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PAIN CATASTROPHIZING IN THE OROFACIAL PAIN POPULATION

by

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A thesis submitted to the Faculty of the
Orofacial Pain Graduate Program
Naval Postgraduate Dental School
Uniformed Services University of the Health Sciences
in partial fulfillment of the requirements for the degree of
Master of Science
in Oral Biology

June 2020

Naval Postgraduate Dental School
Uniformed Services University of the Health Sciences
Bethesda, Maryland

CERTIFICATE OF APPROVAL

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MASTER'S THESIS

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ABSTRACT

PAIN CATASTROPHIZING IN THE OROFACIAL PAIN POPULATION
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M.S., OROFACIAL PAIN, 2020

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Introduction: Pain catastrophizing is a maladaptive cognitive response characterized by an exaggerated negative interpretation of pain experiences. It has been associated with greater disability and poorer outcomes in chronic pain, to include several specific orofacial pain conditions. The goal of this study was to examine pain catastrophizing at a military orofacial pain specialty clinic.

Methods: This retrospective chart review (RCR) examined information collected at initial examination from 699 new patients seen between September 2016 and August 2019 at the Orofacial Pain Center at the Naval Postgraduate Dental School (Bethesda, MD). Pain catastrophizing, pain characteristics, psychosocial factors, and sleep were assessed using standardized scales. Linear regression was used to evaluate associations of patient characteristics and pain intensity with pain catastrophizing. Mediation analyses were done to characterize the extent to which the relationship between pain intensity and pain catastrophizing may be explained by anxiety, depression, and insomnia.

Results: Higher pain intensity, depression, anxiety, insomnia, and younger age were each associated with higher pain catastrophizing (all $p<0.05$). A primary diagnosis of

neuropathic pain was the strongest independent predictor of higher pain catastrophizing. The relationship between pain intensity and pain catastrophizing was partially mediated by anxiety, depression, and insomnia.

Conclusions: In this RCR of a population of orofacial pain patients, those diagnosed with neuropathic pain were most likely to display high levels of pain catastrophizing, a characteristic which is associated with poor long-term pain outcomes. This is the first study to show that, independent of other patient characteristics, those suffering from neuropathic pains displayed the highest levels of pain catastrophizing. This highlights the importance of also addressing psychosocial factors in the treatment of neuropathic pain conditions, which are commonly treated using a predominantly biomedical approach. Additionally, anxiety, depression, and insomnia each partially explain the relationship between pain intensity and pain catastrophizing.

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LIST OF ABBREVIATIONS

1. GAD-7 ..... Generalized Anxiety Disorder-7
2. ISI..... Insomnia Severity Index
3. PHQ-9 ..... Patient Health Questionnaire-9
4. PPTTN .....Painful Post-Traumatic Trigeminal Neuropathy
5. RCR ..... Retrospective Chart Review
6. TMD.....Temporomandibular Disorder
7. TMJ .....Temporomandibular Joint

BACKGROUND

Pain has long been assessed and treated following a "biomedical" approach. A peripheral insult leads to the transmission of a nociceptive impulse, which ultimately reaches the brain causing the person to perceive pain in proportion to the intensity of the insult. Treatments for acute pain are generally guided by this model and are usually very effective. However, such treatments often fail to successfully manage chronic pain, as can be attested by the refractory nature of many chronic pain conditions, frequently without any evidence of tissue damage. Following the seminal paper by Engel in 1977[1], it has become widely accepted that chronic pain is best explained, assessed, and treated through a "biopsychosocial" approach. Under this perspective, the interplay between nociceptive, psychological, and cultural factors ultimately determines the perception of pain and resultant suffering and disability[2].

One psychological factor which has consistently been associated with negative pain outcomes is pain catastrophizing. Pain catastrophizing is a maladaptive cognitive style which can be defined as "an exaggerated negative orientation toward actual or anticipated pain experiences"[2]. The broad construct of "pain catastrophizing" can be further broken down into its subcomponents "rumination" (the inability to inhibit pain-related thoughts), "helplessness" (the perceived inability to do anything to manage pain), and "magnification" (overestimating the threat value of pain)[3]. Pain catastrophizing has been associated with a higher prevalence, increased severity of symptoms, and/or increased disability in many chronic pain conditions, including lower back pain[4], osteoarthritis[5,6], fibromyalgia[6], neuropathic pain[7], and chronic post-surgical pain[8-10]. These associations have been shown both in cross sectional studies and in longitudinal

studies, whereby higher pain catastrophizing at baseline predicted worse pain-related outcomes[11].

Orofacial pain is an umbrella term used to describe pain conditions affecting the face, head, and neck[12]. These include musculoskeletal disorders (to include temporomandibular disorders – TMDs), neurovascular disorders (such as migraine or the trigeminal autonomic cephalalgias), and neuropathic pains. In the realm of orofacial pain, high pain catastrophizing has been correlated with more severe or disabling headaches[13,14], temporomandibular disorders[13,15-17], burning mouth syndrome[18], and painful post-traumatic trigeminal neuropathy (PPTTN)[19], as well as increased utilization of healthcare services[20]. Baseline pain catastrophizing has been shown to predict progression of TMD 18 months later[15]. Pain catastrophizing clearly plays a role in the suffering and prognosis of orofacial pain patients.

Optimal management of chronic pain requires a multimodal approach, targeting central processes in addition to any ongoing peripheral nociceptive input. Pain catastrophizing is one such central therapeutic target. A recent meta-analysis by Schutz[21] highlights that pain catastrophizing is clearly a modifiable characteristic. Furthermore, reduction in pain catastrophizing in high-catastrophizing chronic pain patients leads to clinically meaningful benefit[21]. While several treatment strategies have been shown to be effective at reducing pain catastrophizing, Cognitive Behavioral Therapy boasts the strongest support in the literature[21]. It has demonstrated effectiveness in reducing pain catastrophizing and improving other components of the pain experience across a wide spectrum of chronic pain conditions, including headache and TMD[22-24].

