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Title Page

Bedside clinical tests to assess sensitization in office workers with chronic
neck pain

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Abstract

Objective: This study aimed to assess pain sensitization in individual office workers with chronic neck pain through simple bedside quantitative sensory tests (QST) and to associate the findings with pain intensity and pain catastrophizing.

Methods: One hundred-and-four office workers with chronic neck pain were assessed using pressure pain threshold (PPT) considering pain sensitive if PPTs were lower than 155 kPa in the upper trapezius and 245 kPa in the tibialis anterior. Pain sensitive to temporal summation of pain (TSP) was considered if there was a difference of 2 points in the visual analog scale (VAS) comparing the first and last stimulus. Pain sensitive was considered to conditioned pain modulation (CPM) if the CPM-effect was less than -7.5%. Pain intensity and catastrophizing were measured using VAS and with the Pain Catastrophizing Scale.

Results: There was at least one pain sensitive QST finding in 66 office workers (63.5%). TSP findings were the most common (48.1%), followed by PPT's (31.7%) and CPM (20.2%). Based on the QST findings, office workers were divided based on the number of individual QST findings, and higher pain intensity and pain catastrophizing scores were found in office workers with one (N=38, $P<0.05$) or two (N=28, $P<0.05$) compared with office workers with no QST findings (N=38).

Conclusion: This study demonstrated that most office workers with chronic neck pain exhibit either widespread pressure hyperalgesia, facilitated TSP or impaired CPM, indicating pain sensitization within the central nervous system. This was associated with increased clinical pain and pain catastrophizing rumination scores.

Keywords: office workers, chronic neck pain, pain sensitization, quantitative sensory tests.

1 Introduction

Chronic neck pain prevalence in office workers ranges from 20% to 60% worldwide (Sarquis et al. 2016). Literature suggests that pain chronicity is associated with neuroplastic changes and by having this concept in mind, the identification and classification of the pain related mechanisms as nociceptive, neuropathic or nociplastic, may reveal very useful in designing better pain treatment and management plans (Boudreau et al. 2010; Pavlakovic & Petzke 2010; Arendt-Nielsen et al. 2011; Pelletier et al. 2015; Chimenti et al., 2018). Furthermore, the term nociplastic pain implies an inference of central sensitization, which can be assessed through quantitative sensory tests (QST) (Kosek et al. 2016).

Pressure pain thresholds (PPTs) are often used parameters in the assessment of musculoskeletal pain conditions (Arendt-Nielsen et al. 2011, 2015a, 2018). When compared with asymptomatic office workers, subjects with chronic trapezius myalgia and moderate pain intensity, exhibit lower pain thresholds, when assessed both on the neck and/or at remote non-painful sites (Nunes et al. 2020), indicating localized and widespread pressure hyperalgesia. Normative cut-off points based on data from healthy subjects have been proposed in the literature (Neziri et al. 2011; Waller et al. 2016).

Widespread pain sensitivity can be attributed to changes in wide-dynamic range neurons in the dorsal horn of the spinal cord (Latremoliere and Woolf 2009; Pelletier et al. 2015; Arendt-Nielsen et al. 2018), and in the descending pain pathways, which can inhibit or facilitate pain sensation (Heinricher et al. 2009; Pelletier et al. 2015; Arendt-Nielsen et al. 2018). Temporal summation of pain (TSP) is believed to assess the excitability within the dorsal horn in the spinal cord. Also, it is believed that conditioned pain modulation (CPM) may be used to evaluate the inherent capacity of the endogenous pain modulatory system (Yarnitsky et al. 2010; Arendt-Nielsen et al. 2018). In many chronic pain conditions, TSP is often facilitated, and CPM is often impaired (Arendt-Nielsen et al. 2015b, 2018). A recent study observed a facilitated TSP in office workers with chronic neck pain self-reporting a moderate pain intensity when compared to healthy subjects but with no differences in CPM (Nunes et al. 2020). Also, recently normative cut-off points out of data on healthy subjects were proposed by Schliessbach and colleagues (2019) for determining the possibility of assessing impaired CPM.

