Sensory, Motor, and Psychosocial Characteristics of Individuals With Chronic Neck Pain

A Case-Control Study

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ABSTRACT:

Objective. Given the complex and unclear etiology of neck pain, it is important to understand the differences in central sensitization as well as psychosocial factors in individuals with chronic neck pain and healthy controls. The purpose of this study was to benchmark differences in central sensitization, psychosocial factors, and range of motion between people with nonspecific chronic neck pain and healthy controls and to analyze the correlation between pain intensity, neck disability, and psychosocial factors in people with chronic neck pain.

Methods. Thirty individuals with chronic neck pain and 30 healthy controls were included in this case-control study. Outcome measures were as follows: central sensitization (pressure pain threshold, temporal summation, and conditioned pain modulation), psychosocial factors (depressive symptoms, pain catastrophizing, and quality of life), and active cervical range of motion.

Results. People with neck pain had lower local pressure pain threshold, a decrease in conditioned pain modulation, more depressive symptoms, greater pain catastrophizing, lower quality of life, and reduced range of motion for neck rotation when compared with healthy controls. In people with neck pain, moderate correlations were observed between pain intensity and quality of life ($\rho = -0.479$), disability and pain catastrophizing ($\rho = 0.379$), and disability and quality of life ($\rho = -0.456$).

Conclusions. People with neck pain have local hyperalgesia, impaired conditioning pain modulation, depressive symptoms, pain catastrophizing, low quality of life, and reduced active range of motion during neck rotation, which should be taken into account during assessment and treatment.

Impact. This study shows that important outcomes, such as central sensitization and psychosocial factors, should be considered during assessment and treatment of individuals with nonspecific chronic neck pain. In addition, pain intensity and neck disability are correlated with psychosocial factors.

Introduction

The incidence and prevalence of neck pain has risen in recent years, the latter increasing with age.[1,2] This musculoskeletal disorder may be associated with whiplash injuries, myofascial pain syndrome or degenerative abnormalities such as osteoarthritis and cervical spondylolysis.[3–5] Chronic neck pain is generally persistent and can cause functional disability,[6] limiting activity[7] and lowering quality of life.[6,8]

Central sensitization (CS) is defined as "increased responsiveness of nociceptive neurons in the central nervous system to their normal or subthreshold afferent input."[9] Many individuals with chronic pain, such as fibromyalgia,[10,11] rheumatoid arthritis,[12] osteoarthritis,[13] low back pain,[14] and whiplash[11,15] have presented an involvement of central sensitization and impaired endogenous pain modulation. Nevertheless, in individuals with nonspecific chronic neck pain, the presence of CS is not clear, the available literature provides an inconclusive message and more studies are required[16]. Then, to investigate the presence of central sensitization in nonspecific chronic neck pain compared to healthy controls may lead to more effective therapeutic approaches.

Previous studies have investigated deep tissue hyperalgesia in patients with chronic neck pain compared to healthy controls and evaluated the pressure pain threshold (PPT) in only one or two points on the neck.[17–20] Further, these studies have considered populations consisting of women,[21] adolescents,[22] elderly women,[23] female office workers[24] or patients with chronic whiplash.[25] We found only one study that has investigated the hyperalgesia considering more points on the neck and shoulder girdle area, however, only computers users were recruited.[26] Consequently, there is a lack of studies investigating local hyperalgesia in a larger area of the neck and upper back region in patients with nonspecific chronic neck pain compared to healthy controls.

We have found few studies that have investigated the central sensitization or psychosocial factors and in some cases the sample was composed only by women[21] or adolescents[22] or computers users[26] with neck pain or it was considered only in patients with chronic whiplash.[25] Psychosocial factors play an important role in the chronification of neck pain.[27] Then, the correlation between psychosocial factors and pain intensity or neck disability is also important to promote a better therapeutic approach for patients with neck pain. Some studies have observed that greater pain catastrophizing was associated with greater neck disability[17,22,28] or greater pain intensity.[28] However, until this moment we have found no studies that have investigated the correlation between neck disability, pain intensity and depression symptoms or quality of life.

Individuals with neck pain seem to exhibit reduced active ROM.[29–31] A recent study showed that reduced neck mobility was associated with pain intensity, neck disability, fear of movement and central sensitization, however this study was performed only in females.[32] Therefore, more wide studies are needed to confirm this information. The active neck ROM is important variable that should be investigated in individuals with nonspecific chronic neck pain compared healthy controls in order to promote a more effective treatment.

As such, it is important to highlight that investigating central sensitization and psychosocial factors could contribute to more effective assessments and treatment choices for this population in the future. As such, the first aim of this study was to evaluate the possible differences in central sensitization (PPT, temporal summation (TS) of pain, conditioned pain modulation (CPM)), psychosocial factors (ie, depressive symptoms, pain catastrophizing and quality of life) and active neck range of motion (ROM) between individuals with nonspecific chronic neck pain and healthy controls. The second aim was to analyze the correlation between pain intensity, neck disability and psychosocial factors in individuals with nonspecific chronic neck pain. We hypothesized that individuals with nonspecific chronic neck pain would present central sensitization, presence of psychosocial factors, and reduced active neck ROM. In addition, we also hypothesized that psychosocial factors would be correlated with their pain intensity and/or neck disability.

Methods

Study Design

This is a cross-sectional case-control study that followed STROBE statement.[33] The study was carried out at the Physiotherapeutic Resources Laboratory of the Federal University of São Carlos (UFSCar) and approved by the institutional Research Ethics Committee under protocol number CAAE: 81711417.0.0000.5504. All individuals gave written informed consent. The study was conducted in compliance with the Helsinki declaration.

Participants

We recruited a consecutive, nonprobabilistic convenience sample of individuals via electronic media, posters and oral communication in the city of São Carlos. Individuals with neck pain and healthy controls, aged between 18 and 65 years, were selected. Inclusion criteria were chronic (neck pain lasting more than 3 months),[7] nonspecific (neck pain without known specific causes, such as radiculopathy or trauma)[21,34], bilateral or unilateral neck pain, either localized or radiating to surrounding areas[4], and scores ≥3 on the Numerical Rating Scale (NRS)[35] and ≥ 5 on the Neck Disability Index (NDI).[36]

Pain intensity was assessed by the NRS, an 11-point scale that rates pain from 0 (no pain) to 10 (worst possible pain).[35] Individuals rated their current pain intensity while resting, as well as average intensity in the 24 hours before assessment and during active neck movements. For movement-evoked pain, the highest pain intensity score during neck flexion, extension, tilting and right and left rotation was considered. The NDI was used to assess neck disability.[36] The scores of the 10 items comprising the NDI were added (the higher the total score, the greater the disability).