While it is well-established that higher levels of pain catastrophizing are seen in chronic pain populations, to include chronic orofacial pain populations, little is known about differences in pain catastrophizing among patients with different orofacial pain diagnoses. There have been studies comparing pain catastrophizing in headache and TMD patients[13,25] and among different orofacial pain diagnoses[26,27], but the overall body of literature in this area is limited. Additionally, a positive correlation between pain intensity and pain catastrophizing is consistently seen in the literature. Studies also show a positive correlation between pain catastrophizing and factors such as depression[28], anxiety[29], and insomnia[30]. However, there is a scarcity of research exploring how depression, anxiety, and insomnia influence the relationship between pain intensity and pain catastrophizing.

As pain catastrophizing plays a crucial role in the suffering of those living with orofacial pain and its magnitude may inform treatment decisions, it is important to better characterize pain catastrophizing among the orofacial pain population. The primary aim of the present study was to examine pain catastrophizing characteristics among patients seen at a military orofacial pain clinic with respect to orofacial pain diagnosis, pain characteristics, sleep, and demographic and psychosocial variables. A secondary aim was to assess the degree to which the relationship between pain intensity and pain catastrophizing was influenced by other psychosocial variables and sleep.

MATERIALS AND METHODS

Participants

This was a retrospective chart review study. Information from all new patients seen at the Orofacial Pain Center at the Naval Postgraduate Dental School (Bethesda, MD) was collected following their initial exam from September 2016 through August 2019. The patient population served by this clinic included active duty military service members, retired service members, and family of active duty or retired service members. All patients were evaluated either by an American Board of Orofacial Pain certified dentist or by a supervised orofacial pain resident.

Inclusion/Exclusion Criteria

Inclusion criteria included a primary orofacial pain diagnosis fitting in one of the following diagnostic categories: temporomandibular joint (TMJ) disorders, masticatory muscle disorders, episodic and continuous neuropathic pain, primary headache disorders, and intraoral pain disorders. Exclusion criteria included patients under 18 years of age. All other patients with complete data were included in the study.

Measures

Diagnosis. A primary diagnosis was recorded for each patient at completion of their initial examination and placed into one of five diagnostic categories: TMJ disorders, masticatory muscle disorders, episodic and continuous neuropathic pain, primary headache disorders, and intraoral pain disorders. This was done according to American Academy of Orofacial Pain *Guidelines for Assessment, Diagnosis, and Management* (6^{th} edition)[12]. For the "TMJ disorders" and "masticatory muscle disorders" categories, these diagnoses are consistent with the Diagnostic Criteria for Temporomandibular Disorders

(DC/TMD)[31] Axis I diagnoses. Patients typically met the diagnostic criteria for more than one diagnosis. As an example, a patient may have met the diagnostic criteria for both "myalgia" and "disc displacement with reduction". The condition recorded as the primary diagnosis was the one judged by the clinician to be most pertinent to the patient's chief complaint.

Demographics and Health History Questionnaire. All participants completed a brief demographic and health history questionnaire. Recorded information included sex and age.

Pain measures. Patients rated "average pain intensity" and "worst pain intensity" on a numeric rating scale ranging from zero to ten (with zero indicating "no pain" and ten indicating "the worst pain imaginable"). If a patient gave their answer as a range (e.g., worst pain 5-6/10), the greater number (i.e., 6/10) was recorded. Patients were also asked when their pain first began. Pain duration was then recorded in months. Again, if the patient gave their answer as a range, the greater duration of pain was recorded.

Pain Catastrophizing Scale (PCS). The PCS[3] is a validated 13-item measure of catastrophic thinking associated with pain. The PCS yields a total score and three subscale scores assessing rumination, magnification, and helplessness. The PCS has been shown to have good overall internal consistency (coefficient alphas: total score=0.87)[3].

Generalized Anxiety Disorder-7 GAD-7. The GAD-7[32] is a 7-item measure used to assess the presence of symptoms of generalized anxiety over the previous two weeks. The GAD-7 is a widely used assessment instrument and has demonstrated good psychometric properties in clinical and research applications[32].

Patient Health Questionnaire-9 (PHQ-9). The PHQ-9[33] is a 9-item measure of the presence and severity of depressive symptoms over the previous two weeks. Test-retest reliability, internal consistency, and convergent validity have been established[33].

Insomnia Severity Index (ISI). The ISI[34] is a brief instrument that assesses the severity of both subjective nighttime symptoms as well as daytime consequences of insomnia. The ISI is a 7-item measure assessing severity of sleep onset and sleep maintenance difficulty, satisfaction with current sleep pattern, interference with daily functioning, noticeability of impairment from sleep problems, and degree of distress or concern caused by sleep problems. Each item is rated on a 0-4 scale and the total score ranges from 0-28 with higher scores indicative of more severe insomnia. It has been validated for use as a screening tool to detect sleep disturbances in numerous patient populations and is extensively used in research and clinical settings[34]. The ISI has demonstrated good reliability and validity[34].

