

# A Controlled Study of Biopsychosocial Differences Observed in Masticatory Myalgia With and Without Pain Referral

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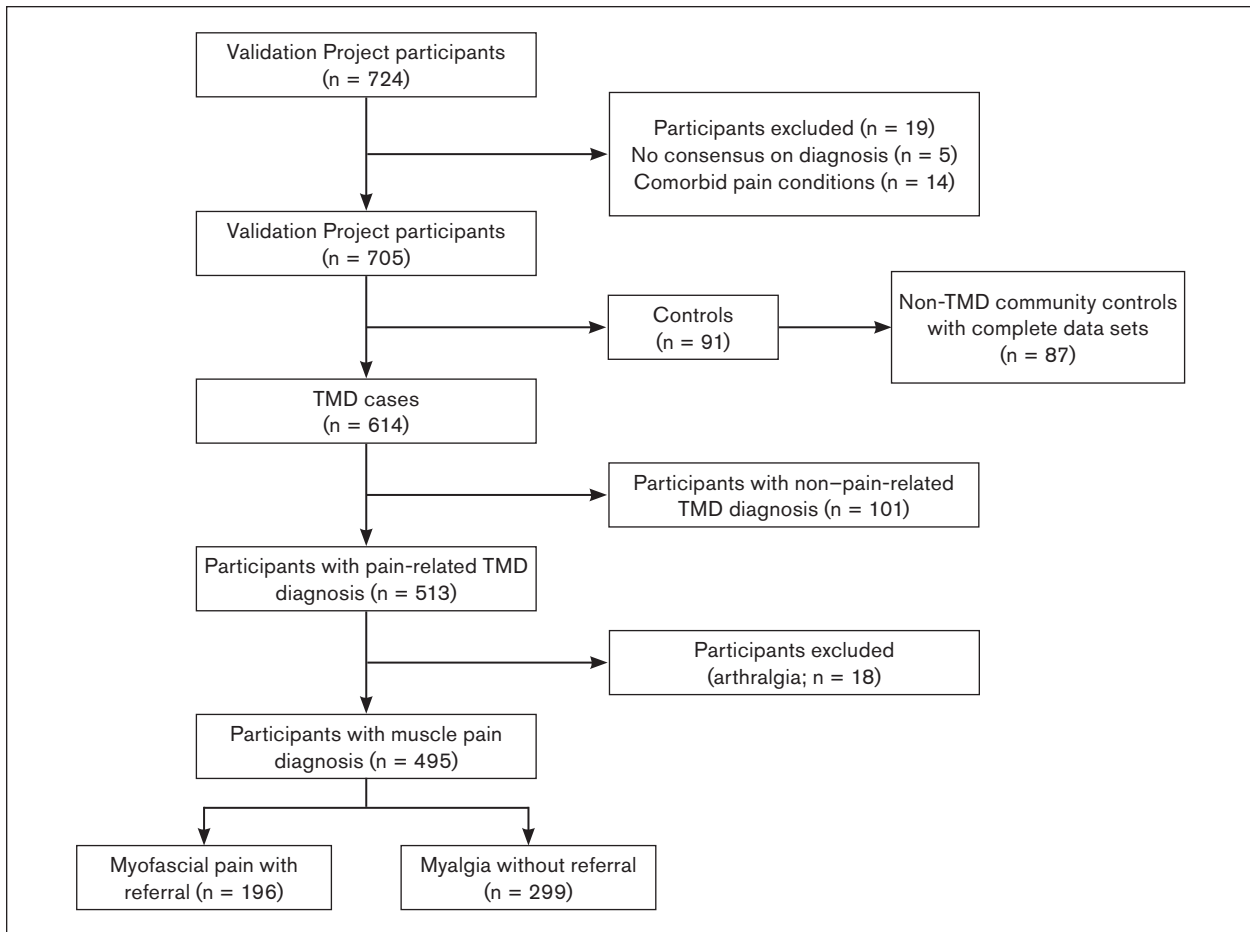
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**Aims:** To assess differences in biopsychosocial factors between participants with masticatory myofascial pain with referral (MFPwR), with myalgia without referral (Mw/oR), and community controls without TMDs. **Methods:** Study participants were diagnosed with MFPwR (n = 196), Mw/oR (n = 299), or as a non-TMD community control (n = 87) by two calibrated examiners at each of three study sites. Pain chronicity, pain on palpation of masticatory muscle sites, and pressure pain thresholds (PPT) at 12 masticatory muscle, 2 trigeminal, and 2 nontrigeminal control sites were recorded. Psychosocial factors assessed included anxiety, depression, and nonspecific physical symptoms (Symptom Checklist-90 Revised); stress (Perceived Stress Scale); and health-related quality of life (Short Form Health Survey). Comparisons among the three groups were adjusted for age, sex, race, education, and income using multivariable linear regression. The significance threshold was set at  $P = .017$  ( $.05 / 3$ ) for subsequent pairwise comparisons. **Results:** Compared to the Mw/oR group, the MFPwR group had significantly greater pain chronicity, number of painful muscle sites, anxiety, depression, nonspecific physical symptoms, and impaired physical health ( $P < .017$ ). The MFPwR group also had significantly lower PPTs for masticatory sites ( $P < .017$ ). Both muscle pain groups differed significantly from the non-TMD community control group for all outcome measures ( $P < .017$ ). **Conclusion:** These findings support the clinical utility of separating MFPwR from Mw/oR. Patients with MFPwR are more complex from a biopsychosocial perspective than Mw/oR patients, which likely affects prognosis and supports consideration of these factors in case management. *J Oral Facial Pain Headache* 2023;37:131–138. doi: 10.11607/ofph.3317

