The Effect of Pressure Pain Sensitivity and Patient Factors on Self-Reported Pain-Disability in Patients with Chronic Neck Pain

Zakir Uddin[*,1,5,6], Joy C. MacDermid[*,1,2], Linda J. Woodhouse[3], John J. Triano[1,4], Victoria Galea[1] and Anita R. Gross[1]

[1]*School of Rehabilitation Science, McMaster University, Hamilton, Ontario, Canada*

[2]*Clinical Research Lab, Hand and Upper Limb Centre, St. Joseph's Health Centre, London, Ontario, Canada*

[3]*Department of Physical Therapy, Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, Alberta, Canada*

[4]*Research Division, Canadian Memorial Chiropractic College, Toronto, Ontario, Canada*

[5]*Department of Rehabilitation Science, Bangladesh University of Health Sciences, Dhaka, Bangladesh*

[6]*Department of Physical Therapy, College of Health and Welfare, Woosong University, Daejeon, South Korea*

Abstract: The study was conducted to estimate the extent to which pressure pain sensitivity (PPS) and patient factors predict pain-related disability in patients with neck pain (NP), and to determine if PPS differs by gender. Forty-four participants with a moderate level of chronic NP were recruited for this cross sectional study. All participants were asked to complete self-reported assessments of pain, disability and comorbidity and then underwent PPS testing at 4-selected body locations. Pearson`s r w was computed to explore relationships between the PPS measures and the self-reported assessments. Regression models were built to identify predictors of pain and disability. An independent sample t-test was done to identify gender-related differences in PPS, pain-disability and comorbidity. In this study, greater PPS (threshold and tolerance) was significantly correlated to lower pain-disability ($r = -.30$ to $-.53$, $p \leq 0.05$). Age was not correlated with pain or disability but comorbidity was ($r = 0.42$-$.43$, $p \leq 0.01$). PPS at the 4-selected body locations was able to explain neck disability (R^2=25-28%). Comorbidity was the strongest predictor of neck disability (R^2 =30%) and pain (R^2=25%). Significant mean differences for gender were found in PPS, disability and comorbidity, but not in pain intensity or rating. This study suggests that PPS may play a role in outcome measures of pain and disability but between-subject comparisons should consider gender and comorbidity issues.

Keywords: Comorbidity, gender, neck pain sensitivity, neck disability, pain threshold, pain tolerance.

INTRODUCTION

Neck pain (NP) is a common musculoskeletal pain disorder [1, 2]. Almost everyone experiences NP at some point in his or her lifetime [3] with a yearly prevalence estimated at roughly 30-50% in the general population [4-7]. Reported incidence and prevalence figures of NP may vary according to patient factors (e.g. age, gender, and comorbidity). The prevalence of pain is reportedly greater among females and older persons [5, 8]. A recent review suggested that gender can influence pain [9] and being female might be associated with higher prevalence and pain intensity. A systematic review reported that the prevalence of NP declines after middle age [10]. Another study suggests an important association between comorbidities and NP [11]. Moreover, it has been demonstrated that accumulated comorbid load is independently associated with chronic pain [12]. This provides a rationale for considering patient factors, including comorbidity, in the assessment of pain-related disability in patients with chronic NP.

NP and its associated disability are a tremendous financial burden to most industrialized nations [13]. The under pinning etiology of NP can be illusive [1]. Evidence suggests it is more closely associated with sensory disturbances than degenerative and radiological findings [14-17]. A large community based British study [18] supported the importance of neurological factors in NP. Poor recovery in NP is associated with widespread sensory hypersensitivity [19, 20]. Research studies [21, 22] and a systematic review [23] have demonstrated evidence of central hyperexcitability in musculoskeletal pain. Generalized sensory hyposensitivity (hypoesthesia) and/or hypersensitivity (hyperesthesia) is a feature in a subset of chronic NP [24]. Abnormal sensory findings are prognostic of poorer clinical outcomes for chronic pain conditions [24, 25] thereby providing substantial rationale for including sensory evaluation in the assessment of patients with NP.

*Address correspondence to these authors at the School of Rehabilitation Science, McMaster University, 1400 Main Street West IAHS (4th floor), Hamilton, Ontario L8S 1C7, Canada;
Tel: 1-905-525-9140, Ext. 22524; Fax: 1-905-524-0069;
E-mails: zakiru@gmail.com, uddinz2@mcmaster.ca, macderj@mcmaster.ca

1874-3250/14

Psychophysical quantitative sensory testing (QST) provides a means for semi-objective measurement of both hypo and hyper-sensory function [25, 26]. QST has the potential to contribute to the assessment of NP conditions if it can be shown to help with diagnosis, treatment selection, or prognosis. Mapping of the anatomical distribution of sensory changes (e.g. hypoesthesia) may be one factor identifying the pathological source in peripheral nerve, plexus, root and central tissues (spinal or cerebral) [26]. QST was associated with neck disability in patients with NP [27]. QST has many demonstrated uses in clinical practice [28-30].