STATISTICAL ANALYSIS

Patient demographic, pain-related, and psychosocial characteristics were compared across primary orofacial pain diagnoses using Fisher's exact tests for categorical variables and analysis of variance or Kruskal-Wallis tests for continuous variables. To evaluate the potential prognostic value of characteristics as predictors of pain catastrophizing, demographic and pain-related characteristics were included as independent variables in an initial multivariable linear regression model of PCS Total Score as the dependent variable (Model 1). A separate, fully adjusted model additionally included ISI, GAD-7, and PHQ-9 scores as hypothesized mediators of the relationship between pain severity and pain catastrophizing (Model 2). Semi-partial correlation

coefficients were used to describe the correlation of each characteristic with PCS Total Score independent of all other model covariates. Patients were excluded from analyses if they had a primary diagnosis of intra-oral pain (N=14), a small and heterogeneous subgroup that could not be well characterized in our study population. Analyses were repeated among patients who had neuropathic pain (N=34), to further characterize predictors of pain catastrophizing in the diagnosis that was associated with highest PCS Total Scores. A parsimonious full model for this subgroup was selected using a forward selection procedure (p-in = 0.20) to avoid model overfitting.

To assess for potential moderating effects of sleep and psychosocial characteristics in the relationship between average pain intensity with PCS Total Score, we additionally tested interactions of ISI, GAD-7, and PHQ-9 scores with pain intensity in the full model. Variances inflation factors <5 indicated collinearity was not a concern. Interactions were not significant ($p>0.5$ for each), suggesting no evidence of moderating effects of psychosocial characteristics.

We also used mediation analyses to evaluate the extent to which psychosocial characteristics may mediate, or account for, the potential causal association of average pain intensity with PCS Total Score. Analyses were done using the general causal mediation framework described by Imai et al.[35] and based on separate linear regression models for the mediator (psychosocial test score) and outcome (PCS total score). Demographic variables were included as covariates in both mediator and outcome models. Average mediation effects were estimated and significance tested using bootstrapping procedures with 1,000 simulated samples. Analyses were done in R (Vienna, Austria) using the mediation package (Tingley, 2019)[36].

RESULTS

Patient Characteristics

Demographic, pain-related, and psychosocial characteristics for the 699 patients included in this study are described in Table 1, broken down by primary orofacial pain diagnosis. Mean age was about 40 years (SD 12.7), with a range from 18 to 89 years. Most patients were female (52%), white (72%), and were currently active duty military service members (72%). Masticatory muscle disorders were the most common primary orofacial pain diagnoses, accounting for about 68% of primary diagnoses. Other diagnoses included TMJ disorders (18%), primary headache disorders (7%), and episodic and continuous neuropathic pain disorders (5%). Intra-oral pain disorders accounted for 2% of the total sample and are not displayed in the table. Median average pain intensity was 4 and median worst pain intensity was 8 on a zero to ten numeric rating scale. The median duration of the chief complaint pain prior to evaluation was 24 months. Patients suffering from neuropathic pain had higher PCS Total Scores (mean=16.9, SD 13.7) than any other diagnostic group. Significant differences by diagnostic group were found for all continuous characteristics other than pain duration ($p<0.05$ for each).

Factors Predicting PCS Total Score

There was a positive linear relationship between pain intensity (both “average” and “worst” pain intensity) and PCS Total Score for both men and women (Figures 1 and 2). Pain duration in the cohort was evaluated as continuous (years) and categorical, because of the wide range of reported pain durations (from a minimum of less than 1 month through a maximum of 61 years) and uncertainty regarding accuracy of reporting pain onset (for example, patients with longstanding pain may have reported their pain

started “10 or 20 years ago”). No association was found between categorical (Figure 3) or continuous pain duration and PCS Total Score.

Table 2 shows results from a multivariable linear regression model with PCS Total Score as the dependent variable and patient and pain characteristics as the independent variables. Pain duration was not significantly associated with PCS Total Score and was not retained in the final models. The diagnosis “masticatory muscle disorders” was used as a reference when evaluating diagnoses, as it was the most commonly encountered diagnosis. In Model 1, higher PCS Total Score was significantly positively associated with younger age ($P<0.01$), average pain intensity ($P<0.001$), and worst pain intensity ($P<0.001$). There were no statistically significant differences among the primary orofacial pain diagnoses, though those with temporomandibular joint pains trended toward lower PCS Total Scores ($P=0.1$) and those with neuropathic pains trended toward higher PCS Total Scores ($P=0.17$), compared to those with masticatory muscle pain disorders. In Model 2, higher PCS Total Score was significantly positively associated with younger age ($P<0.03$), average pain intensity ($P<0.01$), worst pain intensity ($P<0.01$), ISI ($P<0.02$), GAD-7 ($P<0.001$), PHQ-9 ($P<0.001$), and a primary orofacial pain diagnosis of neuropathic pain ($P<0.001$).

Mediation Analyses

Figure 4 shows the conceptual model of the mediation analyses. The proportion of total effect of pain intensity on PCS Total Score that was mediated by GAD-7 was 0.31($P<0.0001$), by PHQ-9 was 0.32 ($P<0.0001$), and by ISI was 0.30 ($P<0.0001$) independent of age, sex, and diagnostic category (Tables 3a-c).

Factors Predicting PCS Total Score in Patients Diagnosed with Neuropathic Pain

As neuropathic pain proved to be the primary orofacial pain diagnosis associated with the highest level of pain catastrophizing, further analysis was performed on this cohort. Table 4 shows results from a multivariable linear regression model with PCS Total Score as the dependent variable. In Model 1, no significant associations were noted between PCS Total Score and age or gender. There was no association between average pain intensity and PCS Total Score (beta coefficient -0.45, $p=0.89$). There was a trend for a strong association with worst pain intensity, though this did not reach statistical significance (beta coefficient 4.82, $p=0.14$). In Model 2, the positive association between worst pain intensity and PCS Total Score persisted and was borderline significant (beta coefficient 3.97, $p=0.06$). There was a positive association between GAD-7 and PCS Total Score ($p<0.01$).

