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Relationship between Temporomandibular Disorders, Widespread Palpation Tenderness and Multiple Pain Conditions: A Case - Control Study

Hong Chen, DDS, MS[1,2], **Gary Slade, BDS, PhD**[1,3], **Pei Feng Lim, BDS, MS**[1,2], **Vanessa Miller, MPH**[1], **William Maixner, DDS, PhD**[1], and **Luda Diatchenko, MD, PhD**[1]

[1]Center for Neurosensory Disorders, University of North Carolina-Chapel Hill, School of Dentistry, Chapel Hill, NC, USA

[2]Oral & Maxillofacial Pain Clinic, University of North Carolina – Chapel Hill, School of Dentistry, Chapel Hill, NC, USA

[3]Department of Dental Ecology, University of North Carolina-Chapel Hill, School of Dentistry, Chapel Hill, NC, USA

Abstract

The multiple bodily pain conditions in temporomandibular disorders (TMD) have been associated with generalized alterations in pain processing. The purpose of this study was to examine the relationship between the presence of widespread body palpation tenderness (WPT) and the likelihood of multiple comorbid pain conditions in TMD patients and controls. This case-control study was conducted in 76 TMD subjects with WPT, 83 TMD subjects without WPT, and 181 non-TMD matched control subjects. The study population was also characterized for clinical pain, experimental pain sensitivity, and related psychological phenotypes. Results showed that (1) TMD subjects reported an average of 1.7 comorbid pain conditions compared to 0.3 reported by the control subjects ($p<0.001$); (2) Compared to control subjects, the odds ratio (OR) for multiple comorbid pain conditions is higher for TMD subjects with WPT [OR 8.4 (95% CI 3.1–22.8) for TMD with WPT versus OR 3.3 (95% CI 1.3–8.4) for TMD without WPT]; (3) TMD subjects with WPT presented with reduced pressure pain thresholds (PPTs) in both cranial and extra-cranial regions compared to TMD subjects without WPT; and (4) TMD subjects with WPT reported increased somatic symptoms. These findings suggest that pain assessment outside of the orofacial region may prove valuable for the classification, diagnosis, and management of TMD patients.

Corresponding author: Luda Diatchenko, Center for Neurosensory Disorders, School of Dentistry, University of North Carolina – Chapel Hill, CB #7450, Chapel Hill, NC 27599, Tel: 919-843-2549, Fax: 919-966-2991, lbdiatch@email.unc.edu.

Institution where the work was done:
Center for Neurosensory Disorders, University of North Carolina-Chapel Hill, School of Dentistry, Chapel Hill, NC, USA,

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Keywords

TMD; temporomandibular disorders; palpation tenderness; multiple pain conditions; comorbid

Introduction

Painful Temporomandibular Disorder (TMD) is a heterogeneous group of musculoskeletal pain conditions affecting approximately 5% of the adult population.[25] In addition to facial pain, patients with TMD frequently report multiple bodily pains outside of the orofacial region.[1, 2, 13, 52, 71] Widespread pain is associated with generalized alteration in pain processing,[33, 45, 53, 54, 66, 67] thereby strongly suggesting that comorbid pain conditions may share common pathophysiological pathways.[15] Pain assessment outside of the orofacial region may be important and useful for the sub-classification of this heterogeneous population thereby informing pain management strategies.

The presence of generalized bodily (non-facial) pain has been associated with an increased risk of developing TMD pain [32, 33] and pain-related disability,[27] persistence of TMD symptoms,[48, 49, 67] and poor treatment outcome.[31, 50] However, TMD patients differ in their experience of bodily pain[45] and the impact and significance of this bodily pain profile needs further clarification. It is unclear if all or only a subgroup of TMD patients differs from non-TMD controls regarding generalized bodily pain experience. This is partly due to the fact that current TMD diagnosis and treatment outcome evaluation are primarily based on facial and cranial pain assessments.[18] The heterogeneity of the TMD patient profile suggests possible, yet-to-be characterized, subgroups of TMD patients with different underlying pain mechanisms.[66] With mounting evidence of the importance of mechanism-based diagnosis for individualized pain management, the bodily pain profile of TMD patients may be an important phenotypic marker of the underlying differential pain mechanisms thereby influencing diagnosis and treatment outcomes.

In addition to comorbid pain conditions, systemically enhanced responses to noxious stimuli, such as pressure pain hypersensitivity at anatomically remote body locations, have also been associated with generalized enhancement in central and/or peripheral pain processing.[19, 29, 30, 63, 64] In TMD and other musculoskeletal pain conditions, subgroup differences in localized versus generalized pressure pain sensitivity have been demonstrated previously[7, 45, 60, 61, 70] suggesting different underlying pain mechanisms. A range of experimental pain modalities have been used to examine generalized pain sensitivity profiles. Digital palpation of tender points on different bodily areas is an effective clinical tool for detecting elevated pressure pain sensitivity in musculoskeletal pain conditions,[23] which allows the quantification of widespread palpation tenderness (WPT). It is, however, unknown if this measure of bodily tenderness is correlated with existing comorbid pain conditions. In addition, based on the biopsychosocial model of complex persistent pain conditions, socio-demographics and psychological variables may have important interactions with these measures.[17, 38]

The aims of this study are to determine if: 1) TMD subjects differed from non-TMD healthy controls regarding the occurrence of multiple (or generalized) bodily pain conditions; 2) the presence of comorbid pain conditions is increased in the presence of WPT in TMD subjects; and 3) the relationship between TMD, WPT and comorbid pain conditions could be explained by two sets of putative confounders, namely demographic variables and psychological variables. In this study, we used anatomically widely distributed palpation tenderness outside of the orofacial region to represent a generalized versus a localized enhancement in pressure pain sensitivity. Psychological characteristics, clinical pain

profiles, and responses to sensory stimuli (i.e., pressure and heat pain) were also detailed for TMD subgroups. Part of this work was presented at American Pain Society's 2011 annual meeting.[8]

Materials and Methods

Study participants and classification

This study is a secondary analysis using existing data from 349 participants in whom palpation tenderness was measured as part of a case-control study investigating genetic risk factors for TMD (R01 DE 16558, LD and WM). Of those, 340 subjects who fulfilled the inclusion/exclusion criteria were included in this study. Data was collected between 2005 and 2009. Female volunteers were recruited from the Orofacial Pain Clinic at the University of North Carolina at Chapel Hill, NC, as well as from the university campus and community by advertisements, flyers and mass email. Participation was limited to female Caucasians due to the higher prevalence of TMD in females than in males, and to avoid problems of population stratification in assessing genetic associations. Participants were aged 18 to 60 years old. Exclusion criteria included the following self-reported medical conditions: diabetes, kidney disease, heart failure, chronic respiratory disease, epilepsy or seizure disorder, or high blood pressure not controlled with medication. Women who were pregnant, nursing, undergoing orthodontic treatment, dialysis, radiation or chemotherapy were similarly excluded from participation as were participants with trauma or surgery on the head, face or neck within the last six months. This study was approved by the Biomedical Institutional Review Board of the University of North Carolina at Chapel Hill. Written informed consent was obtained from all study participants.