Pressure pain sensitivity (PPS) measures are a reliable QST technique for the assessment of pressure (mechanical) pain sensitivity of deep somatic structures in the neck area [31, 32]. PPS measure using algometry is relatively inexpensive and feasible test method. The PPS test protocol is based on the "method of levels" parameter of QST techniques where pressure level is determined by a forced choice option (e.g. yes/no). In this way PPS can target peripheral small fiber based sensory/pain channels (e.g. Aδ, C nerve fibers) [25, 33, 34]. Alterations of pain processing mechanisms (both peripheral and central) may manifest as a reduction in PPS [35].

There are two common test sites on the cervical spine for somatosensory characterization of patients with NP [36-38] - the C2 paraspinal muscles and the upper trapezius muscle. Self-reported physical activity of NP population was related to PPS at these two common testing sites of neck muscles [39]. The upper trapezius pressure pain threshold value has high reliability (minimum detectable change = 0.48 kg/cm^2) in patients with NP [40]. PPS measures over the C2-C3 and C5-C6 cervical zygapophyseal joints correlate with lower activation of the semispinalis cervicis muscle as quantified by intramuscular electromyography (at the levels of C2 and C5 during NP)[41]. Studies of PPS indicate that women were more sensitive than men to pressure pain stimulation in cervico-thoracic areas [42]. Pressure pain threshold was positively associated with muscle strength in healthy individuals [43]. Clinically, PPS measures over bony sites (e.g. tibia) were lower in patients with musculoskeletal pain compared to the healthy population [44] and were used to indicate central sensitization. Moreover, since the periosteum (innervated by unmyelinated small fibers) is sensitive to pressure stimulation [45, 46], the tibial shaft was used to assess periosteum sensitivity.

At present there is insufficient evidence about the relationship between PPS and pain-related disability and which patient factors (e.g. age, gender, and comorbidity) might mediate the relationship. The main objective of this study was to estimate the extent to which the PPS test (threshold and tolerance in selected locations) and patient factors predict pain- related disability in patients with chronic NP. The second objective was to estimate the effect of gender on PPS measures, particularly threshold and tolerance, for this patient population. The final objective was to determine if there were gender differences for self-reported pain-disability and comorbidity in this patient population.

MATERIALS AND METHODS

Study Design and Participants

In a cross-sectional study design, 44 participants (33 female and 11 male) were recruited. All participants were adults with moderate levels of chronic (> 3 months) NP who were actively seeking treatment from local physiotherapy clinics. Recruitment of participants was done through advertisements posted at the clinics. The Hamilton Health Sciences/McMaster University Faculty of Health Sciences Research Ethics Board approved the study protocol and informed consent was obtained from all participants prior to testing. All participants were asked to complete self-reported outcome measures (for pain, disability and comorbidity) and then underwent QST (PPS tests) at the MacHAND clinical research lab at McMaster University.

Participant *inclusion criteria* included: age between 18-85 years, fluency in English (reading and speaking), ability to complete all assessments, complaints of pain in the neck area for more than 3 months, minimum score of 3/10 on visual analogue scale of pain specifically in the neck, documented (physical examination or imaging evidence) of suspected neck pathology. *Exclusion criteria* were: 1) any neurological disorders or pre-existing neuropathic pain as indicated by specific neuropathic pain treatment/diagnostic procedures, 2) scheduled for neck surgery or current pain complaints from prior neck surgery, 3) history of recent neck fracture or any history of tumor or cancer, 4) a history of chronic pain disorder (previously diagnosed), 5) current psychiatric management (from history of medication), 6) a high risk of surgery due to any comorbid condition, and 7) patients unable to complete the test procedures.

According to the patient reported symptom diagram, pain distribution included either 1) symptoms localised to neck/shoulder region (Occiput to the inferior angle of Scapula) or 2) two or more of a) Headache, b) Neck/shoulder, c) Hand/arm symptoms. Participant's characteristics and demographics are described in Table **1**.

Study Measures

NP-Disability Measure

Short Form of the McGill Pain Questionnaire (SF-MPQ). The MPQ was developed to assess pain as a multidimensional phenomenon [47]. The SF-MPQ, introduced in 1987, contained a total of 15 descriptors (11 sensory and 4 affective) each of which are rated on a 4-point (0 to 3) intensity scale [48]. In total, five dimensional pain scores were derived from SF-MPQ: (i) Sensory Pain Rating Index (PRI) was derived from the sum of the intensity rate values for sensory words chosen, (ii) Affective PRI was derived from the sum of the intensity rate values for the affective words chosen, (iii) Total PRI was derived from the sum of the total descriptors (both sensory and affective), (iv) Present Pain Intensity was derived from a 0-10 visual analog scale (VAS), (v) Evaluative Overall Intensity of total pain experience was derived from a 6-point numeric scale (0 to5).

NP and disorder measure. The Neck Disability Index was developed to assess self-reported neck-specific disability and included 10 items (e.g. pain intensity, personal care, lifting, reading, headache, concentration, work, driving, sleeping, and recreation) [49, 50]. Each item was scored out of 5 and a total score of 50 was computed; the lower the score the less the self-rated disability [49, 50].

Pressure Pain Sensitivity (PPS)

Pain threshold and pain tolerance [51-53] for pressure stimuli was measured using the computerized JTech algome-

Table 1. Participants demographics (N = 44).

