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Abstract

To better understand the mechanisms underpinning work-related neck pain, this cross-sectional and single-blinded study compared somatosensory profiles among sonographers with varied neck disability levels. Based on K-mean cluster analysis of scores on the neck disability index (NDI), participants were classified into no (NDI≤8%, n=31, reference group), mild (NDI=10%-20%, n=43) or moderate/severe (NDI≥22%, n=18) disability groups. Data were collected on bodily pain distribution and severity and psychological measures including depression, anxiety, pain-catastrophizing and fear-avoidance beliefs using validated scales. Participants attended one session of quantitative sensory testing performed according to a standardized protocol, including local and remote thermal and mechanical pain thresholds, temporal summation of pain (TSP), conditioned pain modulation (CPM) and an exercise-induced analgesia (EIA) paradigm. Compared to participants with no and mild disability, those with moderate/severe disability showed more widespread pain, cold and mechanical hyperalgesia at a remote non-painful site and significantly higher TSP. Participants with mild disability demonstrated significantly higher TSP than those with no disability. These group differences were attenuated after adjusting for depression or anxiety, indicating these psychological factors may mediate the somatosensory changes associated with neck disability. Group differences were not found for CPM or EIA. These findings suggest that heightened pain facilitation, rather than impaired pain inhibition may underpin nociplastic pain in participants with moderate/severe disability, and it may be associated with depression and anxiety. Clinicians should be aware that individuals with work-related neck pain presenting with moderate/severe disability display distinct somatosensory features and tailor management strategies accordingly.

[Word count: 243]

Keywords: Quantitative sensory measures, Work-related musculoskeletal pain, Central pain mechanisms, Central sensitization.

1. Introduction

Neck pain spreading to the shoulder region is a prevalent occupational health issue imposing a substantial economic burden on workers and organizations.[48] This presentation is commonly termed work-related neck pain and affects 27% to 48% of the general working population annually,[11] with an even higher prevalence among workers in high-risk occupations. Among sonographers, whose work involves ultrasound scanning with sustained static postures and forces and intensive computer-based tasks, it is estimated that 84% experience neck pain, with 55% reporting at least mild disability.[67] Around one in five sonographers prematurely end their careers due to neck disability and other musculoskeletal disorders.[46] Despite significant advancements in management, the global cause of disability-adjusted life years for neck pain has increased rather than decreased over the past years.[48] A potential reason could be the lack of understanding of the underlying pain mechanisms;[66] increasing knowledge about pain mechanisms will enable individualized care and improved health outcomes.[6, 55, 60]

Quantitative sensory testing (QST) is a non-invasive method to examine neurobiological pain mechanisms. QST has been used to assess contributions of somatosensory and central pain modulatory function by analysing an individual's response to innocuous and noxious stimuli.[20] Thermal and/or mechanical hyperalgesia has been demonstrated over painful neck and shoulder regions in different occupational groups, such as office workers[29] violin players,[57] butchers,[42] and secretaries,[24] reflecting sensitization of nociceptive neurons. Our systematic review and meta-analysis[68] suggested that individuals with non-traumatic neck pain, particularly those with moderate/severe disability, have widespread hyperalgesia at a remote non-painful site, indicating nociplastic pain mechanisms involving altered nociceptive processing within the central nervous system (e.g. central sensitization).[27] However, more research is needed to confirm which specific central pain modulation mechanisms are involved.[68] Dynamic QST paradigms such as conditioned pain modulation (CPM), exercise-induced analgesia (EIA), and

temporal summation of pain (TSP) can provide more precise and valuable information regarding pain inhibitory and facilitatory function.[13] Only two studies have examined CPM in individuals with work-related neck pain, with mixed results.[26, 53] Reduced efficacy of EIA has been shown in people with shoulder myalgia, evidenced by a decreased pressure pain threshold during and after an isometric exercise of the painful muscle.[35] Heightened TSP has been reported in other musculoskeletal conditions such as severe knee pain,[50] low back pain[18] and temporomandibular disorders.[34] Investigation using a more comprehensive battery of assessment on somatosensory and central pain modulatory function in a high-risk occupation such as sonographers is warranted to elucidate the pain mechanisms involved and how this relates to the level of disability.

