Pressure pain thresholds in office workers with chronic neck pain

A systematic review and meta-analysis

Maurício Passos Nunes, Alexandre; Paulo Azinheira Martins Moita, João; Margarida Marques Rebelo Espanha, Maria; Kjær Petersen, Kristian; Arendt-Nielsen, Lars

Published in:
Pain Practice

DOI (link to publication from Publisher):
10.1111/papr.13014

Publication date:
2021

Document Version
Accepted author manuscript, peer reviewed version

Citation for published version (APA):
Maurício Passos Nunes, A., Paulo Azinheira Martins Moita, J., Margarida Marques Rebelo Espanha, M., Kjær Petersen, K., & Arendt-Nielsen, L. (2021). Pressure pain thresholds in office workers with chronic neck pain: A systematic review and meta-analysis. *Pain Practice*, *21*(7), 799-814. https://doi.org/10.1111/papr.13014

DR. ALEXANDRE NUNES (Orcid ID : 0000-0002-7450-3933)

Article type : Review

Title Page

Pressure pain thresholds in office workers with chronic neck pain. A systematic review and meta-analysis.

Alexandre Maurício Passos Nunes[1,2,3] (MSc), João Paulo Azinheira Martins Moita[3] (PhD), Maria Margarida Marques Rebelo Espanha[1] (PhD), Kristian Kjær Petersen[4, 5] (PhD), Lars Arendt-Nielsen[4, 5] (Dr. Med. PhD)

[1] *Faculdade de Motricidade Humana da Universidade de Lisboa, Laboratório de Biomecânica e Morfologia Funcional, Cruz-Quebrada, Portugal.*

[2] *Escola Superior de Saúde Jean Piaget do Algarve, Portugal.*

[3] *Escola Superior de Saúde Atlântica, Barcarena, Portugal.*

[4] *SMI, Faculty of Medicine, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark.*

[5] *Center for Neuroplasticity and Pain (CNAP), Department of Health Science and Technology, School of Medicine, Aalborg University, Aalborg, Denmark.*

Corresponding Author:

Alexandre Nunes, MSc

Universidade de Lisboa, Faculdade de Motricidade Humana

Laboratório de Biomecânica e Morfologia Funcional, CIPER

Estrada da Costa, 1499-022 Cruz-Quebrada, Dafundo, Portugal

Phone: +351 965726125

www.neuromechanics.fmh.ulisboa.pt

E-mail: alexandrempnunes@gmail.com

Running head: Pressure pain thresholds in chronic neck pain

Abstract

Objectives: 1) Compare pressure pain threshold (PPT) values between office workers with chronic neck pain and asymptomatic controls; 2) establish reference PPT values in chronic neck pain; 3) evaluate associations between PPTs, pain intensity and disability.

Methods: Seven English/Portuguese databases were searched for relevant literature. Studies investigating adult office workers (age >18) with chronic neck pain were included if PPTs were an outcome. The risk of bias was assessed using the Downs and Black checklist. Meta-analysis was conducted if a cluster contained at least two studies reporting the same PPTs.

Results: Ten high quality, two low quality, and one poor quality studies were included. The meta-analysis revealed decreased PPT values in the upper trapezius, extensor carpi ulnaris, and tibialis anterior in chronic neck pain workers when compared with healthy workers, without a statistical difference (p>0.05). The PPT reference value in the upper trapezius was 263 kPa (95%CI: 236.35, 289.70), and 365 kPa (95%CI: 316.66, 415.12) for the tibialis anterior in office workers with chronic neck pain. No correlations were found between the upper trapezius PPT and pain intensity and disability.

Conclusion: This meta-analysis found that all the pressure pain threshold measurements were not significantly reduced in office workers with chronic neck pain compared with healthy workers. These assumptions were based on a small sample of existing studies, and therefore further studies are necessary to quantify the differences in pressure pain thresholds. Hypersensitivity PPT reference values are proposed for localized and extra-segmental sites in office workers with chronic neck pain.

Key Words: Office workers, neck pain, pressure pain threshold, algometry, upper trapezius.

1 Introduction

Neck pain is a highly prevalent health problem in the general population and one of the leading causes of global disability among the working population.[1-3] The annual prevalence rates range between 30-50%,[1] with office workers (OW) with chronic pain neck pain (CNP) ranging up to 40%.[4,5]

In that sense, the assessment of subjective pain should be made through pain scales, patient complaints, and quantitative sensory tests.[6] Pressure pain threshold (PPT) by algometry is used as a validated and reliable measurement tool for pain sensitivity assessment in the neck region.[7-9] PPTs assessed in a localized pain area can reflect localized hyperalgesia whereas PPTs assessed in areas remote to the painful region reflect widespread hyperalgesia.[10,11] Normative cut-off points reference values corresponding to the 10th and 25th percentiles from the mean in free-pain populations as the lower PPT limit value to be considered as hypersensitive, and the 75th and 90th percentiles to be the upper PPT limit to be considered as hyposensitive.[12,13]

Widespread hyperalgesia can be a component of central sensitization,[14] and has been found to be predictive for development of chronic postoperative pain,[15,16] neck pain associated with whiplash-associated disorders[17,18] and chronic non-specific neck pain.[19,20] In addition, widespread hyperalgesia has been observed in office workers with CNP with high pain and disability compared to healthy workers or office workers with low pain.[20,21] However, those conclusions were made from a control group without OW[20] and from a small sample size in the asymptomatic OW group.[21]

It remains unclear if PPTs can be meaningful in clinical practice to profile and characterize patients with CNP. To our knowledge, this is the first systematic review addressing this topic of CNP in a specific population.

The aims of this systematic review are to: 1) compare PPTs values between office workers with chronic neck pain (CNP) and asymptomatic control office workers (CON); 2) establish reference PPT values in CNP; 3) investigate the strength of association between PPT values with pain intensity and disability in CNP.

2 Methods

The review protocol was registered a priori at the International Prospective Register of Systematic Reviews (registration number: CDR42020164521). This systematic review and meta-analysis are reported according to the PRISMA guidelines.[22]

2.1 Eligibility Criteria

Studies were considered for inclusion if they investigated: (1) adult office workers or computer workers (age > 18); (2) a group with non-specific chronic neck pain (CNP); (3) PPT as one of the main outcomes; (4) and studies written in English and Portuguese. CNP is defined as a condition where pain persists for more than three months,[23,24] is isolated to the neck/shoulder region without any known cause, and is provoked by maintained neck postures, neck movements, or palpation of the cervical musculature.[2,19] PPT is defined as the minimum amount of pressure that elicits a painful sensation.

Review studies (systematic and narrative) were excluded after having their reference lists examined in order to identify appropriate studies for inclusion. Studies not meeting the inclusion criteria were excluded if they presented one or more of the following exclusion criteria : (1) no clear indication of pain duration to be considered chronic definition; (2) not controlling for medical history of cardiovascular diseases, major chronic diseases, a medical diagnosis of fibromyalgia, rheumatoid arthritis or other auto-immune systemic diseases, cervical disc herniation or severe disorders of the cervical spine, whiplash injury, or other existing neurologic and/or metabolic diseases;[25] (3) non-original research, conference proceedings, and doctoral theses; (4) when data was lacking or not clearly described.

2.2 Information Sources and Search Strategy

Two reviewers (AN, JM) created and ran a systematic search of literature on seven databases (PubMed, EBSCO, PEDro, SCIELO, Web of Science, SCOPUS, Cochrane Library) from database inception until 26th March 2019, using the following key terms: office worker, neck pain, pressure pain threshold and algometry (appendix 1 for full search strategy).

2.3 Study Selection

The reviewers (AN, JM), using the predetermined search strategy, independently scanned for potentially relevant articles. References were imported to RefWorks and duplicates removed. After removal, the studies suitable for review through the inclusion and exclusion criteria were retrieved for in-depth analysis. A consensus meeting with a third party (ME) was held if the reviewers were not able to reach an agreement on the inclusion of a study. Corresponding authors of original studies were contacted in an attempt to obtain extra information if necessary.

2.4 Data Collection Process

The following data were extracted: (1) authors and year of publication; (2) study design; (3) office worker group characteristics (number, age, and gender); (4) type of algometer and measurement; (5) PPT location(s) in neck area and non-neck area; (6) outcomes were PPT, pain intensity and disability. After, data were independently checked by a second reviewer.

2.5 Risk of Bias in Individual Studies

Risk of bias was assessed independently by two reviewers (AN, JM), using the same process described recently.[26] Briefly, the same reviewers used the Downs and Black checklist, which is a methodological quality assessment tool shown to have a high internal consistency (KR-20 = 0.89), good test–retest reliability (r = 0.88) and good interrater reliability (r = 0.75).[27] It consists of 27 items across five sections, as follows: (i) Study quality (10 items) –the overall quality of the study based on data reporting; (ii) External validity (3 items) – the ability to generalize findings of the study through their representativeness; (iii) Internal validity concerning study bias (7 items) – to assess bias in the intervention and outcome measure(s); (iv) Internal validity concerning confounding and selection bias (6 items) – to determine bias from sampling or group assignment; and (v) Power of the study (1 item) – to determine if findings are due to chance (for more information see Appendix 2).

Due to some heterogeneity in the included studies design, the checklist was modified. From the original 27 items, 12 items were not applied to the observational studies (4, 8, 9, 13–15, 17, 19, 23–24, 26–27) as they relate specifically to intervention studies, and items 5, 21 and 22 were omitted for studies that did not provide an independent control group. Accordingly, and taking into account the variation of the total item numbers of the checklist, the quality assessment results are presented as percentage scores, as previously suggested.[28] The strength of agreement between reviewers was determined through Cohen's kappa.[29] Interpretation of Kappa values was established using standards proposed by Landis and Koch:[30] 0=poor, 0.01–0.20=slight, 0.21–0.40=fair, 0.41–0.60=moderate, 0.61–0.80=substantial, and 0.81–1=almost perfect.

