American Pain Society
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PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 16, No 11 (November), 2015: pp 1127-1135
Available online at www.jpain.org and www.sciencedirect.com

Evidence for Sustained Mechanical Pain Sensitization in Women With Chronic Temporomandibular Disorder Versus Healthy Female Participants

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Abstract: Generalized dysfunction of the nociceptive system has been hypothesized to be an important pathophysiologic process underlying temporomandibular disorder (TMD) pain. Studies have not identified sensitization to painful stimuli administered prospectively across consecutive days among participants with TMD with chronic pain. We attempted to isolate an empirically derived laboratory-based marker of sustained mechanical pain sensitization. We examined whether this index accounted for variance in prospective assessments of clinical TMD pain. Participants were women with a clinical diagnosis of chronic TMD (n = 30) and healthy female controls (n = 30). Pain thresholds were assessed using digital algometry 4 times at 12-hour intervals over 48 consecutive hours and clinical TMD pain via follow-up telephone assessments. Sustained mechanical pain sensitization, defined by statistically significant linear decrements in pressure pain thresholds across the consecutive testing sessions, discriminated chronic TMD and control participants. An index of sustained sensitization at the masseter accounted for unique variance in clinical TMD pain over the subsequent 3-month assessment period, even controlling for mean pain threshold and baseline pain severity. These preliminary findings highlight discriminant and predictive validity characteristics of a novel marker of protracted pain sensitization among women with chronic TMD pain.

***Perspective:** A laboratory-based and empirically defined marker of sustained mechanical pain sensitization over the course of days with acceptable discriminant and predictive validity was identified. This marker may represent a clinically useful marker of chronic TMD pain in women.*

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***Key words:** Temporomandibular disorder, pain, chronic pain, sensitization, pain threshold, mechanical pain.*

The cause and pathophysiology of temporomandibular disorder (TMD) is not fully understood, although generalized dysfunction of the nociceptive system has been offered as 1 explanation.[24,36-38] Relative to pain-free control individuals, patients with TMD show greater sensitivity to painful mechanical stimuli applied to affected as well as distal, unaffected anatomical sites.[1,7,16-18,25,26,29,36,38,42] In addition, temporal summation (a phenomenon reflecting endogenous facilitation of pain resulting from repeated application of stimuli of equal intensity) may be amplified in patients with TMD relative to healthy control individuals.[26,35,36] Evidence from a recent large-scale prospective case-control study revealed that sensitivity to mechanical pain is associated with greater risk of developing first-onset TMD, although within-session indexes of mechanical pain summation were not associated with greater risk.[21] Despite these findings,[30,41,42] several studies have reported mixed or null findings

Received December 4, 2014; Revised July 14, 2015; Accepted August 4, 2015.

This work was supported by NIH grants NS047168, AR054871, and T32MH075884 and by grant number UL1 RR 025005 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH. Information on NCRR is available at http://www.ncrr.nih.gov/. Information on re-engineering the clinical research enterprise can be obtained from http://nihroadmap.nih.gov/clinicalresearch/overview-translational.asp. M.T.S. holds an equity stake in BMED Technologies, which is managed by the Johns Hopkins Office on Conflict of Interest. There are no additional conflicts of interest to report.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting true views of the Department of the Army or the Department of Defense.

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1526-5900/$36.00

Published by Elsevier Inc. on behalf of the American Pain Society

http://dx.doi.org/10.1016/j.jpain.2015.08.002

concerning hyperalgesic responses to pain-evoking stimuli in TMD.

To our knowledge, studies have not yet investigated the sensitization of patients with TMD to noxious stimuli administered prospectively across consecutive days. Evidence of a progressive and more protracted sensitization to noxious mechanical stimuli over longer periods might be an important laboratory-based model by which investigators can probe more durable nociceptive mechanisms of myofascial pain, especially that of a chronic nature. We propose that nociceptive system sensitization sustained over several days or assessments might represent a prolonged state of nociceptive system sensitization that accounts for variability in chronic TMD pain.