Individuals with more severe neck disability are at greater risk of prolonged recovery and unfavourable prognosis.[64] Comparisons of subgroups might offer novel insights into the pathophysiology underlying poor recovery in individuals with more severe disability and help direct treatments to minimize the personal and economic burden of neck disability. This study aimed to comprehensively document the somatosensory profile in sonographers with different neck disability levels. We hypothesized that sonographers with more severe disability would present thermal and mechanical hyperalgesia at local painful and remote non-painful sites as well as altered central pain modulation compared to those with no or mild disability.

2. Methods

2.1. Study design

Reporting of this cross-sectional and single-blinded study adheres to the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines. Ethical approval was obtained from the University of Queensland Human Research Ethics Committee (approval

#2017001513). The study procedure was clearly explained to participants and signed consent obtained.

2.2. Setting and participants

From June 2018 to August 2019, participants with or without neck pain in the past 12 months were recruited prospectively from 430 volunteers who participated in an online survey examining risk factors of pain and disability in sonographers.[67] The sample of the survey were sonographers from Australia and New Zealand who performed sonography ≥4 hours/week, were not pregnant, without fibromyalgia, uncontrolled diabetes or kidney diseases, or without chemotherapy or radiotherapy for cancers within the past five years. Additional eligibility criteria for the current study were applied through a telephone interview. Participants were eligible if they had pain in the neck region, as defined by The Neck Pain Task Force[23], as the primary musculoskeletal symptom. Participants were also eligible if they had no neck pain or severe pain in the low back or upper or lower limbs that required treatment or interfered with work or home activities in the previous three months. Other general exclusion criteria were a history of surgery in the spine or upper limbs, trauma (for example, whiplash), irritable bowel syndrome, inflammatory conditions, neurological disorders or psychiatric disorders. These additional exclusion criteria were to exclude possible non-work-related sources of neck pain and confounding conditions that may present somatosensory changes. All participants were asked to refrain from taking non-steroidal anti-inflammatory drugs or analgesics 24 hours prior to testing.

2.3. Sample size

An estimated total sample size of 111 participants would be required to detect group differences in pressure pain threshold (PPT), based on calculations undertaken using G*Power (version 3.1.9.2) with an effect size of 0.30, a significance of 0.05 and a power of 0.80. The effect size

was computed using data of PPT measurements derived from two previous studies,[4, 29] which were the only studies available in the literature on comparing QST across varied levels of neck disability.

2.4. Measurements

Data collection was performed in a quiet and temperature-controlled room by one researcher (YX) without knowing the disability levels of participants at the time of measurement. Pilot testing had been performed on six volunteers who were not sonographers to ensure adequate intra-rater reliability of QST measures (all intraclass correlation coefficients were ≥0.83 with lower bounds of 95% confidence of intervals (CIs) ≥0.66 and upper bounds ≥0.88). These volunteers were not included in the study analyses.

2.4.1. Quantitative sensory testing

To control for any potential effect of one test on subsequent tests,[52] QST was conducted in the following order: thermal pain threshold, TSP, CPM, PPT and EIA (**Supplementary 1**). These tests were separated by 5 to 40 minutes to avoid sensitization or habituation due to repetitive stimuli (**Supplementary 1**). Tests were performed unilaterally at the most affected side for symptomatic participants or at the scanning hand side for asymptomatic participants. Prior to data collection, a familiarization trial was performed over an area that was different to the tested sites to ensure that participants clearly understood the tests. All test stimuli were applied for three consecutive trials with 30-second intervals and the averages were used for analysis. Testing protocols and instructions used were based to the German Research Network for Neuropathic Pain QST protocol.[51]

2.4.1.1. Thermal pain threshold

Cold pain threshold (CPT) and heat pain threshold (HPT) were measured using a Thermotest unit (Somedic AB, Sweden), with a 2.5 cm x 5 cm thermode probe. Thermal pain thresholds have shown good to excellent test-retest reliability[44] and are reproducible over 6-9 months in healthy people.[43] Participants were in a prone or supine lying position for this test. The CPT was applied in the following order: the neck (cervical spine at the C5-6 level), upper trapezius (the mid-way between the 7th cervical vertebrae and the acromion), the lateral deltoid (approximately the mid-point between acromion and the deltoid tuberosity), and a remote site which was the tibialis anterior (approximately 2.5 cm lateral and 5 cm inferior to the tibial tuberosity).[2, 10, 65] The HPT was then tested on the same sites in the reverse order to avoid frequent changes of position. For both CPT and HPT, the temperature started at 32°C and changed at a rate of 1°/s,[51] with cut-off temperatures of 5°C and 50°C to reduce the risk of frostbite or burns. Participants were instructed to press a stop button if/when they perceived the cool or warm sensation first became painful to identify CPT and HPT. If the cut-off temperatures were reached before participants felt the first pain, these were used for analysis.