2.6 Data Analysis

The PPT results were reported through means, 95% CI, standard deviations, and p-values. We summarized all mean PPT point values in the selected studies. Normally, PPT measurements are reported in kg/cm^2 or kPa, and for consistency, all scores were converted to kPa.

Studies were grouped based on study design, and PPT protocol (same PPT assessment areas) and further clustered according to pain intensity and disability. If a cluster contained at least two studies reporting means and standard deviation, a meta-analysis was conducted. All analyses used the random-effects model because of the possibility of confounding variables (i.e. age, gender, pain intensity, pain duration) within the inclusion criteria.[31]

Due to the design variability of the included studies, the following meta-analysis approaches were used: a) the baseline mean difference (MD) 95% CI for the same PPT was calculated based on the differences between CNP and CON, where a negative value demonstrates a lower PPT in CNP, and a positive value demonstrates a higher PPT in CON; b) one-arm meta-analysis of the baseline PPT values from CNP groups were employed, in which all studies (RCT, cross-sectional, Cohort) that presented the same PPT assessment area mean value and standard deviations (converted to standard error (SE)) were included.[32] For studies with more than one group, the PPT scores were combined according to the formula in appendix 3;[33] c) associations between PPT with pain intensity and disability were determined through the Pearson product-moment correlation coefficient (*r-value*) when reported. R-values from the different studies were pooled using "Fisher's z' transformation" (i.e. *z*-transformed *r* value) using the following formula: z′=0.5[ln(1+r)-ln(1-r)] where ln is the natural logarithm.[34] Also, the included studies were weighted according to the magnitude of the respective standard error (SE.) The formula used to calculate the SE was: $SE = 1/\sqrt{N-3}$: where N refers to the number of pairs of scores.[34] For the classification and interpretation of correlation sizes, r_z-values were back-transformed to r-values, and interpreted according to the recommendation of Vicent,[35] values of $0 \leq r \geq 0.69$ indicate small, $0.70 \leq r \geq 0.89$ indicate moderate and $r \geq 0.90$ indicate large correlation sizes.[36,37]

Studies not included in the meta-analysis were described separately. Heterogeneity was assessed using I^2. For the interpretation of the I^2 values the following classification was used: 0%-40% might not be important; 30%-60% moderate; 50%-90% substantial heterogeneity; 75%-100% considerable heterogeneity.[33] If heterogeneity was higher than 60% with more than three studies, a subgroup analysis was conducted according to the Downs and Black score, excluding studies with scores below average.[38]

All meta-analytic procedures were conducted using the RevMan software program for Macintosh,[39] and all results were presented in a forest plot. The reliability of the risk of bias assessment scores between the two assessors was examined by k Statistics using SPSS V.25 software.[40]

3 Results

3.1 Study Selection

Figure 1 presents the Flowchart describing the selection process and reasons for exclusion. A total of 315 studies were identified through electronic data base search. After duplicates were removed (n=93), 222 studies were screened in title and abstract for eligibility criteria, out of which 187 were excluded, and 36 retrieved for in-depth analysis. From those, 12 manuscripts met the inclusion criteria and one additional study identified by hand search of the reference list. A total of 13 manuscripts were considered eligible for review.[20,21,41-51]

For meta-analytic purposes, the corresponding authors of eight publications (six authors) were contacted with the request to provide information on additional data. Three authors responded and delivered the requested information, one of the authors did not retrieve the full data required, and two did not respond.

Insert Fig. 1.

3.2 Study Characteristics

Table 1 shows the characteristics and a summary of the findings of all studies included in this review. The 13 studies included consisted of 4 cross-sectional studies,[20,21,43,46] 2 prospective cohort studies,[49,50] 4 randomized controlled trials (RCT),[41,42,44,51] 2 studies with a mixed design (Part A, a cross-sectional and part B an RCT),[45,48] and 1 uncontrolled trial.[47] A total of 692 office workers (92 males/600 females) were included, from those 609 were CNP (87 males/522 females) and 83 were CON (5 males/78 females). Two cross-sectional studies[20,46] with the same sample size from the same author presented the same PPT baseline results, and therefore, the results were pooled only from one study.[20]

Insert Table. 1

All the studies measured PPTs in the neck region, and six studies measured in non-neck areas.[20,21,41,42,45,48] The most common PPT assessment areas in the neck region were: a) the upper trapezius, defined as the midpoint between C7 and acromion in 11 studies;[20,21,41-45,47-50] b) the levator scapulae point (LS) in 2 studies;[20,44] c) the suboccipital point in 2 studies;[43,44] d) the semispinalis muscle in the posterior neck in 2 studies;[43,44] e) the lower trapezius point,[42] the sternocleidomastoid[43] and the C5/6 zygapophyseal joint all measured in one study.[51] In relation to the non-neck area, the regions were: a) the tibialis anterior muscle measured in 5 studies;[20,21,41,42,48] b) the extensor carpi ulnaris in 2 studies;[21,45] c) the median nerve trunk point (cubital fossa medial to and immediately adjacent to the tendon of the biceps) in 1 study;[20] d) and the middle of the sternum bone in 1 study.[42] All PPT points were assessed by palpation.

Pain intensity was assessed in 9 studies[21,41-45,47,50,51] by means of the Visual Analog Scale,[21,41,42,44,47,50,51] and the Numerical Pain Rating Scale.[43,45] Neck Disability Index was measured in 5 studies.[20,43,45,50,51]

3.3 Quality Assessment

Table 2 presents the results of the methodological quality assessment of the included studies. The discrepancies between reviewers regarding quality assessment outcomes were discussed until consensus was reached. The overall level of agreement between reviewers was 87%, with 0.66 (0.44, 0.84) strength of agreement (Kappa (95%CI)), which is considered to be substantial.[29] The Downs and Black quality score ranged from 14.2% to 68.7% (mean 55.1± 14.5). The obtained scores interpretation was done according to a previously published procedure[26] whereas a cut-off point of 50% was established, based on the overall score quality percentage scores mean and standard deviation (SD 55.1±14.5). In line with that procedure we determined the intervals by calculating the mean minus 1 SD (40.6) and then mean plus 1 SD (69.6) for the average quality interval, where studies >69.6 were considered of high quality and studies <40.6 were considered to be of low quality. Based on these criteria, the quality assessment of the 13 studies revealed: 9 high average-quality studies (>50% cut-off point),[20,21,41-43,45,46,49,50] 3 low average-quality study (<50% cut-off point),[44,48,51] and 1 poor-quality study.[47]

Insert Table. 2

3.4 PPT Values Between CNP and CON

The results of the meta-analysis are shown in figures 2a, 2b and 2c. The PPTs measured at the upper trapezius were pooled in 5 studies[21,43,45,48,50] from 152 CNP and 93 CON, without a statistical difference (p=0.13). The lower mean value for CNP compared to CON, with a pooled mean difference of -62.68 kPa (95% CI: -143.58, 18.22), revealed considerable heterogeneity (I^2=89%, Chi^2=35.88, df=4, p<0.00001) (fig 2a).

The PPTs measured at the extensor carpi ulnaris were pooled in 2 studies[21,45] from 67 CNP and 37 CON, without a statistical difference p=0.42. The lower mean value for CNP compared to CON, with a pooled mean difference of -16.31 kPa (95% CI: -56.07, 23.45), revealed insignificant heterogeneity (I^2=0%, Chi^2=0.32, df=1, p=0.57) (fig 2b).

The PPTs measured at the tibialis anterior were pooled in 2 studies[21,48] from 89 CNP and 37 CON, without a statistical difference p=0.29. The lower mean value for CNP compared to CON, with a pooled mean difference of -85.37 kPa (95% CI: -242.03; 71.29), revealed considerable heterogeneity (I^2=87%, Chi^2=7.42, df=1, p=0.006) (fig 2c).

Insert figures 2a, 2b, 2c

3.5 PPT Reference Values in Office Workers with CNP

The PPTs measured at the upper trapezius were pooled in 11 studies[20,21,41-45,47-50] from 549 office workers, and revealed a statistical difference (p<0.001), with a mean value of 263.03 kPa (95%CI: 236.35, 289.70), and considerable heterogeneity (I^2=94%, Chi^2=160.2, df=10, p<0.001) (Figure 3a). The PPTs measured at extensor carpi ulnaris were pooled in 2 studies[21,45] from 67 office workers, and revealed a statistical difference (p<0.001), with a mean value of 253.66 kPa (95%CI: 227.82, 279.51), and insignificant heterogeneity (I^2=0%, Chi^2=0.19, df=1, p=.66) (Figure 3b). The PPTs measured at the tibialis anterior were pooled in 5 studies[20,21,41,42,48] from 419 office workers, and revealed a statistical difference (p<0.001), with a mean value of 365.89 kPa (95%CI: 316.66, 415.12), and considerable heterogeneity (I^2=92%, Chi^2=50.26, df=4, p<.00001) (Figure 3c). Subgroup analysis revealed that I^2 values did not change in the upper trapezius or the tibialis anterior PPTs when taking into account studies with Downs and Black scores below average and poor quality.

Insert figures 3a, 3b, 3c

3.6 Correlations Between Upper Trapezius PPT and Pain Intensity in CNP

Figure 4 illustrates the insignificant correlation analysis between the upper trapezius PPT and pain intensity. The weighted mean r_z value was -0.18 (p=0.15) with insignificant heterogeneity (I^2=0%, Chi^2=0.21, df=1, p=0.65). The back transformed r-value of -.178 indicated a negative small-sized correlation.