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The term *temporomandibular disorders* (TMDs) is a collective term for pain and dysfunction of the masticatory muscles and/or temporomandibular joints (TMJs).<sup>1</sup> The Diagnostic Criteria for TMD (DC/TMD), which are based on the biopsychosocial model of pain, provide reliable and valid Axis I criteria for physical diagnoses and Axis II instruments for assessing behavioral and psychosocial contributing factors.<sup>2</sup> The intent of this dual axis is to provide a physical diagnosis and to identify other relevant factors that could influence the expression and management of a specific case of TMDs.

The most common DC/TMD pain-related diagnoses are masticatory myalgia, TMJ arthralgia, and headache attributed to TMDs.<sup>2</sup> Masticatory myalgia is further subdivided into three types differentiated by provocation testing with palpation: local myalgia, myofascial pain (MFP), and MFP with referral (MFPwR). The diagnostic criteria for masticatory myalgia, as well as the criteria for the MFPwR type of myalgia, have shown acceptable criterion validity using the reference standard of the validation project for the original Research Diagnostic Criteria for TMD.<sup>2,3</sup> Investigation of differences in the clinical presentation of MFPwR compared to the two other types of myalgia (local myalgia and MFP) will provide insight into the clinical utility of this distinction.<sup>4,5</sup> There have been recent reports of differences in biopsychosocial factors associated with MFPwR in retrospective clinical studies of limited size.<sup>6–8</sup>



**Fig 1** Flowchart showing participant inclusion.

The subset of participants from the validation project diagnosed with myalgia and further differentiated into the three types of myalgia provided an opportunity to study a larger sample, with the additional benefit of a non-TMD community control group.<sup>3</sup> Select biopsychosocial factors were compared among a group of participants with MFPwR, a group with local myalgia or myofascial pain (Mw/oR), and a non-TMD community control group. The aims were to investigate potential differences in (1) pain characteristics, including pain chronicity, the number of painful sites, and pain sensitivity to pressure in trigeminal and non-trigeminal sites; and (2) psychosocial characteristics, including patient-reported anxiety, depression, nonspecific physical symptoms, perceived stress, and health-related quality of life (HRQoL). It was hypothesized a priori that participants with MFPwR compared to participants in the combined Mw/oR group and non-TMD community controls would have (1) the greatest pain chronicity, the most painful sites, and the lowest pain pressure thresholds (PPT) with the greatest generalized pain sensitivity; and (2) generally worse psychosocial measures in terms of anxiety,

depression, nonspecific physical symptoms, perceived stress, and HRQoL.

## Materials and Methods

This cross-sectional observational Validation Project conformed to STROBE guidelines for human observational investigations.<sup>9</sup> The Institutional Review Boards at the University of Minnesota (no. 1107M01921), the University of Washington (no. 41390A), and the University at Buffalo (no. SIS0870911B) approved the study. Written informed consent was obtained from all study participants. Participants were compensated \$200.