2.4.1.2. Temporal summation of pain

A single stimulus and then a train of 10 repetitive stimuli at a frequency of 1 Hz (monitored with a metronome) were applied over an area of 1 cm^2 of the cervical spine at the C5-6 level using a pinprick stimulator (256mN). The TSP was determined by the difference in perceived pain on a 0-100 point Numeric Rating Scale (NRS) induced by the single stimulus and the train of 10 repetitive pinprick stimuli.[28, 50] Reliability of TSP has been demonstrated to be fair to good.[44]

2.4.1.3. Conditioned pain modulation

The CPM paradigm is based on the "pain-inhibits-pain" mechanism, in which a reduction of pain perception from a test stimulus is induced by a concurrent application of a noxious

stimulus (conditioning stimulus) at another region of the body.[69] Reliability of this method is fair to excellent.[30] The test stimulus was PPT (described below) at the upper trapezius of the most affected side. The conditioning stimulus was immersion of the contralateral hand (up to the wrist) in a circulating cold-water bath (Polyscience, 912, 6L Basic) maintained at 10 ± 2°C for a maximum of two minutes. Measurements were performed with participants in a sitting position. Prior to hand immersion into the cold water, the PPT was tested for three trials with a 30-second interval between trials. While the hand was immersed in the cold water, participants were asked to rate the pain level of the hand every 10-seconds using a 0-100 NRS until the pain level reached at or above 40 out of 100 on the NRS, after which re-evaluation of PPT on the same site commenced immediately. A cold pain rating of 40 was selected on the basis that a conditioning stimulus of at least moderate intensity is needed to induce CPM.[49] At least one PPT measurement was performed every 30-seconds (maximum of three measurements) while the participant immersed the hand into the cold water before the end of two minutes. Otherwise, the measurement was regarded as missing.[9] Participants were asked to rate their pain levels induced by the cold water again before the 2nd and 3rd PPT measurements. The CPM efficacy was calculated using the following formula: CPM efficacy = (average PPT during conditioning stimulus – average PPT before conditioning stimulus). A positive value reflects endogenous pain inhibition, and the higher the value, the more efficient an individual's pain inhibition.

2.4.1.4. Pressure pain threshold

A hand-held digital algometer (Somedic Production AB) with a probe size of 1 cm^2 was used to measure PPT at a rate of 50kPa/s perpendicularly over the same regions that the thermal pain thresholds were tested. Participants were asked to press a stop button once the sensation of pressure first becomes pain. Measurement of PPT with a hand-held digital algometer has demonstrated good to excellent reliability.[44]

2.4.1.5. An exercise-induced analgesia paradigm

Measurement of pain sensitivity following exercise has been used to evaluate endogenous pain modulation function in humans.[8, 22, 35] The participant's pain response and sensitivity to a pressure stimulus were examined during a standardized exercise. Participants sat on a chair with the trunk upright and performed sustained isometric bilateral shoulder abduction at 90° without external weights until exhaustion (reached to maximum rating of perceived exertion on a scale of 0 to 10 with inability to maintain shoulder abduction angle of 90°) or up to 3 minutes. Participants rated their pain intensity of the neck-shoulder region using a 0-100 NRS before and at the end of the exercise. The PPT was measured at the neck, upper trapezius, deltoid and tibialis anterior before and immediately after the exercise. The EIA was calculated using the following formula: EIA = (average PPT after exercise – average PPT before exercise). Thus a positive change in PPT reflected EIA[56] and the higher the value, the more EIA efficacy. Changes of pain intensity before and after the exercise were also calculated.

2.4.2. Pain, disability and psychological measures

On completion of the QST, participants completed standard questionnaires to collect data on demographics (e.g. age, gender, body mass index (BMI), physical activity assessed using the International Physical Activity Questionnaire-Short Form[12]), work-related information, pain characteristics (e.g. frequency, sick leave and healthcare seeking behavior), and psychological measures.