Insert figure 4

3.7 Correlations Between Upper Trapezius PPT and Disability in CNP

Figure 5 reports the insignificant correlation analysis between the upper trapezius PPT and disability measured by the Neck Disability Index. The weighted mean r_z value was 0.07 (p=0.73) with insignificant heterogeneity (I^2=19%, Chi^2=1.23, df=1, p=0.27). The back transformed r-value of 0.699 indicated a small-sized correlation.

Insert figures 5

4 Discussion

This systematic review and meta-analysis showed insignificant changes in PPTs assessed at the upper trapezius, the extensor carpi ulnaris and the tibialis anterior comparing CNP and CON. The PPT results from the extensor carpi ulnaris and the tibialis anterior were drawn based on only two studies with small sample sizes. The present review provides PPT reference values for the upper trapezius and the tibialis anterior for office workers with chronic neck pain. Finally, no significant correlations were found between PPTs, clinical pain or disability in patients with CNP, in two studies with small sample sizes.

4.1 PPT Between CNP and CON

All the analyses revealed decreased PPT values in CNP when compared to CON, without statistical significance but with a small difference in the extensor carpi ulnaris and the upper trapezius when this analysis was conducted with average quality studies. Also, the sample sizes from all analyses were not representative of an office worker population. Nevertheless, these results were quite similar with the findings of other systematic reviews comparing PPTs between symptomatic and asymptomatic subjects in (1) migraine,[52-54] (2) tension-type headache,[52,53] (3) cervicogenic headache,[53] (4) chronic whiplash-associated disorder,[18] and (5) chronic non-specific neck pain.[38]

Only the reviews from patients with migraine, tension-type headache and cervicogenic headache[53,54] demonstrate localized hyperalgesia (head and neck PPT points) and not widespread hyperalgesia. In a chronic condition, lower PPTs in local and distal points may reflect widespread hyperalgesia.[10,11] Although the current analysis observed lower PPT values remote from the neck region, particularly in the tibialis anterior with a difference of 85 kPA, this was based on one low quality study with considerable heterogeneity and a small sample size. Therefore, future studies should be aimed at investigating this observation.

4.2 PPT Reference Values for CNP

The meta-analysis proposed PPT reference values for the upper trapezius and the tibialis anterior, 263 kPa and 366 kPa, respectively, in office workers with CNP. From the included studies, the upper trapezius PPT value ranged from 183 kPa to 371 kPa, meaning there is substantial variability within CNP. PPTs measured by algometry are a reliable tool in different neck conditions, with a good to almost perfect intra-rater reliability in chronic neck pain,[55] myofascial pain,[56] acute neck pain,[7] and in the cervical region in patients with dizziness.[57] Therefore, this variability has been attributed to gender, different measurement positions, repeated measurements between subjects and peak pressures being more heterogeneous at bone points.[58] In addition, it should be noted that different algometers are used for assessing PPT and this could influence the results. Currently, no studies have investigated the differences in the different algometers. A secondary analysis in the upper trapezius PPT demonstrated higher values in the studies that used a mechanical pressure algometer compared with the studies that used an electronic pressure algometer (Appendix 4). This needs to be interpreted with caution because of considerable heterogeneity and differences in the sample size.

From a clinical perspective, it is crucial that guidelines describe a common methodologic approach, and reference normal/normative PPT values. Normative cut off points with reference values corresponding to the 10th and 25th percentiles from the mean in pain-free populations has been proposed as the lower PPT limit value to be considered as hypersensitive.[12,13] Considering that the PPTs in the upper trapezius and the tibialis anterior in CNP were composed of 88% and 84% females office workers, respectively, and men have higher PPT values[58] in free-pain populations[12,13,52] and in chronic pain populations,[52] it is possible to make some conclusions based on the mentioned studies. Neziri et al.[12] proposed 212 kPa as a normal PPT value in the scapula (30 mm below upper trapezius point)[21] and considered hypersensitivity values below 153 kPa in females. Waller et al.[13] proposed similar results, with normal PPT values above 245 kPa when assessing the upper trapezius, and hypersensitivity values below 155 kPa in females. For the tibialis anterior, 394 kPa was considered a normal PPT value and values below 246 kPa were considered to be hypensensitive in females.[13] The values pooled from the CNP groups in the current review were very similar for females, and so, the values below 155 kPa and 245 kPa in the upper trapezius and the tibialis anterior, can be proposed as hypersensitive values for office workers with chronic neck pain.

Due to the few studies and small sample size with CON, it was not possible to pool PPT values to compare with free-pain populations in this review. Further studies are necessary to investigate PPTs in healthy OW.

4.3 Correlations Between PPT and Pain Intensity and Disability

This meta-analysis found a small association between PPTs measured in the upper trapezius and pain intensity, from only two studies derived from a small sample size (67 office workers).[21,45] No observed association has been described in the literature between PPT values and pain intensity in acute neck pain,[7] in chronic headache,[53] adolescents with chronic pain[59] nor in temporomandibular disorders.[60]

There was a smaller association in Neck Disability Index from two studies with 37 office workers with chronic neck pain.[45,50] A few studies have reported correlations between PPTs in the upper trapezius and disability in patients with neck pain. Walton et al.[8] reported a weak correlation, Beltran-Alacreu et al.[61] reported a moderate negative correlation and no significant correlation in patients with chronic neck pain.[19]

4.4 Limitations

Several limitations were found: a) lack of data in the included studies have limited the robustness of the meta-analysis; b) lack of reporting pain duration made it difficult to conclude if the condition was chronic according to ICD-11 classification;[24] c) to conduct the meta-analysis required at least two studies with the same PPT point and one of the included studies[51] measured in one point that was not repeated by the other studies; d) in two of the excluded studies it was not possible to conclude the PPT assessment points; e) the findings from this review may not be generalizable beyond female gender due to the limited inclusion of male participants in the studies reviewed; f) and finally, across all studies, the PPT points were assessed through palpation, raising questions regarding standardization.[58]

4.5 Conclusion

This meta-analysis found that PPT measurements were not significantly reduced in office workers with chronic neck pain compared with healthy workers. These assumptions were based on a small sample of existing studies, and therefore further studies are necessary to quantify the differences in pressure pain thresholds. Therefore, these conclusions should be interpreted with caution.

This review proposed hypersensitivity reference values for the upper trapezius and the tibialis anterior for localized and extra-segmental assessment of PPTs in chronic neck pain.

Acknowledgements: Lars Arendt-Nielsen and Kristian K. Petersen are part of Center for Neuroplasticity and Pain (CNAP) which is supported by the Danish National Research Foundation (DNRF121).

Disclosure of Funding: No funding

Conflict of Interest: We declare no competing interests.

Reference List

1. Côté P, van der Velde G, Cassidy DJ, Carroll L J, Hogg-Johnson S, Holm LW, et al. Task Force on Neck Pain and its Associated Disorders. The Burden and Determinants of Neck Pain in Workers. *Eur Spine J*. 2008;17:60–74.
2. Hoy D, March L, Woolf A, Blyth F, Brooks P, Smith E, et al. The global burden of neck pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis.* 2014;73:1309–1315.
3. Vos T, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet.* 2016;388:1545-1602.
4. Janwantanakul P, Pensri P, Jiamjarasrangsri V, Sinsongsook T. Prevalence of self-reported musculoskeletal symptoms among office workers. *Occup Med*. 2008;58:436–438.
5. Madeleine P, Vangsgaard S, Andersen JH, Ge H-Y, Arendt-Nielsen L. Computer work and self-reported variables on anthropometrics, computer usage, work ability, productivity, pain, and physical activity. *BMC Musculoskelet Disord*. 2013;14:226.
6. Kumar N. Report of a Delphi Study to determine the need for guidelines and to identify the number and topics of guidelines that should be developed by WHO. WHO Normative Guidelines on Pain Management, 2007.
7. Walton DM, Macdermid J, Nielsen W, Teasell R, Chiasson M, Brown L. Reliability, standard error, and minimum detectable change of clinical pressure pain threshold in people with and without acute neck pain. *J Ortho Sports Phys Ther*. 2011;41:644-650.
8. Walton DM, Levesque L, Payne M, Schick J. Clinical pressure pain threshold testing in neck pain: comparing protocols, responsiveness, and association with psychological variables. *Phys Ther*. 2014;94:827–837.
9. Zamani S, Okhovatian F, Naimi S, Baghban A. Intra-Examiner and between-Day reliability of algometer for pressure pain threshold and pain sensitivity in upper trapezius muscle in asymptomatic young adult women. *J Clin Physiother Res.* 2016;2:15-20.
10. Arendt-Nielsen L, Fernández-de-las-Peñas C, Graven-Nielsen T. Basic aspects of musculoskeletal pain: from acute to chronic pain. *J Man Manip Ther.* 2011;194:186–193.
11. Arendt-Nielsen L, Morlion B, Perrot S, Dahan A, Dickenson A, Kress HG, et al. Assessment and manifestation of central sensitisation across different chronic pain conditions. *Eur J Pain.* 2018;22:216–241.

