

## Temporomandibular Joint Disorders— The View Widens While Therapies Are Constrained

Twenty-five years ago, we measured the electromyographic silent period in the laboratory and delivered occlusal bite splints for patients. Today, we hunt for the molecular fingerprint and the vulnerability alleles that place patients at risk. In the clinic, however, bite splints are still in vogue.

Less than a decade ago, the number of medications addressing pain associated with temporomandibular joint diseases and disorders (TMD) was increasing, but recently, it has decreased. Some medications have been taken off the shelves; the use of others has been restricted because of safety concerns. Once-popular invasive therapies, including occlusal adjustments, orthodontics, prosthodontics, and orthognathic surgeries, all aimed at changing the bite, have fallen out of grace because of unfavorable benefit-risk-cost ratios. In the background also lurks the uncomfortable recognition that the bench-to-bedside discovery process is hampered by questions about the validity of the available animal models.

While the hunt for genes and gene-environment interactions that put patients at risk has widened the discovery process, the road ahead is not without obstacles. Linkage studies are affected by the choice of assays and their relevance to the disease on hand and by issues of statistical power and required resolution to identify loci. Opportunities to advance the field through the use of cytogenetics are limited because the source of cells to test for chromosomal abnormality is itself a question. Phenotype-genotype associations exploring the role of promising candidates are problematic because of concerns linked to multiple testing, variable levels of linkage disequilibrium from population to population, and the scientific challenge of functional confirmation. Single-nucleotide polymorphisms, haplotypes, and diplotypes may or may not be specific for the pain phenotype examined but could reflect downstream processes related to mood, cognition, memory, stress response behaviors, or other comorbid phe-

nomena. Any statistical association is also inherently subject to a certain degree of error; thus, the replication of studies becomes a necessity. At this time, however, too few comparable studies are available to allow estimation using meta-analytic tools of the robustness of particular genotype-phenotype links.

Although occlusal stabilization splints remain a favored therapeutic option and one of the few constants of the past 25 years or so, they have slid downhill from a potentially therapeutic device with mechanistic specificity to one that is indistinguishable from a credible placebo.<sup>1</sup> Nonetheless, many hopeless patients cling to them. It is the one treatment that despite their misery, these patients never want to lose, because the adverse effects of other treatments are more than they can bear. However, it may be possible to harness the brain's reward circuitry to boost the effect of a credible intervention until more definitive treatments become available for this and other chronic, disabling diseases.

Although treatments fall short when it comes to expected outcomes, patient advocates are comfortable with the developments of the past 25 years. TMD have become a complex group of diseases for which easy answers and simple one-fits-all solutions are not an option. While it may not mean very much on the surface, the advances of the past 25 years have fundamentally changed the interaction between providers and patients. Instead of selling certainty, providers are showing respect for patients' pain and acknowledging that professional help is not as good as it should be. In sum, patient-centered care has emerged as an important research outcome.

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1. Kreiner M, Betancor E, Clark GT. Occlusal stabilization appliances. Evidence of their efficacy. *J Am Dent Assoc* 2001;132:770-777.