As sonographers usually present with pain in multiple sites,[67] a novel digital pain drawing method was used to quantify the location and extent of pain. Participants with symptoms were asked to shade precisely every area of pain they typically perceived and had experienced in the previous week, regardless of the intensity, on either female or male body charts displayed on a digital tablet (iPad 6, Apple Inc, Cupertino, California) with a stylus pen.[3] The characteristics

of the stylus pen including the type, size, and colour were standardized. Pain extent (numbers of pixels shaded inside the body chart expressed as a percentage of the total body chart area) was calculated to quantify the percentage of total (frontal and dorsal body regions) pain area.[3] Pain frequency maps were generated to illustrate where pain was most frequently reported. The worst pain level of the shaded body regions was measured using the 0-100 NRS. Disability related to neck pain was assessed using the Neck Disability Index (NDI),[61] with a total score ranging from 0 to 100 (expressed as a percentage). Higher scores indicate greater disability.

Psychological factors assessed included depression, anxiety, pain catastrophizing and fear-avoidance beliefs. Depression and anxiety were assessed using the 8-item Patient Health Questionnaire[33] and Generalized Anxiety Disorder – 7-item scale,[32] respectively. Total depression scores ranged from 0 to 24 while anxiety scores ranged from 0 to 21, with a score of ≥5 being a cut-off score for depression and anxiety.[31, 32] Pain catastrophizing was evaluated by the Pain Catastrophizing Scale, with a total score ranging from 0 to 52.[58] Fear-avoidance beliefs were assessed with two items from the Fear-Avoidance Beliefs Questionnaire[63] ("my work is too heavy for me" and my work might harm my neck"), with a total score ranging from 0 to 12.

2.5. Statistical analysis

All analyses were conducted using R (Version 3.4.2), and the significance level was set at 0.05.

2.5.1. Group classification

K-mean cluster analysis was performed to classify participants into 3 groups. This is a commonly used unsupervised machine learning algorithm for classifying a given dataset into a predefined number of subgroups (clusters) (K=3 in this study), such that the data points within the same subgroup are as similar as possible while data points between subgroups are as different as possible.[41] To better represent the population of working sonographers, NDI scores

obtained from the original full sample (430 sonographers who participated in the online survey) were used to derive the clusters. The cut-off scores for the 3 clusters were: NDI ≤8% (no disability group), NDI=10% - 20% (mild disability group), and NDI ≥22% (moderate/severe disability group). These cut-off scores were replicated when using NDI scores from the current laboratory sample (92 sonographers). The K-mean cluster analysis was performed because the conventional NDI cut-off scores for no, mild and moderate/severe disability have not been validated for non-traumatic neck pain,[39] and may not help to identify homogenous groups of sonographers based on neck disability. Sonographers with no disability whose neck pain might not be clinically meaningful was used as a reference group, because previous research found a high annual prevalence (84%) of neck pain in sonographers,[67] which made it difficult to recruit a true pain-free healthy control group.

2.5.2. Statistical analysis for group comparisons

Chi-square or Fisher's exact test was performed to compare group differences in categorical data. For continuous data, normality was checked using the Shapiro-Wilk test and visual inspection of quantile-quantile plots. Both parametric and non-parametric analyses were conducted for continuous data that were not normally distributed.[40] Parametric analysis was used because results were the same across analyses and it enables us to develop multivariate models and compute effect size (ES) (described below). Furthermore, multivariate and univariate analysis of variance (MANOVA and ANOVA) are reported to be robust to modest departures from normality when there were at least 20 degrees of freedom for error in ANOVA and the violations were not due to outliers.[59] Outliers were examined for each dependent variable and one to two outliers were found for TPS, CPM, and PPT. These outliers were carefully checked to ensure that it was not due to encoding error. To avoid possible data manipulation, outliers were retained in the analyses as results were the same with and without the outliers.