DISCUSSION

Our study supported the findings seen in many other studies, both of orofacial pain and other chronic pain populations, that pain catastrophizing is positively associated with pain intensity. Previous research has shown this relationship to be bidirectional, whereby an early reduction in pain catastrophizing predicts a later reduction in pain intensity and an early reduction in pain intensity predicts a later reduction in pain catastrophizing[7]. Presumably, perception of intense pain may lead a person to catastrophize, while increased catastrophizing will lead a person to perceive their pain as being more intense. We found no correlation between pain duration and pain catastrophizing, which is in line with previous studies of orofacial pain populations demonstrating no[37] or slight[38] correlations. We found that younger patients tended to catastrophize more than older patients, which seems to be in agreement with most[27,39], but not all[38], studies of orofacial pain patients. Whereas most other studies show women catastrophizing more than men[3,40,41], our study found no significant difference between men and women. Interestingly, the mean PCS score found in our study was somewhat lower than the mean scores seen in other studies among TMD or orofacial pain populations, which may be attributable to the unique population served by our clinic[27,37,42].

Similar to previous studies, we found significant correlations between pain catastrophizing and other psychosocial variables[28-30]. Pain catastrophizing was most closely associated with depression, followed by anxiety, followed by insomnia. The same trend was seen in a study of chronic neck pain patients[43]. These variables were each independently responsible for mediating around 30% of the relationship between

pain intensity and pain catastrophizing. However, they had no moderating effect on the relationship between average pain intensity and pain catastrophizing. This means that, regardless of whether a person has high or low average pain intensity, depression, anxiety, and insomnia will contribute to pain catastrophizing in a similar fashion. The implication of these analyses is that, if lowering pain catastrophizing is a treatment goal, interventions should be targeted both at reducing pain catastrophizing directly and also at reducing depression, anxiety, and insomnia.

A novel finding from our study was that pain catastrophizing differs among the orofacial pain diagnoses. Several previous studies have compared psychosocial impairment in patients suffering from muscular versus joint TMDs, mostly showing patients with muscular TMDs having more psychologic comorbidities or impairment[44-46], though these findings are not universal[47]. In our raw data, we found those patients with primarily muscular TMDs had significantly higher mean PCS Total Scores than those with primarily joint TMDs. In our first model, which controlled for pain characteristics and demographic variables, we saw a non-significant trend (P=0.1) toward higher PCS scores in muscle versus joint TMD patients. However, this trend was lost once anxiety, depression, and insomnia were controlled in our second model. This indicates that any difference in pain catastrophizing that exists between muscle and joint TMD groups is attributable to the more severe anxiety, depression, and insomnia seen in the former group. A previous study had found no significant difference in pain catastrophizing in muscular versus joint TMDs[27].

We found no significant difference in pain catastrophizing when comparing masticatory muscle disorders with primary headache disorders. There has been some

previous research comparing pain catastrophizing in TMD and headache patients. One study compared pain catastrophizing in patients with chronic migraine versus those with TMD and found no significant difference, while both groups catastrophized more than controls[13]. Another study compared patients with chronic daily headache versus those with TMD and found increased catastrophizing in the headache patients at initial evaluation and no difference at 6-month follow-up[25]. It must be pointed out that, as an orofacial pain clinic, our headache patients likely differ from those seen at primary care or specialty headache clinics (for example, they are probably more likely to have headache pain perceived in middle or lower thirds of the face). Therefore, it is not clear how generalizable these results are to the headache population at large.

Perhaps the most surprising finding of this study was the degree to which people suffering from neuropathic pains are prone to catastrophize. People suffering from neuropathic pains had the highest mean PCS Total Scores of any diagnostic group. After controlling for demographics, pain intensity, and psychosocial variables, a primary diagnosis of a neuropathic pain disorder was the single strongest predictor of a high PCS Total Score. To the authors' knowledge, only one other study has directly compared pain catastrophizing in orofacial pain patients with neuropathic pains versus other pains. Gustin et al.[26] had shown that patients with neuropathic orofacial pains trended toward higher PCS Total Scores compared to patients with TMDs, though this was a fairly small patient cohort (n=21 neuropathic pain and n=24 TMD) and results were not statistically significant. Our finding of a strong relationship between neuropathic pain and high pain catastrophizing has potentially important clinical ramifications. The fact that this relationship did not emerge until anxiety, depression, and insomnia were controlled for

demonstrates that patients with neuropathic pain may be prone to catastrophizing but may not be especially depressed or anxious. This probably makes it less likely for these patients to be referred to a pain psychologist - the type of healthcare professional most qualified to deliver interventions targeted at reducing pain catastrophizing. It is also noteworthy that, in the realm of back pain, it has been demonstrated that higher levels of pain catastrophizing are more strongly associated with dysfunction in those diagnosed with neuropathic or spinal pain versus those diagnosed with osteoarthritic pain[48]. The implication of such a finding is that people with neuropathic or spinal back pain may see more benefit from interventions aimed at reducing pain catastrophizing than those who suffer from osteoarthritic pain. It would be reasonable to hypothesize that pain catastrophizing contributes to dysfunction variably among patients with different orofacial pain diagnoses, as well. Therefore, interventions aimed at reducing pain catastrophizing may differ in efficacy based on the orofacial pain diagnosis. This has not been studied in orofacial pain populations but is a topic worthy of further research. A final note on this topic is that, while the contribution of cognitive and emotional factors to TMDs is well-recognized and various guidelines and review articles generally place a strong emphasis on treatments targeting behavioral and cognitive change, there seems to be much less emphasis on psychosocial factors in the neuropathic orofacial pain literature. The present study demonstrates that at least one major psychosocial factor (pain catastrophizing) plays a very significant role in the suffering of those diagnosed with neuropathic pain. This argues for greater emphasis on pain catastrophizing in the research, diagnosis, and treatment of neuropathic orofacial pain conditions.