Construct	Variable	Characteristic
PATIENT FACTOR	Age (years)	Mean = 40.1 ± 13.9 (Female = 41.6 ± 13.4 and Male = 35 ± 15)
	Gender	Female = 33 (75%), Male = 11 (25%)
	Comorbidity	Mean = 4 ± 2.8
NP-DISABILITY	McGill Total Pain Rating Index (0-45)	Mean = 12.5 ± 6.9
	Pain Intensity: VAS (0-10 mm)	Mean = 4.5 ± 2.0
	Neck Disability Index (%)	Mean = 31.4 ± 17.8
OTHER DEMOGRAPHICS	Dominant Side	Right = 40 (90.9%), Left = 4 (9.1%)
	Affected side	Right = 8 (18.2%), Left = 9 (20.5%), Bilateral = 27 (61.4%)
	Body Weight (lbs)	Mean = 158.0 ± 33.6

Abbreviation/Symbol: ± = standard deviation; N = number of participants; VAS, Visual Analogue Scale; lb = pounds.

ter (JTECH Medical, Salt Lake City, UT, USA). The hand-held device of the algometer contains a 1 cm^2 circular probe, and it was used to create pressure on the selected body locations using a standardized protocol. Pressure was applied over the posterior cervical spine at the level of the second (C2) and sixth (C6) vertebrae, upper trapezius muscle (Up-Trap) and anterior aspect of the tibia (shin bone) bilaterally. The unaffected side was tested first. In cases of bilateral involvement, the less affected side was tested first. The applied algometric pressure at "uncomfortable" (for pain threshold) and "intolerable" (for pain tolerance) levels were determined by patient response using a standard protocol [40, 54, 55]. The test was repeated 3 times at each site, and the average of these measures was used for data analysis.

Patient Factor (Comorbidity Status)

The Katz comorbidity scale was used to detect the number and severity of 12 co-morbid conditions [56, 57]. Participants were asked to indicate if they currently had the condition (at the time of assessment), whether or not they were receiving treatment for it, and whether their level of physical activity was limited by the condition. The respondent can receive a maximum of 3 points for each condition (1 point if they have been diagnosed with listed health condition, 1 point if it requires treatment, and 1 point if it causes activity limitation) [56]. The total score was calculated by summing across the 12 items [58].

Data Analysis

All data were entered into SPSS 17.0 software (SPSS Inc., Chicago, IL). Descriptive statistics (e.g. skewness, kurtosis) and test of normality (Kolmogorov-Smirnov, Shapiro-Wilk, Histogram, and QQ-Plot) were conducted on all variables. Scatter plots were generated to check violation of assumptions (linearity and homoscedasticity) before performing bivariate correlation (Pearson's) analysis. Assumptions of multiple regressions (e.g. multicollinearity and singularity, outliers, normality, linearity, homoscedasticity) were checked prior to the regression analysis.

Mean and standard deviation were calculated for all variables (e.g. PPS, pain-disability, comorbidity) and then for gender subgroups. Pearson correlation coefficients were computed to determine the relationships between PPS and self-reported NP-disability. Four regression models were built to analyze the relative impact of different PPS measures as predictors of the four neck disability outcome measures (NDI, pain intensity in VAS, SF-MPQ-evaluative score, SF-MPQ-total score). We built four further regression models to analyze patients' factors as predictors of NP-disability. An independent sample t-test (equal variance assumed) was used to evaluate the effect of gender on PPS measure, pain-disability reporting and comorbidity status (tested at α=0.05). Significance level was determined by $p < 0.05$ for all interpretation of data.

RESULTS

The bivariate relationships between PPS and pain-disability are shown in Table **2**. These correlations indicate that greater PPS (both threshold and tolerance) was significantly associated with less pain-disability ($r = -.35$ to $-.53$, $p \leq 0.01$). PPS at the level of C2 was significantly correlated with the total pain rating index of SF-MPQ ($r = -.31$ to -40, $p \leq 0.05$). Age was not correlated with pain-disability, whereas greater comorbidity was correlated with higher pain-disability ($r = 0.42$-$.43$, $p \leq 0.01$).

Table **3** indicates that when multiple PPS test variables were entered as potential predictors of neck disability outcomes all PPS variables (at 4-selected test locations) were significant predictors ($p < 0.03$). The total variability explained by all PPS variables range from 25% to 28%. Table **4** indicates that when patient factors (age, gender and comorbidity) were considered in a multivariate model of NP-disability outcomes, comorbidity was the most consistent predictor that was significantly related to neck disability and evaluative pain. In these multivariate models, comorbidity ($p < 0.01$) was associated with higher pain (in rating, intensity and evaluation). The amount of variability explained by the overall R^2 for these models range from 13% to 30%.

Significant mean differences in gender (male>female) were found in most PPS tests (1.2-5.4, $p < 0.05$), with a few exceptions (mainly at C2 level) (Table **5**). Significant mean differences for gender (male<female) were found in the self-reported disability (18.5, $p = 0.003$) and comorbidity score (2.1, $p = 0.03$) (Table **6**). However, self-reported pain dimensions (SF-MPQ) were independent of gender.

Table 2. Relationship between PPS and patient factors with either disability or pain dimensions.

