Experimental Psychological Stress on Quantitative Sensory Testing Response in Patients with Temporomandibular Disorders

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Aims: To assess the modulatory effects of experimental psychological stress on the somatosensory evaluation of myofascial temporomandibular disorder (TMD) patients. Methods: A total of 20 women with myofascial TMD and 20 age-matched healthy women were assessed by means of a standardized battery of quantitative sensory testing. Cold detection threshold (CDT), warm detection threshold (WDT), cold pain threshold (CPT), heat pain threshold (HPT), mechanical pain threshold (MPT), wind-up ratio (WUR), and pressure pain threshold (PPT) were performed on the facial skin overlying the masseter muscle. The variables were measured in three sessions: before (baseline) and immediately after the Paced Auditory Serial Addition Task (PASAT) (stress) and then after a washout period of 20 to 30 minutes (poststress). Mixed analysis of variance (ANOVA) was applied to the data, and the significance level was set at $P$ = .050. Results: A significant main effect of the experimental session on all thermal tests was found (ANOVA: $F > 4.10$, $P < .017$), where detection tests presented an increase in thresholds in the poststress session compared to baseline (CDT, $P = .012$; WDT, $P = .040$) and pain thresholds were reduced in the stress (CPT, $P < .001$; HPT, $P = .001$) and poststress sessions (CPT, $P = .005$; HPT, $P = .006$) compared to baseline. In addition, a significant main effect of the study group on all mechanical tests (MPT, WUR, and PPT) was found (ANOVA: $F > 4.65$, $P < .037$), where TMD patients were more sensitive than healthy volunteers. Conclusion: Acute mental stress conditioning can modulate thermal sensitivity of the skin overlying the masseter in myofascial TMD patients and healthy volunteers. Therefore, psychological stress should be considered in order to perform an unbiased somatosensory assessment of TMD patients. J Oral Facial Pain Headache 2018;32:428–435. doi: 10.11607/ofph.2046

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Temporomandibular disorders (TMD) are a group of musculoskeletal conditions that affect the temporomandibular joint (TMJ), the masticatory muscles, and associated structures. TMD is the most common chronic orofacial pain condition, with a prevalence in the global population of approximately 12%. The high costs for health care systems and loss of productivity demonstrate the negative impact of TMD at the individual, community, and societal levels. The pathophysiology and underlying pain mechanisms of TMD are not fully understood yet, although previous evidence indicates that somatosensory disturbances can play an important role.

Quantitative sensory testing (QST) encompasses psychophysical tests used to investigate somatosensory functions and has become a promising method for assessing musculoskeletal disorders, including pain-related TMD. The German Research Network on Neuropathic Pain (DFNS) has proposed a comprehensive and standardized battery of QST that primarily uses somatosensory profiles to elucidate mechanisms that contribute to the development and maintenance of neuropathic pain conditions. Somatosensory abnormalities have also been found within and outside the trigeminal area in 82% and 60% of TMD patients, respectively. The most frequent somatosensory abnormalities are gain of function (hyperalgesia) to pressure, pinprick, cold and heat stimuli,
and an increased temporal summation. In addition, it has been possible to identify subgroups of myofascial TMD patients who present with different somatosensory profiles.8

In light of the accumulating evidence attesting to the relevance of standardized QST for phenotyping TMD patients, it is pertinent to assess possible factors that can influence QST results. For instance, QST responses rely on the participant’s perception, and therefore factors such as attention, cooperation, motivation, and emotions can potentially influence the somatosensory assessment.13 Most published QST research has focused on standardization of the procedures,11,12 differentiation between patients and controls,6,7 and estimation of metric properties; eg, reliability and agreement.14,15 On the other hand, psychological factors (such as stress) that can modulate responses evoked by QST in areas supplied by spinal nerves8,16,17 have not been sufficiently investigated in the orofacial pain field. Therefore, the aim of this study was to assess the modulatory effects of experimental psychological stress on the somatosensory evaluation of myofascial TMD patients. It was hypothesized a priori that (1) psychological stress would modulate responses evoked by QST and (2) psychological stress would modulate the responses differently between myofascial TMD patients and healthy volunteers.