### Study Sample

Participants were recruited from 2003 to 2006 at the University of Minnesota, the University of Washington, and the University at Buffalo. Details regarding the project's methods, including inclusion/exclusion criteria and participants' clinical characteristics, have been reported previously.<sup>3</sup> Figure 1

describes the flow of participants into the study groups. The two groups with myalgia included 495 total participants: the MFPwR group with 196 and the Mw/oR combined group with 299. The non-TMD community control group included 87 participants.

### Clinical Assessment and Diagnoses

Two calibrated orofacial pain experts at each site used a semi-structured interview that included a review of questionnaire responses and a comprehensive exam to independently examine participants and establish consensus-based TMD criterion diagnoses for cases with myalgia, including the differentiation of the three types of myalgia, and to identify non-TMD community controls. All three types of myalgia have content validity, as their criteria were developed by the expert panel of the Validation Project based on the current literature available at that time. Reliability ( $\kappa = 0.85$ ) and criterion validity (sensitivity = 0.86; specificity = 0.98) using a credible reference standard have been previously reported for MFPwR.<sup>2</sup>

Participants in the MFPwR group presented with familiar pain at the site of muscle palpation and a report of familiar pain beyond the boundary of the muscle being palpated. Participants in the Mw/oR group met the criteria for either the local myalgia or the MFP (without referral) types of myalgia. The Mw/oR group demonstrated familiar pain at the site of muscle palpation, with any familiar pain spreading on palpation confined within the boundary of the muscle being palpated. Mw/oR is not a recognized DC/TMD type of myalgia, but it is a convenient and accurate description of the participants included in this combined group of myalgia types. Non-TMD community controls were normal pain-free participants with no TMD diagnosis. The complete diagnostic criteria for the three types of myalgia as used in this project have since been included in the DC/TMD criteria.<sup>2,10</sup> Note that in the context of the DC/TMD, *familiar pain* is defined as pain like or similar to the participant's pain complaint. Muscle pain on palpation and pain referral were provoked with calibrated application of 1.0 kg of force with a single finger for 5 seconds to multiple sites covering the entire surface of the temporalis and masseter muscles.

### Outcomes

#### **Pain characteristics.**

##### *Pain chronicity.*

Participants completed questions from the history questionnaire of the RDC/TMD,<sup>3</sup> which included chronicity in years of pain in the face, jaw, jaw joint, and temple.

##### **Number of painful sites on palpation.**

Manual muscle palpation was applied bilaterally to three temporalis muscle regions, three masseter

muscle regions, the posterior mandibular regions, the submandibular regions, the lateral pterygoid areas, and the temporalis muscle tendons, for a total of 20 muscle sites for each participant. Pain on palpation of each site was noted as present or absent by the participant. If present, the pain required confirmation by the participant as their "familiar pain." A TMD palpation composite score for the number of painful sites was the sum of positive responses to palpation of these 20 sites.

##### **Pressure pain threshold.**

PPTs were quantitatively assessed using a pressure algometer (Somedic Algometer, Somedic). Increasing pressure was applied at a rate of 30 kPa/second with a 1.0-cm<sup>2</sup> probe to each site with a minimum of 3 seconds between repeated stimuli. Participants terminated each measurement with a switch when they perceived the pressure as painful. The PPT was bilaterally assessed for three temporalis muscle sites, three masseter muscle sites, the frontalis (trigeminal control site), and the lateral palm site, located on the palm just below the palmar crease of the little finger and 1 cm medial to the lateral border of the palm (nontrigeminal control site). The average of two measurements from each site was used in this analysis. Greater pain sensitivity was associated with lower values.

##### **Psychosocial characteristics.**

Participants self-reported the following data using standardized reliable and valid instruments.