Multiple MANOVAs were performed to compare group differences in variables that are related conceptually, such as psychological variables (anxiety, depression, pain catastrophizing and fear-avoidance beliefs), pain thresholds at local sites (the model included cold, heat and pressure pain thresholds at the neck, upper trapezius and deltoid), and pain thresholds at the remote site (cold, heat and pressure pain thresholds at the tibialis anterior). When MANOVA showed a significant result, post-hoc ANOVA was performed to analyse which specific variable significantly differed between groups. Variables that did not fit in the MANOVA (e.g. demographics, pain, disability, TSP, CPM, EIA) were analysed by ANOVA. As pain ratings of the conditioning stimulus were different between groups, ANOVA of CPM was performed with and without the inclusion of this variable. Considering the potential effect of psychological variables on QST,[21, 45, 47, 71] models for all QST outcomes were performed with and without the inclusion of each psychological variable as a covariate. When significant group differences were found, pairwise comparison was performed with Bonferroni correction, and ESs and 95% CIs were computed using Hedge's *g* for pairwise group comparisons. An ES was: <0.20 = negligible; 0.20 – 0.49 = small; 0.50 – 0.79 = moderate; and ≥0.80 = large effect.[7]

3. Results

Ninety-two sonographers were recruited; 31 were classified into the no disability group (NDI = 4.06% ± 2.90%), 43 into mild disability group (NDI = 15.00% ± 3.22%) and 18 into moderate/severe disability group (NDI = 30.60% ± 13.70%) (**Figure 1**). These three groups were comparable ($P > 0.30$ for all demographics) in age (whole group mean ± SD: 39.91 ± 10.70 years), gender (83.7% female), BMI (23.59 ± 3.65 kg/m^2), physical activity levels (2431.49 ± 1918.35 MET-minutes/week) and work-related characteristics (sonography experience: 13.37 ± 10.32 years; scanning time: 25.88 ± 9.52 hours/week). Almost all sonographers in the mild and moderate/severe disability groups reported pain in the neck region at least once a week and a higher proportion of them had sick leave in the past three months,

compared to the no disability group (**Table 1**). Regarding psychological characteristics, the moderate/severe disability group scored significantly higher than no and mild disability groups on questionnaires of anxiety, depression and pain catastrophizing (**Table 1**). For fear-avoidance beliefs, significant differences were only found between moderate/severe and no disability groups (**Table 1**).

3.1. Pain distribution and intensity in the previous week

The percentage of participants that reported pain in a specific body region is illustrated using a heat map in **Figure 2**, with the most frequently reported areas displayed in red. The total area of bodily pain (as a percentage) was significantly different between all three groups ($F_{(2, 89)}$ = 18.46, $P < 0.01$), ranging from 1.23% ± 1.55% (no disability), 4.68% ± 3.21% (mild disability) and 7.20% ± 5.75% (moderate/severe disability). Worst pain intensity was also significantly different between all three groups for the neck, shoulder, upper and lower back (**Figure 3**). For the elbow and wrist/hand, only the moderate/severe group had higher pain intensity than the no disability group (**Figure 3**). There were no group differences for pain intensity for lower limb regions.

3.2. Thermal and pressure pain thresholds

Significant group differences were only found in CPT ($F_{(2, 88)}$ = 6.22, $P < 0.01$) and PPT ($F_{(2, 89)}$ = 4.40, $P = 0.02$) at the tibialis anterior, although there was a trend of group differences at local sites (**Figure 4**). Pairwise comparisons revealed higher CPT and lower PPT (cold and mechanical hyperalgesia) at the tibialis anterior in the moderate/severe disability group, compared to mild disability with moderate effect sizes (CPT: ES (95%CI) = 0.66 (0.09, 1.22); PPT: -0.68 (-1.24, -0.12)) and compared to no disability groups with large effect sizes (CPT: 1.06 (0.44, 1.68); PPT: -1.00 (-1.61, -0.39)) (**Supplementary 2**). No group differences were found in HPT across all tested sites (**Figure 4**).

3.3. Temporal summation of pain

There were significant group differences in TSP ($F_{(2, 89)}$ = 5.42, P = 0.01), with the moderate/severe disability group reporting highest TSP (**Figure 5A**). Post-hoc analysis revealed that the between-group effect was moderate between mild and no disability groups (ES (95%CI) = 0.67 (0.19, 1.14)), and large between moderate/severe and no disability groups (0.94 (0.33, 1.54)) (**Supplementary 2**).