Healthy individuals were also selected as controls, matched for sex, body mass, height, body mass index (BMI) and age to individuals with nonspecific chronic neck pain. Inclusion criteria for controls were no reports of neck pain for more than 7 days in the last 12 months and a score <5 on the NDI.

General exclusion criteria for both groups were signs of radiculopathy in the upper limbs (loss of myotome muscle strength, sensory loss at dermatomes and/or changes in reflexes), whiplash associated disorder, other chronic pain conditions, pregnancy, history of trauma, fractures or neck surgeries, inflammatory rheumatic, neurological or cardiorespiratory diseases, cardiac pacemaker, systemic hypertension or uncontrolled diabetes, and tumors. Also excluded were individuals who had received physical therapy or cervical injections in the last 3 months, started engaging in any physical activity in the last two weeks or used analgesics, use of anti-inflammatory drugs or muscle relaxants in the 24 hours prior to assessment.

Procedure

First, all included individuals were asked to their demographics and clinical characteristics. Subsequently, they completed the questionnaires related to psychosocial factors. Afterward, an experienced researcher (VRS)c performed the tests to investigate the central sensitization and active neck ROM.

Outcome Measures

Central Sensitization

Pressure pain threshold (PPT)

The PPTs were evaluated using a digital pressure algometer (Somedic®, Hörby, Sweden), with a 1 cm^2 rubber probe and pressure rate of approximately 40 kPa/s. Individuals held the stop button of the algometer with the hand contralateral to the limb being assessed and were instructed to press it when the pressure stimulus became a clear sensation of pain, whereupon the pressure was recorded. The following points were evaluated bilaterally: C2 and C5: 2 cm laterally from the spinous processes of C2[37] and C5,[38] respectively; UT (upper trapezius): midway between the spinous process of C7 and the lateral edge of the acromion[39]; LS (levator scapulae): 2 cm above the superior angle of the scapula[40,41]; T4 and T8: 2 cm laterally from the spinous processes of T4 and T8, respectively (Suppl. Appendix 1); and the middle third of the right tibialis anterior muscle (TA), considered an asymptomatic distant site to verify the presence of distant hyperalgesia[23,24]. The average of three measurements was considered for each point, with a 30-second interval between them to prevent temporal summation (TS).[42]

The intrarater reliability of these measurements was tested before the study, with ten healthy individuals and a 48-hour interval between assessments. The intraclass correlation coefficient ($ICC_{2,3}$) was considered excellent for average values measured at points C2, C5, UT, LS, T4 and T8 (bilaterally) (0.866; 95% CI = 0.460 to 0.967) and for the TA muscle (0.956; 95% CI = 0.824 to 0.988).

Topographical pressure pain sensitivity maps of the neck and shoulder girdle areas

Individuals' posture and the position of the points were standardized in order to design and compile topographical sensitivity maps of the neck and shoulder girdle areas.[42] A schematic diagram of the points based on the average body mass, height and BMI was used to establish the x and y coordinates of each point. The absolute mean of the PPT values at the twelve points assessed (C2, C5, UT, LS, T4 and T8, bilaterally) was used. Inverse distance weighted interpolation was applied to obtain the distribution of the PPT values for all 60 individuals, in agreement with.[43] The sensitivity maps of the neck and shoulder girdle areas were generated in Matlab (The Mathworks, Natick, MA, USA).

Temporal summation of pain was analyzed on the most painful side of the UT or the dominant side in the absence of a more painful side or when pain intensity was the same on both sides. Ten pressure stimuli were applied, at the pressure value previously obtained in algometry and a rate of 40 kPa/s, with a 1-second interval between them. Individuals were instructed to quantify the pain intensity of the first, fifth and tenth stimuli based on the NRS scale[44]. Pain intensity of the tenth stimuli was subtracted from that of the first. The intrarater reliability of these measurements was tested before the study, with ten healthy individuals and a 48-hour interval between assessments. Good reliability was observed according to the intraclass correlation coefficient ($ICC_{2,3}$) (0.710; 95%CI = 0.295 to 0.930).

For CPM, the conditioning stimulus used was the cold pressor test and the test stimulus, the PPT on the least painful side of the UT (the least painful side was chosen because before this test we have performed the TS of pain test using the most painful side and this point could be more sensitive due to temporal summation[42]) or the nondominant side in the absence of radiating pain to the shoulder girdle or when pain intensity was the same on both sides. Individuals were instructed to immerse their hand (up to the wrist) in a bucket of water (22°C) for 1 minute to standardize hand temperature,[21] and then immerse it in a bucket of ice water (4°C),[45] moving it back and forth to prevent heat buildup around the hand[46]. After 30 seconds of immersion, individuals were asked to rate their pain intensity in the hand based on the NRS (0-10) to verify the magnitude of effect of this noxious stimulus that was used to induce a reduction in the perception of pain from another test stimulus (PPT at the upper trapezius).[47,48] Then, it was recorded the pain intensity the immersed hand. Thirty seconds later they were instructed to remove their hand from the water to prevent distraction bias and the PPT of the UT was measured again.[46,47] The average values obtained before and after immersion were subtracted to assess the efficacy of CPM, whereby the lower the result the less effective the endogenous pain inhibition.

Psychosocial factors

The Beck Depression Inventory (BDI) was applied to assess depressive symptoms,[49]. Pain Catastrophizing Scale (PCS) was used to evaluate pain catastrophizing.[50] High scores indicating greater presence of depressive symptoms and greater pain catastrophizing, respectively. Quality of life was assessed by the 12-Item Short-Form Health Survey – version 2 (SF-12v2).[51] An algorithm is used to measure the physical and mental component summary scores on a scale of zero to 100, whereby higher scores are associated with better quality of life.[51,52]

Active range of motion (ROM)

Active ROM was measured using a fleximeter (Sanny, São Paulo, Brazil). The fleximeter was positioned on the temporal bone to measure flexion and extension movements, on the forehead for tilting and on top of the head to measure rotation.[53]

The intrarater reliability of these measurements was tested before the study, with ten healthy individuals and a 48-hour interval between assessments. The intraclass correlation coefficient ($ICC_{2,3}$) was considered excellent for flexion (0.917; 95% CI = 0.665 to 0.979), extension (0.964; 95% CI = 0.854 to 0.991), right tilting (0.941; 95% = CI = 0.761 to 0.985), left tilting (0.982; 95% CI = 0.927 to 0.996), right rotation (0.984; 95% CI = 0.574 to 0.974) and left rotation (0.907; 95% CI = 0.624 to 0.977).