12. Neziri AY, Scaramozzino P, Andersen OK, Dickenson AH, Arendt-Nielsen L, Curatolo M. Reference values of mechanical and thermal pain tests in a pain-free population. *Eur J Pain*. 2012;15:376–383.
13. Waller R, Smith A, O'Sullivan PB, Slater H, Sterling M, McVeigh JA, Straker, et al. Pressure and cold pain threshold references values in a large, young adult, free-pain population. *Scand J Pain.* 2016;13:114-122,
14. Graven-Nielsen T, Arendt-Nielsen L. Assessment of mechanisms in localized and widespread musculoskeletal pain. *Nav Rev Rheumatol*. 2010;6:599-606.
15. Wylde V, Palmer S, Learmonth ID, Dieppe P. The association between pre-operative sensitisation and chronic pain after knee replacement: an exploratory study. *Osteoarthritis Cartilage*. 2013;21:1253-1256.
16. Petersen K, Graven-Nielsen T, Simonsen O, Laursen MB, Arendt-Nielsen L. Preoperative pain mechanisms assessed by cuff algometry are associated with chronic postoperative pain relief after total knee replacement. *Pain*. 2016;157:1400-1406.
17. Wallin M, Liedberg G, Börsbo B, Gerdle B. Thermal detection and pain thresholds but not pressure pain thresholds are correlated with psychological factors in women with chronic whiplash-associated pain. *Clin J Pain*. 2012;28:211–221.
18. Stone A, Vicenzino B, Lim E, Sterling M. Measures of central hyperexcitability in chronic whiplash associated disorder – A systematic review and meta-analysis. *Man Ther.* 2013;18:111-117.
19. La Touche R, Fernández-de-las-Peñas C, Fernandez-Carnero J, Díaz-Parreño S, Paris-Alemany A, Arendt-Nielsen L. Bilateral mechanical-pain sensitivity over the trigeminal region in patients with chronic mechanical neck pain. *J Pain.* 2010;11:256-263.
20. Johnston V, Jimmieson N, Jull G, Souvlis T. Quantitative sensory measures distinguish office workers with varying levels of neck pain and disability. *Eur J Appl Physiol*. 2008;137:257-265.
21. Ge H-Y, Vangsgaard S, Omland Ø, Madeleine P, Arendt-Nielsen L. Mechanistic experimental pain assessment in computer users with and without chronic musculoskeletal pain. *BMC Musculoskelet Disord*. 2014;15:412–10.
22. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P). *Systematic Reviews*. 2015, 4:1.

23. Furlan AD, Pennick V, Bombardier C, van Tulder M. Updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine*. 2009;34:1929e41.
24. Smith B, Fors E, Korwisi B, Barke A, Cameron P, Colvin L, et al. The IASP classification of chronic pain for ICD-11: applicability in primary care. *Pain*. 2019;160:83-87.
25. Søgaard K, Blangsted A, Nielsen P, Hansen L, Andersen L, Vedsted P, et al. Changed activation, oxygenation, and pain of chronically painful muscles to repetitive work after training interventions: a randomized controlled trial. *Eur J Appl Physiol*. 2012;112:173-181.
26. Moita JP, Nunes A, Esteves J, Oliveira R, Xarez L. The relationship between muscular strength and dance injuries. A systematic review. *Med Probl Perform Art.* 2017;32:40-50.
27. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomized and non-randomised studies of health care interventions. *J Epidemiol Community Health*.1998;52:377–84.
28. Butterworth PA, Landorf KB, Smith SE, et al. The association between body mass index and musculoskeletal foot disorders: a systematic review. *Obes Rev.* 2012;13:630–42
29. Cohen J. Statistical Power Analysis for the Behavioral Sciences, 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Assoc, 1998.
30. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33:159–74.
31. Borenstein M, Hedges L, Higgins J, Rothstein H. Introduction to meta-analysis. Chichester, West Sussex, UK: John Wiley & Sons, Ltd; 2009.
32. Rosa M, Perracini M, Ricci N. Usefulness, assessment and normative data of the Functional Reach Test in older adults: A systematic review and meta-analysis. *Archives of Gerontology and Geriatrics.* 2019;81:149-170.
33. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions. The Cochrane Collaboration, Version 5.1.0, 2011.
34. Kenny DA. Statistics for the social and behavioral sciences. London: Longman; 1987
35. Vincent WJ. Statistics in Kinesiology. Champaign, IL: Human Kinetics; 1995.
36. Muehlbauer T, Gollhofer A, Granacher U. Associations between measures of balance and lower-extremity muscle strength/power in healthy individuals across the lifespan: A systematic review and meta-analysis. *Sports Med.* 2015;45:1671-1692.

37. Kiss R, Schedler S, Muehlbauer T. Associations between types of balance performance in healthy individuals across the lifespan. A systematic review and meta-analysis. *Front Physiol.* 2018;9:1366.
38. Bandt HLDH, Paulis WD, Beckwée D, Ickamns K, Nijs J, Voogt L. Pain mechanisms in low back pain: a Systematic Review and Meta-analysis of mechanical Quantitative Sensory Testing outcomes in people with non-specific low back pain. *J Orthop Sports Phys Ther*. 2019;49:698-715.
39. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.
40. IBM Corp. [Computer program]. IBM SPSS Statistics for Macintosh Version 25.0. Armonk, NY: IBM Corp, 2017.
41. Andersen L, Andersen C, Sundstrup E, Jakobsen M, Mortensen O, Zebis M. Central adaptation of pain perception in response to rehabilitation of musculoskeletal pain: randomized controlled trial. *Pain Physician.* 2012;15:385-393.
42. Andersen CH, Andersen LL, Zebis MK, Sjøgaard G. Effect of scapular function training on chronic pain in the neck/shoulder region: A randomized controlled trial. *J Occup Rehabil.* 2014;24:316-324.
43. Bragatto M, Bevilaqua-Grossi D, Regalo SCH, Sousa JD, Chaves TC. Associations among temporomandibular disorders, chronic neck pain and neck pain disability in computer office workers: a pilot study. *J Oral Rehabil.* 2016;43:312-332.
44. He D, Veiersted K, Hostmark A, Mebdo J. Effect of acupuncture treatment on chronic neck and shoulder pain in sedentary female workers: a 6 month and 3 year follow-up study. *Pain*. 2004;109:299-307.
45. Heredia-Rizo, A, Petersen K, Madaleine P, Arendt-Nielsen L. Clinical outcomes and central pain mechanisms are improved after trapezius eccentric training in female computer users with chronic neck/shoulder pain. *Clin J Pain.* 2019;35:65-76.
46. Johnston V, Jimmieson N, Jull G, Souvlis T. Contribution of individual, workplace, psychosocial and physiological factors to neck pain in female office workers. *Eur J Pain.* 2009;13:985-991.
47. Kimura M, Fuji H, Sato H. Effects of hot water baths containing carbon dioxide and 3-Octylphthalide on work-related chronic shoulder-neck pain muscle. *J Phys Ther Sci*. 2008;20:15-21.

48. Nielsen P, Andersen L, Olsen H, Rosendal L, Sjogaard G, Sogaard K. Effect of physical training on pain sensitivity and trapezius muscle morphology. *Muscle Nerve.* 2010;41:836-844.
49. Shahidi B, Curran-Everett D, Maluf K. Psychosocial, physical, and neurophysiological risk factors for chronic neck pain: a prospective inception cohort study. *J Pain.* 2015;16:1288-1299
50. Shahidi B, Maluf K. Adaptations in evoked pain sensitivity and conditioned pain modulation after development of chronic neck pain. *BioMed Res Int.* 2017;2017: Artcile ID 8985398.
51. Valera-Calero A, Lluch E, Callego-Izquierdo T, Malfliet A, Pecos-Martin D. Endrocrine response after cervical manipulation and mobilization in people with chronic mechanical neck pain: a randomized controlled trial. *Eur J Phys Rehabil Med*. 2019;55:792-805.
52. Andersen S, Petersen M, Svendsen A, Gazerani P. Pressure pain thresholds assessed over temporalis, masseter, and frontalis muscle in healthy individuals, patients with tension-type headache, and those with migraine – a systematic review. *Pain.* 2015;156: 1409-1423.
53. Castien R, van der Wouden J, De Hertogh W. Pressure pain thresholds over the cranio-cervical region in headache: a systematic review and meta-analysis. *J Headache Pain.* 2018;19:9.
54. Nahman-Averbuch H, Shefi T, Schneider V, Li D, Ding L, King C, et al. Quantitative sensory testing in patients with migraine: a systematic review and meta-analysis. *Pain*. 2018;159:1202-1223.
55. Ylinen J, Nykanen M, Kautiainen H, Hakkinen A. Evaluation of repeatability of pressure algometry on the neck muscles for clinical use. *Man Thera.* 2007;12:192–197.
56. Park G, Kim C, Park S, Kim M, Jang S. Reliability and usefulness of the pressure pain threshold measurement in patients with myofascial pain. *Ann Rehabil Med.* 2011;35:412-417.
57. Knapstad MK, Nordahl SHG, Naterstad IF, Ask T, Skouen JS, Goplen FK. Measuring pressure pain threshold in the cervical region of dizzy patients-The reliability of a pressure algometer. *Physiother Res Int.* 2018;23:e1736–6.
58. Melia M, Geissler B, König J, Ottersbach H, Umbreit M, Letzel S, et al. Pressure pain thresholds: subject factors and the meaning of peak pressures. *Eur J Pain.* 2019:23;167-182

59. Tham SW, Palermo TM, Holley AL, Zhou C, Stubhaug A, Furberg A-S et al. A population-based study of quantitative sensory testing in adolescents with and without chronic pain. *Pain*. 2016;157:2807–2815.
60. Sanches ML, Juliano Y, Novo NF, Guimarães AS, Conti PCR. Correlation between pressure pain threshold and pain intensity in patients with temporomandibular disorders who are compliant or non-compliant with conservative treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015;120:459-468.
61. Beltran-Alacreu H, Lopez-de-Uralde-Villanueva I, Calvo-Lobo C, Fernandez-Carnero, J, La Touche R. Clinical features of patients with chronic non-specific neck pain per disability level: A novel observational study. *Rev Assoc Med Bras.* 2018;64:700–709

Figure Legends

Figure 1 - Flow diagram for selection articles included in the review.

Figure 2a – Results of meta-analysis pressure pain threshold (kPa) for the upper trapezius muscle in CNP versus CON. a) all included studies; b) only studies with high quality above average. CNP: chronic neck pain; CON: asymptomatic control; IV: inverse-variance; kPa: kilopascal; Random: random-effects; SD: standard deviation; 95% CI: 95% confidence interval.

