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Potential Autonomic Risk Factors for Chronic TMD: Descriptive Data and Empirically Identified Domains from the OPPERA Case-Control Study

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Abstract: **Several case-control studies have been conducted that examine the association between autonomic variables and persistent pain conditions; however, there is a surprising dearth of published studies in this area that have focused on temporomandibular disorders (TMD). The current study presents autonomic findings from the baseline case-control study of the OPPERA (Orofacial Pain: Prospective Evaluation and Risk Assessment) cooperative agreement. Measures of arterial blood pressure, heart rate, heart rate variability, and indirect measures of baroreflex sensitivity were assessed at rest and in response to a physical (orthostatic) and psychological (Stroop) stressors in 1,633 TMD-free controls and 185 TMD cases. In bivariate and demographically adjusted analyses, greater odds of TMD case status were associated with elevated heart rates, reduced heart rate variability, and reduced surrogate measures of baroreflex sensitivity across all experimental procedures. Principal component analysis was undertaken to identify latent constructs revealing 5 components. These findings provide evidence of associations between autonomic factors and TMD. Future prospective analyses in the OPPERA cohort will determine if the presence of these autonomic factors predicts increased risk for developing new onset TMD.**

Perspective: ***This article reports autonomic findings from the OPPERA Study, a large prospective cohort study designed to discover causal determinants of TMD pain. Findings indicate statistically significant differences between TMD cases and controls across multiple autonomic constructs at rest and during both physical and psychologically challenging conditions. Future analyses will determine whether these autonomic factors increase risk for new onset TMD.***

Key words: *Temporomandibular disorders, heart rate variability, blood pressure, heart rate, baroreflex sensitivity, stroop, orthostatic.*

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There is considerable evidence that enhanced pain sensitivity and psychological distress are risk factors* for the onset and maintenance of temporomandibular joint disorders (TMD; for reviews, see Maixner et al in this volume, Diatchenko et al[19] and Maixner[59]). In addition to these relatively well-studied risk domains, emerging evidence indicates that dysregulation of the autonomic nervous system contributes to the onset and persistence or chronicity of TMD and related conditions.[8,10,16,52,57,59,83] To date only a handful of studies have systematically examined and compared autonomic function in TMD cases and controls under resting conditions and in response to physical and psychological stressors.[8,10,16,52,81,83] However, there is a rather substantial literature on the autonomic profiles associated with fibromyalgia syndrome (FMS), a chronic musculoskeletal condition where over 50% of affected people also experience chronic TMD.[22,53,54,60-62,68] Some individuals with FMS display autonomic dysregulation that involves increased sympathetic nervous system (SNS) drive at rest coupled with deficient SNS-mediated responses to specific challenges such as postural change or exercise.[28,60,62] Decreased heart rate variability (HRV) under awake resting conditions and during sleep is seen in FMS and is consistent with lesser parasympathetic and greater β-adrenergic tone.[13,62,68] Arterial baroreflexes, a brain stem system that is involved in regulating cardiovascular dynamics and pain perception, is also blunted in individuals with FMS.[7,37,60,79]

Consistent with blunted baroreflex sensitivity, people with FMS show reduced heart rate (HR) and blood pressure (BP) responses during orthostatic challenges.[7,26] Further evidence for a central nervous system (CNS) dysregulation in autonomic function in FMS patients is the finding of reduced plasma epinephrine (EPI) and norepinephrine (NE) responses, as well as decreased NE metabolites in cerebrospinal fluid, to stressors such as exercise or hypoglycemia.[28,31,48,92] Compared to controls, individuals with TMD express lower ambulatory BP than controls[16] and reduced plasma NE levels at rest and during a stressful public speaking procedure.[15,52] Thus, an emerging literature implicates a CNS-mediated dysregulation of autonomic function at rest and in response to both physical and psychological stressors. This dysregulation contributes to the clinical signs and symptoms seen in patients with FMS, suggesting that it may also contribute to the signs and symptoms of TMD.

One aim of the baseline case-control study of the OPPERA project (Orofacial Pain: Prospective Evaluation and Risk Assessment) was to assess autonomic profiles of people diagnosed with TMD arthralgia, myalgia or both (TMD cases) and people who were found not to have TMD when examined (controls). Autonomic profiles were measured under resting conditions and in response to a physical stressor (ie, orthostatic challenge) and a psychological/cognitive stressor (ie, Stroop color-word and pain-word tests).

Methods

Study Setting and Participants

As described elsewhere (see Slade et al in this volume for detailed description), the OPPERA baseline case-control study used advertisements, emails, flyers, and word of mouth to recruit people who had chronic TMD (cases) and people who did not (controls). They were recruited between May 2006 and November 2008 from communities in and around academic health centers at 4 US study sites: Baltimore, MD; Buffalo, NY; Chapel Hill, NC; and Gainesville, FL. At each study site, the target was to recruit 800 controls and variable numbers of cases based on local operational requirements, for a total of 3,200 controls and 200 cases. The actual number enrolled was 3,263 controls and 185 cases.

The classification of TMD was based on the Research Diagnostic Criteria for Temporomandibular Disorder.[18] In summary, cases met all 3 of the following criteria: during the telephone interview: 1) pain reported with sufficient frequency in the cheeks, jaw muscles, temples, or jaw joints during the preceding 6 months (at least 15 days in the preceding month and at least 5 days per month in each of the 5 months preceding that); during the examination, 2) pain reported in the examiner-defined orofacial region for at least 5 days out of the prior 30 days; and 3) pain reported in at least 3 masticatory muscles or at least 1 temporomandibular joint in response to palpation or to maneuvering of the jaw. Examiners defined the orofacial region by touching the following anatomical areas bilaterally: temporalis, preauricular, masseter, posterior mandibular, and submandibular. Controls met all 5 of the following criteria: during the telephone interview, 1) pain reported infrequently in the cheeks, jaw muscles, temples, or jaw joints (no orofacial pain in the preceding month and no more than 4 days per month in any of the 5 months preceding that); 2) no more than 4 headaches per month within the preceding 3 months; 3) never diagnosed with TMD; 4) no use of a night guard occlusal splint; and during the examination, 5) pain reported in the examiner-defined orofacial region for no more than 4 days in the prior 30 days. However, controls could be positive or negative with respect to pain in response to palpation or jaw maneuver. Additional studywide criteria for all study participants were; aged 18 to 44 years, fluent in English, not receiving orthodontic treatment, and not pregnant or nursing, and had negative responses to each of 10 questions about significant medical conditions and no history of facial injury or surgery.

This analysis uses data from all 185 recruited TMD cases and one-half of the 3,263 recruited controls (1,633 people). The controls for this analysis were selected at random so that data from people in the reserved sample could be used for validation studies that will be reported elsewhere. The accompanying paper (see Slade et al in this volume) gives a more detailed account of study

* Here, we define a risk factor as "an attribute or exposure that is associated with an increased probability of a specified outcome, such as the occurrence of a disease; not necessarily a causal factor.[46]