Pain intensity and neck disability in individuals with chronic neck pain

The average intensity pain in the last 24 hours before assessment and neck disability were evaluated using the NRS[35] and the NDI,[36] respectively. These variables were correlated with psychosocial factors.

Sample size calculation

The sample size was calculated to detect a difference of 80 kPa between groups and a standard deviation of 100 obtained from a previous data on PPT and neck pain.[24,54] At a significance level of 0.05 and power of 80%, the required sample size in each group was 26 individuals (Minitab, v.15, State College, PA). Allowing for attrition, 30 individuals were therefore recruited for neck pain group and 30 individuals for healthy control, for a total of 60 individuals.

Statistical Analysis

All the statistical analyses were performed with IBM SPSS Statistics 19 software (IBM SPSS, Armonk, New York). Descriptive statistics, mean and standard deviation, or median and interquartile range were calculated for each variable. The Shapiro-Wilk test was applied to assess data normality and Levene's test for homogeneity of variance. Parametric and nonparametric tests were used to analyze data with normal and non-normal distribution, respectively.

The Shapiro-Wilk test showed normal distribution for neck range of motion; as such, the independent t test was applied to determine differences in degrees for flexion, extension, left and right tilting and rotation between individuals with neck pain and healthy controls. Non-normal data distribution was identified (Shapiro-Wilk) for PPT, TS, CPM, depressive symptoms, pain catastrophizing and quality of life, which were then analyzed by the Mann-Whitney U test to compare the two groups. Cohen's d was used to assess effect size, classified as small (0.2), medium (0.5) or large (0.8).[55] Spearman correlation coefficient was applied to correlate pain intensity, neck disability and the psychosocial factors studied (depressive symptoms, pain catastrophizing and quality of life) in patients with chronic neck pain, with values < 0.3 considered low, 0.3 to 0.5 moderate and > 0.5 strong correlation.[55] A 95% CI was used and statistical significance was set at $p < 0.05$.

[H2] Role of the funding source

The funder had no role in the study design, data collection, management, analysis, or interpretation, writing the report or the decision to submit the manuscript for publication, nor does it have ultimate authority over any of these activities.

Results

Participant characteristics

Thirty individuals with nonspecific chronic neck pain and thirty healthy controls were included in the study, with no missing data for any individuals. Demographic and clinical characteristics are presented in Table 1. Both groups were matched for sex, age, body mass, height and BMI.

Central sensitization

The bilateral PPT at points C2, C5, LS, T4 and T8 were significantly lower in the neck pain group, with a moderate to large effect size (*d* = -0.47 to 0.74), when compared to healthy controls (all: *P* < .05) (Fig. 1). There were no significant differences between groups for PPT at points on the right and left upper trapezius (both: *P* > .05) and right TA muscle (*P* = .133) (Tab. 2 and Fig. 1). Figure 2 shows the topographical maps of individuals with nonspecific chronic neck pain and healthy controls indicating pressure hyperalgesia at C2, C5, LS, T4 and T8 points bilaterally in neck pain group as compared to healthy controls. No statistically significant between groups differences were observed for TS (*P* = .774). The magnitude of CPM (PPT after the cold pressor test minus the PPT before testing) was significantly lower in the neck pain group when compared to controls (*P* = .002), with a large effect size (*d* = -0.77) (Tab. 2 and Suppl. Appendix 2). Pain intensity mean (SD) in the hand during the conditioning test was 7.9 (2.0) in individuals with neck pain and 7.9 (2.0) in healthy controls.

Psychosocial measures

Scores on the BDI and PCS were significantly higher in the neck pain group as compared healthy controls (both: *P* < .001) (Tab. 2). Individuals with chronic neck pain reported significantly lower scores on the SF-12v2 (*P* = .004) when compared to healthy controls (Tab. 2).

Active Range of motion

There was a significant decrease in ROM for right and left rotations (*P* < .05) in individuals with neck pain when compared to healthy controls (Tab. 3). No significant differences between groups were observed for active flexion, extension or tiltings (all: *P* > .05) (Tab. 3).

Correlation between average pain intensity in the last 24 hours, neck disability, BDI, PCS and SF-12 in individuals with chronic neck pain

Spearman correlation identified a significant moderate negative correlation between pain intensity and quality of life (ρ = -0.479; P = .007), and moderate positive correlation between pain intensity and neck disability (ρ = 0.496; P = .005) (Tab. 4).There was also a significant moderate positive correlation between disability and pain catastrophizing (ρ = 0.379; P = .039) and a significant moderate negative correlation between disability and quality of life (ρ = -0.456; P = .011) (Tab. 4).

Discussion

The results of this study revealed lower PPT in the neck and shoulder girdle areas, a decrease in CPM, the presence of depressive symptoms, greater pain catastrophizing, lower quality of life, and reduced active ROM for rotation in individuals with chronic neck pain compared to healthy controls. In addition, as hypothesized, greater pain intensity and neck disability were moderately correlated with psychosocial factors.

Similarly to our findings in relation to PPT of the neck, other studies reported a decline in PPT in individuals with chronic NP when compared to controls[17,22,23,56–58]. However, these studies investigated only one or two points on the neck and in our study PPT was measured in twelve points on neck and shoulder girdle areas.

With respect to PPT in TA muscle, our findings are in line with those of other studies that also reported no distant hyperalgesia in individuals with neck pain compared to healthy controls[17,19,21,23,24,26,59]. By contrast, other studies have observed lower PPT values of the anterior tibialis muscle in individuals with neck pain when compared to healthy individuals[22,24,57,60]. Given the controversial results regarding secondary hyperalgesia in individuals with neck pain, further research is needed to assess the presence of this variable.