Figure 2b - Results of meta-analysis pressure pain threshold (kPa) for the extensor carpi ulnaris in CNP versus CON. CNP: chronic neck pain; CON: asymptomatic control; IV: inverse-variance; kPa: kilopascal; Random: random-effects; SD: standard deviation; 95% CI: 95% confidence interval.

Figure 2c - Results of meta-analysis pressure pain threshold (kPa) for the tibialis anterior in CNP versus CON. CNP: chronic neck pain; CON: asymptomatic control; IV: inverse-variance; kPa: kilopascal; Random: random-effects; SE: standard deviation; 95% CI: 95% confidence interval.

Figure 3a - Results of meta-analysis pressure pain threshold (kPa) for the upper trapezius reference values in CNP. CNP: chronic neck pain; IV: inverse-variance; kPa: kilopascal; Random: random-effects; SD: standard error; 95% CI: 95% confidence interval.

Figure 3b - Results of meta-analysis pressure pain threshold (kPa) for the extensor carpi ulnaris reference values in CNP. CNP: chronic neck pain; IV: inverse-variance; kPa: kilopascal; Random: random-effects; SD: standard error; 95% CI: 95% confidence interval.

Figure 3c - Results of meta-analysis pressure pain threshold (kPa) for the tibial anterior reference values in CNP. CNP: chronic neck pain; IV: inverse-variance; kPa: kilopascal; Random: random-effects; SD: standard error; 95% CI: 95% confidence interval.

Figure 4 - Pearson's *r*-values (z-transformed) for correlation between pressure pain threshold (kPa) and pain intensity in CNP. CNP: chronic neck pain; IV: inverse-variance; Random: random-effects; SD: standard error; 95% CI: 95% confidence interval.

Figure 5- Pearson's *r*-values (z-transformed) for correlation between pressure pain threshold (kPa) and neck disability index in CNP. CNP: chronic neck pain; IV: inverse-variance; Random: random-effects; SD: standard error; 95% CI: 95% confidence interval.

Table 1 – Study characteristics

Author/ year of publication	Study Design	Population: CNP N Age Gender (M/F)	Population: CON N Age Gender (M/F)	Device and measurement: Electronic / mechanical	Device and measurement: Probe size / rate/ outcome	PPT Location(s): Neck area	PPT Location(s): Non-neck area	Outcomes: PPT kPa Mean±SD	Outcomes: Pain Intensity	Outcomes: NDI	R
Andersen et al[41]	RCT	**Group 1** n=66 44±11 8/58 **Group 2** n=66 42±11 8/58 **Group 3** n=66 43±10 8/58		Electronic pressure algometer (Wagner Instruments, Greenwich, CT, USA)	1cm^2 30 KPa.s^{-1} kPa	**UT** Midpoint between C7 and acromion	**TA** Midway between the lateral condyle of the tibia and the lateral malleolus of the fibula	**UT** Group 1 239±92 Group 2 260±108 Group 3 219±73 **TA** Group 1 329±124 Group 2 331±127 Group 3 309±120	**VAS (0-10)** (3 months) Group 1 5.2±1.9 Group 2 5.2±2.1 Group 3 4.5±1.9	NA	**PPT between UT and TA** r=.60
Andersen et al[42]	RCT	**Group 1** n=23 45±11		Electronic Pressure Algometer	1cm^2 30 KPa.s^{-1} kPa	**UT** Midpoint between C7	**Sternum** Middle part **TA**	**UT** Group 1 303±127	**VAS (0-9) (last month)**	NA	NA

		5/18 **Group 2** n=24 44±13 5/19		(Algometer Type 2; Somedic, Horby, Sweden)		and acromion **LT** 2/3 down between angulus superior and the spinal attachment	muscle belly	Group 2 277±155 **LT** Group 1 383±145 Group 2 308±161 **Sternum** Group 1 254±154 Group 2 225±128 **TA** Group 1 381±135 Group 2 321±93	Group 1 5.4±1.5 Group 2 5.7±1.9		
Bragatto et al[43]	Cross-sectional	n=26 36.5 (33-4-36.6) (0/26)	n=26 33.81 (30.6 - 36.9) (0/26)	Digital Dynamometer model DDK-20	NA 0.5 Kg /cm^2s^1 Kg/cm^2	**UT** midpoint between C7 and acromion **ECM** Insertion fibers below the mastoid	NA	**UT** CNP 183±67 CON 180±59 **ECM** CNP 235±99 CON	**NPRS (0-10) (on the day)** CNP 4.85±1.58	**NDI** CNP 8.23±2.35	NA

						process **Suboccipital** Point immediately below the mastoid process		256±100 **Suboccipital** CNP 185±63 CON 196±64			
Ge et al 2014[21]	Cross sectional	n=47 47.6 ± 1.5 14/33	N=17 43.2 ± 2.3 5/12	Pressure algometer (Somedic, Horby, Sweden)	1cm2 30 kPa / sec kPa	**UT** midpoint between C7 and acromion	**ECU** muscle belly. 4cm bellow lateral epicondyle and then 2cm posterior **TA** muscle belly	**UT** CNP 240±112 CON 278±110 **ECU** CNP 258±113 CON 266±78 **TA** CNP 419±174 CON 421±166	**VAS (0-10)** **(on the day)** CNP 2.3±0.3 **(last 24 hours)** 3.2±1.8	NA	**UT** **Between PPT/VAS** r=-.217
He at al [44]	RCT	**Group 1** n=14 49±8		Algometer (Somedic production	$1cm^2$ $30 KPa.s^{-1}$ kPa	**UT** midpoint between C7	NA	**UT** Group 1 192±10	**VAS (0-10)** **(on the day)**	NA	NA

		0/14 **Group 2** n=10 45±10 0/10		AB, Sollentuna, Sweden)		and acromion **Levator scapula** **Suboccipital** insertion of the suboccipital tendons		Group 2 268±18 No data from other muscles	Group 1 5.7±0.7 Group 2 4.8±0.9		
Heredia-Rizo et al[45]	**Part A** Cross sectional **Part B** RCT	n=20 46.8 ± 1.3 0/20	n=20 41.7 ± 2.5 0/20	Eletronic pressure algometer (Somedic AB, Horby, swden)	$1cm^2$ 30 $KPa.s^{-1}$ kPa	**UT** Midpoint between C7 and acromion	**ECU** Muscle belly. 4cm bellow lateral epicondyle and then 2cm posterior.	**UT** CNP 189± 72 CON 209±81 **ECU** CNP 246±98 CON 278±119	**NPRS (last 24h)** CNP 5.30±0.42 CON 0.27±0.12 **NPRS (last week)** CNP 5.30±0.42 CON 0.75±0.19	**NDI** CNP 10.95±1.51 CON 1.15±0.31	**UT between PPT/NPRS** r=-.09 **UT Between PPT/NDI** r=.246
Johnston el al[20,46]	Cross-sectional	**Group 1** n=33 43±10.5 0/33 **Group 2**		Digital Algometer (Somedic AB, Farsta, Sweden)	$1cm^2$ 40 $KPa.s^{-1}$ kPa	**UT** Midpoint between C7 and acromion	**Median nerve trunk** Cubital fossa medial to and immediately	**Posterior Neck** Group 1 322±160 Group 2	NA	**NDI** Group 1 4.2 ± 2.6 Group 2 19.5 ± 5.9	NA

		n=38 43.8 ± 9.4 0/38 **Group 3** n=14 45.4 ± 10.3 0/14				**Levator Scapulae** Muscle belly medial to insertion on superior angle of scapulae **Posterior neck** Semispinalis capitis, just distal to its origin and 2cm from the midline.	adjacent to the tendon of the biceps. **TA** Upper 1/3 of the muscle belly	295±122 Group 3 237±72 **Levator Scapulae** Group 1 510±193 Group 2 447±155 Group 3 377±136 **UT** Group 1 389±128 Group 2 329±120 Group 3 303±112 **Median Nerve** Group 1 291±100 Group 2 255±78 Group 3 213±69		Group 3 33.5 ± 3.6	

								TA Group 1 499±173 Group 2 426±174 Group 3 393±175			
Kimura et al[47]	Uncontrolled trial	n=8 30.8±4.5 0/8		Algesiometer (Igarashi Medical Corp. Tokyo, Japan)	NA 1kgf/cm^2 kgf/cm^2	**UT** Midpoint between C7 and acromion	NA	**UT** **Right** 225.5±68.6 **Left** 186.3±39.2	**VAS (0-10) (on the day)** 6.8 (5.4-7.8)	NA	NA
Nielsen et al[48]	**Part A** Cross-sectional **Part B** RCT	n=42 44±8 0/42	n=20 45±9 0/20	Electronic Pressure Algometer (Algometer Type 2; Somedic, Horby, Sweden)	1cm^2 30 KPa.s^{-1} kPa	**UT** Midpoint between C7 and acromion	**TA** Middle distance between lateral condyle of the tibia and the lateral malleolus of the fibula	**UT** CPN-CW 280±82 CON 479±119 **TA** CPN-CW 302±110 CON 464±134	NA	NA	NA
Shahidi et al[49]	Prospective	n=35 29.8±6.8		Mechanical digital	1cm^2 1 kgF/s	**UT** Muscle belly	NA	**UT** CNP	NA	NA	NA

	Cohort	4/31		pressure algometer (FPIX 50, Wagner Instruments, Greenwich, CT)	kg/cm^2	dominant point		382±177			
Shahidi and Maluf[50]	Prospective Cohort	n=17 27.9±7.0 3/14	n=10 26.3 ±3.3 1/9	Mechanical digital pressure algometer (Wagner Instruments, Greenwich, CT)	$1cm^2$ 1 kgF/s kg/cm^2	**UT** Muscle belly dominant point	NA	**UT** CNP 371±177 CON 453±564	**VAS (0-10) (on the day)** CNP 1.62±0.69	**NDI** CNP 3.41±3.48 CON 0.5±0.97	**Between PPT NDI** r=-.141
Valera-Calero et al[51]	RCT	**Group 1** n=28 35±8 12/16 **Group 2** n=28 37±10. 10/18 **Group 3** n=27 36±8		Electronic Pressure Algometer (Wagner FDX-25-Wagner Instruments, Greenwich, CT)	$1cm^2$ $1kg/cm^2/s$ $1kg/cm^2$	**C5/6 zygapophyseal joint**	NA	**Group 1** 187±37 **Group 2** 195±40 **Group 3** 198±44	**VAS (0-10) (on the day)** Group 1 6.39±1.07 Group 2 6.41±1.24 Group 3 6.50±1.62	**NDI (0-50)** Group 1 23.78±10.19 Group 2 23.07±10.25 Group 3 25.24±8.88	NA

		10/17									

Legend: CNP – Chronic neck pain; CON – Asymptomatic controls; ECU – Extensor Carpal Ulnaris; kPA – kilopascal; LT – Lower Trapezius; NA- not attributed; NDI – Neck Disability Index; NPRS – Numerical Pain Rating Scale; PPT – pressure pain threshold; RCT - randomized controlled trials; TA – Tibial Anterior; UT – Upper Trapezius; VAS – Visual Analogue Scale.