TMD case classification—Case classification of TMD was based on the following criteria: 1) a self-reported history of pain in the temporomandibular region for at least 5 days in the month preceding the clinical examination; and 2) the presence of myalgia and/or arthralgia of TMD based on a modified version of Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) (for detailed examination and classification method description, see Slade[56] and Ohrbach[43] 2011). This RDC/TMD clinical examination was performed by calibrated examiners on all subjects to determine TMD case or non-case status. Myalgia was present when pain was reported in response to jaw movements or digital palpation of three or more of eight orofacial muscle groups (each assessed bilaterally): temporalis, masseter, lateral pterygoid, and submandibular. Arthralgia was present when pain was reported in response to jaw movements or digital palpation of one or both temporomandibular joints. The digital pressure used for palpation of extraoral muscle sites, intraoral muscle sites, and temporomandibular joints were 2 lbs., 1lb. and 1 lb. respectively, and the duration of applied force was 2 seconds for each site.

Classification of widespread palpation tenderness (WPT)—WPT was determined by digital palpation examination at 18 pre-defined bodily sites. Three pounds of digital palpation pressure were applied bilaterally for 2 seconds to each of the following pre-defined locations modeled after ACR's 1990 criteria[72] for fibromyalgia tender points examination: occiput, trapezius, supraspinatus, lower cervical, second rib, lateral epicondyle, knee, gluteal, and greater trochanter. At each location, a response of pain to palpation was recorded as "tenderness". WPT was classified as present when palpation tenderness was elicited bilaterally and above and below the waist, i.e., at least in diagonal locations.

Control subjects reported no history of orofacial pain within the preceding 6 months and no prior diagnosis of TMD. In addition, the RDC/TMD clinical examination determined the absence of arthralgia and myalgia, and the criteria for WPT were not met.

Clinical pain measures

Pain characteristics such as pain intensity, duration, location, and impact of pain on usual activities were assessed to measure the severity and impact of facial pain and other bodily pain in TMD and control participants.

Comprehensive Pain Symptom Questionnaire (CPSQ)—The CPSQ is a self-report instrument assessing presence of multiple pain symptoms and their associated characteristics, and the lifetime presence of multiple pain conditions. In particular, the comorbidity of 7 complex persistent pain conditions, namely, fibromyalgia (FM), chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), interstitial cystitis (IC), chronic pelvic pain (CPP), headaches, and low back pain (LBP), were examined. The presence of FM, CFS, IBS, IC, and CPP were determined by the following question: "Do you have any of the following conditions or symptoms?". The presence of frequent headache(s) was determined by headaches that have been presented for at least 3 months or at least 10 episodes in the last year, and on an average of 1 or more day per month. The presence of frequent LBP was determined by a positive history and at least 11 episodes of LBP in the past 12 months. Psychometric properties of the instrument have been assessed for items such as presence of jaw pain (in past 30 days and lifetime), headache in the past year, and jaw pain frequency. The validity coefficients range 0.85 to 1.0 versus expert interview, and temporal stability ranges 0.7 to 0.9 over 3–7 days (Ohrbach R et al unpublished).

Graded Chronic Pain Scale (GCPS)—The GCPS includes 6 items that rate the intensity of current pain as well as intensity and pain interference with activities in the past 6 months. All items are rated from 0 to 10. The derived pain severity score is graded into 4 hierarchical classes: Grade I, low disability-low intensity; Grade II, low disability-high intensity; Grade III, high disability-moderately limiting; and Grade IV, high disability-severely limiting. GCPS has been validated in primary care and chronic pain patients[68]. We assessed GCPS rating for both "facial pain" and "other pain" (i.e., bodily pain other than facial pain).

Screening Pain Self Report (SPSR)—The SPSR is a 5-item questionnaire which rates the recent pain intensity (i.e., average, highest, and lowest; range 0–100), average percentage of waking day during which individuals experience pain, and a rating of current pain corresponding to descriptive words that represent sensory (intensity) and affective (unpleasantness) domains of the pain experience.[22]

Short Form McGill Pain Questionnaire (MPQ)—The Short Form MPQ consists of 15 descriptors that reflect the sensory (11 items) and affective (4 items) aspects of pain. The intensity of the pain feelings are rated on a Likert scale from 0 to 3 where 0 is "none" and 3 is "severe". Three pain scores are derived from the sum of the intensity ratings for sensory, affective and total descriptors.[40]

Experimental pain measures

Pressure pain thresholds were assessed in the orofacial as well as non-facial regions to evaluate pressure pain sensitivity in all subjects. Heat pain threshold and tolerance were assessed in the ventral forearm to evaluate thermal pain sensitivity.

Pressure Pain Threshold (PPT)—The PPT was measured using a flat-tipped algometer (Pain Diagnosis and Treatment, Great Neck, NY, USA) applied to facial muscle sites (i.e., temporalis and masseter muscles), the temporomandibular joints, and non-facial sites (i.e., trapezius muscle and lateral epicondyle). Pressure was applied at a steady rate of 1kg/second until the participant indicated that she felt pain. After an initial test trial two subsequent and

consecutive readings that differed by no more than 0.2 kg were averaged and recorded as the PPT at each site. Two reproducible reading were generally obtained within 3 trials after the initial test trial.