In this study, topographical mapping confirmed that individuals with chronic neck pain showed greater pressure pain sensitivity. Additionally, the neck region was more sensitive than the shoulder girdle area in both groups, in agreement with Binderup at al.[43] In contrast with our findings, Ge et al, 2014 reported no significant differences in topographical pressure pain sensitivity maps between computer users with and without chronic pain in the neck.[26] However, it should be noted that the authors analyzed individuals who reported pain on the day of the experiment or in the last 24 hours, whereas individuals in the present study had experienced pain for more than 3 months.

Our findings are in line with other studies that also found no increase in TS in individuals with whiplash-associated disorders[25] and musculoskeletal shoulder pain[61] compared to healthy controls. In this study, the effectiveness of CPM decreased in individuals with nonspecific chronic neck pain in relation to healthy controls. These findings indicate changes in the endogenous pain inhibition mechanism also observed in individuals with chronic low back pain.[62] However, in those with chronic neck pain, other studies found no decrease in the effectiveness of CPM in individuals with nonspecific chronic neck pain when compared to healthy controls.[21,63]

The PPTs, TS of pain and CPM tests were used to investigate the presence of central sensitization in individuals with nonspecific chronic neck pain. As previously mentioned, the results obtained for these outcomes are controversial, however, central sensitization may be present in some individuals with neck pain[26] even though it is not characteristic in this population[16].

As in our study, other studies displayed the presence of depressive symptoms,[64,65] pain catastrophizing[17,22,64] and lower quality of life[18,21] in individuals with chronic neck pain compared to controls. Assessing and treating these psychological factors are important in order to optimize the effectiveness of pain therapy for these individuals.

Individuals with neck pain exhibited reduced ROM for neck rotation when compared to healthy controls. Recent reviews concluded that individuals with neck pain seem to exhibit reduced active ROM for flexion, extension and rotation in relation to healthy individuals.[29,30] It is important to highlight that these differences in findings may be related to the different measuring instruments used. In our investigation, active ROM of the cervical spine was measured with a fleximeter, whereas previous studies used other devices.[29,30] In addition, some limitations are mentioned by aforementioned reviews[29,30]: studies with no difference between patients and healthy controls are more likely to keep unpublished than those reporting positive results, inadequate blinding of evaluators may have enlarged the difference in measurements and there is a poor reporting in relation to test methods and evaluator background and training. Then, additional research with better quality and more detailed descriptions of the individuals and methods to obtain more consistent findings are needed.

Correlation between pain intensity, neck disability and psychosocial factors in individuals with neck pain.

The present study demonstrated that higher pain intensity is correlated with greater neck disability and low quality of life. In contrast with our results, Muñoz-García et al, 2017 found no correlation between pain intensity and neck disability.[17] Our study also showed that neck disability is correlated with poor quality of life. In addition, the neck disability also is moderately correlated with pain catastrophizing, as reported in other studies with patients with neck pain.[17,22,28] Therefore, pain intensity and disability can affect quality of life, while neck disability may influence pain catastrophizing or vice versa, since a causal relation cannot be established. Based on these findings, these aspects should be evaluated, and the therapeutic approach requires more than analgesics and physical treatment modalities (electrophysical agents, manual therapy or exercises) to improve ROM. The presence of central sensitization and psychosocial factors makes it important to adopt a multidisciplinary approach as well as neurophysiological pain education to effectively rehabilitate these individuals.

Limitations

The PPT at distant sites was only assessed in the middle third of the TA muscle and additional points should be evaluated to analyze the distant hyperalgesia mechanism in this group. Anxiety was not evaluated, and we think it is important to investigate it, and to verify if it is correlated with pain intensity or neck disability. It will provide more information that can be used for a better approach in the assessment and treatment of individuals with nonspecific chronic neck pain.

Conclusions

Local hyperalgesia, impaired conditioning pain modulation, depressive symptoms, pain catastrophizing, poor quality of life and reduced active ROM for neck rotation were observed in individuals with nonspecific chronic neck pain. Additionally, there is a significant correlation between intensity pain, neck disability and psychosocial factors. As such, pain management, neck mobility and psychosocial components should be assessed and taken into account in the therapeutic approach adopted for this population.

Author Contributions

Concept/idea/research design: É.P. Rampazo, P.M. Madeleine, R.E. Liebano

Writing: É.P. Rampazo, P.M. Madeleine, L. Arendt-Nielsen, R.E. Liebano

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Consultation (including review of manuscript before submitting): P.M. Madeleine, R.E. Liebano

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Ethics Approval

The study was approved by the Research Ethics Committee of the Physiotherapeutic Resources Laboratory of the Federal University of São Carlos (CAAE: 81711417.0.0000.5504). All individuals gave written informed consent.

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Disclosure

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

References

1. Blanpied PR, Gross AR, Elliott JM, et al. Neck Pain: Revision 2017. *J Orthop Sport Phys Ther* 2017; 47: A1–A83.
2. Safiri S, Kolahi AA, Hoy D, et al. Global, regional, and national burden of neck pain in the general population, 1990-2017: systematic analysis of the Global Burden of Disease Study 2017. *BMJ* 2020; 368: m791.
3. Borghouts J a, Koes BW, Bouter LM. The clinical course and prognostic factors of non-specific neck pain: a systematic review. *Pain* 1998; 77: 1–13.
4. Kroeling P, Gross A, Graham N, et al. Electrotherapy for neck pain. *Cochrane database Syst Rev* 2013; CD004251.
5. Kjaer P, Kongsted A, Hartvigsen J, et al. National clinical guidelines for non-surgical treatment of patients with recent onset neck pain or cervical radiculopathy. *Eur spine J*.
6. Wong JJ, Shearer HM, Mior S, et al. Are manual therapies, passive physical modalities, or acupuncture effective for the management of patients with whiplash-associated disorders or neck pain and associated disorders? An update of the Bone and Joint Decade Task Force on Neck Pain and Its Ass. *Spine J* 2016; 16: 1598–1630.
7. Koyuncu E, Ökmen BM, Özkuk K, et al. The effectiveness of balneotherapy in chronic neck pain. *Clin Rheumatol* 2016; 35: 2549–55.
8. Alayat MSM, Mohamed AA, Helal OF, et al. Efficacy of high-intensity laser therapy in the treatment of chronic neck pain: a randomized double-blind placebo-control trial. *Lasers Med Sci* 2016; 31: 687–694.
9. Nijs J, Leysen L, Vanlauwe J, et al. Treatment of central sensitization in patients with chronic pain: time for change? *Expert Opin Pharmacother* 2019; 20: 1961–1970.
10. Sluka KA, Clauw DJ. Neurobiology of fibromyalgia and chronic widespread pain. *Neuroscience* 2016; 338: 114–129.
11. Coppieters I, Ickmans K, Cagnie B, et al. Cognitive performance is related to central sensitization and health-related quality of life in patients with chronic whiplash-associated disorders and fibromyalgia. *Pain Physician* 2015; 18: E389–E402.
12. Zhang A, Lee YC. Mechanisms for Joint Pain in Rheumatoid Arthritis (RA): from Cytokines to Central Sensitization. *Curr Osteoporos Rep* 2018; 16: 603–610.
13. Lluch E, Torres R, Nijs J, et al. Evidence for central sensitization in patients with osteoarthritis