Test Location		Neck Disability Index	Short Form of the McGill Pain Questionnaire				
			Sensory-PRI	Affective-PRI	Total-PRI	Pain Intensity-VAS	Evaluative Overall Pain
PPS Variables							
Cervical spine at level of C2	Left Threshold	**-.50****	-.28	-.29	**-.31***	-.14	-.12
	Left Tolerance	**-.51****	**-.32***	-.30	**-.33***	-.13	-.15
	Right Threshold	**-.51****	**-.36***	**-.33***	**-.37***	-.15	-.14
	Right Tolerance	**-.52****	**-.40****	**-.35***	**-.40****	-.17	-.15
Cervical spine at level of C6	Left Threshold	**-.47****	-.22	-.27	-.28	-.11	-.05
	Left Tolerance	**-.44****	-.28	-.28	**-.30***	-.12	-.07
	Right Threshold	**-.47****	-.27	-.23	-.26	-.05	-.01
	Right Tolerance	**-.43****	**-.33***	-.24	-.29	-.10	-.06
Upper Trapezium muscle	Left Threshold	**-.40****	-.21	-.18	-.20	.00	-.06
	Left Tolerance	**-.43****	-.27	-.22	-.24	-.05	-.14
	Right Threshold	**-.49****	-.16	-.20	-.21	-.10	-.14
	Right Tolerance	**-.46****	-.21	-.18	-.20	-.12	-.18
Anterior Tibia (shine bone)	Left Threshold	**-.48****	-.20	-.19	-.21	-.28	-.21
	Left Tolerance	**-.49****	-.25	-.24	-.26	**-.36***	-.30
	Right Threshold	**-.38****	-.12	-.27	-.25	**-.40****	-.25
	Right Tolerance	**-.35****	-.24	-.24	-.26	**-.46****	-.26
Patient Factors							
	Age	.16	.03	.09	.06	.07	.04
	Comorbidity	**.42****	.31	.20	.31	.30	**.43****

Abbreviation/Symbol: PPS, Pressure Pain Sensitivity; PRI, Pain Rating Index; VAS, Visual Analogue Scale;
** Correlation (Pearson's r) is significant at 0.01 level; * Correlation is significant at 0.05 level. Significant correlations are **bolded**.

Table 3. Regression models describing Pressure Pain sensitivity predictors of neck disability (depended variable = neck disability index, N=44).

Test Locations	Pressure Pain Sensitivity in the Model: Beta (p Values) are Shown				Model	
	Left Threshold	Left Tolerance	Right Threshold	Right Tolerance	R^2	p Value
Cervical spine at level of C2	-.13 (.79)	-.11 (.85)	-.13 (.83)	-.19 (.79)	**.28**	**.02***
Cervical spine at level of C6	.01 (.99)	-.62 (.32)	-1.02 (.20)	1.12 (.24)	**.26**	**.03***
Upper Trapezium muscle (UpTrap)	.38 (.54)	-.27 (.68)	-.66 (.22)	.08 (.88)	**.25**	**.03***
Anterior aspect of Tibia (shine bone)	.23 (.66)	-.91 (.13)	-.45 (.34)	.64 (.23)	**.28**	**.02***

Abbreviation/Symbol: * R^2 are significant at 0.05 level. Significant R^2 are **bolded**.

Table 4. Regression models describing patient's factors predictors of pain-disability (n=44).

Construct	Dependent Variable	Patient Factors in the Model: Beta (p Values) are Shown			Model	
		Age	Gender	Comorbidity	R^2	p Value
NP-DISABILITY	McGill Total Pain Rating Index	-.22 (.28)	-.05 (.78)	**.43 (.04)***	.13	.17
	Pain Intensity: VAS	.19 (.36)	-.08 (.64)	**.44(.04)***	.12	.22
	Evaluative overall pain	-32 (.09)	-.01 (.94)	**.62 (.01)****	**.25**	**.02***
	Neck Disability Index	-.15 (.43)	**.35 (.03)***	**.39 (.05)***	**.30**	**.007****

Abbreviation/Symbol: PRI, Pain Rating Index; VAS, Visual Analogue Scale; ** beta and R^2 are significant at 0.01 level; * beta and R^2 are significant at 0.05 level. Significant beta and R^2 are **bolded**.

DISCUSSION

This study provided preliminary evidence suggesting that both pain threshold and tolerance affect pain-disability, as indicated by medium to large size bivariate correlations. The impact of PPS was further evident in multivariate modeling where individual PPS (at four test locations) explained 25 to

Table 5. Effect of gender on PPS measure (n=44). Both threshold and tolerance tests were done on 4 LOCATIONS (C2, C5, Up-Trap and shin bone) in each side of neck-shoulder and leg area.