It has been argued that there is an association between higher clinical pain intensities and decreased PPTs, facilitated TSP and impaired CPM in patients with musculoskeletal pain (Graven-Nielsen and Arendt-Nielsen. 2010; Arendt-Nielsen et al. 2015b). Recent studies indicate that pain catastrophizing might be associated with both QST findings (Christensen et al. 2020) and clinical pain intensities (Lee et al. 2013). Nevertheless, those associations need further elaboration.

Also, QST is found not to be widely implemented in the clinic practice due to the lack of standardized protocols with established normative data for assessing somatosensory dysfunctions (Arendt-Nielsen et al. 2009; Arendt-Nielsen et al. 2015a; Curatolo et al. 2015; Arendt-Nielsen et al. 2018; Chimenti et al. 2018;), expensive equipment and the time-consuming nature of the tests (Rolke et al. 2006; Cruz-Almeida and Fillingim 2014; Zhu et al. 2019).

The primary aim of this study was to assess sensitization through simple bedside QST findings in individual office workers with chronic neck pain and to identify pain sensitive subjects based on previously proposed normative data. The secondary aim was to assess the differences between the number of individual pain sensitive QST findings, clinical pain intensity and pain catastrophizing.

2 Methods

This study complies to the tenets of the Declaration of Helsinki and was approved by the Ethic Council (CEFMH) at the Faculty of Human Kinetics – Lisbon University (Approval Number:23/2017). All participants gave written informed consent.

2.1 Subjects

A total of 104 office workers with chronic neck pain were recruited to participate in the study. The study population was retrieved from a larger sample composed of 171 office workers from Lisbon University, Algarve University, and Albufeira City Council, which had participated in a previous observational analytic and correlational cross-sectional study. In the present work, data were collected from February 2018 to May 2019. The eligibility criteria were adult office workers from 25 to 60 years of age, working at least for more than one year in the same job position and spend at least 3/4 of the working hours on a computer (Sjörs et al. 2011, Andersen et al. 2014). The criteria for chronic neck pain was defined to be present for more than three months (Smith et al. 2019). The exclusion criteria were: medical history of

cardiovascular and cerebrovascular events; major chronic diseases; neurologic diseases; metabolic diseases; pregnancy; rheumatologic diseases; fibromyalgia; whiplash disorders; cervical disc herniation or severe disorders of the cervical spine such as severe osteoarthritis and past neck fractures; signs of tendinitis or joint affection in the shoulders at examination; and pregnancy (Søgaard et al. 2012).

A standard clinic examination was performed, by one examiner with more than 15 years of clinic experience, to ensure that the subjects met the above criteria. This examination included questions about pain duration; pain intensity; pain localization; tiredness and stiffness in the neck and shoulder region on the day of the examination; neck and shoulder range of motion according to Ohlsson and Kristensen (Ohlsson et al. 1994; Juul-Kristensen et al. 2006). Office workers were asked to not take any analgesics or nonsteroidal anti-inflammatory drugs (NSAIDs) 24 hours before the examination.

2.2 Demographics

The demographic variables included were age, gender, BMI, working hours on the computer per week, working hours on the computer per day, number of years working with computers, pain intensity, pain duration, analgesics or NSAIDs taken for more than 24h for the neck pain, and current treatment for neck pain.

2.3 Self-Reported Measures

2.3.1 Pain Intensity

The pain intensity at present day and the average from the last seven days, were assessed on a Visual Analog Scale (VAS), anchored at 0: no pain and 10: worst pain imaginable.