pain: A systematic literature review. *Eur J Pain (United Kingdom)* 2014; 18: 1367–1375.

14. Nijs J, Apeldoorn A, Hallegraeff H, et al. Comprehensive Review Low Back Pain: Guidelines for the Clinical Classification of Predominant Neuropathic, Nociceptive, or Central Sensitization Pain. *Pain Physician* 2015; 18: E333–E346.
15. Van Oosterwijck J, Nijs J, Meeus M, et al. Evidence for central sensitization in chronic whiplash: A systematic literature review. *Eur J Pain (United Kingdom)* 2013; 17: 299–312.
16. Malfliet A, Kregel J, Cagnie B, et al. Lack of evidence for central sensitization in idiopathic, non-traumatic neck pain: A systematic review. *Pain Physician* 2015; 18: 223–235.
17. Muñoz-García D, López-de-Uralde-Villanueva I, Beltrán-Alacreu H, et al. Patients with Concomitant Chronic Neck Pain and Myofascial Pain in Masticatory Muscles Have More Widespread Pain and Distal Hyperalgesia than Patients with Only Chronic Neck Pain. *Pain Med* 2017; 18: 526–537.
18. Yalcinkaya H, Ucok K, Ulasli AM, et al. Do male and female patients with chronic neck pain really have different health-related physical fitness, depression, anxiety and quality of life parameters? *Int J Rheum Dis* 2017; 20: 1079–1087.
19. Scott D, Jull G, Sterling M. Widespread sensory hypersensitivity is a feature of chronic whiplash-associated disorder but not chronic idiopathic neck pain. *Clin J Pain* 2005; 21: 175–181.
20. Chien A, Sterling M. Sensory hypoaesthesia is a feature of chronic whiplash but not chronic idiopathic neck pain. *Man Ther* 2010; 15: 48–53.
21. Coppieters I, De Pauw R, Kregel J, et al. Differences Between Women With Traumatic and Idiopathic Chronic Neck Pain and Women Without Neck Pain: Interrelationships Among Disability, Cognitive Deficits, and Central Sensitization. *Phys Ther* 2017; 97: 338–353.
22. Sá S, Silva AG. Repositioning error, pressure pain threshold, catastrophizing and anxiety in adolescents with chronic idiopathic neck pain. *Musculoskelet Sci Pract* 2017; 30: 18–24.
23. Uthaikhup S, Prasert R, Paungmali A, et al. Altered pain sensitivity in elderly women with chronic neck pain. *PLoS One*; 10. Epub ahead of print 3 June 2015. DOI: 10.1371/journal.pone.0128946.
24. Johnston V, Jimmieson NL, Jull G, et al. Quantitative sensory measures distinguish office workers with varying levels of neck pain and disability. *Pain* 2008; 137: 257–65.
25. Ickmans K, Malfliet A, de Kooning M, et al. Lack of gender and age differences in pain

measurements following exercise in people with chronic whiplash-associated disorders. *Pain Physician* 2017; 20: E829–E840.

26. Ge H-Y, Vangsgaard S, Omland Ø, et al. Mechanistic experimental pain assessment in computer users with and without chronic musculoskeletal pain. *BMC Musculoskelet Disord* 2014; 15: 412.

27. Cohen SP, Hooten WM. Advances in the diagnosis and management of neck pain. *Bmj* 2017; j3221.

28. Thompson DP, Urmston M, Oldham JA, et al. The association between cognitive factors, pain and disability in patients with idiopathic chronic neck pain. *Disabil Rehabil* 2010; 32: 1758–1767.

29. Hesby BB, Hartvigsen J, Rasmussen H, et al. Electronic measures of movement impairment, repositioning, and posture in people with and without neck pain - A systematic review. *Systematic Reviews*; 8. Epub ahead of print 27 August 2019. DOI: 10.1186/s13643-019-1125-2.

30. Stenneberg MS, Rood M, de Bie R, et al. To what degree does active cervical range of motion differ between patients with neck pain, patients with whiplash, and those without neck pain? A systematic review and meta-analysis. *Arch Phys Med Rehabil* 2017; 98: 1407–1434.

31. Madeleine P, Prietzel H, Svarrer H, et al. Quantitative posturography in altered sensory conditions: A way to assess balance instability in patients with chronic whiplash injury. *Arch Phys Med Rehabil* 2004; 85: 432–438.

32. De Pauw R, Coppieters I, Palmans T, et al. Motor impairment in patients with chronic neck pain: does the traumatic event play a significant role? A case-control study. *Spine J* 2018; 18: 1406–1416.

33. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). *Epidemiology* 2007; 18: 805–835.

34. Cerezo-Téllez E, Torres-Lacomba M, Fuentes-Gallardo I, et al. Effectiveness of dry needling for chronic nonspecific neck pain: a randomized, single-blinded, clinical trial. *Pain* 2016; 157: 1905–17.

35. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. *Pain* 2011; 152: 2399–2404.

36. Cook C, Richardson JK, Braga L, et al. Cross-cultural adaptation and validation of the Brazilian Portuguese version of the Neck Disability Index and Neck Pain and Disability Scale. *Spine (Phila Pa 1976)* 2006; 31: 1621–1627.

37. Cheung J, Kajaks T, Macdermid JC. The relationship between neck pain and physical activity. *Open Orthop J* 2013; 7: 521–9.

38. Dailey DL, Rakel BA, Vance CGT, et al. Transcutaneous electrical nerve stimulation reduces pain, fatigue and hyperalgesia while restoring central inhibition in primary fibromyalgia. *Pain* 2013; 154: 2554–62.