Test Variables	Male, Mean ± SD	Female, Mean ± SD	Mean Difference (Male-Female)	P Value
Test location: Cervical spine level two (C2)				
Left Threshold	5.3 ± 2.2	3.9 ± 1.6	**1.4**	**.02**
Left Tolerance	9.4 ± 4.2	6 ± 2.5	**3.3**	**.03**
Right Threshold	5.7 ± 3.0	4.2 ± 1.7	1.5	.14
Right Tolerance	9.3 ± 5.5	5.9 ± 2.5	3.5	.07
Test location: Cervical spine level six (C6)				
Left Threshold	6.1 ± 2.5	4.2 ± 1.8	**1.9**	**.01**
Left Tolerance	9.9 ± 5	6.5 ± 3.3	3.4	.06
Right Threshold	7.1 ± 3.7	4.5 ± 1.8	**2.6**	**.04**
Right Tolerance	10.8 ± 4.6	6.4 ± 3.0	**4.1**	**.05**
Test location: Upper Trapezium muscle (UpTrap)				
Left Threshold	10.8 ± 4.6	7.7 ± 3.4	**3.1**	**.02**
Left Tolerance	16.8 ± 7.2	11.9 ± 5.3	**4.9**	**.02**
Right Threshold	11.4 ± 5	7.7 ± 3.8	**3.7**	**.01**
Right Tolerance	17.5 ± 7.3	12.2 ± 6.7	**5.4**	**.03**
Test location: Anterior aspect of Tibia (Shin bone)				
Left Threshold	6 ± 1.9	4.2 ± 1.9	**1.8**	**.01**
Left Tolerance	9.5 ± 3.5	6.5 ± 3.4	**2.9**	**.02**
Right Threshold	5.8 ± 2	4.6 ± 1.6	**1.2**	**.05**
Right Tolerance	8.4 ± 3.4	6.7 ± 2.9	1.7	.12

Abbreviation/Symbol: SD = Standard Deviation; Significant mean differences and p values are **bolded**.

Table 6. Effect of Gender on self-reported Pain-Disability and Comorbidity status (n=44).

Variables	Male, Mean ± SD	Female, Mean ± SD	Mean Difference (Female-Male)	p Value
Short Form of the McGill Pain Questionnaire				
Sensory Pain Rating Index (0-33)	8.8 ± 5.9	11.1 ± 5.9	2.26	.29
Affective Pain Rating Index (0-12)	1.8 ± 1.39	2 ± 1.8	.23	.75
Total Pain Rating Index (0-45)	10.6 ± 6.9	13 ± 6.9	2.4	.34
Present Pain Intensity-Visual Analog Scale (0-10)	4.4 ± 1.5	4.6 ± 2.1	.15	.83
Evaluative overall intensity of total pain experience (0-5)	2.1 ± 0.6	2.3 ± 0.9	.23	.46
Disability and Comorbidity				
Neck Disability Index (in %)	17.4 ± 9	35 ± 17.6	**18.5**	**.003**
Comorbidity Status (0-39)	2.4 ± 2.3	4.5 ± 2.7	**2.1**	**.03**

Abbreviation/Symbol: SD, Standard Deviation; Significant mean differences and p values are **bolded**.

28% of neck disability. Conversely, when age, gender and comorbidity were entered into multivariate models, although higher R^2's were not achieved, comorbidity was the primary determinant of pain-disability. This suggests that the role of comorbidity in pain-related disability may partially be related to the extent to which it *sensitizes* the pain-neurophysiology of the individual.

Male participants demonstrated higher pain threshold and tolerance. However, gender was not associated with differences in pain dimensions when multivariate modeling was considered. Previous studies found that pressure pain threshold was lower in women than men [59,60]. Moreover, it was demonstrated that self reported NP was higher among women than men [4,5]. Our study suggested that pressure pain tolerance was also gender dependent. Gender was acknowl-

edged as an important consideration in NP conditions because of differences in prevalence of different NP conditions by gender. The prevalence and incidence of NP is higher in females than males [65]. Furthermore, gender differences in pain threshold and tolerance was well accepted [66,67]. This study also demonstrated that PPS measures (threshold and tolerance) was more sensitive (lower threshold and tolerance) in females. Females also had more pain-related disability and comorbid health conditions. As gender influences the PPS scores obtained, multivariate models should be powered sufficiently to allow for separate modeling of males and females to identify the true impact of PPS on outcomes or, at minimum, sufficient power to allow for gender interactions to be tested. The relatively small sample precluded testing interactions between PPS and other variables in a gender specific analysis.

Prevalence of NP declines after middle age (i.e. 60 years of age) [10], with middle-aged individuals having more than a two-fold risk of developing NP compared to younger aged individuals [61]. A recent study reported that age was an important moderator between pain and cognition relationships [62]. Although, we did not assess cognition in this study, we did not find age to be related to pain or disability. Similarly, whereas others have found age to be associated to QST [63] and pressure pain threshold [60], we did not find a similar relationship.

Dominick *et al*. demonstrated that accumulated comorbid load was independently associated with chronic pain in a large population based study [12]. Recently, Johansen *et al*. speculated that painful comorbid conditions influence pain sensitivity based on findings from their large population-based study of pain and health status determined by medical examination [60]. That study and our findings concur about the potential importance of comorbid health conditions to "prime" the pain system.

One of the main limitations of this study was that our sample was too small to explore more variables and their interactions. PPS measures provide somatosensory information based on stimulus-response parameters, and are limited by semi-objective psychophysical evaluation. A recent review suggested that it was preferable to assess both sensory and modulatory elements of pain sensitivity [9]. The type of stable threshold-based pain sensitivity measure used in this study provided limited information on complex pain processing since the measure was based on the static parameter of QST [26, 64]. It was suggested that dynamic QST may be better at assessing spatial and temporal summation as well as descending modulation of pain [9, 26]. In addition, suprathreshold pain processing can be assessed by the magnitude rating for a suprathreshold stimulus [9, 26]. We used threshold and tolerance parameters for the QST measures in this study because these are commonly used in clinical practice. Our findings reaffirmed the importance of PPS and patient factors in explaining pain-disability. Stimulus intensity/magnitude rating parameters of QST may be more relevant to clinical features (e.g. pain, disability).

