Commentary 3

Temporomandibular Disorders—Casting the Net to Find Answers

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I was asked to share my reflections on three papers in this issue: "Attributes Germane to Tempromandibular Disorders and Their Associations with Five Chronic Overlapping Pain Conditions," by Sharma et al; "Associations of Sleep Disturbance, Atopy, and Other Health Measures with Chronic Overlapping Pain Conditions," by Sanders et al; and "Associations of Psychologic Factors with Multiple Idiopathic Pain Conditions," by Fillingim et al. Their research designs are well-established, and the employed methodologies are time-tested.

The intent of this commentary is to generate an overarching analysis, placing these three contributions in the context of scientific advances in the understanding of temporomandibular disorders (TMD) that originated in the early 1990s and continues to present times. This operational framework sets the stage for what has been learned and what should come next.

When it comes to the evolution of knowledge over this time period—summarized by Ohrbach and Dworkin in 2016[1]—TMD diagnostic assignments moved away from a focus on structural aberrations towards the Research Diagnostic Criteria for TMD (RDC/TMD) in the 90s, which emphasize a dual-axis system based on the biopsychosocial model of disease, the reliability of measurements, and the allowance of multiple diagnoses. This initial step was followed by the current Diagnostic Criteria for TMD (DC/TMD) and work contracted by the National Institutes of Health (OPPERA-1 and OPPERA-2), among other works that further advanced our understanding of TMD as a family of complex conditions framed within a biopsychosocial illness model, considering the overwhelming number of cases overlapping with other persistently painful conditions.[1] Although much was intuitively apparent for two decades, research on the commonality of clinically observable phenomena among cases with TMD and other pain conditions (the present three studies are prime examples) have brought us to a point where continuing the journey of discovery calls for a new map to be drawn.

The three papers I was asked to consider provide some interesting actionable insights. The paper by Sharma et al investigates whether clinically observable phenomena associated with TMD are indeed specific to TMD or whether they are also found in other persistent pain conditions. Study findings reject the assumption that attributes germane to TMD are specific to painful TMD based on TMD measures from a range of domains, including physical examination measures; reported jaw-related functional limitations; beliefs; and behaviors. Clinically recordable attributes assumed to be germane to only painful TMD were recorded in other persistent pain conditions as well.

The paper by Sanders et al provides an initial assessment regarding the presence of atopy and sleep disorders among a series of DC/TMD cases enrolled in the OPPERA-2 study. Atopy refers to a person's tendency to develop a host of possible allergic reactions. Yes/no answers were requested from the study subjects regarding allergic rhinitis, asthma, atopic dermatitis, urticaria, itching or burning eyes, and food allergies. The presence of sleep disturbances was measured with the Pittsburgh Sleep Quality Index, evaluating dimensions such as subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction over a 1-month reference period. Additionally, a simple 4-item scale was included to assess the obstructive sleep apnea risk. Results showed that atopic disorders, previously recognized as predictors of poor sleep, are associated with multiple chronic overlapping pain conditions (COPCs). Sleep disturbances were also associated with each COPC and with the total number of COPCs.

The paper by Fillingim et al assesses psychologic functioning across five persistent pain conditions: TMD, fibromyalgia or widespread pain, low back pain, headache, and irritable bowel syndrome. The results are not surprising to anyone who has worked in a pain clinic, with a focus on pain location as opposed to an anatomical domain. While some limitations can be typical for the anatomical structures impacted by a specific condition, pain and distress represent the key drivers of negative psychologic functioning.

The three contributions have solidified an ensemble view of overlapping persistent pain conditions. While this kind of phenomenologic approach to disease—ie, the systematic collection and analysis

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of clinical observations using credible methods—is comforting for patients (eg, validating poorly acknowledged symptoms; inducing the feeling of "me, too") and may instill needed corrective change in the mindset of treatment providers, the underlying pathogenetic drivers of patients' symptoms remain speculative. The next and likely most challenging segment of this journey of discovery calls for the elucidation of the mechanistic network underlying these observed phenomena in order for treatments to emerge that are better, and certainly not worse, than placebo.