Thermal Pain Sensitivity—Thermal pain sensitivity was assessed using a commercially available thermal stimulator (TSA, Medoc Inc). This device delivered computer-controlled slowly increasing thermal stimuli to the skin on the left medial ventral forearm at a rate of 0.5°Celcius/second from an adapting temperature of 39°Celcius. The subject terminated the stimuli by pressing a button when it became painful (thermal pain threshold) or when intolerable (thermal pain tolerance) respectively. Four sites were tested for threshold and 4 sites were tested for tolerance with each site being at least 1.5 inches apart. Four trials each of the threshold and tolerance were conducted to obtain an average temperature value. The difference between mean tolerance and mean threshold measures was also calculated, which represents a metric of an individual's thermal heat pain range.

Psychological measures

All subjects completed a battery of psychological inventories that have been shown to be associated with TMD and other persistent pain conditions.[6, 55, 65, 69]

Pain Catastrophizing Scale (PCS)—The PCS consists of 14 thoughts or feelings, including anxiety, coping, and helplessness in response to pain. Subjects rate the degree to which they experience each item while feeling pain using a 5-point scale from 0 ("not at all") to 4 ("all the time").[62]

Pennebaker Inventory of Limbic Languidness (PILL)—The PILL assesses the frequency of occurrence of 54 common physical symptoms and sensations using a 5-point scale, ranging from 1 ("never or almost never have"), to 5 ("more than once every week"). The total score of PILL represents somatic awareness. It has high internal consistency and sufficient test retest reliability.[44]

Perceived Stress Scale (PSS)—The PSS is a 10-item measure of the degree to which respondents appraise stressful situations that occurred during the last month. Items are scored on a 5-point scale from 0 to 4. Total scores range from 0 to 40, with higher scores denoting greater perceived stress.[9] Test-retest reliability, calculated in a community samples at approximately 6 weeks apart yielded coefficients of 0.85 and 0.55, respectively.

Profile of Mood States-Bipolar (POMS-BI)—The POMS- BI consists of 72 mood-related items rated using a 4-point scale. Questions refer to current mood state. Responses for the POMS-BI range from 0 ("much unlike this") to 3 ("much like this"). The POMS-BI is scored creating 6 bipolar subscales measuring positive and negative affective dimensions of mood. These dimensions are: (1) Agreeable - Hostile; (2) Elated - Depressed; (3) Confident – Unsure; (4) Energetic - Tired; (5) Clearheaded - Confused; and (6) Composed - Anxious. The POMS-BI has been well validated with other mood measures and is sensitive to subtle differences in affective state.[34]

Spielberger State-Trait Anxiety Inventory (STAI)—The STAI includes two 20-item instruments measuring situational state anxiety (STAI-Y1) and trait anxiety (STAI-Y2). It includes statements such as "I feel calm" or "I am worried" with response options scored on a 4-point scale from 1 ("not at all") to 4("very much so"). Ten of the items are reversely scored to create an overall score of anxiety for each of the instruments.[57, 58]

Symptom Checklist – 90 Revised (SCL-90-R)—The SCL-90-R consists of 90 items, each describing a feeling or thought, scored on a 5-point scale from 1 ("not at all distressed") to 5 ("extremely distressed"). It provides ratings of psychological distress in nine symptom areas: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.[14] In the current study, only the rating for depression was reported and used for analysis.

Data Reduction and Statistical Analysis

For statistical analyses, Stata for Windows (version 11) was used. To address our study hypothesis regarding the association between TMD, pressure tenderness and multiple pain conditions, we first needed to identify likely confounders of that association. Potential confounders were measures of demographic, clinical and psychological characteristics. They were compared between TMD cases with WPT, without WPT and controls. Statistical significance was evaluated using Pearson's Chi-square test for categorical variables and analysis of variance for continuous variables. Bonferroni correction was used to determine the threshold for statistical significance according to the number of characteristics within each group of potential confounders: $P<0.003$ for demographic and clinical characteristics, and $P<0.004$ for psychological characteristics. The second step in evaluating confounding investigated bivariate associations between each potential confounder and presence or absence of 2 or more persistent pain conditions (arbitrarily chosen to reflect the presence of multiple pain conditions). The same Bonferroni correction was applied to determine criteria for statistical significance. The percentage of people with 2 or more persistent pain conditions was then compared among subgroups of TMD cases with and without WPT and controls, and odds ratios were computed to provide an unadjusted estimate of the association. Two multivariate binary logistic regression models were then created to calculate adjusted estimates of the association: the first adjusted only for age as a continuous variable, and the second additionally adjusted for putative confounders that had been identified in preceding steps to be associated both with 2 or more persistent pain conditions and with TMD subgroups. For this final model, continuous measures of confounders were transformed to unit-normal deviates to provide a comparable scale for the odds ratio quantifying their association with persistent pain.

Results

A total of 181 controls and 159 TMD cases were included in this study of women aged 18–60 years (mean = 32.8 years, sd = 12.1 years). The majority of TMD cases (91.1%) were diagnosed with both arthralgia and myalgia. Forty-eight percent (48%) of TMD cases had WPT. Significant age differences were found across the groups (Table 1a).

Clinical pain characteristics

Overall, TMD subjects reported an average of 9.5 ± 8.4 years of facial pain (Table 1a). The mean facial pain intensity during past 6 months and during past 1–2 weeks was "moderate". After Bonferroni correction, none of the facial pain characteristics differed significantly between TMD subjects with and without WPT (Table 1a). However, Graded Chronic Pain Scale (GCPS) scores regarding severity of non-facial pain was greater in the former (Table 1b, $p<0.001$).

Experimental pain profiles

Pressure Pain Threshold (PPT)—TMD subjects exhibited lower PPTs in all (facial and non-facial) sites compared to controls (Table 1c, p's<0.001). In particular, TMD subjects without WPT exhibited lower PPTs only in the facial sites, while TMD subjects with WPT showed lower PPTs in both facial and non-facial sites (Table 1c, p's<0.001). Reduced PPTs

in all sites was also noted in subjects who reported multiple comorbid pain conditions (Table 4c, p's<0.001).

Heat Pain Threshold and Tolerance—TMD subjects and controls did not differ with regards to heat pain threshold and tolerance at the site outside of orofacial region. Heat pain tolerance in TMD subjects with WPT was slightly lower than that in TMD subjects without WPT and in controls (Table 1c). Slightly reduced heat pain tolerance was also noted in subjects who reported multiple comorbid pain conditions (Table 4c, p<0.05). However, these differences did not reach statistical significance after Bonferroni correction.