So as not stigmatize chronic orofacial pain patients in a box labeled “it’s all in your head”, it is important for clinicians to be aware of biological substrates that underlie and influence brain regions that govern pain and affect. Three dimensions of pain have been described by Melzack and Casey: The sensory-discriminative aspect of pain (governed by the somatosensory cortex of the brain) allows one to identify the location and intensity of nociceptive impulses. The affective-motivational aspect of pain (governed by limbic brain areas, such as the amygdala, hippocampus, and hypothalamus) influences pain unpleasantness, pain behavior, and negative affect. The cognitive-evaluative dimension of pain (governed by the prefrontal cortex) allows for appraisal and decision-making[49-51]. These brain regions and their involved neurotransmitters have profound direct or indirect modulatory effects on nociception via inhibitory or facilitatory neural pathways[52]. While this paper argues for recognition of and treatment targeting the cognitive-evaluative dimension of pain, one would be mistaken to offer treatment *only* targeted at this dimension. Biomedical interventions aimed at the sensory-discriminative dimension, as well as an appreciation of the affective-motivational burden of pain, remain vital components of pain treatment and should be included in comprehensive pain management plans.

Some notes must be made concerning limitations of our study, particularly relating to diagnoses. First, most of the patients seen at this clinic presented with multiple diagnoses. It was not uncommon, for example, to see a patient presenting with co-occurring masticatory myalgia, TMJ arthralgia, and chronic migraine. This study only looked at the primary orofacial pain diagnosis and, therefore, did not account for these potential secondary and tertiary diagnoses. Additionally, it is not always clear which

diagnosis should be considered the "primary" diagnosis. While an attempt is always made to replicate the patient's chief complaint on exam, the decision on what constitutes the "primary" diagnosis often comes down to the clinician's judgment. Second, each of the primary diagnostic categories contain an extremely heterogenous group of conditions. This is perhaps most notable in the "episodic and continuous neuropathic pain" category. One would not be surprised to find pain catastrophizing characteristics differ substantially between trigeminal neuralgia patients, who suffer from unpredictable attacks of brief but excruciatingly severe pain, and PPTTN patients, who are more likely so suffer from continuous unremitting pain but without the fear of unexpected attacks. It is interesting to note that when the neuropathic pain cohort was examined in this study, there was a trend toward PCS Total Score having a stronger association with worst pain intensity than with average pain intensity. As the pain attacks associated with trigeminal neuralgia are by definition "severe", one must wonder if the trigeminal neuralgia patients skewed the results for the neuropathic pain cohort as a whole. Indeed, previous research has shown differences in the psychosocial burden experienced by trigeminal neuralgia versus PPTTN patients, though pain catastrophizing was not assessed[53]. Similarly, previous research has shown higher pain catastrophizing in patients with myofascial pain with referral compared to patients with myalgia[27], two conditions which both fell under the diagnostic category of "masticatory muscle disorders" in the present study

Another limitation concerns generalizability to other patient populations. This study was performed at a military treatment facility and the majority of patients were active duty military service members. This patient group may differ substantially from civilian patient groups. For example, roughly half our study sample was male, whereas

most studies of orofacial pain patients, and of chronic pain patients in general, demonstrate samples that are overwhelmingly female.

Another limitation was sample size. While the overall sample size was large, nearly 90% of the patients fell into the TMD diagnoses, leaving relatively small samples in the other diagnostic categories. Particularly given our findings regarding neuropathic pain, studies of larger samples of pain catastrophizing in orofacial neuropathic pain populations are warranted. One final limitation to note is that this was a cross-sectional study. While this study design is useful at detecting correlations among variables, one cannot use it to infer causation.

CONCLUSIONS

In this orofacial pain population, higher pain catastrophizing was associated with higher pain intensity, depression, anxiety, insomnia, and younger age. Anxiety, depression, and insomnia may each partially explain the relationship between pain intensity and pain catastrophizing. A primary diagnosis of neuropathic pain was the strongest independent predictor of higher pain catastrophizing. Thus, pain management strategies should target cognitive-behavioral change and improved sleep, in addition to more traditional biomechanical and pharmacologic treatment paradigms.

Table 1. Patient characteristics by primary orofacial pain diagnosis.					
	Muscle N=476 (68%)	Joint N=129 (18%)	Headache N=46 (7%)	Neuropathy N=34 (5%)	Total N=699 (100%)
Age – years (SD)	39.6 (12.4)	38.7 (12.6)	46.6 (13.1)	46.8 (13.1)	40.4 (12.7)
Male – N (%)	226 (47.5)	66 (51.2)	17 (37.0)	17 (50.0)	335 (47.9)
Military Status – N (%)					
--Active Duty	348 (73.1)	93 (72.1)	29 (63.0)	20 (58.8)	501 (72.0)
--Family Member	75 (15.8)	23 (17.8)	11 (23.9)	6 (17.6)	115 (16.5)
--Retired	50 (10.5)	13 (10.1)	6 (13.0)	8 (23.5)	80 (11.5)
Race – N (%)					
--White	294 (61.8)	84 (65.1)	25 (54.3)	18 (52.9)	429 (72.1)
--Black	80 (16.8)	21 (16.3)	8 (17.3)	8 (23.5)	120 (20.2)
--Asian	25 (5.3)	7 (5.4)	3 (6.5)	3 (8.8)	39 (6.6)
--Other	4 (0.8)	1 (0.8)	1 (2.2)	1 (2.9)	7 (1.2)
Pain Intensity – mean (SD)					
--Average (0-10)*	4.5 (1.8)	4.0 (2.1)	5.2 (2.4)	4.4 (1.9)	4.4 (1.9)
--Worst (0-10)*	7.4 (1.9)	6.7 (2.4)	7.9 (2.1)	7.7 (2.3)	7.3 (2.1)
Pain Duration, months– median (max, min)	24 (0, 480)	18 (0, 732)	24 (1, 600)	12.5 (1, 300)	24 (0, 732)
PCS Total – mean (SD)*	14.6 (12.1)	11.3 (10.5)	16.1 (12.5)	16.9 (13.7)	14.2 (12.0)
PHQ-9 – mean (SD)*	6.9 (5.9)	4.3 (4.9)	6.1 (5.9)	3.9 (4.5)	6.2 (6.2)
GAD-7 – mean (SD)*	6.8 (6.0)	4.6 (4.9)	5.8 (5.4)	4.7 (5.3)	6.2 (5.8)
ISI – mean (SD)*	11.1 (7.2)	8.8 (6.5)	11.8 (7.6)	8.2 (6.8)	10.5 (7.1)