Materials and Methods

Sample and Ethics

The study was conducted at Bauru School of Dentistry from August 2016 to February 2017. A total of 20 healthy women and 20 women with myofascial TMD who were between 18 and 50 years of age were recruited from the local community through advertisements. Only female participants were included in order to avoid the confounding effect of sex on pain perception.18

Healthy volunteers were free of any complaint or pain syndrome at the time of study enrollment. Patients with TMD were examined by an orofacial pain specialist (D.M.A.O.F) and met the criteria for myofascial pain with or without jaw opening limitation (Ia and Ib) according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)19 with pain duration of at least 3 months. Exclusion criteria for all participants were: pregnancy; present or previous pathology or any other skin lesions in the face (testing site); diseases causing potential neural damage ipsilateral to the dominant hand of healthy volunteers; these were cold detection threshold (CDT), warm detection threshold (WDT), cold pain threshold (CPT), heat pain threshold (HPT), mechanical pain threshold (MPT), wind-up ratio (WUR), and pressure pain threshold (PPT). Thermal tests were performed using a TSA 2001-II (Medoc, Israel) thermal sensory testing device. The contact area of the thermode was 16 × 16 mm. CDT and WDT were measured first, and then CPT and HPT were determined. The thermode baseline temperature was 32°C, and it was raised or lowered respectively at a rate of 1°C/second to the upper limit of 50°C or the lower limit of 0°C. The participants were instructed to press a button as soon as they perceived the sensation of cold, warm, cold pain, or heat pain. The threshold was considered the mean of three consecutive trials.11,12

MPT was measured using a standardized set of Semmes-Weinstein monofilaments (Touch-Test TM Sensory Evaluators; North Coast Medical) that exert forces between 0.008 g/mm² and 300 g/mm². The monofilaments were applied in a vertical and perpendicular position to the site of examination, and the contact time was approximately 2 seconds. Participants were instructed to verbally report the first sharpness/pinprick sensation. The method of limits technique, which uses a series of ascending and descending stimulus intensities to yield five suprathreshold and five subthreshold reports, was used to determine the threshold. The geometric mean of these measurements was considered the MPT.11,12
WUR was measured with the same set of Semmes-Weinstein monofilaments. For this test, the perceived intensity of a single pinprick stimulus was compared to a series of 10 repetitive pinprick stimuli of the same physical intensity (1/second applied within an area of 1 cm²). The monofilament was perceived as “slightly painful” and individually determined for each participant. The participant was asked to rate the pain intensity immediately after the single stimulus and the series of 10 stimuli by using a 0 to 100 numeric rating scale (NRS). The entire procedure was repeated three times. WUR was calculated as the mean rating of the three series divided by the mean rating of the three single stimuli.11,12

PPT was performed with a digital dynamometer (Kratos) with a probe area of 1 cm² and flat circular-shaped tip. The participants were instructed to press a button at the first painful sensation. The PPT was determined as the arithmetic mean of three consecutive trials of ascending stimulus intensities that were applied with an increasing ramp of approximately 0.5 kgf/cm² (the device provided a visual feedback of the force rate).

In addition, the following psychometric questionnaires were applied: validated Brazilian Portuguese translations of the Perceived Stress Scale (PSS),20 State-Trait Anxiety Inventory (STAI),21 and Pain Catastrophizing Scale (PCS).22 Finally, the reported stress was evaluated by means of a visual analog scale (VAS), which consisted of a 10-cm line with 2 anchors at its extremities (0 = no stress; 10 = worst imaginable stress). The participants were requested to place a vertical mark on the line at the point that they best felt represented their perception of their current state of stress.

