle perfusion and spasticity in patients with
48 poststroke hemiparesis treated by robotic assistance (gloeha) of the
49 hand. *J Phys Ther Sci* 2016;28:769–73.
- 50 21. Bishop L, Stein J. Three upper limb robotic devices for stroke reha-
51 bilitation: a review and clinical perspective. *NeuroRehabilitation*
52 2013;33:3–11.
22. Mehrholz J, Pohl M, Platz T, Kugler J, Elsner B. Electromechanical
and robot-assisted arm training for improving activities of daily liv-
ing, arm function, and arm muscle strength after stroke [review].
Cochrane Database Syst Rev 2018:CD006876.
23. Gassert R, Dietz V. Rehabilitation robots for the treatment of sensori-
motor deficits: a neurophysiological perspective [review]. *J Neuroeng*
Rehabil 2018;15:46.
24. Hakim RM, Tunis BG, Ross MD. Rehabilitation robotics for the upper
extremity: review with new directions for orthopaedic disorders.
Disabil Rehabil Assist Technol 2017;12:765–71.
25. Vanoglio F, Bernocchi P, Mule C, Garofali F, Mora C, Taveggia G,
et al. Feasibility and efficacy of a robotic device for hand rehabilitation
in hemiplegic stroke patients: a randomized pilot controlled study.
Clin Rehabil 2017;31:351–60.
26. Hall T, Coppieters MW, Nee R, Schafer A, Ridehalgh C. Neurodynamic
treatment improves leg pain, back pain, function and global per-
ceived effect at 4 weeks in patients with chronic nerve-related leg
pain. *J Physiother* 2017;63:59.
27. Butler D, Jones M, Gore R. Mobilisation of the nervous system.
London: Churchill Livingstone; 1991.
28. Villafañe JH, Silva GB, Fernandez-Carnero J. Short-term effects of neu-
rodynamic mobilization in 15 patients with secondary thumb carpo-
metacarpal osteoarthritis. *J Manipulative Physiol Ther* 2011;34:449–56.
29. Villafañe JH, Silva GB, Bishop MD, Fernandez-Carnero J. Radial nerve
mobilization decreases pain sensitivity and improves motor perfor-
mance in patients with thumb carpometacarpal osteoarthritis: a ran-
domized controlled trial. *Arch Phys Med Rehabil* 2012;93:396–403.
30. Oskay D, Meric A, Kirdi N, Firat T, Ayhan C, Leblebicioglu G.
Neurodynamic mobilization in the conservative treatment of cubital
tunnel syndrome: long-term follow-up of 7 cases. *J Manipulative*
Physiol Ther 2010;33:156–63.
31. Villafañe JH, Valdes K, Imperio G, Borboni A, Cantero-Tellez R, Galeri S,
et al. Neural manual vs. robotic assisted mobilization to improve motion
and reduce pain hypersensitivity in hand osteoarthritis: study protocol
for a randomized controlled trial. *J Phys Ther Sci* 2017;29:801–6.
32. Villafañe JH, Cleland JA, Fernandez-de-Las-Penas C. The effec-
tiveness of a manual therapy and exercise protocol in patients with
thumb carpometacarpal osteoarthritis: a randomized controlled trial.
J Orthop Sports Phys Ther 2013;43:204–13.
33. Ylinen J. Pressure algometry. *Aust J Physiother* 2007;53:207.
34. Kamper SJ, Maher CG, Hush JM, Pedler A, Sterling M. Relationship
between pressure pain thresholds and pain ratings in patients with
whiplash-associated disorders. *Clin J Pain* 2011;27:495–501.
35. Pedersini P, Negrini S, Cantero-Tellez R, Fernandez-Carnero J, Bishop
MD, Villafañe JH. Neural manual mobilization vs. robotic assisted mobi-
lization to reduce pain hypersensitivity in hand osteoarthritis: a ran-
domised controlled pilot trial. *Ann Rheum Dis* 2019;78 Suppl:1046–7.
36. Pedersini P, Negrini S, Cantero-Tellez R, Bishop MD, Villafane JH.
Pressure algometry and palpation of the upper limb peripheral ner-
vous system in subjects with hand osteoarthritis are repeatable and
suggest central changes. *J Hand Ther* 2019;33:103–11.
37. Villafañe JH, Valdes K. Letter regarding “conservative treatment of
thumb base osteoarthritis: a systematic review”. *J Hand Surg Am*
2015;40:1058–9.
38. Villafañe JH, Valdes K. Reliability of pinch strength testing in elderly
subjects with unilateral thumb carpometacarpal osteoarthritis. *J*
Phys Ther Sci 2014;26:993–5.
39. Emshoff R, Bertram S, Emshoff I. Clinically important difference
thresholds of the visual analog scale: a conceptual model for iden-
tifying meaningful intraindividual changes for pain intensity. *Pain*
2011;152:2277–82.
40. Citrome L, Magnusson K. Paging Dr Cohen, paging Dr Cohen...
an effect size interpretation is required STAT!: visualising effect
size and an interview with Kristoffer Magnusson. *Int J Clin Pract*
2014;68:533–4.
41. Villafañe JH, Cleland JA, Fernandez-de-Las-Penas C. Bilateral sen-
sory effects of unilateral passive accessory mobilization in patients
with thumb carpometacarpal osteoarthritis. *J Manipulative Physiol*
Ther 2013;36:232–7.
42. Singh JA, Luo R, Landon GC, Suarez-Almazor M. Reliability and clin-
ically important improvement thresholds for osteoarthritis pain and
function scales: a multicenter study. *J Rheumatol* 2014;41:509–15.
43. Pham T, van der Heijde D, Altman RD, Anderson JJ, Bellamy N,
Hochberg M, et al. OMERACT-OARSI Initiative: Osteoarthritis
Research Society International set of responder criteria for osteoar-
thritis clinical trials revisited. *Osteoarthritis Cartilage* 2004;12:389–99.