39. Celenay ST, Kaya DO, Akbayrak T. Cervical and scapulothoracic stabilization exercises with and without connective tissue massage for chronic mechanical neck pain: A prospective, randomised controlled trial. *Man Ther* 2016; 21: 144–150.

40. Bablis P, Pollard H, Bonello R. Neuro Emotional Technique for the treatment of trigger point sensitivity in chronic neck pain sufferers: A controlled clinical trial. *Chiropr Osteopat* 2008; 16: 4.

41. Alburquerque-Sendín F, Camargo PR, Vieira A, et al. Bilateral myofascial trigger points and pressure pain thresholds in the shoulder muscles in patients with unilateral shoulder impingement syndrome: a blinded, controlled study. *Clin J Pain* 2013; 29: 478–486.

42. Alburquerque-Sendín F, Madeleine P, Fernández-De-Las-Peñas C, et al. Spotlight on topographical pressure pain sensitivity maps: A review. *J Pain Res* 2018; 11: 215–225.

43. Binderup AT, Arendt-Nielsen L, Madeleine P. Pressure pain sensitivity maps of the neck-shoulder and the low back regions in men and women. *BMC Musculoskelet Disord* 2010; 11: 234.

44. Corrêa JB, Costa LOP, Oliveira NTB, et al. Effects of the carrier frequency of interferential current on pain modulation and central hypersensitivity in people with chronic nonspecific low back pain: A randomized placebo-controlled trial. *Eur J Pain* 2016; 20: 1653–1666.

45. Shahidi B, Maluf KS. Adaptations in Evoked Pain Sensitivity and Conditioned Pain Modulation after Development of Chronic Neck Pain. *Biomed Res Int* 2017; 2017: 8985398.

46. Valencia C, Kindler LL, Fillingim RB, et al. Stability of conditioned pain modulation in two musculoskeletal pain models: Investigating the influence of shoulder pain intensity and gender. *BMC Musculoskelet Disord* 2013; 14: 182–192.

47. Yarnitsky D, Bouhassira D, Drewes AM, et al. Recommendations on practice of conditioned pain modulation (CPM) testing. *Eur J Pain (United Kingdom)* 2015; 19: 805–806.

48. Yarnitsky D. Conditioned pain modulation (the diffuse noxious inhibitory control-like effect): Its relevance for acute and chronic pain states. *Curr Opin Anaesthesiol* 2010; 23: 611–615.

49. Gomes-Oliveira MH, Gorenstein C, Lotufo Neto F, et al. Validation of the Brazilian Portuguese version of the Beck Depression Inventory-II in a community sample. *Rev Bras Psiquiatr* 2012; 34: 389–94.

50. Sehn F, Chachamovich E, Vidor LP, et al. Cross-Cultural Adaptation and Validation of the Brazilian Portuguese Version of the Pain Catastrophizing Scale. *Pain Med* 2012; 13: 1425–1435.

51. Damásio BF, Andrade TF, Koller SH. Psychometric properties of the Brazilian 12-item short-form health survey version 2 (SF-12v2). *Paideia* 2015; 25: 29–37.

52. Silveira MF, Almeida JC, Freire RS, et al. Propriedades psicométricas do instrumento de avaliação da qualidade de vida: 12-item health survey (SF-12). *Cien Saude Colet* 2013; 18: 1923–1932.

53. Dibai-Filho AV, de Oliveira AK, Girasol CE, et al. Additional effect of static ultrasound and diadynamic currents on myofascial trigger points in a manual therapy program for patients with chronic neck pain. *Am J Phys Med Rehabil* 2017; 96: 243–252.

54. Walton DM, Levesque L, Payne M, et al. Clinical Pressure Pain Threshold Testing in Neck Pain: Comparing Protocols, Responsiveness, and Association With Psychological Variables. *Am Phys Ther* 2014; 94: 827–838.

55. Cohen J. *Statistical power analysis for the behavioral sciences*. 2nd ed. New Jersey: Lawrence Erlbaum Associates, 1988.

56. Szikszay TM, Luedtke K, Harry von P. Increased mechanosensivity of the greater occipital nerve in subjects with side-dominant head and neck pain–a diagnostic case-control study. *J Man Manip Ther* 2018; 26: 237–248.

57. Beinert K, Englert V, Taube W. After-effects of neck muscle vibration on sensorimotor function and pain in neck pain patients and healthy controls–a case-control study. *Disabil Rehabil* 2019; 41: 1906–1913.

58. Piña-Pozo F, Heredia-Rizo AM, Madeleine P, et al. Local and Widespread Pressure Pain Hyperalgesia Is Not Side Specific in Females with Unilateral Neck Pain that Can Be Reproduced during Passive Neck Rotation. *J Clin Med* 2019; 8: 1246.

59. Chien A, Sterling M. Sensory hypoaesthesia is a feature of chronic whiplash but not chronic idiopathic neck pain. *Man Ther* 2010; 15: 48–53.

60. Javanshir K, Ortega-Santiago R, Mohseni-Bandpei MA, et al. Exploration of somatosensory

impairments in subjects with mechanical idiopathic neck pain: A preliminary study. *J Manipulative Physiol Ther* 2010; 33: 493–499.

61. Haik MN, Evans K, Smith A, et al. People with musculoskeletal shoulder pain demonstrate no signs of altered pain processing. *Musculoskelet Sci Pract* 2019; 39: 32–38.

62. Correa JB, Pena Costa LO, de Oliveira NT, et al. Central sensitization and changes in conditioned pain modulation in people with chronic nonspecific low back pain: a case-control study. *Exp BRAIN Res* 2015; 233: 2391–2399.

63. Chua NHL, Timmerman H, Vissers KC, et al. Multi-modal Quantitative Sensory Testing in Patients with Unilateral Chronic Neck Pain: An Exploratory Study. *J Musculoskelet Pain* 2012; 20: 292–299.

64. López-de-Uralde-Villanueva I, Sollano-Vallez E, Del Corral T. Reduction of cervical and respiratory muscle strength in patients with chronic nonspecific neck pain and having moderate to severe disability. *Disabil Rehabil* 2018; 40: 2495–2504.

65. Liu F, Fang T, Zhou F, et al. Association of Depression/Anxiety Symptoms with Neck Pain: A Systematic Review and Meta-Analysis of Literature in China. *Pain Res Manag* 2018; 2018: 3259431.