3.4. Conditioned pain modulation

There were no group differences in the time of exposure to the conditioning stimulus ($F_{(2, 89)}$=0.77, P=0.47), with mean ± SD time being 109.60 ± 23.02 seconds for the whole sample. The mean ± SD hand pain ratings (0-100 NRS) during the conditioning stimulus for no, mild and moderate/severe disability groups were 64.30 ± 13.55, 67.85 ± 11.81, and 74.07 ± 11.32, respectively (**Supplementary 2**). There were significant group differences in hand pain rating ($F_{(2, 89)}$ = 3.58, P = 0.03), with the moderate/severe disability group rating significantly higher pain levels than the no disability group (ES (95%CI) = 0.76 (0.17, 1.36)). Almost all participants from all groups had increased PPT (decreased mechanical sensitivity) at the upper trapezius during exposure to the conditioning stimulus (**Figure 5B**). However, no group differences were found in changes in PPT ($F_{(2, 89)}$=2.35, P=0.10), and the result remained the same after including hand pain rating as a covariate.

3.5. Exercise-induced analgesia

All participants completed the 3-minute exercise, except one in the moderate/severe disability group who had to interrupt after 2 minutes due to reaching the maximum rating of perceived exertion. The pain scores prior to exercise were 5.13 ± 8.89, 9.51 ± 9.69 and 27.22 ± 21.57, with an increase of pain (0-100 NRS) of 21.55 ± 22.22, 38.28 ± 20.39, and 31.78 ± 17.80 after

exercise for the no, mild and moderate/severe disability groups, respectively. The mild disability group had significantly higher magnitude of pain increase than the no disability group (ES (95%CI) = 0.78 (0.30, 1.27)). All groups had increased PPT (decreased mechanical sensitivity) at all tested sites after exercise, but no significant group differences were found in changes of PPT at all tested sites (**Figure 6**).

3.6. Role of psychological measures as covariates

Group differences in thermal and pressure pain thresholds at the tibialis anterior changed from statistically significant ($F_{(6, 174)} = 2.84$, $P = 0.01$) to non-significant when each of the following psychological variables were included as a covariate in the MANOVA: anxiety ($F_{(6, 172)} = 2.03$, $P = 0.06$), depression ($F_{(6, 172)} = 1.72$, $P = 0.119$), pain catastrophizing ($F_{(6, 172)} = 2.13$, $P = 0.05$), or fear-avoidance belief ($F_{(6, 172)} = 2.11$, $P = 0.06$). Results of TSP remained similar after including depression, pain catastrophizing or fear-avoidance beliefs as a covariate. However, group differences in TSP changed from statistically significant to non-significant after including anxiety ($F_{(2, 88)} = 2.48$, $P = 0.09$) as a covariate. Results of other QST variables did not change when including psychological measures as covariates.

4. Discussion

This is the first study examining somatosensory features in sonographers with different levels of neck disability. The main finding was that sonographers with moderate/severe neck disability demonstrated significantly more widespread pain, cold and mechanical hyperalgesia at a remote site, and higher TSP, compared to those with mild or no disability. The mild disability group showed significantly higher TSP and pain intensity in response to an isometric exercise compared to the no disability group. All groups demonstrated normal CPM function and no significant group differences were found in efficacy of CPM and EIA. These findings

offer new insights regarding possible pain mechanisms that may underpin subgroups with work-related neck disability.

4.1. Comparison of QST between different neck disability levels

Multi-modal hyperalgesia at a site remote from the painful site, as reflected by increased sensitivity to cold and pressure pain at the tibialis anterior, was found in the moderate/severe neck disability group compared to both no and mild disability groups. This could be considered as evidence of nociplastic pain processing characterized by sensitization within the central nervous system.[14, 19] Although all groups included some participants reporting pain in the lower limb, the mean pain levels were lower than 10 out of 100 on a NRS (**Figure 3**), which is not clinically relevant. Furthermore, no group differences in lower limb symptoms were observed between groups. Therefore, cold and mechanical hyperalgesia at the tibialis anterior is unlikely to be due to peripheral sensitization of nociceptive neurons. Contrary to our hypothesis, localized hyperalgesia was not statistically evident in sonographers with mild or moderate/severe disability, although there was a trend of group differences in CPT and PPT at the local symptomatic sites. Similar phenomena was observed in other occupations such as pianists[37] and office workers[26, 29] with neck pain in that hyperalgesia was only found at the remote sites but not the symptomatic neck-shoulder region. It is possible that the localized neck-shoulder region has been sensitized in sonographers with no disability due to long-term exposure to repetitive ultrasound scanning with awkward neck and shoulder postures and static muscle force, making it more difficult to find statistically significant group differences in CPT and PPT at local sites. Further investigation of localized hyperalgesia by comparing sonographers with non-worker healthy controls is warranted to confirm this hypothesis.