Psychological characteristics

TMD subjects reported higher mean levels of psychological distress than control subjects on all tested psychological measures (Table 2, p≤0.001). Compared to TMD subjects without WPT, TMD subjects with WPT reported higher distress on a number of psychological measures, with statistically significant difference only in somatic symptoms between the 2 groups based on the PILL (p<0.001; after Bonferroni correction).

Comorbid pain conditions

Seven persistent pain conditions were assessed in this study including fibromyalgia (FM), chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), interstitial cystitis (IC), chronic pelvic pain (CPP), headaches, and low back pain (LBP), Twenty two percent of the study participants reported 2 or more comorbid pain conditions (outside of the orofacial region). This included 4% of the control subjects, 59% of TMD subjects with WPT and 27% of TMD subjects without WPT (Figure 1. p<0.001). The mean age of subjects who reported multiple comorbid pain conditions was significantly greater than that of subjects who reported 0–1 comorbid pain condition (Table 4a). In addition, all pain characteristics and psychological distress measures were also significantly elevated in the former (Tables 4a, 4b & 5, p's<0.001). TMD subjects reported an average of 1.7 comorbid pain conditions compared to 0.3 reported by the control subjects (p<0.001). In the former, the percentage of subjects ranged from 1.3% for IC, to 86.2% for frequent headaches (Table 3). TMD subjects with WPT reported higher numbers of comorbid pain conditions than TMD subjects without WPT (2.2 ± 1.5 vs. 1.2 ±0.6 respectively, p<0.001). Three of the 7 comorbid pain conditions examined, namely FM, CFS, and LBP, were more frequently reported in TMD subjects with WPT than those without WPT (Table 3, p<0.007). IBS (p=0.01) and CPP (p=0.02) also showed higher prevalence in TMD subjects with WPT compared to those without WPT, however, these differences did not reach statistically significant levels after Bonferroni correction.

Bivariate and multivariate analyses of the association between TMD with and without WPT status and multiple comorbid pain conditions

Bivariate analysis revealed that TMD subjects without WPT had 6.5 times the odds of reporting multiple comorbid pain conditions (95% CI: 2.7, 15.6 - Table 6, Model 1), while TMD subjects with WPT had 32.5 times the odds of reporting multiple comorbid pain conditions (95% CI: 13.7, 77.0), both compared to controls. Putative confounders that had been identified in preceding steps to be associated both with 2 or more comorbid pain conditions and with TMD subgroups (with and without WPT) included age and PILL (i.e., somatic symptom report). Multivariate regression analyses were then performed adjusting for potential confounders. Although statistically significant, GCPS-other pain and PPT measures were not included in the multivariate models due to the close proximities to case definitions of multiple pain and WPT. After adjusting only for age, the preceding odds ratios were attenuated only slightly (Table 6, Model 2). However, after additional adjustment for

somatic symptoms, the odds of reporting multiple (2 or more) comorbid pain conditions was elevated only 3-fold (OR 3.3, 95% CI = 1.3, 8.4) for TMD subjects without WPT relative to controls, and 8-fold (OR 8.4, 95% CI = 3.1, 22.8) for TMD subjects with WPT. Other findings from Model 3 showed that an increase of one standard deviation in age (i.e., 12 years) or in somatic symptom report (i.e., 24 points in PILL score) was associated with approximately twice the odds of reporting multiple comorbid pain conditions.

Discussion

Main Results

The present study compared the self-report of seven chronic persistent pain conditions in females with painful TMD with or without widespread palpation tenderness and control subjects, which were characterized in both clinical and psychological domains. The results revealed elevated, but substantially different likelihoods of reporting multiple pain conditions between TMD subgroups as compared to controls. These outcomes indicate that assessments of pain outside of the orofacial region can provide important information regarding sub-classification of TMD that may prove valuable for the diagnosis and management of TMD patients.

Generalized versus localized pain profiles in TMD cases

Having multiple pain conditions in different body locations have been associated with generalized alteration in pain processing [33, 45, 53, 54, 66, 67] that may share common pathophysiological pathways in developing chronic pain conditions [15] and may represent different pain mechanisms in subgroups of TMD.[66] Having multiple pain conditions in non-facial regions have also been associated with increased risk of developing painful TMD,[32, 33] pain-related disability,[27] persistence of TMD symptoms,[48, 49, 67] and poor treatment outcomes in patients with TMD,[31, 50] Therefore, identifying patients with a profile of generalized pain is important for improving mechanism-based diagnosis and treatments.

In addition to having multiple clinical pain conditions, systemically enhanced responses to noxious stimuli, such as the presences of pressure pain hypersensitivity at anatomically remote body locations, have also been associated with generalized enhancement in central and/or peripheral pain processing [19, 29, 30, 63, 64] and may attribute to the generalized pain profile observed in TMD patients and patients with related persistent pain conditions. In TMD and other persistent pain conditions, subgroup differences in localized vs. generalized pressure pain hypersensitivity have been demonstrated previously[7, 45, 60, 61, 70] suggesting a diversity of neurobiological mechanisms contributing to the presentation and report of clinical pain.

Although generalized enhancement in pain has been suggested as a potential risk factor for persistent pain conditions, systemic pain profiles have not been routinely assessed and integrated into the evaluation of TMD patients. Current patient assessments and treatment outcome evaluations have primarily been focused on pain and dysfunction in the masticatory system. In the present study, approximately 40–50% of the TMD cases presented with characteristics of a more generalized pain profile, i.e., multiple pain sites or WPT. Similar to previous studies,[45, 46, 50, 66] this emphasizes the heterogeneity in this population and the importance of integrating bodily pain assessments into the evaluation of TMD patients.