Table 2. Included studies quality assessment scores (from modified Downs and Black checklist)

	Items																												
	Reporting										External validity			Internal validity (Bias)							Internal validity (Confounding)						Pwr		
Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Score	%
Observational studies n=; max. achievable score 16																													
Bragatto et al[43]	1	1	1	*	1	1	1	*	*	1	1	0	*	*	*	0	*	1	*	1	0	1	*	*	0	*	*	11	68.7
Ge et al[21]	1	1	1	*	1	1	0	*	*	1	0	0	*	*	*	0	*	1	*	1	1	0	*	*	0	*	*	9	56.2
Heredia-Rizo et al[45]	1	1	1	*	1	1	1	*	*	1	0	0	*	*	*	0	*	1	*	1	1	0	*	*	0	*	*	10	62.5
Johnston et al[20]	1	1	1	*	1	1	1	*	*	1	0	0	*	*	*	0	*	1	*	1	0	0	*	*	1	*	*	10	62.5
Johnston et al[46]	1	1	1	*	1	1	1	*	*	1	0	0	*	*	*	0	*	1	*	1	0	0	*	*	1	*	*	10	62.5
Nielsen et al[48]	1	1	1	*	0	1	0	*	*	0	0	0	*	*	*	0	*	1	*	1	0	1	*	*	0	*	*	7	43.7
Shahidi et al[49]	1	1	1	*	1	1	1	*	*	1	0	0	*	*	*	0	*	1	*	1	0	0	*	*	1	*	*	10	62.5
Shahidi & Maluf[50]	1	1	1	*	0	1	0	*	*	1	0	0	*	*	*	0	*	1	*	1	1	1	*	*	0	*	*	9	56.2
Experimental studies with no independent control group n=; max. achievable score 28																													
Kimura et al[47]	1	1	0	1	*	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	*	*	0	0	0	0	0	4	14.2
Experimental studies n=; max. achievable score 32																													
Andersen et al[41]	1	1	1	1	1	1	1	0	0	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	0	1	2	22	68.7
Andersen et al[42]	1	1	1	1	0	1	1	1	1	0	1	1	1	0	0	0	1	1	1	1	1	1	1	0	0	1	1	20	62.5
He et al[44]	1	1	1	1	1	1	1	0	1	1	0	0	1	1	0	0	1	0	0	1	0	0	1	1	0	1	0	16	50.0
Valera-Calero et al[51]	1	1	0	1	0	1	1	0	0	1	0	0	0	0	1	0	0	1	0	1	0	0	1	1	0	0	4	15	46.8
																												Mean % score	55.1

All questions were scored on the following scale: yes = 1, no = 0, unable to determine = 0; Question 5 is an exception, with scores allocated: yes = 2, partially = 1; no = 0; Question 27 is also an exception with scores ranging from 0 – 5; *Not applicable;.Pwr, power

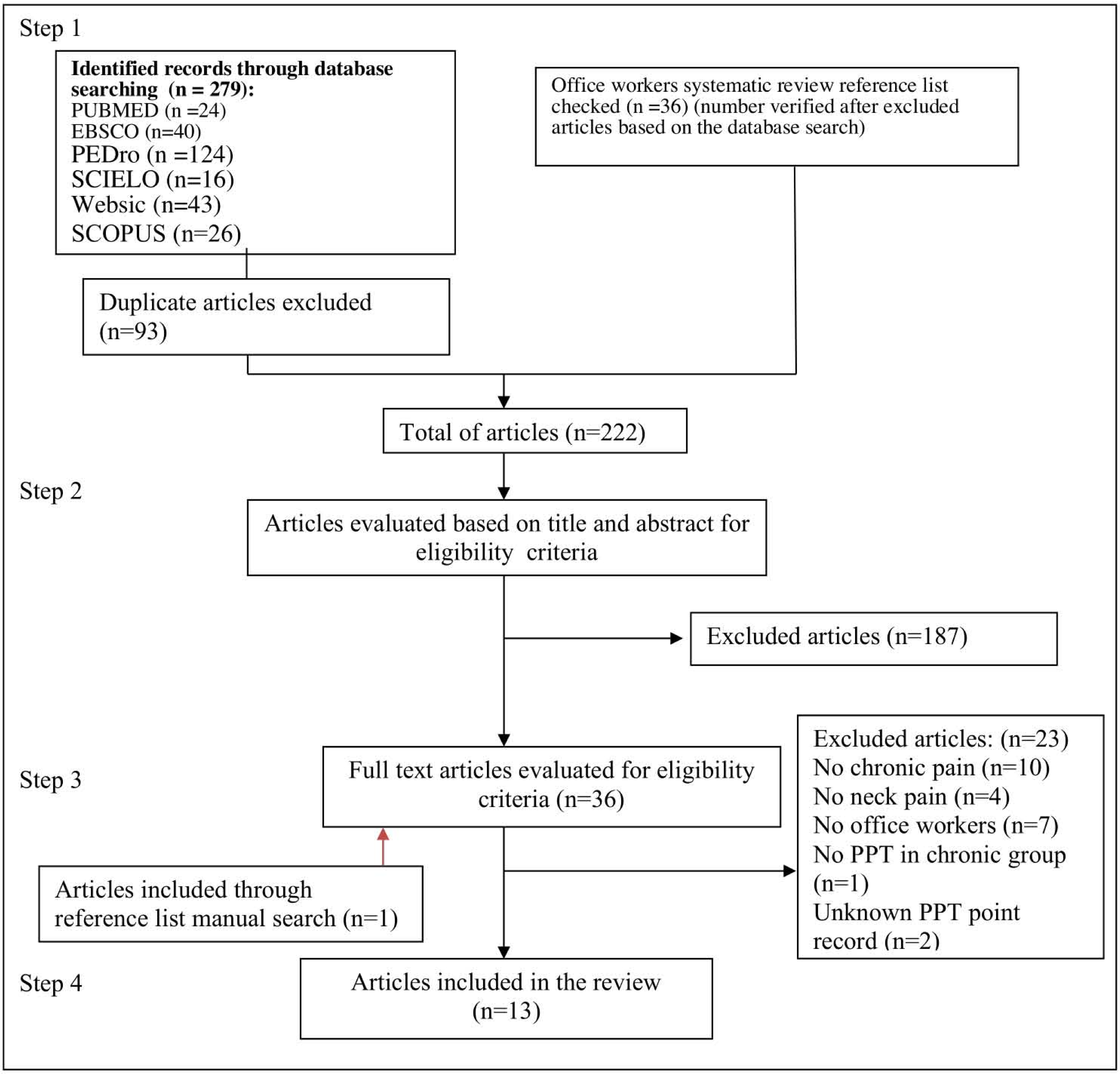
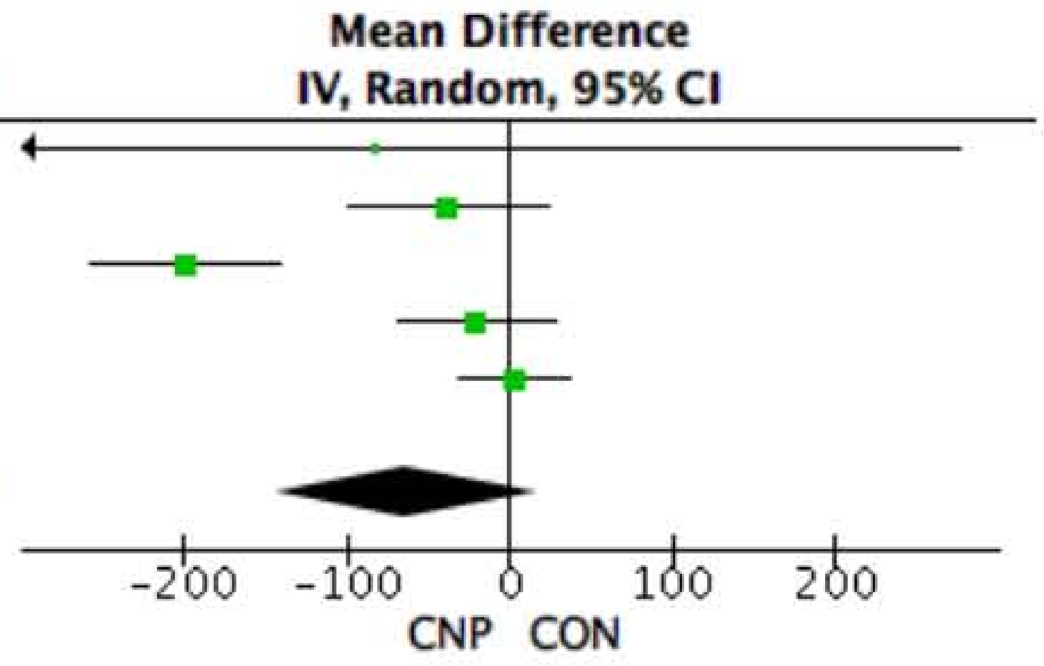


Figure 1 - Flow diagram for selection articles included in the review.