**Psychological Stress Task**
The Paced Auditory Serial Addition Task (PASAT) was applied to induce psychological stress. This test has been shown to be an effective mental stressor and consists of a mental arithmetic task where a series of single digit numbers is presented to the participant, who must add each new digit to the one immediately prior to it.25 For instance, if the digits 3, 6, and 2 were presented, the participant would respond with the correct sums, which are 9 and then 8. The participant must respond prior to the presentation of the next digit for a response to be scored as correct. Single digits were presented at four different interstimulus intervals25; ie, every 2.4, 2.0, 1.6, and 1.2 seconds, and the total application time of one PASAT trial was approximately 8 to 10 minutes.

Prior to the task, the participant was informed that the average performance was about 70% to 80% of correct answers and that she would receive a performance feedback at the end of the task. The examiner (D.M.A.O.F) pretended that she was taking notes on the subject’s performance during the trial. After the end of the first trial, the participant received a negative performance feedback (below the average), and a second trial was requested in order to achieve the average of correct answers. In fact, feedback was not based on performance and all participants were scored below average. Following a similar second trial of PASAT, the subject received negative feedback again and the test was finished. This procedure aimed to enhance the stress response and, thus, the complete stress task lasted approximately 20 minutes.

**Study Design**
The psychometric questionnaires were applied only before the stress task, while reported stress and the subsequent somatosensory evaluation were measured at three sessions: before (baseline) and immediately after the PASAT session (stress) and then after a washout period of 20 to 30 minutes (poststress). QST = quantitative sensory testing; STAI = State-Trait Anxiety Inventory; PSS = Perceived Stress Scale; PCS = Pain Catastrophizing Scale.
25°C ± 1°C). The participants were asked to abstain from smoking, drinking, and eating 30 minutes before the procedures. Blinding assessments were not possible, considering that only one examiner (D.M.A.O.F.), trained by one certified expert in QST by the DFNS (Y.C), assessed the eligibility criteria, collected the data, and applied the stress task.

**Statistical Analyses**

Reported stress and somatosensory assessment outcomes were reported as mean ± standard deviation (SD) and were assessed for normal distribution with the Kolmogorov-Smirnov test, and a log10 transformation was performed when the test results were significant at an alpha level of 5% (P < .05). Thus, the following variables were log10 transformed: reported stress (VAS) and the raw data of the CDT, WDT, MPT, WUR, and PPT. In addition, the psychometric questionnaire scores were also reported as mean ± SD. A t test for independent samples was applied to compare the age and STAI and PSS scores between TMD patients and healthy volunteers, and the Mann-Whitney U test was applied to compare PCS scores.

Mixed analysis of variance (ANOVA) was performed to assess the effect of one between-group factor (group: two levels) and one within-group factor (session: three levels) on the reported stress and QST values. When appropriate, post hoc analyses were performed using Tukey’s HSD. The significance level was set at P < .05 (Table 1).

**QST Assessment**

The QST descriptive data are shown in Table 2, and the mixed ANOVA results are reported in Table 3. A significant main effect of the study group on all thermal tests (CDT, WDT, HPT, and CPT) was found (ANOVA: F = 33.97, P < .001, partial $\eta^2 = .47$), where an increased stress level was reported immediately after PASAT compared to baseline and poststress levels (Tukey: P < .001). However, there was no significant main effect of group (ANOVA: F = 3.41, P = .072) or interaction between group and session (ANOVA: F = 0.99, P = .374), which indicates that group stress levels throughout the sessions were not significantly different between the TMD patients and healthy volunteers.

**Results**

### Demographic and Psychological Assessments

There was no significant age difference between the healthy volunteers and TMD patients (P = .183). In addition, both groups reported similar amounts of anxiety (P = .896 for trait dimension and P = .132 for state dimension) and perceived stress (P = .744). However, pain catastrophizing was higher in the TMD patients (P = .001) (Table 1).