In the present study, we attempted to isolate a laboratory-based and empirically derived index of sustained pain sensitization by examining changes in mechanical pressure pain thresholds (PPTs) assessed across serial testing sessions conducted over 2 consecutive days. Empirical evidence for this hypothesized somatosensory phenomenon could provide insight into an untapped but potentially clinically relevant pathophysiologic process of chronic TMD pain. We hypothesized that compared with healthy female control individuals, women with chronic TMD would show increased mechanical pain sensitivity (diminished PPTs) at affected (masseter) and unaffected (forearm) anatomical sites across 4 consecutive pain testing sessions conducted over a contiguous 48-hour period. We also examined the predictive validity of sustained sensitization by examining the association of an empirically derived index of the proposed phenomenon with self-reported clinical TMD pain outcomes over a subsequent 3-month telephone-based assessment epoch.

Methods

Participants

We recruited women with TMD (n = 30) from a dental school–based, tertiary care, orofacial pain clinic and by media advertisements for a larger prospective study concerning sleep disturbance and TMD pain and function. To be eligible, participants with TMD had to receive a primary myofascial TMD diagnosis based on published research diagnostic criteria (RDC).[8] All TMD diagnostics were conducted by an experienced dentist who had completed formal training in RDC procedures and undergone periodic reliability calibration. Additional major eligibility criteria for patients with TMD included typical pain severity graded as >2 out of 10 and minimum symptom duration ≥6 months. We excluded patients reporting primary pain conditions or serious medical disorders other than TMD, current alcohol or drug abuse problems, and use of narcotics, antidepressants, anticonvulsants, or muscle relaxants within 2 weeks of study participation. In addition, for the purposes of the present study, only participants with TMD who did not meet diagnostic criteria for primary insomnia were included in the analysis. This approach minimized the potential influence of sleep-related characteristics on hypothesized between-group differences in sustained sensitization.

Female healthy control individuals (n = 30) were recruited from fliers posted at a major teaching hospital and medical school and from newspaper advertisements. Major eligibility criteria for healthy control individuals included the absence of a significant medical/psychiatric history within the previous 6 months; the absence of a lifetime history of Raynaud disease, bipolar or psychotic disorder, recurrent major depression, or substance abuse disorder; the absence of use of antidepressant medications within the past 6 months; the absence of any history of chronic pain (ie, lifetime history of persistent pain for ≥6 months); and the absence of insomnia or other sleep disorders.

Procedure

All procedures took place in a university hospital–based clinical research unit. Participants with TMD were enrolled in a larger study aimed at characterizing associations between objective polysomnography sleep architecture and continuity indexes and pain sensitivity, and healthy controls were enrolled in a study of the effects of sleep deprivation on pain sensitivity. Sleep data from the full sample of participants with TMD from which the current sample was selected were presented in a previous publication.[40] Although insomnia was ruled out for participants with TMD in the current study, we found that individual differences in self-reported sleep quality (assessed with the Pittsburgh Sleep Quality Index[2]) were not associated with mean pain sensitivity or between-session changes in pain sensitivity at any testing site ($P > .20$). Questionnaires were completed as part of a larger packet of questionnaires provided on study entry. The analyses of the present investigation are based on mechanical pain testing procedures (see later discussion). Afternoon sessions were conducted between 3:00 PM and 5:00 PM hours, and morning sessions were conducted 40 minutes after awakening (all participants were allotted an uninterrupted 8-hour period for sleep structured around participants' habitual sleep-wake times ascertained from a 2-week daily sleep diary). The control afforded by the inpatient environment ensured that all participants had not smoked, eaten, ingested caffeinated or calorie-rich beverages, or exercised vigorously before morning or within 2 hours of afternoon pain testing sessions, effectively ruling out these potential confounding factors.

All participants underwent a standardized 45-minute pain testing battery consisting of thermal (heat) and mechanical (pressure) pain threshold testing, temporal summation of heat pain, always followed by cold pain testing.[11,14,40] For the purposes of the present study, we were interested in mechanical pain sensitization given the myofascial nature of TMD and because PPT appears to be a particularly robust concurrent and prospective correlate of TMD.[39] All participants completed 4 consecutive pain testing batteries over a 48-hour period: an initial afternoon session was followed by a morning and an afternoon session the next day, and