##### *Symptom Checklist-90 Revised*

The Symptom Checklist-90 Revised (SCL-90R) is a 90-item self-report questionnaire where each item represents a symptom of psychologic distress and is rated on a 5-step ordinal scale, with 0 being "not at all" and 4 being "extremely" in terms of how bothersome the symptom has been within the past 7 days.<sup>11</sup> The symptoms are assigned to 9 dimensions, including anxiety, depression, and nonspecific physical symptoms (somatization), which have shown good reliability and validity in previous TMD investigations.<sup>12-14</sup> For each of these 3 dimensions, the statistical analysis used the mean score derived by adding the values (0 to 4) and dividing by the number of items endorsed in that dimension.<sup>15</sup> In the case of missing responses, if at least 2 out of 3 items in a dimension had responses, the score was created as a sum of the provided responses divided by the number of valid responses. If at least 2 out of 3 were not provided, the score was not included.

##### *Perceived Stress Scale.*

The Perceived Stress Scale (PSS) is a 10-item self-report instrument measuring the degree to which respondents appraise situations as stressful and the extent to which they perceive themselves as capable of coping with the situations.<sup>16</sup> Responses are on a

**Table 1 Demographics of Participants with MFPwR (Group 1), Mw/oR (Group 2), and the Non-TMD Community Control Group (Group 3)**

Characteristic	Group 1 (n = 196)	Group 2 (n = 299)	Group 3 (n = 87)	P value for differences among groups	P values for pairwise comparisons between groups
Age (y), mean (SD)	37.8 (12.6)	35.6 (13.4)	36.0 (12.8)	.18	
Sex (female), n (%)	178 (90.8)	253 (84.6)	53 (60.9)	< .0001*	1 vs 2: .04 1 vs 3: < .0001* 2 vs 3: < .0001*
Race (non-Hispanic white), n (%)	182 (92.9)	264 (88.3)	71 (81.6)	.020*	1 vs 2: .10 1 vs 3: .005* 2 vs 3: .11
Education (> 16 y), n (%)	44 (22.6)	77 (25.8)	25 (28.7)	.75	
Income (> \$40,000), n (%)	107 (55.7)	151 (51.0)	28 (32.6)	.001*	1 vs 2: .31 1 vs 3: .0004* 2 vs 3: .003*

\*Statistically significant. The thresholds of statistical significance were  $P < .05$  for differences among groups and  $P < .017$  for pairwise comparisons.

5-category ordinal scale: never, almost never, sometimes, fairly often, and very often. The overall perceived stress score is a sum of the numeric weights of each item after reverse scoring 4 items; the lower the number, the lower the perceived stress. Good internal consistency has been demonstrated, with a Cronbach alpha of 0.86 and moderate convergent, concurrent, and predictive validity.<sup>17-19</sup>

*Short Form-12, version 2*

The Short-Form 12, version 2 (SF-12) is a self-report instrument assessing HRQoL<sup>20,21</sup> composed of two scales, a Physical Component Summary (PCS) and a Mental Component Summary (MCS), with each scale transformed to a mean of 50 and an SD of 10 when applied to the general US population. Low scores indicate poor HRQoL, and high scores reflect well-being. The PCS measures the impact of health on limitations with any physical activity, including climbing chairs, moving heavy objects, household work, and low-impact sports such as bowling and golf. The MCS evaluates the frequency of feelings of nervousness, depression, happiness, and calmness.

**Statistical Methods**

To describe differences among the three groups, mean and SD values are presented for continuous measures and proportions for dichotomous measures (eg, sex). Pearson chi-square test was used to test for differences in categorical measures. For pain chronicity, anxiety, depression, nonspecific physical symptoms, and number of sites with pain, which had skewed distributions, Kruskal-Wallis test was used. A general linear model (GLM) was used for the multivariable linear regression to compare groups, adjusting for age, sex, race, education, and income, as GLM is not sensitive to skewed data with a large sample size. For post hoc pairwise compari-

son between groups, the threshold of statistical significance was set at  $P = .017$  ( $0.05 / 3$ ).

**Results**

**Demographics**

Table 1 shows participant demographic characteristics. The groups did not differ significantly for age or education, but did for sex, race, and income ( $P < .05$ ), with the highest proportions of female, non-Hispanic white, and highest income in the MFPwR group, followed in order by the Mw/oR and non-TMD community control groups. Multivariable linear regression was used to adjust for age, sex, race, education, and income.

**Pain characteristics.**

*Pain chronicity and number of painful sites on palpation.*

Both pain chronicity and number of painful sites on palpation were significantly higher in the MFPwR group compared to the Mw/oR group ( $P < .017$ ; Table 2).