Remarkably, when using WPT as a clinical “marker” for generalized pain profile to sub-classify TMD cases, we found no subgroup differences in facial pain measures, while non-facial pain measures differed in both clinical and experimental domains. When comparing between TMD ± WPT subgroups, facial pain characteristics such as pain intensity, duration, impact on usual activities, overall severity assessment (i.e., GCPS of facial pain), and

pressure pain sensitivity (i.e., PPT), both of which are commonly used in TMD evaluations, have shown no group differences. Our results clearly demonstrated that both self-reported characteristics of facial pain and PPT measures at cranial sites did not differ between TMD subgroups. However, at non-facial locations, both measures of clinical pain severity (i.e., GCPS of other pain) and PPT were elevated in the subgroup with a more generalized pain profile (i.e., WPT). These results indicate that signs and symptoms of facial pain alone do not reflect a generalized enhancement in pain processing and perception. Therefore, assessing pain in the masticatory system alone is not sufficient to draw conclusions regarding the overall pain phenotype of TMD cases. As suggested in previous studies,[33, 50, 67, 70] TMD pain should not be considered in isolation. Evaluating signs and symptoms of systemically generalized enhancement in pain, such as WPT, may therefore be considered into TMD evaluation. Future studies will need to be conducted to validate the clinical significance of such stratification especially in relation to the determination of treatment outcomes.

Psychological profiles in TMD cases

Heightened psychological distress has been documented extensively in the TMD population. TMD subjects in this study also showed greater distress compared to controls in all psychological measures, which highlights the importance of reducing distress for effective management of TMD. In addition, TMD subjects with WPT reported higher somatic symptoms (i.e., elevated PILL scores) compared to TMD participants without WPT. The PILL questionnaire provides a measure of somatic awareness with respect to common physical symptoms or sensations resulting in a quantitative measure of how people physically perceive their body in response to internal visceral and external somatic stimuli. These sensations serve as monitors through which we perceive our own existence (e.g. self) and we act (consciously and subconsciously) upon these sensations to make adjustments to the external world we experience. In this context, pain serves as part of a “surveillance” system for noxious stimuli. This system is highly integrated in that both internal and external sensations are integrated to maintain homeostasis, survive external threats, and protect the integrity of the body.[10, 11, 35, 37, 47] Different lines of research have shown both anatomical and functional integration of pain and information from other sensory modalities through cortical and subcortical neuronal pathways.[3, 5, 41] The multisensory integration facilitates the perception of internal and external environment.[35, 37, 59] Increased somatic symptom report has been frequently seen in chronic pain population. [6, 12, 16, 21, 42, 51] The frequent co-existence and correlation between pain and other somatic symptoms may indicate a shared pathophysiology such that enhanced sensitivity is not limited to pain, but also exists in other sensory modalities due to converging neuronal networks in the central nervous system,[21] particularly in the somatosensory system. From this perspective, PILL values or elevated somatic complaints can be considered, at least in part, as a marker of peripheral and/or central sensory sensitization, in addition to a psychological construct.

WPT as a potential clinical assessment method for generalized pain sensitivity in musculoskeletal conditions

Quantitative sensory testing for mechanical pressure hypersensitivity has been broadly used in research settings to study altered pain sensitivity in musculoskeletal pain conditions. As a simple proxy, digital palpation tenderness has been suggested for clinical use of assessing pressure pain hypersensitivity and psychological distress.[23] Previous studies have shown that in patients with persistent pain, palpation tenderness expresses widely to remote body sites and represents a generalized sensitivity to mechanical pressure pain.[4, 26, 28]

In the current study, we adopted the American College of Rheumatology’s “widespread” concept to represent a generalized pattern in contrast to a localized pattern of pain

sensitivity. Compared to controls, TMD cases with WPT showed reduced PPTs in both cranial and extra-cranial regions, while TMD cases without WPT showed reduced PPTs only in cranial region. These results imply that WPT may represent anatomically generalized mechanical pressure hypersensitivity to pain, thereby, serving a potential clinical marker for generalized pressure pain hypersensitivity in musculoskeletal conditions such as TMD and represent a more “mechanism-based” approach for classification and management when the mechanism(s) for comorbid pain conditions is still poorly understood.

In contrast, heat pain measures did not discriminate between TMD subgroups (with and without WPT) and controls in this study, which is inconsistent with previous reports.[20, 24, 36, 45] One explanation is that due to the heterogeneity of TMD populations studied.[20] A second possibility is an insufficient sample size (note that TMD cases tended to exhibited higher sensitivity to heat but fell short of statistical significance). Nevertheless, and consistent with previous studies,[24, 45] pressure pain measures differed markedly between TMD subgroups and controls in the present study raises the question of whether there is a generalized enhancement of pain sensitivity across stimulus domains in deep tissue musculoskeletal pain conditions, and if so, what modalities of quantitative sensory stimuli will be clinically appropriate and sufficiently sensitive to detect such generalized changes in pain sensitivity in these conditions.

Implications and limitations

As an earlier effort to develop a mechanism-based evaluation for TMD, our study provides valuable insights into the clinical and psychological characteristics associated with pain mechanisms in TMD subgroups using a simple assessment procedure. Our findings may ultimately lead to validated clinical methods that identify TMD patients with generalized pain, which inform and enable tailored therapeutic approaches. The treatment implication lies in the importance of an integrated interdisciplinary approach, whereby the management of both local factors (e.g., oral parafunctions) and biopsychosocial factors that contribute to pain amplification and psychological distress may improve the treatment outcomes.[39]

This study has several limitations. First, the reported comorbid pain conditions may be inaccurate due to self-report, recall bias, and differences in diagnostic criteria adopted by different physicians. Also, the comorbidities were assessed mostly based on life-time history, and information regarding their current status was not collected. Thereby, their current impact on TMD pain was unknown. Second, the reported findings result from a secondary data analysis in a study sample limited to females, which limits the generalizability of our findings. Third, information regarding current pain treatments (such as medication use) was not accounted for and its potential impact on pain assessment was not determined. Future studies will need to address these weaknesses.

Summary

TMD is commonly viewed by healthcare providers and the public as a local or regional pain condition, and patient assessments and treatment outcome evaluations have primarily been focused on pain and dysfunction in the masticatory system. This study investigated bodily widespread palpation tenderness (WPT) and self-reported comorbid pain conditions in female TMD subjects versus non-TMD control subjects. In general, TMD subjects with WPT presented with greater self-report of multiple comorbid pain conditions, higher levels of somatic symptoms, and reduced PPTs in both cranial and extra-cranial regions, compared to TMD subjects without WPT or controls. In contrast, localized facial pain is not reflective of generalized pain enhancement and is associated with less psychological symptoms than TMD with WPT. These findings are of substantial clinical significance as they emphasize the importance of integrating bodily pain assessment and psychological (i.e., measures of

somatic awareness) assessment in the evaluation of TMD patients and may guide the development of individualized management programs for specific TMD groups.