Table 2. Beta coefficients estimated from a multivariable linear regression model of PCS total score as the dependent variable								
	Model 1*				Model 2**			
	Beta	SE	p	sr****	Beta	SE	p	sr****
Characteristic								
Age (scaled)	-1.20	0.43	<0.01	-0.09	-0.76	0.36	0.03	-0.06
Male	-0.95	0.86	0.27	--	-1.27	0.69	0.07	--
Average pain (scaled)	1.83	0.54	<0.001	0.10	1.39	0.44	<0.01	0.09
Worst pain (scaled)	2.72	0.54	<0.001	0.16	1.37	0.45	<0.01	0.10
Diagnosis								
Muscle (reference)	--	--	--	--	--	--	--	--
Joint	-1.83	1.12	0.10	--	0.48	0.91	0.60	--
Headache	0.86	1.74	0.62	--	1.79	1.42	0.21	--
Neuropathy	2.76	2.00	0.17	--	5.90	1.62	<0.001	--
ISI (scaled***)	--	--	--	--	1.21	0.50	0.02	0.06
GAD7 (scaled***)	--	--	--	--	2.78	0.60	<0.001	0.10
PHQ9 (scaled***)	--	--	--	--	3.48	0.68	<0.001	0.09
*Model 1 includes age, sex, average pain, worst pain, and diagnosis as independent variables.								
**Model 2 includes all Model 1 independent variables + ISI, GAD-7, and PHQ-9 scores.								
*** Scaled = Variable is standardized by subtracting its mean and dividing by its standard deviation.								
**** sr = Semi-partial correlation of the characteristic with PCS total score controlling for all other continuous covariates.								

Table 3a. Mediating effect of GAD-7 (scaled) on the relationship between average pain (scaled) and PCS total.			
Effect	Estimate	95% CI	p
Indirect effect	1.089	0.620, 1.603	<0.0001
Direct effect	2.405	1.644, 3.101	<0.0001
Total effect	3.494	2.575, 4.375	<0.0001
Proportion of total effect mediated by GAD-7	0.31		
Model 1 covariates (age, sex, and diagnosis category) were included as covariates in all mediation analyses.			

Table 3b. Mediating effect of PHQ9 (scaled) on the relationship between average pain (scaled) and PCS total.			
Effect	Estimate	95% CI	p
Indirect effect	1.108	0.613, 1.609	<0.0001
Direct effect	2.353	1.620, 3.101	<0.0001
Total effect	3.461	2.632, 4.367	<0.0001
Proportion of total effect mediated by PHQ-9	0.32		
Model 1 covariates (age, sex, and diagnosis category) were included as covariates in all mediation analyses.			

Table 3c. Mediating effect of ISI (scaled) on the relationship between average pain (scaled) and PCS total.			
Effect	Estimate	95% CI	p
Indirect effect	1.056	0.640, 1.478	<0.0001
Direct effect	2.416	1.619, 3.231	<0.0001
Total effect	3.473	2.641, 4.403	<0.0001
Proportion of total effect mediated by ISI	0.30		
Model 1 covariates (age, sex, and diagnosis category) were included as covariates in all mediation analyses.			

Table 4. Beta coefficients estimated from a multivariable linear regression model of PCS total score as the dependent variable and average pain, worst pain, and patient characteristics as independent variables, among patients diagnosed with neuropathy (N=34).