2a(a)

Study or Subgroup	CNP Mean	CNP SD	CNP Total	CON Mean	CON SD	CON Total	Weight	Mean Difference IV, Random, 95% CI
Shahidi and Maluf (50)	371	177	17	453	564	10	4.2%	-82.00 [-441.55, 277.55]
Ge et al (21)	240	112	47	278	110	17	23.0%	-38.00 [-99.31, 23.31]
Nielsen et al (48)	280	82	42	479	119	20	23.3%	-199.00 [-256.75, -141.25]
Heredia-Rizo et al (45)	189	72	20	209	81	20	24.2%	-20.00 [-67.50, 27.50]
Bragatto et al (43)	183	67	26	180	59	26	25.2%	3.00 [-31.32, 37.32]
Total (95% CI)			**152**			**93**	**100.0%**	**-62.68 [-143.58, 18.22]**

Heterogeneity: $Tau^2 = 6442.55$; $Chi^2 = 35.88$, df = 4 ($P < 0.00001$); $I^2 = 89\%$
Test for overall effect: Z = 1.52 (P = 0.13)



2a(b)

Study or Subgroup	CNP Mean	CNP SD	CNP Total	CON Mean	CON SD	CON Total	Weight	Mean Difference IV, Random, 95% CI
Shahidi and Maluf (50)	371	177	17	453	564	10	0.5%	-82.00 [-441.55, 277.55]
Ge et al (21)	240	112	47	278	110	17	17.0%	-38.00 [-99.31, 23.31]
Nielsen et al (48)	280	82	42	479	119	20	0.0%	-199.00 [-256.75, -141.25]
Heredia-Rizo et al (45)	189	72	20	209	81	20	28.3%	-20.00 [-67.50, 27.50]
Bragatto et al (43)	183	67	26	180	59	26	54.2%	3.00 [-31.32, 37.32]
Total (95% CI)			**110**			**73**	**100.0%**	**-10.89 [-36.16, 14.38]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.67$, df = 3 ($P = 0.64$); $I^2 = 0\%$
Test for overall effect: Z = 0.84 (P = 0.40)

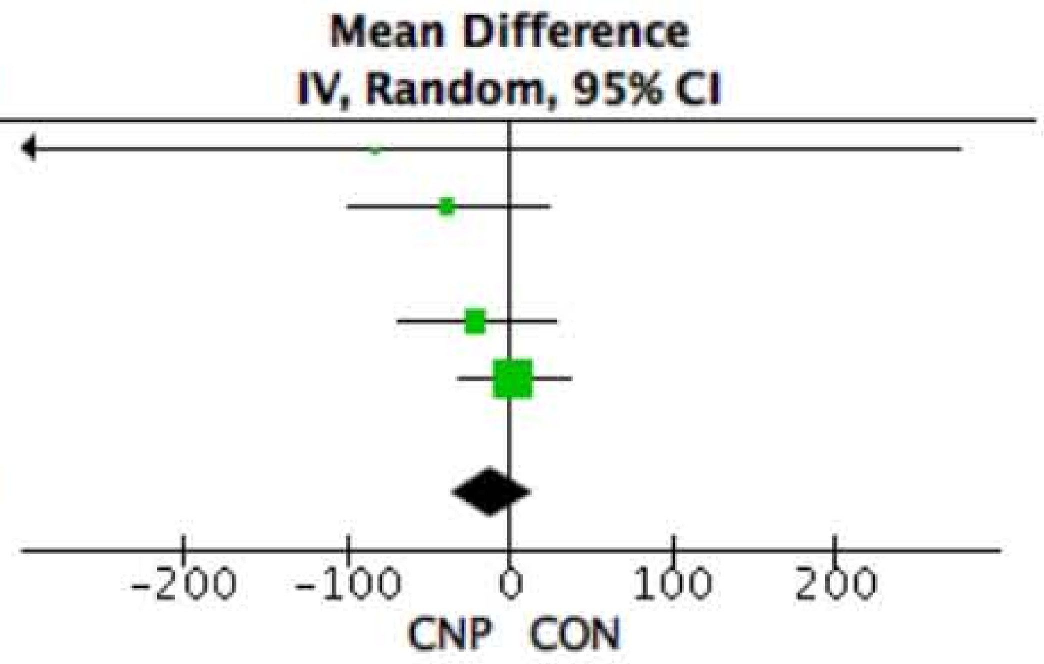


Figure 2a – Results of meta-analysis pressure pain threshold (kPa) of upper trapezius muscle in CNP versus CON. a) all included studies; b) only studies with high quality above average.

2b

Study or Subgroup	CNP Mean	CNP SD	CNP Total	CON Mean	CON SD	CON Total	Weight	Mean Difference IV, Random, 95% CI
Ge et al (21)	258	113	47	266	78	17	65.4%	-8.00 [-57.18, 41.18]
Heredia-Rizo et al (45)	246	98	20	278	119	20	34.6%	-32.00 [-99.56, 35.56]
Total (95% CI)			**67**			**37**	**100.0%**	**-16.31 [-56.07, 23.45]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.32$, df = 1 ($P = 0.57$); $I^2 = 0\%$
Test for overall effect: Z = 0.80 (P = 0.42)

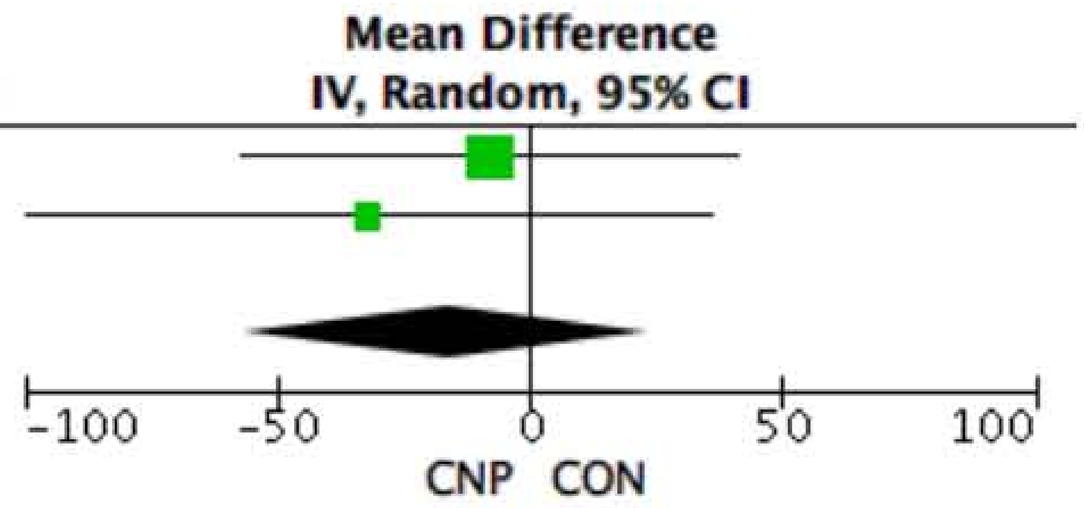


Figure 2b - Results of meta-analysis pressure pain threshold (kPa) of extensor carpi ulnaris in CNP versus CON

2c

Study or Subgroup	CNP-CW Mean	CNP-CW SD	CNP-CW Total	CON-CW Mean	CON-CW SD	CON-CW Total	Weight	Mean Difference IV, Random, 95% CI
Ge et al (21)	419	174	47	421	166	17	47.9%	-2.00 [-95.28, 91.28]
Nielsen et al (48)	302	110	42	464	134	20	52.1%	-162.00 [-229.49, -94.51]
Total (95% CI)			**89**			**37**	**100.0%**	**-85.37 [-242.03, 71.29]**

Heterogeneity: $Tau^2 = 11074.50$; $Chi^2 = 7.42$, df = 1 ($P = 0.006$); $I^2 = 87\%$
Test for overall effect: Z = 1.07 (P = 0.29)

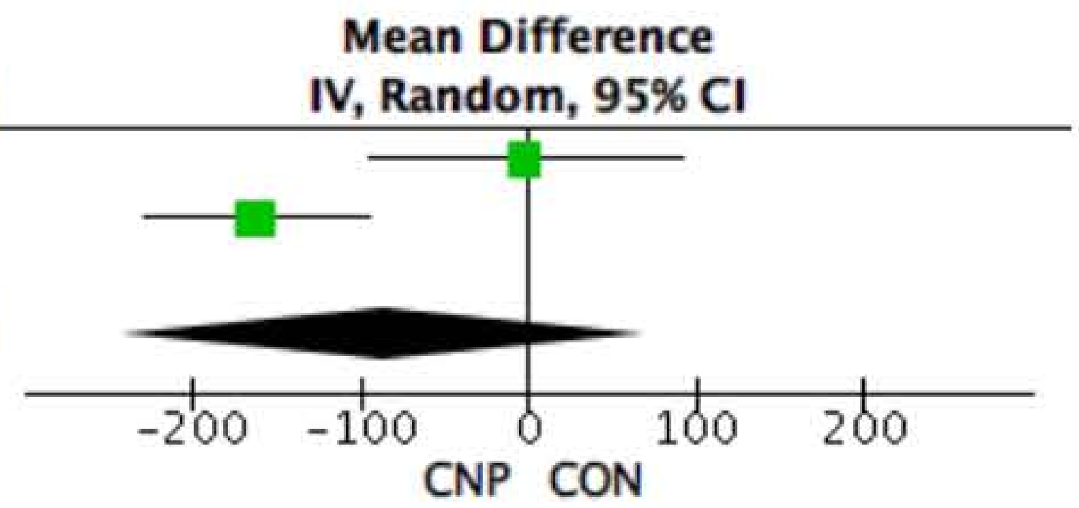


Figure 2c - Results of meta-analysis pressure pain threshold (kPa) of tibialis anterior in CNP versus CON.