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Perspective

TMD subjects with WPT experience a greater level of multiple comorbid pain conditions, compared to TMD subjects without WPT and non-TMD controls. Integration of bodily pain assessments can be informative for evaluation, diagnosis, and management of TMD.

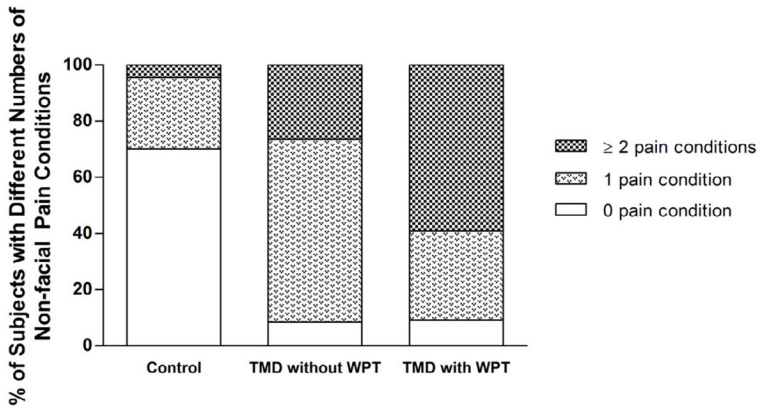

Figure 1.

Percentage of each study group reporting different numbers of persistent pain conditions
X-Axis: TMD-Pain group status
Y-Axis: % of subjects in each group reported different # of persistent pain conditions (fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, interstitial cystitis, chronic pelvic pain, frequent headache, and frequent lower back pain)
1. Overall, $p<0.001$
2. $p<0.001$ for the followings: control vs. TMD with WPT; control vs. TMD without WPT; TMD with WPT vs. TMD without WPT.

Table 1a

Characteristics of the study population – age and clinical characteristics of facial pain

Characteristic	Controls Mean(SD) or %	All TMD cases Mean(SD) or %	TMD w/o WPT Mean(SD) or %	TMD with WPT Mean(SD) or %
Age (years) *	29.7 (11.0)	36.3 (12.3)	33.1 (12.1)[a]	39.8 (11.8)[b,c]
Months since facial pain onset *	6.8 (25.3)	113.7 (100.8)	107.7 (100.8)[a]	120.4 (101.0)[b]
Average facial pain intensity (6-mon) *	0.1 (0.5)	4.5 (2.2)	4.7 (2.1)[a]	4.3 (2.2)[b]
Impact due to facial pain (6-mon) *				
Missed usual activities (days) *	0 (0.1)	7.0 (22.8)	6.7 (21.6)[a]	7.4 (24.2)[b]
Less than 50% efficiency(days) *	0 (0.4)	23.0 (64.8)	28.5 (83.4)[a]	16.8 (32.8)[b]
Facial pain in the past 1–2 weeks (0–100)				
1. Average intensity *	0.5 (3.6)	40.1 (22.6)	39.0 (21.6)[a]	41.4 (23.7)[b]
2. Highest intensity *	0.7 (6.3)	60.2 (24.6)	59.9 (24.4)[a]	60.5 (24.9)[b]
3. Lowest intensity *	0.3 (3.1)	15.9 (18.1)	12.9 (15.5)[a]	19.2 (20.2)[b],
4. % of wake days with pain *	0.5 (3.9)	52.0 (33.4)	47.0 (33.3)[a]	57.5 (32.9)[b]
5. Unpleasantness rating *	0.1 (0.8)	8.4 (3.9)	7.8 (3.6)[a]	9.1 (4.0)[b]
Grade chronic pain scale-facial(%) *,a, b				
GCPS-0	97.2	2.0	1.3	2.8
GCPS-I	2.2	42.4	38.8	46.5
GCPS-II	0.6	45.7	50.0	40.9
GCPS-III	0	4.6	3.8	5.6
GCPS-IV	0	5.3	6.3	4.2

Abbreviations: TMD, temporomandibular disorders; WPT, widespread palpation tenderness; w/o, without; 6-mon, 6 months; GCPS, Grade Chronic Pain Scale.

Note: Number of study subjects included in each group for pain characteristics varies based on available information.

For controls: n=180–181; for TMD cases: n=151–159 (TMD without WPT: 77~83, TMD with WPT: 71~76)

*Controls vs. all TMD cases: p<0.003

[a]Controls vs. TMD without WPT: p<0.003

[b]Controls vs. TMD with WPT: p<0.003

[c]TMD without WPT vs. TMD with WPT: p<0.003

Table 1b

Characteristics of the study population – other clinical pain characteristics

Characteristic	Controls	All TMD cases	TMD w/o WPT	TMD with WPT
MPQ (Mean, sd)				
Affective*	11.2 (1.0)	17.4 (5.2)	16.5 (4.6)[a]	18.3 (5.6)[b]
Sensory*	4.1 (0.5)	5.1 (1.5)	4.9 (1.1)[a]	5.4 (1.9)[b]
Grade chronic pain scale-other(%)*,[a,b,c]				
GCPS-0	88.3	45.2	59.0	29.7
GCPS-I	10.6	16.6	18.1	14.9
GCPS-II	1.1	19.8	16.9	23.0
GCPS-III	0	12.1	6.0	18.9
GCPS-IV	0	6.4	0	13.5

Abbreviations: TMD, temporomandibular disorders; WPT, widespread palpation tenderness; w/o, without; 6-mon, 6 months; GCPS, Grade Chronic Pain Scale; MPQ, McGill Pain Questionnaire-Short Form.

Note: Number of study subjects included in each group for pain characteristics varies based on available information.