### Reported Stress

Table 2 presents the reported stress levels for healthy volunteers and TMD patients throughout the PASAT sessions. A significant main effect of the experimental session on reported stress was found (ANOVA: F = 33.97, P < .001, partial $\eta^2 = .47$), where an increased stress level was reported immediately after PASAT compared to baseline and poststress levels (Tukey: P < .001). However, there was no significant main effect of group (ANOVA: F = 3.41, P = .072) or interaction between group and session (ANOVA: F = 0.99, P = .374), which indicates that group stress levels throughout the sessions were not significantly different between the TMD patients and healthy volunteers.
volunteers. Although the main effect of session was presented for MPT, post hoc analyses did not show any significant difference between specific sessions (Tukey: \( P > .050 \)). However, WUR showed a significant interaction between group and session (ANOVA: \( F = 4.25, P < .001 \), partial \( \eta^2 = .07 \)) (Table 3), where TMD patients had decreased pain ratings in the stress session compared to baseline (Tukey: \( P = .012 \)) and poststress (Tukey: \( P < .001 \)) sessions compared to baseline values. In addition, TMD patients reported higher WUR compared to healthy volunteers in the baseline session (Tukey: \( P = .001 \)) (Table 3).

Analogous findings were evident when \( z \) scores were generated (Fig 2). Both groups were less sensitive to thermal detection (ie, CDT and WDT [significant main effect of the experimental session]) in the poststress session compared to baseline (CDT, Tukey: \( P = .012 \); WDT, Tukey: \( P = .040 \)) and were
more sensitive to thermal pain detection (ie, CPT and HPT) in the stress (CPT, Tukey: $P < .001$; HPT, Tukey: $P = .005$; HPT, Tukey: $P = .006$) compared to baseline (Figs 2a and 2b). On the other hand, TMD patients presented overall higher $z$ scores for mechanical pain detection (significant main effect of the study group, regardless of session); ie, MPT (Tukey: $P = .037$) and PPT (Tukey: $P = .015$) (Fig 2c). Furthermore, WUR $z$ scores of TMD patients were decreased in the stress session compared to baseline (Tukey: $P = .018$), and they were increased in the healthy volunteers in the stress (Tukey: $P = .001$) and poststress (Tukey: $P < .001$) sessions compared to baseline (Fig 2d). Finally, the TMD patients reported higher WUR scores than the healthy volunteers in the baseline session (Tukey: $P = .001$) (Fig 2d). However, individual abnormal $z$ scores were not detected in the great majority of TMD patients and healthy volunteers; ie, the values were within the 95% CI of the normative range.

**Discussion**

The main findings of this study, which aimed to investigate the effects of experimental psychological stress on somatosensory evaluation of the facial skin overlying the masseter muscle of myofascial TMD patients and healthy volunteers, were: (1) both groups were less sensitive to thermal detection (CDT and WDT) and more sensitive to thermal pain detection (CPT and HPT) after exposure to acute mental stress; and (2) TMD patients were more sensitive to mechanical pain detection (MPT, WUR, and PPT) than healthy volunteers.
All participants reported a significant increase in reported stress following the PASAT, which is in line with previous reports showing that this mental arithmetic task is able to evoke acute stress.\textsuperscript{23,24} Although a physiologic stress marker was not measured in this study, previous investigations have demonstrated that PASAT can activate the sympathetic nervous system\textsuperscript{23,24} and hypothalamic-pituitary-adrenocortical axis.\textsuperscript{26} In addition, healthy volunteers presented higher mean values of reported stress than TMD patients in stress and poststress sessions, although these differences were not significant in the mixed ANOVA model. This may be related to the fact that both groups reported similar levels of perceived stress at baseline, and so significant differences between the groups would be more difficult to detect.