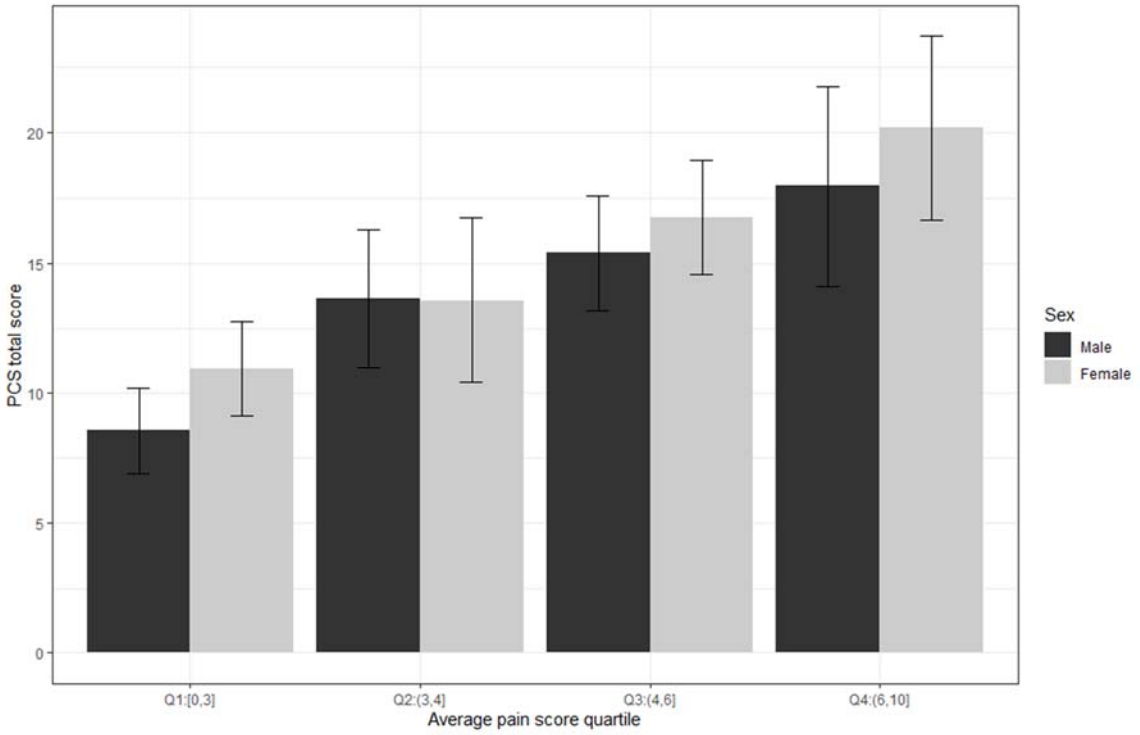
	Model 1*			Model 2**		
	Beta	SE	p	Beta	SE	p
Characteristic						
Age (scaled)	-1.89	2.41	0.44	--	--	--
Male	0.40	4.85	0.94	--	--	--
Average pain (scaled)	-0.45	3.24	0.89	--	--	--
Worst pain (scaled)	4.82	3.18	0.14	3.97	2.04	0.06
ISI (scaled)	--	--	--	--	--	--
GAD7 (scaled)	--	--	--	6.29	2.04	<0.01
PHQ9 (scaled)	--	--	--	--	--	--

*Model 1 includes age, sex, average pain, and worst pain as independent variables.

**Model 2 was selected from Model 1 independent variables + ISI, GAD7 and PHQ9 scores using a forward procedure (p-in = 0.2).

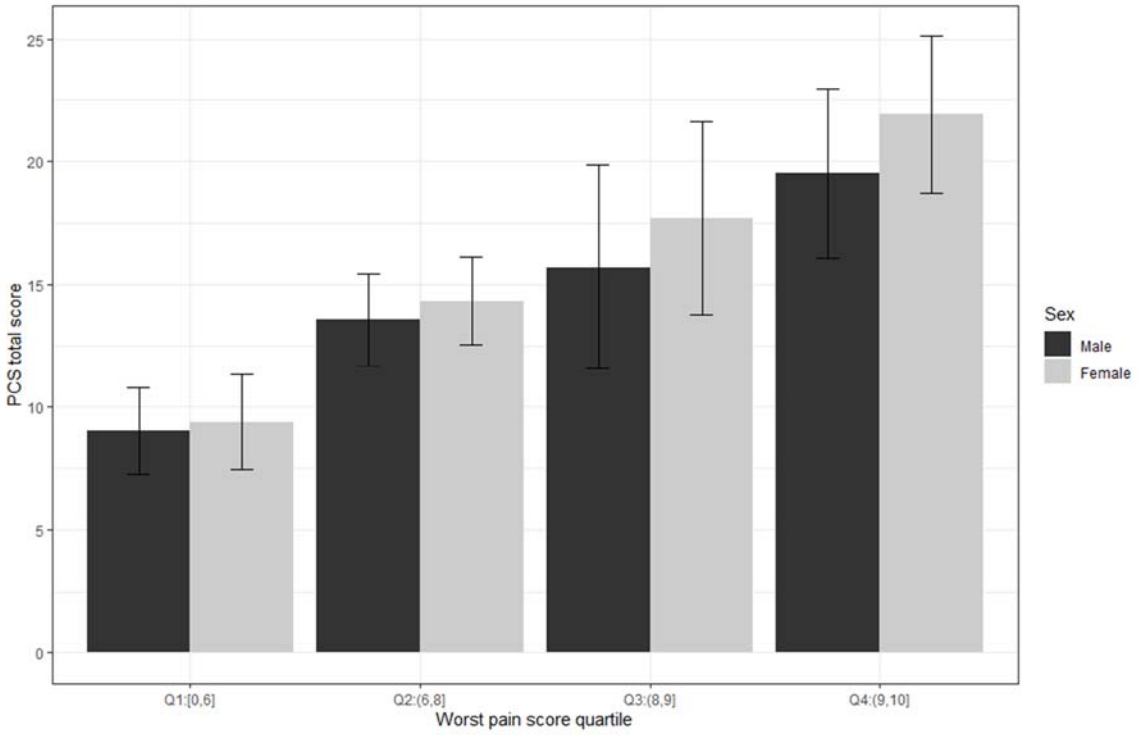
Scaled = Variable is standardized by subtracting its mean and dividing by its standard deviation.

