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Parasympathetic Reactivity in Fibromyalgia and Temporomandibular Disorder: Associations With Sleep Problems, Symptom Severity, and Functional Impairment

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Abstract: **Despite evidence of autonomic disturbances in chronic multisymptom illnesses such as temporomandibular disorder (TMD) and fibromyalgia, additional work is needed to characterize the role of parasympathetic reactivity in these disorders. Given the high levels of comorbidity with psychiatric disorders characterized by stronger parasympathetic decline than controls in safe contexts (leading to higher arousal), it was hypothesized that individuals with TMD and fibromyalgia would respond similarly. In this preliminary investigation, 43 women with TMD (n = 17), TMD + fibromyalgia (n = 11), or neither (controls; n = 15) completed a baseline assessment of respiratory sinus arrhythmia (a measure of parasympathetic activity) followed by ongoing parasympathetic assessment during a questionnaire period. As predicted, patients showed greater parasympathetic decline during psychosocial assessment, suggesting an autonomic stance that supports defensive rather than engagement behaviors. Individual differences in parasympathetic reduction during the questionnaire period were related to a variety of physical and psychosocial variables. Although this study has a number of key limitations, including a convenience sampling approach and small group sizes, if replicated in larger samples, the findings would have important implications for the treatment of patients with these disorders.**

Perspective: ***Compared to controls, individuals with TMD or TMD and fibromyalgia demonstrated greater parasympathetic decline during psychosocial assessment, and individual differences in parasympathetic decline predicted negative patient outcomes. Such parasympathetic decline may demonstrate a tendency to readily perceive danger in safe environments.***

Key words: *Autonomic reactivity, polyvagal theory, respiratory sinus arrhythmia, fibromyalgia, temporomandibular disorder, chronic pain.*

Chronic multisymptom illnesses such as temporomandibular disorder (TMD) and fibromyalgia (FM) often co-occur and share many features.[7,26,34,53,54] There is no universal known cause of either disorder, although numerous overlapping risk factors have been identified.[1,26,56] Altered functioning of the autonomic nervous system (ANS) represents one such overlapping risk factor.

The 2 branches of the ANS have antagonistic effects on autonomic arousal. However, arousal is under tonic inhibitory control of the parasympathetic branch via the myelinated vagus nerve (termed the "vagal brake" or "parasympathetic maintenance"), which allows for efficient upregulation of arousal via parasympathetic reduction (or "vagal withdrawal"). According to Porges's polyvagal theory, parasympathetic maintenance promotes calm engagement, whereas vagal withdrawal facilitates quick escape from danger.[36,37,39] FM and TMD are linked to higher baseline sympathetic activity or

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predominance, especially at night[12,14,30,32,36,42,46] and lower baseline parasympathetic activity.[12,42,45] With regard to ANS *reactivity* in these disorders, some evidence points toward blunted sympathetic responding coupled with greater increases in arousal,[11,31,42,55] from which one might infer greater parasympathetic reduction in response to the environment. However, very little is known about the nature of *parasympathetic reactivity* in these conditions.[42]

Some reduction in parasympathetic activity in response to safe stimuli facilitates task engagement.[39] However, rapid or exaggerated parasympathetic decline in response to safe stimuli is associated with hypersensitivity to environmental danger[36] and has been described as a "nonspecific marker of emotional lability."[3] Consistent with this perspective, greater parasympathetic reductions in response to objectively safe laboratory stimuli have been associated with various reactive emotional disorders such as panic,[52] generalized anxiety,[48] and borderline personality disorder.[2] Given the frequent comorbidity of FM and TMD with such disorders,[7,34] we hypothesize a similar pattern of parasympathetic reactivity among individuals with TMD or FM.[38]

The current study examined the physiologic functioning of controls, individuals with TMD, and individuals with both TMD and FM at rest and while completing psychosocial measures. Questionnaire completion was conceptualized as a safe task that mirrors the assessment protocol used in pain clinics, where patients fill out assessment paperwork prior to examination.[34] Given the objectively safe nature of this context, the polyvagal theory would specify the adaptive response as relative maintenance of parasympathetic activity to facilitate task engagement, whereas relatively greater parasympathetic reduction would represent an inappropriate defensive response related to the inaccurate perception of danger.[38]

Hypotheses

The following specific hypotheses were tested:

1. Baseline parasympathetic functioning is suppressed among individuals with TMD or TMD + FM.
2. Individuals with TMD and TMD + FM will exhibit greater parasympathetic decline during the assessment period. Such decline would be greater among individuals with both diagnoses than individuals with one or neither diagnosis, and greater among individuals with TMD than with neither diagnosis.
3. Individual differences in rate of parasympathetic decline during the assessment period will be associated with poorer sleep, poorer general physical and mental functioning, greater chronic pain symptom severity, greater impact of symptoms on functioning, and greater distress and depression.

Methods

Participants

Participants were 43 females between the ages of 18 and 65. Pain patients were diagnosed with TMD with or without comorbid FM. Diagnosis of TMD was made by a clinician using the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD).[19,43] Patients were included if they presented with painful TMD. Overall, 88.3% of participants in the TMD-only group and 90.9% of participants in the TMD + FM group were diagnosed with myalgia; the majority of those participants were also diagnosed with another type of TMD pain (ie, disc disorders or arthralgia/osteoarthritis). Diagnosis of comorbid FM was made by a rheumatologist using 1990 American College of Rheumatology classification criteria and/or 2010 American College of Rheumatology criteria. Patients with TMD were recruited from a university-based tertiary orofacial pain clinic, from the Kentucky Women's Health Registry (KWHR), or from advertisements by flier or in the newspaper. The KWHR is a longitudinal cohort study containing self-report information including the presence of painful conditions including TMD and FM in which patients agree to be contacted for studies for which they may qualify based on inclusion and exclusion criteria. Controls were recruited from the KWHR or from the community using fliers. Potential participants were excluded from the study if they were pregnant or nursing; were prisoners or institutionalized; were severely obese as defined by body mass index $\geq$40; were current alcohol or other substance abusers; were current smokers of $\geq$1 pack of cigarettes daily; were taking or received oral, inhaled, or injected corticosteroids within 3 months; were unable to discontinue medications that affect heart rate variability (HRV), such as beta blockers; had a currently active Axis I psychiatric diagnosis other than simple phobia as assessed by the Mini-International Neuropsychiatric Interview structured diagnostic interview; or had presence of any active or unstable medical condition, including chronic infection or inflammatory/autoimmune condition.

Table 1 contains descriptive data regarding demographic (and substantive) variables in the full sample and by group. Racial makeup of the sample was as follows: 95.3% white (control group = 93.3%; TMD group = 100%; TMD + FM group = 90.9%) and 4.7% African American (control group = 6.7%; TMD group = 0%; TMD + FM group = 9.1%).

Procedures

All procedures were reviewed and approved by the University of Kentucky institutional review board. During the initial visit, patients provided informed consent and were examined by a clinician to determine eligibility for the study. Informed consent included an explanation of the measures included in the packet, with an emphasis on the anonymous nature of responses, and also included an explanation of physiological recording procedures, emphasizing that these would be noninvasive and not painful. Patients were classified as TMD (n = 17), TMD + FM (n = 11), or control (n = 15), and the Mini-International Neuropsychiatric Interview was completed. If it was necessary to discontinue any medications that could affect the heart rate, instructions were provided.

Participants returned to the clinical research center for autonomic and psychosocial assessment. The participant was seated in a comfortable dental exam chair in a clean