The greater sensitivity of females to pain threshold and tolerance may reflect differences in how sensory inputs are received at the tissue level or how they are processed from the periphery to the brain. However, this study indicated that gender differences in pain threshold and tolerance was not necessarily indicative of gender differences in all NP-related health outcomes, including self-reported pain. This differential suggested that gender needs to be carefully considered when examining NP, and that all hypotheses should be tested separately between male and female subjects to assure that conclusions made apply across genders. However, sex/gender differences in pain processing may not necessarily lead to differences in the pain experiences or related disability. Differences in pain processing may be a reason for differences in treatment response. Again, these requirements suggested the need for larger sample sizes; and prespecified gender analyses.

CONCLUSION

This descriptive cross-sectional study suggested that PPS (both threshold and tolerance) may play a role in self-reported outcome measures (e.g. pain and disability) in NP. However, given the findings that PPS tests was gender dependent, and comorbidity also affected these outcomes, these observations must be considered with caution until larger samples are used to confirm any interactions between comorbidity and PPS measures. Future studies that investigate the effects of PPS or other indicators of pain processing in humans should consider both gender and comorbidity as potential confounders and be powered sufficiently to test/control for their effects and to run analyses in subgroups to insure that findings are generalizable. This is certainly important before the potential role for PPS to provide useful information in managing NP can be determined. Future studies may consider using alternative sensory evaluations including dynamic QST and pain magnitude ratings (for a suprathreshold stimulus) to elucidate the relationship between suprathreshold pain processing, descending control or central integration of pain and other clinical features of NP.

ABBREVIATIONS

C2 = Cervical spine level two

C6 = Cervical spine level six

NP = Neck Pain

PPS = Pressure Pain Sensitivity

PRI = Pain Rating Index

QST = Quantitative Sensory Testing

SF-MPQ = Short Form of the McGill Pain Questionnaire

CONFLICT OF INTEREST

We, the authors of the manuscript, do not have a direct/indirect financial relation with the commercial/non-commercial identities mentioned in the paper that might lead to a conflict of interests.

ACKNOWLEDGEMENTS

The project was funded by the Neuro Resource Group, Inc. Zakir Uddin was supported by the McMaster University School of Rehabilitation Science Graduate Scholarship, Canadian National Graduate Scholarship in Rehabilitation Science and Islamic Development Bank Merit scholarship for PhD study. Dr. Joy C. MacDermid was supported by a CIHR Chair award (Gender in Measurement and Rehabilitation of Musculoskeletal Work Disability).

REFERENCES

[1] Borghouts JAJ, Koes BW, Vondeling H, Bouter LM. Cost-of-illness of neck pain in The Netherlands in 1996. Pain 1999; 80(3): 629-36.

[2] Bot S, Van der Waal J, Terwee C, *et al*. Incidence and prevalence of complaints of the neck and upper extremity in general practice. Ann Rheum Dis 2005; 64(1): 118-23.

[3] Haldeman S, Carroll L, Cassidy JD, Schubert J, Nygren Å. The Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders. Eur Spine J 2008; 17: 5-7.

[4] Bovim G, Schrader H, Sand T. Neck pain in the general population. Spine 1994; 19(12): 1307-9.

[5] Côté P, Cassidy JD, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: a population-based cohort study. Pain 2004; 112(3): 267-73.

[6] Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: a systematic critical review of the literature. Eur Spine J 2006; 15(6): 834-48.

[7] Hogg-Johnson S, van der Velde G, Carroll LJ, *et al*. The burden and determinants of neck pain in the general population. Eur Spine J 2008; 17: 39-51.

[8] Tsang A, Von Korff M, Lee S, Alonso J, *et al*. Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. Pain 2008; 9(10): 883-91.

[9] Hashmi JA, Davis KD. Deconstructing sex differences in pain sensitivity. Pain 2014; 155(1): 10-3.

[10] Fejer R, Leboeuf-Yde C. Does back and neck pain become more common as you get older? A systematic literature review. Chiropr Man Therap 2012; 20: 24.

[11] Côté P, Cassidy JD, Carroll L. The factors associated with neck pain and its related disability in the Saskatchewan population. Spine 2000; 25(9): 1109-17.

[12] Dominick CH, Blyth FM, Nicholas MK. Unpacking the burden: understanding the relationships between chronic pain and comorbidity in the general population. Pain 2012; 153(2): 293-304.

[13] Ferrari R, Russell AS. Neck pain. Best Pract Res Clin Rheumatol 2003; 17(1): 57-70.

[14] Abdulkarim J, Dhingsa R, L Finlay D. Magnetic resonance imaging of the cervical spine: frequency of degenerative changes in the intervertebral disc with relation to age. Clin Radiol 2003; 58(12): 980-4.

[15] van der Donk J, Schouten JS, Passchier J, van Romunde LK, Valkenburg HA. The associations of neck pain with radiological abnormalities of the cervical spine and personality traits in a general population. J Rheumatol 1991; 18(12): 1884-9.