For controls: n=180–181; for TMD cases: n=151–159 (TMD without WPT: 77~83, TMD with WPT: 71~76)

Controls vs. all TMD cases: p<0.003

[a]Controls vs. TMD without (w/o) WPT: p<0.003

[b]Controls vs. TMD with WPT: p<0.003

[c]TMD w/o WPT vs. TMD with WPT: p<0.003

Table 1c

Characteristics of the study population – experimental pain measures

Characteristic	Controls Mean(SD)	All TMD cases Mean(SD)	TMD w/o WPT Mean(SD)	TMD with WPT Mean(SD)
Heat Pain (C°)				
Threshold	42.5 (2.1)	42.5 (2.2)	42.5 (2.0)	42.6 (2.3)
Tolerance	47.2 (1.4)	47.0 (1.8)	47.3 (1.4)	46.7 (2.1)
Delta (Tolerance – Threshold)	4.7 (2.0)	4.5 (2.1)	4.8 (1.9)	4.1 (2.2)
PPT in Facial Region (kg/cm^2)				
Temporalis*	3.2 (0.7)	2.3 (0.7)	2.6 (0.6)^{a,c}	2.1 (0.7)^{b,c}
Masseter*	3.0 (0.8)	1.9 (0.6)	2.0 (0.6)^{a}	1.9 (0.7)^{b}
Temporomandibular Joint*	3.1 (0.7)	2.1 (0.7)	2.2 (0.6)^{a}	2.0 (0.7)^{b}
PPT in Non-facial Region (kg/cm^2)				
Trapezius*	4.5 (1.2)	3.7 (1.3)	4.2 (1.2)^{c}	3.2 (1.2)^{b,c}
Lateral Epicondyle*	5.2 (1.1)	4.5 (1.3)	5.0 (1.1)^{c}	4.0 (1.2)^{b,c}

Abbreviations: TMD, temporomandibular disorders; WPT, widespread palpation tenderness; w/o, without; PPT: pressure pain threshold.

Note: Number of study subjects included in each group varies based on available information.

For controls: n=180–181; for TMJD cases: n=151–159 (TMD without WPT: 77~83, TMD with WPT: 71~76)

Controls vs. all TMD cases: $p<0.006$

^{a}Controls vs. TMD without WPT: $p<0.006$

^{b}Controls vs. TMD with WPT: $p<0.006$

^{c}TMD without WPT vs. TMD with WPT: $p\leq0.006$

Table 2

Characteristics of the study population – psychological characteristics

Characteristic	Controls Mean(SD)	All TMD cases Mean(SD)	TMD w/o WPT Mean(SD)	TMD with WPT Mean(SD)
Perceived stress*	17.0 (4.6)	20.4 (5.3)	20.6 (5.5)[a]	20.3 (5.3)[b]
STAI				
State anxiety*	29.9 (6.5)	34.5 (7.6)	34.4 (7.1) [a]	34.6 (8.2)[b]
Trait anxiety*	32.7 (8.3)	37.8 (9.7)	37.9 (9.3) [a]	37.7 (10.1)[b]
SCL-90-R depression*	16.4 (4.3)	19.8 (6.9)	18.9 (5.7)[a]	20.9 (7.8)[b]
Pain catastrophizing scale*	6.8 (6.3)	11.2 (10.6)	10.7 (9.9) [a]	11.8 (11.4)[b]
Somatic awareness*	88.8 (17.6)	115.4 (24.6)	107.6 (21.8) [a,c]	123.8 (24.9)[b,c]
POMS-BI				
Agreeable-hostile*	30.4 (4.8)	27.6 (5.9)	28.1 (5.9) [a]	27.0 (5.9)[b]
Elated-depressed*	28.4 (5.8)	25.2 (6.7)	25.9 (6.2)[a]	24.4 (7.2)[b]
Confident-unsure*	26.2 (5.8)	23.5 (6.5)	24.2 (6.0)	22.7 (6.9)[b]
Energetic-tired*	25.4 (7.5)	19.5 (8.4)	21.6 (7.5)[a]	17.1 (8.9)[b]
Clearheaded-confused*	30.0 (5.4)	27.7 (6.3)	28.4 (5.5)	26.7 (7.1)[b]
Composed-anxious*	28.8 (5.9)	24.8 (6.7)	25.0 (6.6)[a]	24.4 (6.7)[b]

Abbreviations: TMD, temporomandibular disorders; WPT, widespread palpation tenderness; w/o, without; STAI, Spielberger State-Trait Anxiety Inventory; POMS-BI, Profile of Mood States-Bi-Polar; SCL-90-R, Symptoms Checklist – 90 Revised.

Note: Number of study subjects included in each group for age and all psychological measures:

1. Controls: maximum 181, range 168–181
2. All TMD cases: maximum 159, range 149–159
3. TMD without WPT: maximum 83, range 78–83
4. TMD with WPT: maximum 76, range 68–76

Controls vs. all TMD cases: $p<0.004$

[a] Controls vs. TMD without (w/o) WPT: $p<0.004$

[b] Controls vs. TMD with WPT: $p<0.004$

[c] TMD w/o WPT vs. TMD with WPT: $p<0.004$

Table 3

Percentage of people reporting persistent pain conditions in TMD cases and controls

Conditions	Controls (%)	All TMD cases (%)	TMD w/o WPT (%)	TMD with WPT (%)
Fibromyalgia *	0	18.2	1.2 *c*	36.8 *a,c*
Chronic fatigue syndrome *	0.6	9.6	0 *c*	20.3 *a,c*
Irritable bowel syndrome *	5.0	22.6	14.5	31.6 *b*
Interstitial cystitis	1.1	1.3	2.4	0
Chronic pelvic pain*	0.6	7.0	2.4	12.0 *b*
Frequent headaches*	21.4	86.2	83.1 *a*	89.5 *b*
Frequent low back pain*	6.3	25.2	16.1	35.3 *a,c*

Abbreviations: TMD, temporomandibular disorders; WPT, widespread palpation tenderness; w/o, without.