Pressure pain threshold.

The PPTs differed significantly between groups for all pairwise comparisons ( $P < .017$ ), except for between the MFPwR group and the Mw/oR group for the two nonmasticatory sites (the frontalis muscle and the lateral palm).

**Psychosocial characteristics.**

*Symptom Checklist-90 Revised.*

Using the SCL-90R, the MFPwR group had the highest adjusted mean scores for anxiety, depression, and nonspecific physical symptoms. The Mw/oR group scores were greater than the non-TMD community control group. The adjusted scores for anxiety, depression, and nonspecific physical symptoms

**Table 2 Pain Chronicity, Number of Painful Muscle Sites, and PPTs by Site for the MFPwR (Group 1), Mw/oR (Group 2), and Non-TMD Control (Group 3) Groups**

Measure	Group 1 (n = 196)	Group 2 (n = 299)	Group 3 (n = 87)	P value for differences among groups	P value for pairwise comparisons between groups
Pain chronicity, y	10.1 (9.2)	7.9 (8.3)	0	.008*	1 vs 2: .009*
No. of painful muscle sites (0–20)	10.3 (0.5)	6.2 (0.4)	0	< .0001*	1 vs 2: < .0001* 1 vs 3: < .0001* 2 vs 3: < .0001*
PPT for masseter muscle, kPa	147 (5.3)	159 (4.6)	209 (6.0)	< .0001*	1 vs 2: .005* 1 vs 3: < .0001* 2 vs 3: < .0001*
PPT for temporalis muscle, kPa	182 (6.6)	196 (5.7)	248 (7.4)	< .0001*	1 vs 2: .008* 1 vs 3: < .0001* 2 vs 3: < .0001*
PPT for frontalis muscle, kPa	211 (6.8)	223 (5.9)	279 (7.6)	< .0001*	1 vs 2: .03 1 vs 3: < .0001* 2 vs 3: < .0001*
PPT for lateral palm, kPa	405 (13.0)	410 (11.1)	497 (14.5)	< .0001*	1 vs 2: .64 1 vs 3: < .0001* 2 vs 3: < .0001*

All data are reported as mean (SE). \*Statistically significant. The thresholds of statistical significance were  $P < .05$  for differences among groups and  $P < .017$  for pairwise comparisons.

**Table 3 Anxiety, Depression, Nonspecific Physical Symptoms, Perceived Stress, and HRQoL for the MFPwR (Group 1), Mw/oR (Group 2), and Non-TMD Control (Group 3) Groups**

Measure	Group 1 (n = 196)	Group 2 (n = 299)	Group 3 (n = 87)	P value for differences among groups	P value for pairwise comparison between groups
Anxiety, SCL-90R (0–4)	0.46 (0.06)	0.33 (0.05)	0.09 (0.06)	< .0001*	1 vs 2: .004* 1 vs 3: < .0001* 2 vs 3: .0002*
Depression, SCL-90R (0–4)	0.64 (0.06)	0.50 (0.05)	0.26 (0.07)	< .0001*	1 vs 2: .004* 1 vs 3: .0001* 2 vs 3: .0003*
Nonspecific physical symptoms, SCL-90R (0–5)	0.79 (0.05)	0.53 (0.05)	0.13 (0.06)	< .0001*	1 vs 2: .0001* 1 vs 3: .0001* 2 vs 3: .0001*
Perceived stress, PSS (0–100)	14.2 (0.8)	13.8 (0.7)	10.2 (0.9)	< .0001*	1 vs 2: .55 1 vs 3: .0001* 2 vs 3: .0001*
PCS, SF-12 (0–100)	49.7 (0.9)	52.5 (0.8)	55.4 (1.0)	< .0001*	1 vs 2: .0002* 1 vs 3: .004* 2 vs 3: .0001*
MCS, SF-12 (0–100)	48.3 (1.1)	48.5 (0.9)	52.3 (1.2)	.004*	1 vs 2: .77 1 vs 3: .002* 2 vs 3: .002*

Data are reported as adjusted mean (SE). \*Statistically significant. The thresholds of statistical significance were  $P < .05$  for differences among groups and  $P < .017$  for pairwise comparisons.

differed significantly among the three groups ( $P < .05$ ), and all pairwise comparisons differed significantly ( $P < .017$ ; Table 3).