The presence of nociplastic pain processing in sonographers with moderate/severe disability is further supported by the finding of a large magnitude of heightened TSP, a human surrogate model involving a wind-up in the dorsal horn and activation of N-methyl-D-aspartate

receptor.[17] In contrast, no evidence was found for impaired CPM in all groups, indicating endogenous pain inhibition function may be normal in sonographers. Similarly, at the group level, EIA seemed to be normal in sonographers with moderate/severe disability as decreased mechanical sensitivity was found after the 3-minute shoulder isometric exercise and changes in pain rating after exercise did not differ with the no disability group. The EIA efficacy as demonstrated by changes of PPT had high standard deviations, indicating that some sonographers may present impaired EIA, but this is unlikely a common feature of sonographers with disability. Collectively, our findings provide novel evidence that heightened pain facilitation rather than impaired pain inhibition may underpin the nociplastic pain processing in sonographers with moderate/severe neck disability.

Compared to sonographers with moderate/severe neck disability, signs of central involvement in those with mild disability is less clear. Sonographers with mild disability did not show statistically evident thermal and mechanical hyperalgesia compared to those with no disability. In contrast, they displayed a moderate magnitude of higher TSP, indicating that heightened pain facilitation may be present, at least for some individuals in this subgroup. Additionally, sonographers with mild disability showed significantly higher increase in pain perception during the 3-minute shoulder isometric exercise task compared to those with no disability. Exercise-induced pain and hyperalgesia were found in fibromyalgia[16] and chronic whiplash associated disorders,[56] and have been linked to changes in central nervous system function.[36] However, whether the increased pain perception to exercise points to central mechanisms in sonographers with mild disability group, or simply reflects a discrepancy in pain perception compared to other groups, requires further investigation.

4.2. Potential effect of pain distribution and psychological measures on QST

According to a mechanisms-based classification list from Smart et al,[54] ‘diffuse or widespread areas of pain’ and ‘maladaptive psychosocial factors’ have been recognized as key signs and

symptoms in classifying central sensitization. This is also supported by recent study, involving patients with knee osteoarthritis, which showed that widespread pain is associated with signs and symptoms of central sensitization.[38] In our study, sonographers with mild and moderate/severe disability groups demonstrated more widespread pain than those with no disability, and those with moderate/severe disability also presented significantly more widespread pain compared to those with mild disability. This may explain why the moderate/severe disability group displayed more somatosensory changes associated with central sensitization while the mild disability group showed a lesser extent of central changes. However, there was a large amount of variation in the total area of bodily pain within each group as reflected by the broad standard deviations, suggesting that the area of bodily pain may not exclusively account for the group differences seen in the somatosensory changes.

Sonographers with moderate/severe disability also showed more psychological impairments when compared to those with mild and no disability, and this was particularly the case for anxiety and depression. When scores were dichotomized according to the recommended cut-off for anxiety and depression,[31, 32] it was found that 61% and 78% of sonographers in the moderate/severe disability group presented anxious and depressive symptoms. Group differences in CPT and PPT at the tibialis anterior and TSP were attenuated and approached significance when assessed psychological factors were entered as covariates in the analysis. This contrasts with previous studies of people with whiplash-associated disorders which showed that somatosensory changes were independent of psychological impairments.[5, 52] In our sample, individuals with trauma were excluded and different psychological constructs were studied using different questionnaires, which may explain the discrepancy. Our study suggests that somatosensory changes identified in sonographers with disability may be partially mediated by psychological factors. However, the direction of this relationship cannot be established in a cross-sectional design.