[16] Pettersson K, Hildingsson C, Toolanen G, Fagerlund M, Björnebrink J. MRI and neurology in acute whiplash trauma: No correlation in prospective examination of 39 cases. Acta Orthop 1994; 65(5): 525-8.

[17] Karlsborg M, Smed A, Jespersen H, *et al*. A prospective study of 39 patients with whiplash injury. Acta Neurol Scand 1997; 95(2): 65-72.

[18] Coggon D, Cyrus Cooper D. Prevalence and occupational associations of neck pain in the British population. Scand J Work Environ Health 2001; 27(1): 49-56.

[19] Sterling M, Jull G, Vicenzino B, Kenardy J, Darnell R. Physical and psychological factors predict outcome following whiplash injury. Pain 2005; 114(1-2): 141-8.

[20] Sterling M, Jull G, Kenardy J. Physical and psychological factors maintain long-term predictive capacity post-whiplash injury. Pain 2006; 122(1-2): 102-8.

[21] Sterling M. Differential development of sensory hypersensitivity and a measure of spinal cord hyperexcitability following whiplash injury. Pain 2010; 150(3): 501-6.

[22] Desmeules J, Cedraschi C, Rapiti E, *et al*. Neurophysiologic evidence for a central sensitization in patients with fibromyalgia. Arthritis Rheum 2003; 48(5): 1420-9.

[23] Lim EC, Sterling M, Stone A, Vicenzino B. Central hyperexcitability as measured with nociceptive flexor reflex threshold in chronic musculoskeletal pain: a systematic review. Pain 2011; 152(8): 1811-20.

[24] Chien A, Eliav E, Sterling M. Whiplash (grade II) and cervical radiculopathy share a similar sensory presentation: an investigation using quantitative sensory testing. Clin J Pain 2008; 24(7): 595.

[25] Backonja M, Attal N, Baron R, Bouhassira D, *et al*. Value of quantitative sensory testing in neurological and pain disorders: NEUPSIG consensus. Pain 2013; 154(9): 1807-19.

[26] Arendt-Nielsen L, Yarnitsky D. Experimental and clinical applications of quantitative sensory testing applied to skin, muscles and viscera. Pain 2009; 10(6): 556-72.

[27] Uddin Z, MacDermid JC, Ham HH. Test–retest reliability and validity of normative cut-offs of the two devices measuring touch threshold: Weinstein Enhanced Sensory Test and Pressure-Specified Sensory Device. Hand Ther 2014: 19(1): 3-10.

[28] Courtney CA, Kavchak AE, Lowry CD, O'Hearn MA. Interpreting joint pain: quantitative sensory testing in musculoskeletal management. J Orthop Sports Phys Ther 2010; 40(12): 818-25.

[29] Uddin Z, MacDermid J, Packham T. Clinical implementation of two quantitative Sensory Tests: Cold Stress Test and the Ten Test. Physiother Pract Res 2014; 35(1): 33-40.

[30] Uddin Z, MacDermid J, Packham T. The ten test for sensation. J Physiother 2013; 59(2): 132-2.

[31] Ylinen J, Nykänen M, Kautiainen H, Häkkinen A. Evaluation of repeatability of pressure algometry on the neck muscles for clinical use. Man Ther 2007; 12(2): 192-7.

[32] Ylinen J, Takala E, Kautiainen H, *et al*. Effect of long-term neck muscle training on pressure pain threshold: A randomized controlled trial. Eur J Pain 2005; 9(6): 673.

[33] Chong PST, Cros DP. Technology literature review: quantitative sensory testing. Muscle Nerve 2004; 29(5): 734-47.

[34] Hansson P, Backonja M, Bouhassira D. Usefulness and limitations of quantitative sensory testing: clinical and research application in neuropathic pain states. Pain 2007; 129(3): 256-9.

[35] Hogeweg JA, Kuis W, Oostendorp RA, Helders PJ. General and segmental reduced pain thresholds in juvenile chronic arthritis. Pain 1995; 62(1): 11-7.

[36] Chien A, Eliav E, Sterling M. Hypoaesthesia occurs with sensory hypersensitivity in chronic whiplash–further evidence of a neuropathic condition. Man Ther 2009; 14(2): 138-46.

[37] Johnston V, Jimmieson NL, Jull G, Souvlis T. Quantitative sensory measures distinguish office workers with varying levels of neck pain and disability. Pain 2008; 137(2): 257-65.

[38] Sterling M, Treleaven J, Edwards S, Jull G. Pressure pain thresholds in chronic whiplash associated disorder: further evidence of altered central pain processing. J Musculoskelatal Pain 2002; 10(3): 69-81.

[39] Cheung J, Kajaks T, Macdermid JC. The relationship between neck pain and physical activity. Open Orthop J 2013; 7: 521-9.

[40] Walton D, Macdermid J, Nielson W, Teasell R, Chiasson M, Brown L. Reliability, standard error, and minimum detectable change of clinical pressure pain threshold testing in people with and without acute neck pain. J Orthop Sports Phys Ther 2011; 41(9): 644-50.

[41] Schomacher J, Boudreau SA, Petzke F, Falla D. Localized pressure pain sensitivity is associated with lower activation of the semispinalis cervicis muscle in patients with chronic neck pain. Clin J Pain 2013; 29(10): 898-906.