Perceived Stress Scale.

The MFPwR group had the highest adjusted mean PSS, followed by the Mw/oR and the non-TMD community control groups, respectively. The MFPwR and the Mw/oR groups did not differ significantly, but both groups differed significantly from the non-TMD community control group ( $P < .017$ ).

Short Form-12, version 2.

The adjusted scores for PCS and MCS differed significantly among the three groups. The MFPwR group had the lowest adjusted score for both physical and mental health, followed by the Mw/oR group and the non-TMD community control group. For PCS, all pairwise comparisons showed significant differences ( $P < .017$ ). The two muscle groups did not differ significantly for MCS, but both groups differed significantly from the non-TMD community control group ( $P < .017$ ).

## Discussion

A consistent pattern of differences in biopsychosocial factors in individuals diagnosed with MFPwR compared to Mw/oR and the non-TMD community controls was found. Those with MFPwR had significantly greater pain chronicity, more painful sites, and lower PPTs in trigeminal sites (ie, the highest pain sensitivity). Participants with MFPwR also had significantly higher rates of self-reported symptoms of anxiety, depression, and nonspecific physical symptoms and a lower physical component of HRQoL. The two muscle pain groups did not differ significantly for perceived stress or the mental component of HRQoL.

The only difference in diagnostic criteria distinguishing the DC/TMD type of myalgia (MFPwR) from the two myalgia types without referral (local myalgia and MFP) is the clinical provocation of familiar pain at a site distant from the muscle being palpated with 1.0 kg of force for 5 seconds. These findings suggest that the presence of referred pain is associated with more complex pain and psychosocial characteristics.

The age and sex distributions in this TMD sample were similar to other studies involving clinical cases of TMDs, with more women than men and with a peak prevalence during reproductive ages.<sup>1,22</sup> The non-TMD community control group differed from the pain groups in sex, race, and income, which were adjusted for in the multivariable linear regression model.

Previous studies have compared biopsychosocial factors in participants identified with generalized masticatory myalgia diagnoses to pain-free controls and to nonpainful TMJ articular diagnoses. There are also a limited number of more recent investigations using the DC/TMD diagnosis of MFPwR for comparison to types of myalgia without the clinical signs of referral.<sup>7,8</sup>

### Pain Characteristics

#### ***Pain chronicity and number of sites painful to palpation.***

Masticatory muscle pain of greater chronicity was associated with more painful sites in an investigation by Rammelsberg et al.<sup>23</sup> These results are consistent with the present study, as MFPwR had significantly greater pain chronicity and more painful sites compared to Mw/oR. Widespread pain outside the head and neck region was more frequent in MFPwR compared to Mw/oR in another clinical sample.<sup>7</sup> Although this study did not assess the presence of widespread pain beyond the trigeminal region, the observation of more sites painful to palpation is consistent with this broader pain pattern.

#### ***Pain pressure threshold.***

Several studies have found that TMD patients with muscle pain have significantly lower PPTs in masticatory muscles than healthy controls.<sup>24–27</sup> Higher pain

sensitivity has also been reported for nontrigeminal sites among TMD patients compared to controls, suggesting that central sensitization may be a factor.<sup>26–30</sup> These findings are consistent with the observed masticatory muscle and nontrigeminal PPTs in the present study, which were significantly lower for both MFPwR and Mw/oR compared to controls.

### Psychosocial Characteristics

In the present study, both muscle pain groups had greater psychologic distress compared to controls, with significantly higher scores for anxiety, depression, nonspecific physical symptoms, and lower HRQoL. This is consistent with other studies in which TMD patients displayed higher levels of anxiety, depression, catastrophizing, and psychologic distress in comparison to controls and patients with TMJ disorders without pain, as measured using a variety of assessment instruments.<sup>24,31–33</sup> A significant association of psychologic disorders with masticatory muscle disorders, but not for TMJ disorders, was reported by Kight et al.<sup>34</sup> Psychosocial measures were compared between patients with chronic MFP and TMD-free controls, and the MFP group scored higher for the anxiety, depression, and nonspecific physical symptoms scales of the SCL-90R in a case-control study.<sup>15</sup> TMD cases also had higher mean scores than non-TMD controls across all SCL-90R subscales in the OPPERA case-control study.<sup>35</sup>

Significant differences in anxiety, depression, and nonspecific physical symptoms between patients diagnosed with MFPwR and local myalgia using the DC/TMD have been reported.<sup>9</sup> Although these groups did not differ in pain chronicity, these findings are largely consistent with the current study.