Figure 1: Average Pain Intensity versus PCS Total Score



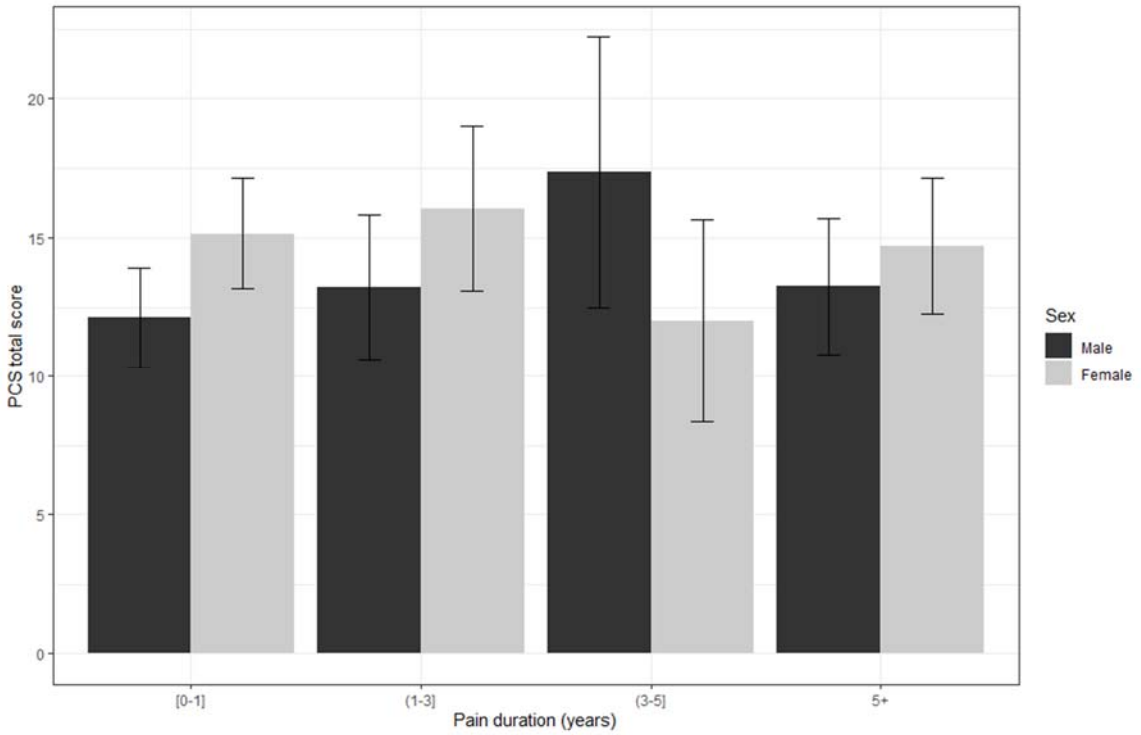
Average pain intensity (divided into quartiles) versus Pain Catastrophizing Scale Total Score, divided by sex. Bars represent 95% confidence interval.

Figure 2: Worst Pain Intensity versus PCS Total Score



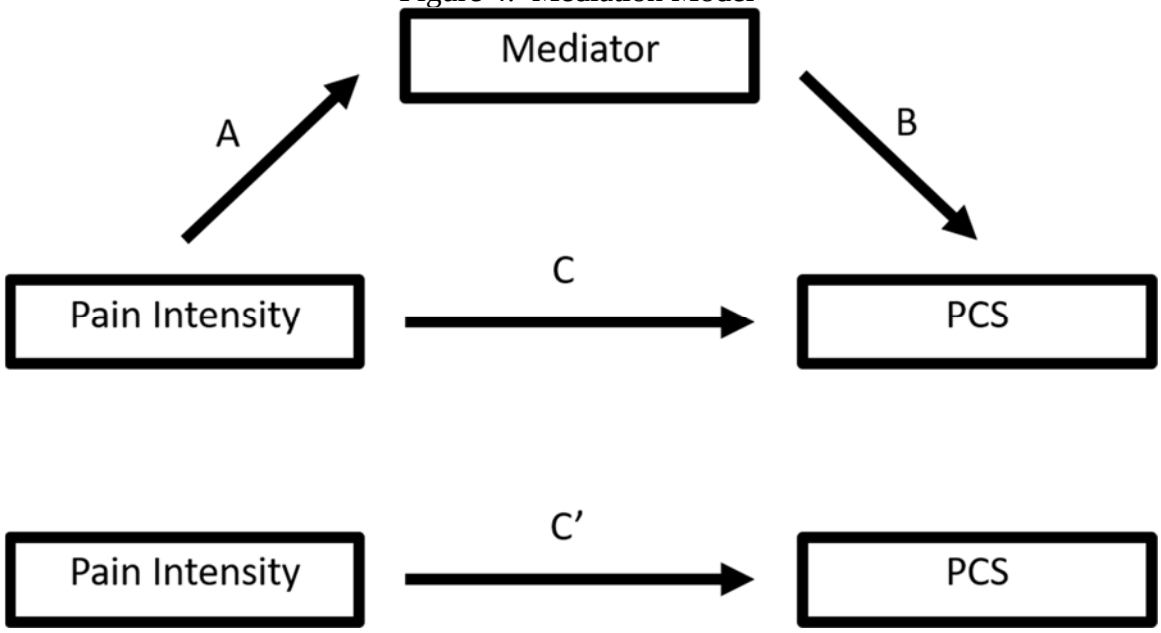
Worst pain intensity (divided into quartiles) versus Pain Catastrophizing Scale Total Score, divided by sex. Bars represent 95% confidence interval.

Figure 3: Pain Duration versus PCS Total Score



Pain duration versus Pain Catastrophizing Scale Total Score, divided by sex. Bars represent 95% confidence interval.

Figure 4: Mediation Model



Conceptual model demonstrating how anxiety, depression, or insomnia may mediate the relationship between pain intensity and pain catastrophizing. C represents the direct effect of pain intensity on pain catastrophizing. AxB represents the indirect effect of pain intensity on pain catastrophizing, as mediated by anxiety, depression, or insomnia. C' represents the total effect of pain intensity on pain catastrophizing (the sum of the direct and indirect effects).

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