Table 1. Demographics and Clinical Characteristics of Participants With Neck Pain and Healthy Subjects (Control)[a]

Variable	Groups		*p*
	Neck Pain (n = 30)	Control (n = 30)	
Sex - n (%)			
Male	14 (47%)	14 (47%)	1.000[b]
Female	16 (53%)	16 (53%)	
Age, years - Mean ± SD	27.17 ± 4.76	27.63 ± 4.46	.697[c]
Body mass, Kg - Mean ± SD	68.77 ± 10.00	68.88 ± 10.44	.967[c]
Height, m - Mean ± SD	1.70 ± 0.09	1.69 ± 0.10	.737[c]
BMI, Kg/m² - Mean ± SD	23.82 ± 2.23	24.07 ± 2.33	.656[c]
Ethnicity - n (%)			
Caucasian	22 (73%)	27 (90%)	.095[b]
Others	8 (27%)	3 (10%)	
Education - n (%)			
High school or less	9 (30%)	4 (13%)	.117[b]
Some college or above	21 (70%)	26 (87%)	
Marital Status - n (%)			
Single	23 (77%)	28 (93%)	.145[d]
Married	7 (23%)	2 (7%)	
Physically active (≥ 3/week) - n (%)	16 (53%)	20 (67%)	.292[b]
Smoker - n (%)	3 (10%)	0 (0%)	.237[d]
Dominance upper limb - n (%)			
Right	28 (93%)	25 (83%)	.424[d]
Pain intensity (NRS) - Mean ± SD			
At rest	4.20 ± 2.09	-	
Pain average in the last 24 hours	5.16 ± 2.03	-	
Worst pain during movement	6.06 ± 2.28	-	
Pain duration - n (%)			
3 months - < 1 year	4 (13)	-	
1 year - < 3 years	12 (40)	-	
3-5 years	5 (17)	-	
> 5 years	9 (30)	-	
Disability (NDI) - Mean ± SD	12 ± 4.58	-	
Duration of pain crisis (days) - Mean ± SD	1.7 ± 1.0	-	
Crisis per month - Mean ± SD	13 ± 10	-	
Consumption of medicines - n (%)			
If necessary	16 (53)	-	
Daily	2 (7)	-	
Weekly	2 (7)	-	
Monthly	0 (0)	-	
None	10 (33)	-	
Pain Medication - n (%)			
Opioid	0 (0)	-	
Non-opioid	13 (43)	-	
Combo	0 (0	-	
Muscle relaxants	7 (23)	-	
Topical anti-inflammatories	0 (0)	-	

None	10 (33)	-	
Headache - n (%)	23 (76)	17 (56)	.100[b]
Relationship between neck pain and headache - n (%)			
Headache - neck pain	3 (10)	-	
Neck pain - headache	17 (57)	-	
No relation	10 (33)	-	

[a] BMI = body mass index; Kg: kilograms; m = meters; n = number of participants; NDI = neck disability index; NRS = numerical rating scale; SD = standard deviation.

[b] Statistical analysis were performed using a Pearson Chi-Square test.

[c]Data that were normally distributed and analyzed with Independent *t* test.

[d] Statistical analyses were performed using Fisher Exact test.

Table 2. Outcome Measures of Central Sensitization and Psychosocial Factors Between Individuals With Nonspecific Chronic Neck Pain and Healthy Controls[a]

Outcome measures	Groups: Neck Pain (n = 30)	Groups: Control (n = 30)	*p*	ES (d)
Pressure Pain Threshold (kPa)				
Right C2	141 [111, 190]	210 [162, 266]	.004[b]	-0.74
Left C2	146 [109, 184]	198 [154, 257]	.007[b]	-0.67
Right C5	156 [113, 208]	191 [147, 259]	.024[b]	-0.52
Left C5	140 [114, 176]	203 [146, 278]	.004[b]	-0.69
Right Upper trapezius	174 [138, 204]	200 [141, 252]	.249	-0.22
Left Upper trapezius	184 [136, 221]	204 [155, 243]	.315	-0.26
Right Levator scapulae	181 [136, 275]	245 [181, 346]	.009[b]	-0.47
Left Levator scapulae	163 [148, 248]	255 [212, 320]	.001[b]	-0.64
Right T4	206 [143, 316]	260 [221, 402]	.011[b]	-0.64
Left T4	227 [173, 278]	284 [244, 389]	.006[b]	-0.71
Right T8	237 [167, 306]	306 [231, 415]	.012[b]	-0.66
Left T8	246 [178, 295]	336 [240, 404]	.016[b]	-0.70
Right Tibialis anterior muscle	279 [228, 389]	364 [234, 481]	.133	-0.47
Pain temporal summation (10º- 1º) (0-10)	1 [0, 2.5]	1 [0.25, 2]	.774	-0.10
CPM (Difference scores, kPa)	82.7 [59.9, 97.2]	116 [87.1, 141]	.002[b]	-0.77
Depressive symptoms (BDI) (0-63)	7 [6, 13]	4 [2.25, 6]	< .001[b]	1.21
Pain catastrophizing (PCS) (0-52)	15 [8, 22]	3.5 [0, 11]	< .001[b]	1.12
Quality of life (SF-12v2)				
PCS - Physical Component Summary	50.8 [46, 56.9]	57 [55.1, 59]	.004[b]	-0.89
MCS - Mental Component Summary	45.4 [38.2,	52.7 [44.9,	.004[b]	-0.73

	49.5]	56.8]

[a]Values are presented in median and interquartile range. Abbreviations: BDI: Beck Depression Inventory; CPM: Conditioned Pain Modulation; d: Cohen´s;ES: effect size; n: number of individuals; IQR: interquartile range; kPa: kiloPascal; PCS: Pain Catastrophyzing Scale; SF-12v2: 12-Item Short-Form Health Survey - version 2.

[b]Statistically significant difference: p < .05.