2.3.2 Pain Catastrophizing Scale (PCS)

Pain Catastrophizing Scale (PCS) is a 13-item self-reported measure designed to assess catastrophic thoughts or feelings when experiencing pain. It is composed of three subscales: rumination, magnification and, helplessness; items are rated on a 5-point scale ranging from 0 (not at all) to 4 (all the time), the maximum score is 52 being 30 points considered to be a clinically relevant level of catastrophizing (Sullivan and Bishop, 1995). This questionnaire was translated, adapted, and validated to the Portuguese population with chronic pain, and has revealed a good internal consistency in all subscales: rumination (0.796), magnification (0.789) and helplessness (0.897) (Azevedo et al. 2007).

2.4 Quantitative Sensory Testing

2.4.1 Pressure Pain Threshold

PPTs were assessed using a hand-held pressure algometer consisted of a 1 cm² rubber tip applicator, placed perpendicularly to the skin, mounted on a force transducer at an application rate of 1 kg/seg (JTech Medical, Salt Lake City, USA). The PPT's were defined as the minimum pressure first evoking a pain sensation. An upper cut-off limit of 500 kPa was used (Nunes et al. 2020). PPTs were measured twice with an interval of 10 seconds for each point, and the mean value was used for statistical analysis, as previously described (Balaguier et al. 2016).

Three different assessment sites were used: upper trapezius in the most painful side/dominant side and the same point in the contralateral muscle and tibialis anterior. The upper trapezius point was localized in the midpoint between C7 and acromion (Ge et al. 2014); the tibialis anterior point was defined approximately 2.5 cm lateral and 5 cm inferior to the tibial tubercle (Walton et al. 2011). The tibialis anterior point was on the same side as the most painful side/dominant side in upper trapezius. For upper trapezius measurement the participants were in prone position and for tibialis anterior in supine position. Each PPT localization was marked with a pen marker.

2.4.2 Temporal Summation of Pain (TSP)

A modified von Frey stimulator (Aalborg University, Aalborg, Denmark) with a weighted load of 25.6 g was used to induce TSP. The procedure consisted on the application of ten consecutive stimulations with a 1-second interval between stimulations, in the upper trapezius on the most painful side/dominant side in the same point previously described with the subjects in a sitting position. Each subject was asked to rate the pain intensity from the first and last stimulus on the VAS (0-10). TSP was calculated as the difference in pain intensity between the first and the last stimuli, as previously described (Petersen et al. 2015; Kurien et al. 2018).

2.4.3 Conditioned Pain Modulation (CPM)

CPM was measured as the difference in PPTs at the upper trapezius before and after the cold pressor test (CPT) (Petersen et al., 2015). Measurements were done with the subject in a sitting position, the contralateral hand of the most painful side/dominant side immersed up to

the wrist in a cold water bath maintained at 2-3°C. The subjects were asked maintain the hand immersed for a maximum time of 2 minutes or to remove it when a pain intensity of 7 out of 10 was reached on a 0 (no pain) to 10 (worst imaginable pain) scale. The CPM effect was calculated as the ratio between the test stimulus with and without the conditioning stimulus.

2.5 Experimental protocol

The sequence of the quantitative sensory procedures were: 1) PPT measured in the upper trapezius in the most painful side/dominant, the same point in the contralateral muscle and in the tibialis anterior (ipsilateral); 2) TSP measurement; 3) CPM assessment. A five-minute interval was set between PPT and TSP and between TSP and CPM. The measurements were performed during workdays, from 9am to 1pm, in the different workplaces.

2.6 Statistics

Descriptive statistics were used for age, gender, BMI, number of working hours per week, number of working hours on the computer, number of years working on the computer, pain intensity at present day, pain duration, analgesics or nonsteroidal anti-inflammatory drugs (NSAIDs) taken from more than 24 hours, and current treatment for the neck pain. The Shapiro-Wilk test was used to test the normal distribution of the variables.