4.3. Clinical implications

Our findings have important clinical implications for guiding the design of management strategies for neck pain in sonographers where the current focus has largely been on ergonomic interventions.[1, 25] Management might need to address the somatosensory alterations and tailor interventions to individual sonographers with different disability levels. The findings of heightened pain facilitation without widespread hyperalgesia in sonographers with mild disability, suggest that this subgroup is an important group to focus strategies to reduce the progression to more severe disability. For this group, clinicians should consider that repetitive noxious or non-noxious stimuli (e.g. by sustained isometric contraction) may lead to summation of pain. As sonographers typically perform sustained shoulder abduction during their typical scanning activities,[62] it may be important to monitor their pain levels and institute frequent periods of rest between scans. Furthermore, activity-based treatment strategies may need modification to account for increase of pain during a single bout of isometric exercise for sonographers with mild disability. It might be important to start exercising asymptomatic body regions to activate endogenous pain inhibitory mechanisms[35] and then progress to exercising the neck and shoulder muscles following the principles of progressive overload and periodization with adequate recovery periods.[15, 70] For sonographers with moderate/severe disability, additional multidisciplinary therapeutic approach including interventions aiming to reduce anxiety, depression, and maladaptive beliefs about their pain, as well as graded exposure therapy might be appropriate. Further investigation is needed to identify optimal management strategies for different subgroups of sonographers to improve disability and reduce professional attrition.

4.4. Strength and limitations

A strength of this study is that the investigator who conducted QST was not aware of the group allocation, thus reducing study bias. Moreover, a broad set of QST across multiple modalities and sites was conducted to characterize the somatosensory profiles. Some limitations should be considered. First, QST was conducted in a fixed order without randomization which may increase study bias. However, pain ratings were repeatedly asked to ensure no systematic increase in pain during the testing occurred and there were sufficient intervals between tests which should minimize the sensitization due to repeated application of multiple stimuli. Second, not all sonographers with no disability were completely pain-free and this may have resulted in an underestimation of differences in somatosensory features in sonographers with varied disability levels. Third, due to the difficulty in recruiting sonographers with moderate/severe neck disability, the current sample size was smaller than the estimated size needed, which may have reduced statistical power potentially explaining the lack of group differences in other outcomes such as pain thresholds at local sites. Finally, the cause-effect relationship of observed impairments could not be elucidated from this study due to the nature of a cross-sectional design.

5. Conclusions

This study showed that more widespread pain, remote cold and mechanical hyperalgesia and heightened TSP, but not dysfunctional CPM and EIA, distinguish sonographers with moderate/severe neck disability from no disability. Sonographers with mild neck disability presented a moderate effect of heightened TSP and increased pain ratings in response to exercise compared to those with no disability. Psychological factors, particularly anxiety and depression, were found to influence the results of group differences in somatosensory features. Specific somatosensory changes and psychological factors should be considered when tailoring management strategies for sonographers with different levels of disability.

Conflict of Interest: There are no conflicts of interest.

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Figure legends

Figure 1. Study participant flow. NDI, neck disability index.

Figure 2. Pain frequency maps generated separately for no, mild and moderate/severe disability groups by superimposing the pain drawings of all participants within the group. The color grid indicates both the number and the percentage of participants who reported pain in

that specific area. Female and male participants shaded their pain areas on a female and male body chart, respectively. For illustrative purposes, all data is presented on a female body chart.

Figure 3. Mean intensity of worst pain experienced in different body regions in the previous week for the no, mild and moderate/severe disability groups. Error bars depict standard deviations. *P<0.05; **P<0.001.

Figure 4. Mean cold (A), heat (B) and pressure (C) pain thresholds at local (neck, upper trapezius and deltoid) and remote (tibialis anterior) sites for the no, mild, and moderate/severe disability groups. A higher score indicates worse (hyperalgesia) for cold pain threshold while a lower score is worse for heat and pressure pain thresholds. Error bars depict standard deviations. *P<0.05; **P<0.001

Figure 5. Individual data plots for temporal summation of pain (A) and conditioned pain modulation (B) for the no, mild, and moderate/severe disability groups. (A) Changes in pain rating from a single to 10 repeated pinprick stimuli, with higher values representing greater temporal summation of pain. (B) Changes in pressure pain threshold from before to during the conditioning stimulus, with positive changes reflecting endogenous pain inhibition and higher values representing greater pain inhibition. Black diamonds and lines depict group means and standard deviations. *P<0.05

Figure 6. Mean changes of pressure pain threshold (PPT) at local (neck, upper trapezius, deltoid) and remote (tibialis anterior) sites in response to an isometric exercise for the no, mild, and moderate/severe disability groups. A positive change reflects exercise-induce analgesia and higher values represent greater efficacy of analgesia. Error bars depict standard deviations.