In previous studies, TMD participants have reported greater stress compared to pain-free controls.<sup>35,36</sup> Higher mean PSS scores in an MFP group compared to controls were reported by Maślak-Bereś et al.<sup>37</sup> Baseline measures of perceived stress using the PSS were significant predictors of new-onset TMD in a prospective sample of healthy young women, as reported by Slade et al.<sup>38</sup> These outcomes are consistent with the present study's results, as mean PSS scores were significantly higher in the muscle pain groups compared to the control group.

Lower HRQoL compared to healthy controls using the SF-12 has been found for a variety of chronic pain conditions, such as fibromyalgia,<sup>39</sup> tension-type headache,<sup>40</sup> and migraine.<sup>41</sup> The SF-12 PCS and MCS were both lower (indicating poorer function and lower HRQoL) for TMD cases vs controls in the OPPERA case-control study.<sup>27</sup> These results are consistent with the lower HRQoL of the present masticatory myalgia participants.

In addition to statistical significance, the clinical importance of these differences must be considered. In terms of pain-related measures, the greater chronicity of pain, more painful sites, and higher pain sensitivity observed with MFPwR are all features generally thought to be associated with poorer clinical prognosis and a more difficult clinical course. In the clinical setting, SCL-90R levels of depression have been previously categorized as normal (< 0.5), moderate (0.5 to 1.1), and severe (> 1.1). Levels of nonspecific symptoms (somatization) have also been categorized as normal (< 0.5), moderate (0.5 to 0.99), and severe (> 0.99).<sup>12,13,42</sup> Using these clinical categories, the MFPwR group in the present study had, on average, both moderate depression and moderate nonspecific physical symptoms, in contrast with the Mw/oR group, which had normal levels on average. The MFPwR group also reported greater symptoms of anxiety and lower physical HRQoL compared to Mw/oR. Previous clinical reports and the broad scope of the differences observed in this study give strong support to the clinical importance of distinguishing MFPwR from masticatory muscle pain without referral.

The primary limitation of the study is that it is a secondary analysis of a convenience sample specifically recruited to include an appropriate mix of TMD pain conditions necessary to test the diagnostic accuracy of TMD diagnostic criteria.<sup>3</sup> Also, data regarding specific referral patterns (eg, dental pain) were not collected. However, the present study included a large sample typical of TMD subjects described in other studies, as well as settings enabling multiple comparisons of a wide range of biopsychosocial variables among different masticatory muscle pain subtypes.

## Conclusions

These findings suggest the following:

- Diagnosis of MFPwR is associated with increased complexity of pain characteristics, including greater pain chronicity, more painful sites, and greater pain sensitivity, compared to masticatory muscle pain without referral.
- Diagnosis of MFPwR is associated with increased complexity of psychosocial symptoms, including greater anxiety, depression, nonspecific physical symptoms, perceived stress, and lower physical HRQoL, compared to those with masticatory muscle pain without referral and those without pain.
- Assessment and management of the associated biopsychosocial signs and symptoms is an important component of care for those diagnosed with MFPwR.

## Clinical Implications and Key Findings

These results support the clinical utility for distinguishing MFPwR from masticatory muscle pain without referral. Patients with MFPwR are more complex from a biopsychosocial perspective than Mw/oR patients, which likely affects prognosis and supports consideration of these factors in case management.

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Drs Varun, Anderson, and Schiffman contributed to the study design, interpretation of results, and writing and editing of the manuscript. Dr Hodges directed the data analysis and interpretation of the results and contributed to the editing of the manuscript. Lei Zhang performed the statistical analysis, interpreted the results, and contributed to the editing of the manuscript. The authors wish to thank the other principal investigators of the Validation Project, Drs Richard Ohrbach and Edward Truelove, and the rest of the Project's research team.

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