Office workers were analyzed for pain sensitization using previously published normative data score according to the following criteria: a) PPT points were considered to be hypersensitive if values were below 155 kPa (upper trapezius) and 245 kPa (tibialis anterior) (Neziri et al. 2011; Waller et al. 2016; Nunes et al. 2021). Since the scores from the above studies were found to be similar the lowest scores from Neziri et al. (2011) were chosen as cut-off. A widespread pressure hyperalgesia was found to be present if all the three PPT values (both trapezius and tibialis anterior) were below the cut-off point, and were dichotomized as yes or no; b) facilitated TSP was present if the difference between the first and the last stimulus increased 2 points in VAS (Rabey et al. 2019), being that increased dichotomized as yes or no; c) impaired CPM was considered when the CPM effect was lower than -7.5% (Schliessbach et al. 2019), being also dichotomized as yes or no. Widespread pain sensitivity was considered present if all the three QST values were below the cut-off points.

Office workers were grouped into the following groups based on the number of positive QST findings: no findings (QST0), one positive finding (QST1), and two positive findings (QST2). Differences between groups in pain intensity, PCS and PCS subscales were examined

using a one-way analysis of variance (ANOVA) with Tukey HSD post hoc tests for statistical significance ($p < 0.05$). A Pearson's chi-squared test was used to determine whether there were a statistically difference between the average of the three QST tests in QST1 and QST2 ($p < 0.05$).

Power analysis and sample size details were presented in a previous study (Nunes et al. 2020). In the current study was analyzed the 104 office workers with chronic neck pain from the total sample size. The statistical analyses were performed using SPSS 25.0 software (SPSS Inc., Chicago, IL, USA).

3 Results

3.1 Office Workers Demographics

One-hundred-and-four office workers (age 44.0 ± 7.82 ; weight 65.5 ± 12.7 kg, height 164.2 ± 8.6 cm) were recruited from the Albufeira City Council (59.6%), from Lisbon University (25.0%), and from Algarve University (15.4%). Office workers were divided into three groups accordingly with QST findings: QST0 ($n=38$), QST1 ($n=38$), and QST2 ($n=28$) (flow-chart in fig. 1). No significant differences were found in the demographics when comparing the groups (table 1).

Insert table 1, fig. 1

3.2 Quantitative Sensory Testing Findings.

In total 38 office workers (36.5%) exhibited no QST finding and 66 (63.5%) had at least one QST finding. From positive QST findings, and based on previously published normative values, 33 office workers (31.7%) have demonstrated widespread pressure hyperalgesia (figure 2a), 50 office workers (48.1%) show facilitated TSP (figure 2b), and 21 office workers (20.2%) demonstrated an impaired CPM (figure 2c).

A statistically significant difference in PPTs, TSP and CPM averages between QST1 and QST2, was found in all analyses, $p < 0.005$ (table 2). In QST2, 10 office workers had all the three QST findings, representing 9.6% of the total sample.

Insert table 2, fig. 2

3.3 Self-Reported Measures

A significant difference was found concerning pain intensity [$F(2,101)=9.865$, $p<0.001$], with the Tukey HSD post hoc analysis showed a higher pain intensity in QST2 when compared with QST0 ($p<0.001$), and in QST1 when compared with QST0 ($p=0.011$) (fig 3).

Also, a significant difference was observed in the rumination subscale [$F(2,101)=3.060$, $p=0.05$], with the Tukey HSD post hoc analysis revealing a higher rumination score in QST2 when compared with QST0 ($p=0.047$). There were no differences between groups in the other subscales or in the full PCS (table 3).

Insert table 3, and Fig. 3.

4 Discussion

This study aimed to assess sensitization in office workers with chronic neck pain through simple bedside QST findings and by using an already published normative data set from PPT (Neziri et al. 2011; Waller et al. 2016) and CPM (Schliessbach et al. 2019) in healthy subjects and from PPT in office workers with chronic neck pain (Nunes et al. 2021).

From the 104 participants, 63.5% exhibited either widespread hyperalgesia, facilitated TSP or impaired CPM. Also, it was found that clinical pain intensity and pain catastrophizing rumination scores increase with the increasing number of positive QST findings.