Note: Number of study subjects included in each group:

1. Controls: maximum 181, range 175–181
2. All TMD cases: maximum 159, range 155–159
3. TMD without WPT: maximum 83, range 81–83
4. TMD with WPT: maximum 76, range 74–76

Controls vs. all TMD cases: $p<0.007$

a Controls vs. TMD without (w/o) WPT: $p<0.007$

b Controls vs. TMD with WPT: $p<0.007$

c TMD w/o WPT vs. TMD with WPT: $p<0.007$

Table 4a

Characteristics of subjects reporting 0–1 and ≥2 persistent pain conditions

	0~1 pain conditions	≥ 2 pain conditions
	Mean (SD)	Mean (SD)
Age (in years) *	30.6 (11.2)	40.5 (12.1)
Facial Pain duration from onset (months) *	39.6 (78.9)	117.6 (109.7)
Average facial pain intensity (past 6-mon) *	1.7 (2.6)	4.5 (2.5)
Impact due to facial pain (past 6-mon)		
Missed usual activities (days) *	2.5 (15.6)	6.1 (16.6)
Reduced efficiency to <50% (days) *	8.8 (48.4)	17.1 (31.4)
Facial pain in the past 1–2 weeks		
1. Average intensity *	13.3 (21.9)	38.7 (26.3)
2. Highest intensity *	20.9 (31.6)	54.8 (31.0)
3. Lowest intensity *	4.9 (12.1)	17.1 (19.0)
5. % of wake days with pain *	15.7 (28.6)	55.1 (35.7)
6. Unpleasantness rating *	2.7 (4.4)	8.0 (4.7)
Grade chronic pain scale-facial pain (%) *		
GCPS-0	65.1	12.7
GCPS-I	16.9	33.8
GCPS-II	15.3	42.3
GCPS-III	0.8	7.0
GCPS-IV	1.9	4.2

Abbreviations: TMD, temporomandibular disorders; WPT, widespread palpation tenderness; w/o, without; 6-mon, 6 months; GCPS, Grade Chronic Pain Scale.

Note: Number of study subjects included in each group for clinical pain measures:

1. 0–1 pain condition group: range 258–265;
2. ≥2 pain conditions group: range 71–75.

* P<0.004

Table 4b

Subject characteristics by reporting different numbers of persistent pain conditions – other clinical pain characteristics

	0~1 pain conditions	≥ 2 pain conditions
	Mean (SD)	**Mean (SD)**
MPQ		
1. Affective *	13.3 (4.0)	17.2 (5.8)
2. Sensory *	4.4 (0.8)	5.3 (2.0)
Grade chronic pain scale-other pain (%) *		
GCPS-0	78.3	32.4
GCPS-I	12.9	14.9
GCPS-II	6.8	20.3
GCPS-III	1.5	20.3
GCPS-IV	0.4	12.2
% of cases-controls within each group *		
Controls	62.3	10.7
TMD without WPT	23.0	29.3
TMD with WPT	11.7	60.0

Abbreviations: GCPS, Grade Chronic Pain Scale; MPQ, McGill Pain Questionnaire-Short Form.

Note: Number of study subjects included in each group for clinical pain measures:

1. 0–1 pain condition group: range 258–265;
2. ≥2 pain conditions group: range 71–75.

* $P<0.003$

Table 4c

Subject characteristics by reporting different numbers of persistent pain conditions – experimental pain measures

Characteristic	0~1 pain conditions	≥ 2 pain conditions
	Mean (SD)	Mean (SD)
Heat Pain (C°)		
Threshold	42.5 (2.1)	42.6 (2.2)
Tolerance	47.2 (1.4)	46.7 (2.1)
Delta (Tolerance – Threshold)	4.7 (1.9)	4.1 (2.2)
PPT in Facial Region (kg/cm^2)		
Temporalis *	3.0 (0.8)	2.3 (0.7)
Masseter *	2.7 (0.9)	2.0 (0.7)
Temporomandibular Joint *	2.8 (0.8)	2.1 (0.7)
PPT in Non-Facial Regions (kg/cm^2)		
Trapezius *	4.3 (1.3)	3.6 (1.2)
Lateral Epicondyle *	5.0 (1.2)	4.3 (1.2)

Abbreviations: PPT, pressure pain threshold

Note: Number of study subjects included in each group varies based on available information.

* $p<0.006$

Table 5

Subject characteristics by reporting different numbers of persistent pain conditions – psychological characteristics

	0~1 pain conditions Mean (SD)	≥ 2 pain conditions Mean (SD)
Perceived stress *	17.9 (5.1)	21.2 (4.9)
STAI		
State anxiety *	31.1 (6.7)	35.6 (8.6)
Trait anxiety *	34.0 (9.0)	39.0 (9.3)
SCL-90-R depression *	17.1 (5.1)	21.1 (7.3)
Pain catastrophizing scale *	8.0 (8.1)	12.1 (10.5)
Somatic awareness *	94.9 (20.8)	124.1 (25.5)
POMS-BI		
Agreeable-hostile *	29.9 (5.0)	26.6 (6.5)
Elated-depressed *	27.8 (6.0)	23.9 (6.8)
Confident-unsure *	25.7 (6.0)	22.4 (6.6)
Energetic-tired *	24.4 (7.6)	16.5 (8.6)
Clearheaded-confused *	29.7 (5.4)	25.9 (6.8)
Composed-anxious *	27.9 (6.2)	23.6 (6.7)

Abbreviations: STAI, Spielberger State-Trait Anxiety Inventory; SCL-90-R, Symptoms Checklist – 90 Revised; POMS-BI, Profile of Mood States-Bi-Polar.

Note: Number of study subjects included in each group for age and all psychological measures:

1. 0–1 pain condition group, range 247–265;
2. ≥2 pain conditions group, range 69–75.

* $p<0.004$

Table 6

Unadjusted and adjusted odds ratios comparing subject characteristics reporting multiple persistent pain conditions

	Model 1 Odds Ratio (95% CI)	Model 2 Odds Ratio (95% CI)	Model 3 Odds Ratio (95% CI)
Control	1.0 (reference)	1.0	1.0
TMD without WPT	6.5 (2.7, 15.6)	5.8 (2.4, 14.2)	3.3 (1.3, 8.4)
TMD with WPT	32.5 (13.7, 77.0)	23.1 (9.6, 55.9)	8.4 (3.1, 22.8)
Age-z	NA	1.8 (1.3, 2.4)	1.9(1.4, 2.7)
Somatic symptoms-z	NA	NA	2.3 (1.5, 3.6)

Abbreviations: CI, confidence interval; TMD, temporomandibular disorders; WPT, widespread palpation tenderness; NA, not applicable; z, standardized z score, one unit change equals one standard deviation change.

Note: For all models, n=315 with participants who have complete information on all tested variables in the final model (i.e., Model 3).

Model 1: unadjusted logistic regression model

Model 2: adjusted for age

Model 3: adjusted for age and somatic symptoms (PILL)