[42] Binderup A, Arendt-Nielsen L, Madeleine P. Pressure pain sensitivity maps of the neck-shoulder and the low back regions in men and women. BMC Musculoskelet Disord 2010; 11(1): 234.

[43] Henriksen M, Klokker L, Bartholdy C, Graven-Nielsen T, Bliddal H. The associations between pain sensitivity and knee muscle strength in healthy volunteers: a cross-sectional study. Pain Res Treat 2013; 787054.

[44] Tunks E, Crook J, Norman G, Kalaher S. Tender points in fibromyalgia. Pain 1988; 34(1): 11-9.

[45] Finocchietti S, Andresen T, Arendt-Nielsen L, Graven-Nielsen T. Pain evoked by pressure stimulation on the tibia bone–Influence of probe diameter on tissue stress and strain. Eur J Pain 2012; 16(4): 534-42.

[46] Grönblad M, Liesi P, Korkala O, Karaharju E, Polak J. Innervation of human bone periosteum by peptidergic nerves. Anat Rec 1984; 209(3): 297-9.

[47] Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. Pain 1975; 1(3): 277-99.

[48] Melzack R. The short-form McGill pain questionnaire. Pain 1987; 30(2): 191-7.

[49] Vernon H, Mior S. The Neck Disability Index: a study of reliability and validity. J Manipulative Physiol Ther 1991; 14(7): 409-15.

[50] MacDermid JC, Walton DM, Avery S, *et al*. Measurement properties of the neck disability index: a systematic review. J Orthop Sports Phys Ther 2009; 39(5): 400-17.
[51] Chesterton LS, Sim J, Wright CC, Foster NE. Interrater reliability of algometry in measuring pressure pain thresholds in healthy humans, using multiple raters. Clin J Pain 2007; 23(9): 760-6.
[52] Bernhardt O, Schiffman EL, Look JO. Reliability and validity of a new fingertip-shaped pressure algometer for assessing pressure pain thresholds in the temporomandibular joint and masticatory muscles. J Orofac Pain 2007; 21(1): 29-38.
[53] Kosek E, Ekholm J, Nordemar R. A comparison of pressure pain thresholds in different tissues and body regions. Long-term reliability of pressure algometry in healthy volunteers. Scand J Rehabil Med 1993; 25(3): 117-24.
[54] Finocchietti S, Andresen T, Arendt-Nielsen L, Graven-Nielsen T. Pain evoked by pressure stimulation on the tibia bone–Influence of probe diameter on tissue stress and strain. Eur J Pain 2012; 16(4): 534-42.
[55] Walton DM, Macdermid JC, Nielson W, Teasell RW, Nailer T, Maheu P. A descriptive study of pressure pain threshold at 2 standardized sites in people with acute or subacute neck pain. J Orthop Sports Phys Ther 2011; 41(9): 651-7.
[56] Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? Med Care 1996; 34(1): 73-84.
[57] Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The self-administered comorbidity questionnaire: A new method to assess comorbidity for clinical and health services research. Arthritis Care Res 2003; 49(2): 156-63.
[58] Tashjian RZ, Henn RF, Kang L, Green A. The effect of comorbidity on self-assessed function in patients with a chronic rotator cuff tear. J Bone Joint Surg 2004; 86(2): 355-62.
[59] Castro-Sánchez AM, Matarán-Peñarrocha GA, López-Rodríguez MM, *et al*. Gender differences in pain severity, disability, depression, and widespread pressure pain sensitivity in patients with fibromyalgia syndrome without comorbid conditions. Pain Med 2012; 13(12): 1639-47.
[60] Johansen A, Schirmer H, Stubhaug A, Nielsen CS. Persistent postsurgical pain and experimental pain sensitivity in the Tromsø study: Comorbid pain matters. Pain 2014; 155(2): 341-8.
[61] Cagnie B, Danneels L, Van Tiggelen D, De Loose V, Cambier D. Individual and work related risk factors for neck pain among office workers: a cross sectional study. Eur Spine J 2007; 16(5): 679-86.
[62] Oosterman J, Gibson S, Pulles W, Veldhuijzen D. On the moderating role of age in the relationship between pain and cognition. Eur J Pain 2013; 17(5): 735-41.
[63] Costantini M, Tunks K, Wyatt C, Zettel H, MacDermid JC. Age and upper limb tension testing affects current perception thresholds. J Hand Ther 2006; 19(3): 307-17.
[64] Hübscher M, Moloney N, Leaver A, *et al*.. Relationship between quantitative sensory testing and pain or disability in people with spinal pain–a systematic review and meta-analysis. Pain 2013; 154(9): 1497-504
[65] Cassou B, Derriennic F, Monfort C, Norton J, Touranchet A. Chronic neck and shoulder pain, age, and working conditions: longitudinal results from a large random sample in France. Occup Environ Med 2002; 59(8): 537-44.
[66] Rolke R, Baron R, Maier C, *et al*. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. Pain 2006; 123(3): 231-43.
[67] Berkley KJ. Sex differences in pain. Behav Brain Sci 1997; 20(3): 371-80.

Received: March 28, 2014 Revised: June 26, 2014 Accepted: June 30, 2014