The present study results are in line with previous studies reporting QST findings in office workers with chronic neck pain (Johnston et al. 2008; Ge et al. 2014; Shahidi et al. 2015; Shahidi and Maluf, 2017; Heredia-Rizo et al. 2019). However, the QST findings in patients with chronic neck pain are still open for debate. As an example, the evidence for widespread hyperalgesia measured by PPT in chronic neck pain in office workers is conflicting. While some studies report no PPT differences (Ge et al. 2014) other studies report widespread pressure hyperalgesia in office workers with chronic neck pain compared with asymptomatic office workers (Johnston et al. 2008; Nielsen et al. 2010; Nunes et al. 2020). Nevertheless, the findings of this study concerning PPT results, were found to be in line with the aforementioned studies and a recent systematic review and meta-analysis from Xie et al. (2020) for neck pain. The systematic review from Xie et al. (2020) found a moderate effect size with moderate-quality evidence for mechanical hyperalgesia in PPTs in the tibialis anterior when comparing patients with non-traumatic neck pain with healthy controls. This suggests the presence of an altered central pain processing. However, the review did not specifically address to office

workers and both participants with acute and chronic pain were considered, therefore caution is recommended when extrapolating conclusions out of the results.

The conflicting results concerning QST found across the literature, can also be applied to CPM, where no differences between office workers with chronic neck pain and healthy workers have been reported (Ge et al. 2014; Heredia-Rizo et al. 2019; Nunes et al. 2020). Nonetheless, in the studies from Shahidi et al. (2015) and Shahidi and Maluf (2017), CPM was considered to be a risk factor for developing chronic interfering neck pain in a twelve-month prospective cohort study with office workers. In the present study, 20% of the population were found to have impaired CPM, which may suggest that only a subpopulation of patients might display impairment of descending pain pathways, as seen in other musculoskeletal pain conditions [50,51] (Petersen et al. 2016; Vægter et al. 2016).

TSP can be elicited by different modalities such as thermal, electric, or pressure (Graven-Nielsen and Arendt-Nielsen 2010; Arendt-Nielsen et al. 2018). In the study from Heredia-Rizo et al. (2019), TSP was collected with a cuff-algometer in the lower limb, with no observed differences when compared to healthy office workers. In a previous study, eliciting TSP by a pinprick in the upper trapezius (painful side/dominant side), proved to enhance TSP in office workers with moderate pain intensity when compared to asymptomatic (Nunes et al. 2020). The TSP test-retest reliability with a pinprick demonstrated moderate to good reliability in long term reliability in healthy subjects (Marouzzi et al. 2017; Nothnagel et al. 2017), with good to excellent reliability in acute musculoskeletal trauma (Middlebrook et al. 2020) and good reliability in neurologic conditions (Geber et al. 2011). The 48.1% of office workers with facilitated TSP found in the present study, suggests that only a subpopulation of patients with chronic neck pain might exhibit facilitated TSP.

Previous studies have reported a correlation between pain intensity with less efficient CPM (Ge et al. 2014) and enhanced TSP (Nunes et al. 2020). Our results revealed that the QST2 and QST1 groups had a significantly higher intensity pain comparing with QST0. Moreover, in the QST2 group, there was an association between pain intensity with the rumination subscale in the Pain Catastrophizing Scale. This result is in accordance with previous studies where an association was verified between pain catastrophizing and higher pain intensity in subjects with CNP (Thompson et al. 2010; Park et al. 2016). Also, in a recent review of systematic reviews of prospective cohort studies, pain catastrophizing identified as a longitudinal psychological risk factor associated with pain intensity and dysfunction in persistent musculoskeletal pain cases (Martinez-Calderon et al. 2020).