3a

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Andersen et al (41)	238	6.61	10.4%	238.00 [225.04, 250.96]
Andersen et al (42)	288	20.43	8.6%	288.00 [247.96, 328.04]
Bragatto et al (43)	183	13.13	9.7%	183.00 [157.27, 208.73]
Ge et al (21)	240	16.4	9.3%	240.00 [207.86, 272.14]
He et al (44)	222	2.6	10.7%	222.00 [216.90, 227.10]
Heredia-Rizo et al (45)	189	16.08	9.3%	189.00 [157.48, 220.52]
Johnston et al (20)	332	12.7	9.8%	332.00 [307.11, 356.89]
Kimura et al (47)	225	24.32	8.0%	225.00 [177.33, 272.67]
Nielsen et al (48)	280	12.65	9.8%	280.00 [255.21, 304.79]
Shahidi and Maluf (50)	371	28.52	7.3%	371.00 [315.10, 426.90]
Shahidi et al (49)	382	29.86	7.1%	382.00 [323.48, 440.52]
Total (95% CI)			**100.0%**	**263.02 [236.35, 289.70]**

Heterogeneity: $Tau^2 = 1730.16$; $Chi^2 = 169.20$, df = 10 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: $Z = 19.32$ ($P < 0.00001$)

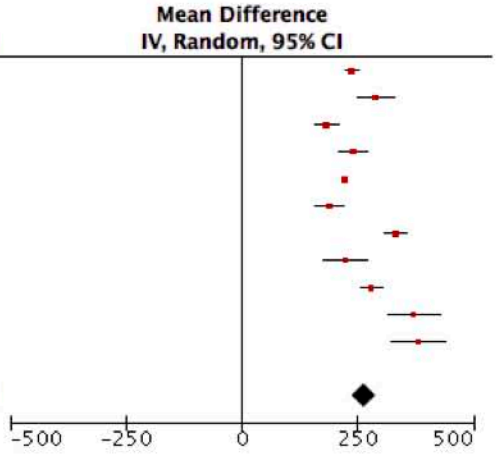


Figure 3a - Results of meta-analysis pressure pain threshold (kPa) for upper trapezius reference values in CNP.

3b

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Ge et al (21)	258	16.5	63.9%	258.00 [225.66, 290.34]
Heredia-Rizo et al (45)	246	21.94	36.1%	246.00 [203.00, 289.00]
Total (95% CI)			**100.0%**	**253.66 [227.82, 279.51]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.19$, df = 1 ($P = 0.66$); $I^2 = 0\%$
Test for overall effect: $Z = 19.24$ ($P < 0.00001$)

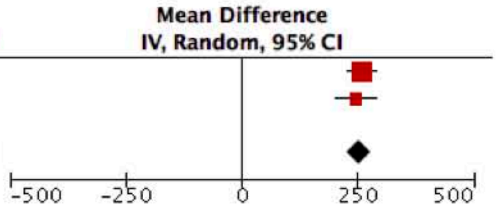


Figure 3b - Results of meta-analysis pressure pain threshold (kPa) for extensor carpi ulnaris reference values in CNP.

3c

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Andersen et al (41)	323	8.6	21.7%	323.00 [306.14, 339.86]
Andersen et al (42)	349	16.35	20.3%	349.00 [316.95, 381.05]
Ge et al (21)	419	25.4	18.1%	419.00 [369.22, 468.78]
Johnston et al (20)	447	19	19.7%	447.00 [409.76, 484.24]
Nielsen et al (48)	302	17	20.2%	302.00 [268.68, 335.32]
Total (95% CI)			**100.0%**	**365.89 [316.66, 415.12]**

Heterogeneity: $Tau^2 = 2837.83$; $Chi^2 = 50.26$, df = 4 ($P < 0.00001$); $I^2 = 92\%$
Test for overall effect: $Z = 14.57$ ($P < 0.00001$)

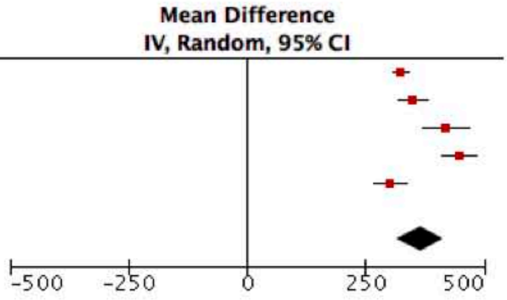


Figure 3c - Results of meta-analysis pressure pain threshold (kPa) for tibial anterior reference values in CNP.

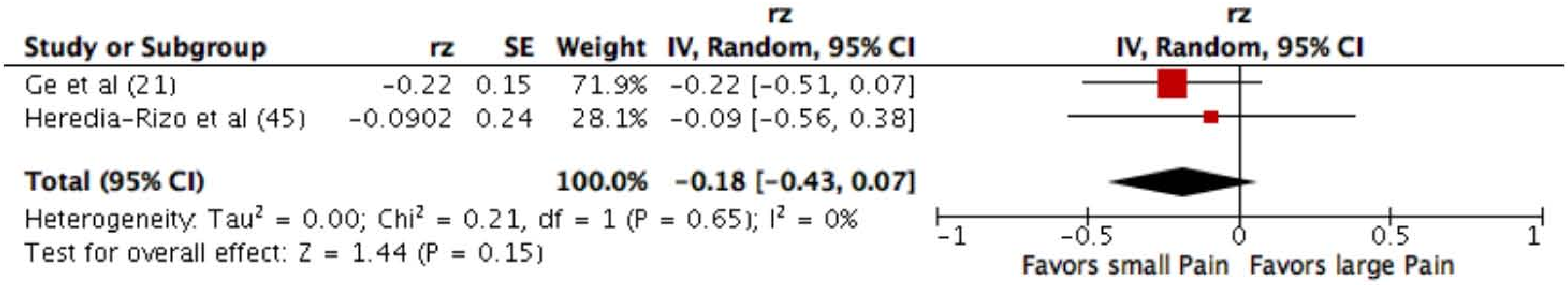


Figure 4 - Pearson's *r*-values (z-transformed) for correlation between pressure pain threshold (kPa) and pain intensity in CNP.

Study or Subgroup	Rz	SE	Weight	Rz IV, Fixed, 95% CI
Heredia-Rizo et al (45)	0.251	0.24	54.0%	0.25 [-0.22, 0.72]
Shahidi and Maluf (50)	-0.141	0.26	46.0%	-0.14 [-0.65, 0.37]
Total (95% CI)			**100.0%**	**0.07 [-0.27, 0.42]**

Heterogeneity: Chi^2 = 1.23, df = 1 (P = 0.27); I^2 = 19%
Test for overall effect: Z = 0.40 (P = 0.69)

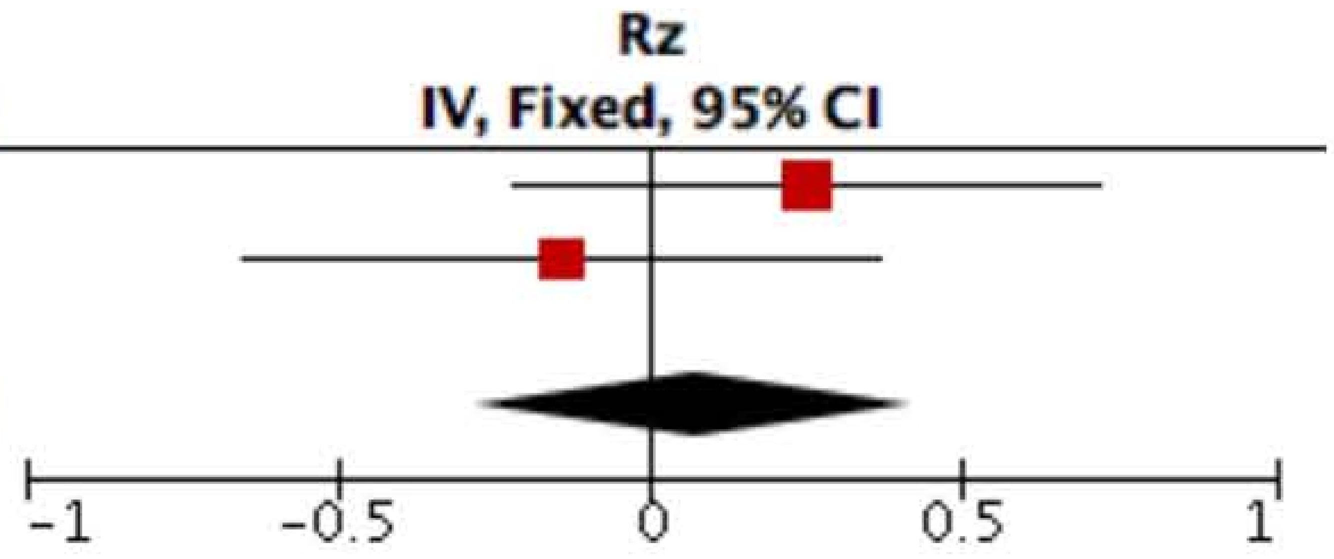


Figure 5- Pearson's *r*-values (z-transformed) for correlation between pressure pain threshold (kPa) and neck disability index in CNP.