Table 3. Mean (SD) ROM and Mean Difference (95% CI), *P*, and Effect Sizes (Cohen's D) Between Groups[a]

Outcome	**Groups**				
	Neck pain (n = 30)	**Control (n = 30)**	**Mean Difference (95% CI)**	***p***	**ES (d)**
Range of motion (°C) - Mean ± SD					
Flexion	62.4 ± 11.8	59.9 ± 13.6	2.48 (-4.12 to 9.10)	.455	0.19
Extension	67.5 ± 13.7	72.7 ± 12.8	-5.21 (-12.10 to 1.67)	.135	-0.39
Right tilting	50.8 ± 9.3	48.2 ± 10.0	2.62 (-2.38 to 7.62)	.299	0.27
Left tilting	48.6 ± 8.1	48.7 ± 10.8	-0.04 (-4.99 to 4.90)	.986	-0.00
Right rotation	69.2 ± 8.6	74.6 ± 10.5	-5.43 (-10.43 to -0.43)	.034[b]	-0.56
Left rotation	74.1 ± 11.0	79.9 ± 8.9	-5.80 (-11.01 to -0.58)	.030[b]	-0.57

[a]ES = effect size; d = Cohen´s; n = number of individuals; ROM = range of motion; SD = standard deviation.

[b]Statistically significant difference; p < 0.05 (Independent t test).

Table 4. Correlations Between Average Pain Intensity in the Last 24 Hours, Neck Disability and Psychosocial Factors in Individuals With Nonspecific Chronic Neck Pain Individuals (n = 30)[a]

	Measure			Measure		
	Pain Intensity Related Variables			Neck Disability Related Variables		
Variable	***p***	**95% CI**	**correlation (ρ)**	***p***	**95% CI**	**correlation (ρ)**
BDI	.648	-0.443 to 0.292	-0.087	.197	-0.140 to 0.562	0.242
PCS	.092	-0.064 to 0.612	0.313	.039[b]	0.010 to 0.657	0.379
SF-12v2 - PCS	.007[b]	-0.721 to -0.133	-0.479	.011[b]	-0.706 to -0.103	-0.456
SF-12v2 - MCS	.645	-0.298 to 0.443	0.088	.339	-0.516 to 0.203	-0.181
NDI	.005[b]	0.155 to 0.732	0.496	-	-	-

[a]n = number of individuals; PCS = Pain Catastrophizing Scale; SF-12v2 - MCS = Short-Form Healthy Survey version 2 - Mental Component Summary; SF-12v2 - PCS = Short-Form Healthy Survey version 2 - Physical Component Summary.

[b] The Spearman correlation was significant ($p \leq 0.05$).

FIGURE LEGENDS

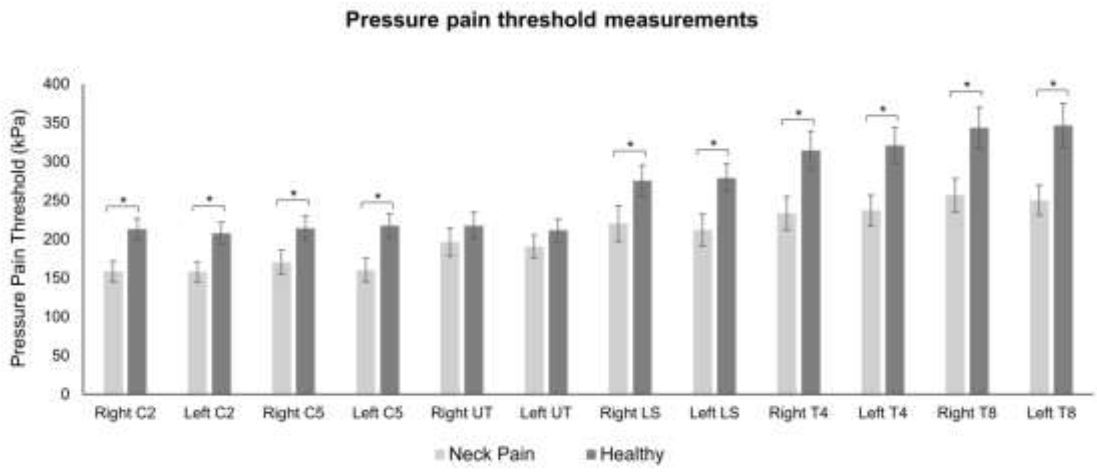

FIGURE 1. Pressure pain threshold (PPT) measurements. Median value and interquartile range of ppt measurements at each point in the neck and shoulder girdle areas. *p < .025 (Mann-Whitney Test / Bonferroni correction: .05/2). kPa = kilopascal; LS = levator scapulae; TA = tibialis anterior muscle; UT = upper trapezius.

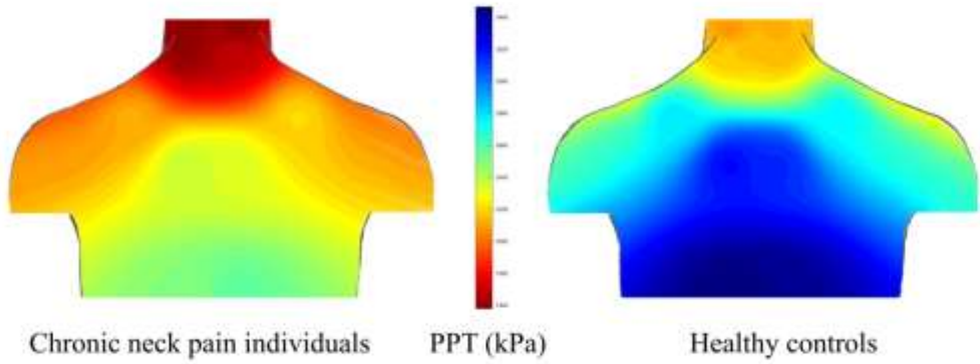

FIGURE 2. Pressure pain sensitivity maps of the neck and shoulder girdle areas in individuals with neck pain and healthy controls. The maps show lower PPTs at C2. C5. levator scapulae. T4 and T8 (x) bilaterally in individuals with neck pain when compared to healthy controls. kPa = kiloPascal.

Supplementary Appendix 1. Representation of the 12 points used for pressure pain threshold assessment in the neck and shoulder girdle areas. 1: left C2; 2: right C2; 3: left C5; 4: right C5; 5: left upper trapezius (UT); 6: right UT; 7: left levator scapulae (LS); 8: right LS; 9: left T4; 10: right T4; 11: left T8; 12: right T8.

Supplementary Appendix 2. Conditioned pain modulation (CPM). Score differences (kPa) between individuals with neck pain and healthy controls. kPa: kiloPascal; Mann-Whitney test. p = .002**.**