Quantitative Sensory Testing normative values and cut-off points

The current study used normative data and cut-off points for easiness of use in the clinical practice. For PPT assessment, the reference scores were established based on the ones previously reported in the literature (Neziri et al. 2011; Waller et al. 2016; Nunes et al 2021), which allowed us to identify the subjects with hypersensitivity PPT values in the upper trapezius and the tibialis anterior. Furthermore, the reference values from PPT hypersensitivity in the tibialis anterior identified as the non-painful region in subjects with chronic neck pain, suggest widespread pressure hyperalgesia which is a clinical sign of central sensitization (Arendt-Nielsen et al. 2011; 2018).

The cut-off of 2 points in VAS was used for an enhanced TSP (Rabey et al. 2019). Further research will be needed to determine if this is actually the ideal cut-off point regarding the different methods to induced TSP. Nevertheless, this cut-off point was used with a pinprick for eliciting TSP (Rabey et al. 2019). In clinical practice, the problem of calculating a wind-up ratio comes up when the self-reported pain intensity of the first stimulus by the patient is zero. Typically, another heavier pinprick is used (Marcuzzi et al. 2017). In our study, oftenly the first stimulus did not elicited pain.

With concern to CPM, also variability can be observed, namely between healthy female and male subject (Bulls et al., 2015; Graven-Nielsen et al. 2015; Hermans et al. 2016; Skovberg et al. 2017), and between younger and older ages (Grashorn et al. 2013, Hermans et al. 2016). For these reasons, there is a need for reference CPM values to be used in the clinical practice to assess dysfunctional pain modulation. Schliessback et al. (2019) study provided percentiles for CPM with the cold pressor test as the conditioning stimulus for assessing dysfunctional pain modulation. This study used the 5th percentile proposed by the same author as a cut-off point for a normal CPM which is very conservative in identifying dysfunctional pain modulation and a negative CPM value which may not necessarily reflect an abnormal CPM (Schliessback et al. 2019). Nonetheless, the existence of self-reported moderate pain intensity plus other QST test findings in office workers with chronic neck pain, should be considered as being consistent results for impaired endogenous pain modulation.

Finally, time-consuming, expensive equipment, multiple QST tests, lack of normative data between symptomatic and asymptomatic populations were identified as potential barriers to implementing QST in the clinical practice (Rolke et al. 2006; Cruz-Almeida and Fillingim 2014). The present work used standard procedures for assessing signs of sensitization in a chronic musculoskeletal condition (Graven-Nielsen and Arendt-Nielsen 2010; Petersen et al.

2015; Arendt-Nielsen et al. 2018) with non-expensive equipment (algometer, pinprick, ice, and water), quicker and simple, with normative data and cut-off points which might introduce a more straightforward QST assessment than the ones previously found in the literature.

4.1 Clinical Implications

The current study is the first to use normative reference values and cut-off points from the literature in patients with chronic neck pain, meaning that it is possible to assess sensitization through simple bedside QST findings in clinical practice.

Limitations

In the current study, it was not possible to measure all the outcomes at the same workweek day for all office workers. Fatigue resulting from working on computer can influence the QST results and therefore it might be considered to be a limitation (Grimby-Ekman et al. 2020).

4.2 Conclusion

This study demonstrated that 63.5% of office workers with chronic neck pain revealed either widespread pressure hyperalgesia, facilitated temporal summation of pain or impaired conditioned pain modulation, indicating pain sensitization within the central nervous system. Furthermore, increasing positive signs of central pain sensitization were associated with higher clinical pain intensity and pain catastrophizing rumination scores.

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Figure 1 – Flowchart diagram of office workers

Figure 2 – A) Pressure pain threshold (kPa) in all office workers. Grey line indicates hypersensitivity values below 155 kPa for both upper trapezius points. Black line indicates hypersensitivity values below 245 kPa for tibialis anterior point; B) Temporal summation of pain in all office workers. Values above grey line indicates values higher than 2 in VAS; C) Conditioned pain modulation effect in all office workers. Values below grey line indicates values below -7.5%.

Figure 3 – Pain intensity last 7 days per group, *between QST2 with QST0, Tukey post hoc test $p < 0.001$; # between QST1 with QST0, Tukey post hoc test $p = 0.011$.

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