Anatomical domains exhibit well-recognized and often legally accepted boundaries that define the scope of medical/dental specialty practices. On the other hand, comorbidity in its newer definition describes the altered risk for a given person to develop a second, possibly third, or even fourth ailment when already affected by a specific one. Recognizing that correlative and causal relationships are often difficult to discern, are these co-occurring ailments influenced by shared pathogenetic processes—or even caused by the primary condition of concern—in a person who happens to exhibit a particular pathogenetic vulnerability?

With the recent emergence of comprehensive health records providing health systems with access to big data—enabling massive data mining beyond the primary domain of interest—the concept of comorbidity is attracting increasing attention, with promising avenues for precision medicine and the prevention of likely subsequent ailments in a person's path to multimorbidity. Consideration of anatomical domains is of little relevance in these computational endeavors. However, the role of molecular factors leading to the appearance of symptoms linked to illnesses in bodily domains other than the primary condition remain largely underinvestigated. For TMD research to thrive in the immediate future, it is mandatory to go beyond clinically observable phenomena and correlative findings established in catered TMD case cohorts. The promise of big data combined with a steadily growing catalog of disease-linked genetic variations, as well as the availability of high-throughput technologies, inspires excitement that both the mechanistic similarities and differences among these increasingly ill-delineated, overlapping persistent pain conditions will become better understood.

Based on these three papers and others, I increasingly question the experimental framework employed in the study of TMD, particularly if there is little germane to the condition. Can future research be founded on case series of persons who fit criteria that are insufficiently specific in the first place? Wouldn't we better served by having a case construct of all signs and symptoms associated with any of the overlapping persistent pain conditions to understand how they cluster phenomenologically? In fact, a more biologically plausible alternative conceptualizes these overlapping conditions as a familial cluster of complex clinical manifestations founded on a common pathogenesis that expresses itself through a molecular network with embedded individual vulnerabilities. Are individual downstream vulnerabilities the reason for symptoms to be prominently centered on the face as opposed to the gut? If so, neither the term "comorbidity" nor "multimorbidity" would apply, as the pathogenetic autonomy of the conditions is in question. Instead, Chapman's "painful multi-symptom disorders" would become a more acceptable diagnostic label to use.[2]

Defining the next frontier: With barely anything germane to TMD, what more can we find out from a fixed cohort of defined and reliably selected TMD cases? Recognizing the dilemma, big data—huge datasets of structured and unstructured medical information of all sorts—hold promise to cast the net of discovery far beyond the scientific fishing hole that we call TMD. Besides big data applications for the performance enhancements of health systems or the management of individual health, applications in human research are also being launched. In contrast to longitudinal cohort and case-control studies, as well as randomized controlled trials, investigations employing big data analytics happen in a real-life situation without any a priori assumptions and with a better handle on confounding variables. Big data analytics build on existing knowledge and complement established investigative methodologies.

Based on the three papers that I was asked to reflect upon, and many others that have appeared in recent times, I have learned much about what TMD are not. The time has come to establish what they are, phenomenologically and mechanistically. Big data will undoubtedly accelerate medical discovery and enable a wide net to be cast over all conditions without biased centrality on TMD. The challenge will be to make sure that data on TMD are not buried in inaccessible dental records and instead become represented in thousands of health records as real-life datapoints, similar to those available on irritable bowel syndrome and other conditions.

References

1. Ohrbach R, Dworkin SF. The evolution of TMD diagnosis: Past, present, future. J Dent Res 2016;95:1093–1101.
2. Chapman CR. Painful multi-symptom disorders: A systems perspective. In: Kruger L, Light AR (eds). Translational Pain Research: From Mouse to Man. Boca Raton, FL: CRC, 2010: 1–30.