The significant increase in thermal detection thresholds after exposure to acute psychological stress was an interesting finding. Animal studies have reported that thermal hypoesthesia following experimental stress could be attributed to a general warming of the skin due to an increase in body temperature at the same time that peripheral vasoconstriction induces a marked cooling of the extremities.\textsuperscript{27,28} Considering that the study did not monitor skin temperature, it is difficult to argue that such peripheral changes were mainly responsible for the thermal detection modulation. Previous evidence of experimental stress effects on QST measured at the forearm did not find significant changes in CDT and WDT.\textsuperscript{29} Nonetheless, taking into consideration that the temperature of the face is slightly higher than that of the limbs,\textsuperscript{30} it is plausible to suppose that differences in the thermoregulation between body sites could account for these different findings. Further investigations are warranted to elucidate this issue.

On the other hand, thermal pain thresholds were lowered after exposure to stress. This confirms earlier reports.\textsuperscript{29,31} Two possibilities could explain this: (1) less intense stressors with low to moderate arousal are associated with hyperalgesic responses\textsuperscript{32,33}; and (2) the release of pro-inflammatory cytokines mediated by activation of the sympathetic nervous system is able to exert a sensitization effect on cutaneous nociceptive fibers.\textsuperscript{34} Likewise, although autonomic responses were not monitored in this study, preclinical evidence has shown that stress-induced thermal hyperalgesia requires sympathetic nervous system activity.\textsuperscript{35}

The mechanical sensitivity of myofascial TMD patients was an expected finding, considering the weight of evidence that supports this state of neuronal hyperexcitability of TMD patients.\textsuperscript{6–9,36} In fact, neurophysiologic investigations have shown that mechanical hyperalgesia is related to long-term potentiation of nociceptive neurons in the central nervous system, which is expressed as central sensitization.\textsuperscript{5,37} On the other hand, the psychological stress did not significantly influence pinprick (MPT) or blunt pressure (PPT) sensitivity. This dissociation of thermal and mechanical sensitivity modulation due to experimental stress has also been previously reported.\textsuperscript{29} Mechanical pain tests seem more prone to measurement errors than thermal pain tests, probably due to technical aspects.\textsuperscript{38} Therefore, greater threshold changes in a repeated measures design would be necessary to reveal whether significant differences do occur.

The exposure to acute mental stress evoked different effects on temporal summation, reflected in the WUR scores of TMD patients and healthy volunteers. The former were less sensitive to repetitive mechanical stimuli in the stress session, while the latter were more sensitive in the stress and poststress sessions. In addition, the groups were significantly different in their WUR scores in the baseline session. Pragmatic explanations for this crossover interaction could be related to the low reliability of WUR.\textsuperscript{14} However, experimental psychological stress can elicit hypalgesic\textsuperscript{16} and hyperalgesic\textsuperscript{17} responses, which are dependent on the nature and duration of the stressor, baseline state of the physiologic stress system, the psychological effects that the stressor exerts on the individual’s emotions, and the interactions among these factors.\textsuperscript{16,17,32,33} It might have been possible that the stressor effects of PASAT, other than the reported stress intensity, were different between the TMD patients and healthy volunteers.

The present study had some limitations that need to be addressed. Variables that could be associated with the stress responses were not controlled throughout the sessions; eg, autonomic monitoring and degree of anxiety. Comprehensive psychosocial assessments were also not performed, such as evaluations of depression and sleep quality. However, symptoms of anxiety are associated with a low and moderate stress level, which seemed to be the case for this investigation, and depression symptoms with a high stress level.\textsuperscript{39} In addition, the inclusion of only female patients hampers the external validity of the results. Finally, the small sample size can be considered insufficient to detect small effect differences for repeated measurements on some QST parameters; eg, mechanical pain tests.

Conclusions

Acute mental stress conditioning can modulate thermal sensitivity of the skin overlying the masseter in myofascial TMD patients and healthy volunteers. Therefore, psychological stress should be considered in order to perform an unbiased somatosensory assessment of TMD patients.
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