

Animal Models of Chronic Orofacial Pain

Over the past 3 decades, considerable advances have been made in acute pain management and in the understanding of the mechanistic basis of acute pain. Our understanding of chronic pain is much more limited, and most of our knowledge of the pathogenesis of chronic pain states comes from animal and human experimental models of persistent pain associated with spinally innervated tissues. Studies using animal models of chronic pain have documented over the last 20 years various structural, neurochemical, and physiologic changes in the nervous system in these models, such as peripheral and central sensitization, phenotypic alterations in neurons, and activation of glial cells, and these processes have been implicated in the pathogenesis of several chronic pain states.

Some of the most common chronic pain conditions are manifested in the orofacial region. These conditions include various headaches, musculoskeletal pain states such as temporomandibular disorders (TMD), neuropathic pains such as post-herpetic neuralgia and trigeminal neuralgia, and other less well-defined conditions such as burning mouth syndrome, atypical odontalgia, and atypical facial pain. While the development of orofacial chronic pain models has lagged behind that of the spinal models, in the past 10 years greater emphasis has been placed on developing animal models of chronic orofacial neuropathic or inflammatory pain states affecting various tissues, eg, temporomandibular joint (TMJ), muscle, tooth pulp, sinus, and parotid gland tissues. Details of many of these models have been presented in recent articles in the *Journal of Orofacial Pain*.¹⁻⁵ A case in point is TMD; understanding of its etiology and pathogenesis is very limited. Several animal models of TMD have recently been developed, but as the lead article in this issue of the *Journal* notes, each of these TMD models has its limitations. This article presents a study by Thut and colleagues⁶ in which they sought to overcome many of these limitations. The researchers used an established model whereby a chronic inflammatory state is produced in the rat TMJ by application of the inflammatory agent complete Freund's adjuvant. A notable feature of this study is that the investigators monitored changes in the animals' feeding behavior as an assay of hyper-

algesia associated with the chronic TMJ inflammatory condition. The model shows promise for further development and use for investigations of mechanisms related to TMD and of therapeutic interventions to manage pain in TMD conditions manifesting inflammation. The need to develop new models of chronic orofacial pain and to adopt novel approaches to assess the various dimensions of pain behavior was recognized by the National Institute of Dental and Craniofacial Research in the United States in its recent call for applications for studies using new pain models in animals and humans. Ideally, such models should provide a comprehensive reflection of the chronic pain experience, including its emotional distress and disabling effects, along the lines of Dr Palla's recent argument in this journal⁷ that the very definition of chronic pain needs to be reconsidered to include these features of chronic pain states.



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References

1. Dubner R, Ren K. Brainstem mechanisms of persistent pain following injury. *J Orofac Pain* 2004;18:299-305.
2. Henry JL. Future basic science directions into mechanisms of neuropathic pain. *J Orofac Pain* 2004;18:306-310.
3. Iwata K, Tsuboi Y, Shima A, et al. Central neuronal changes after nerve injury: Neuroplastic influences of injury and aging. *J Orofac Pain* 2004;18:293-298.
4. Ro JY. Bite force measurement in awake rats: A behavioral model for persistent orofacial muscle pain and hyperalgesia. *J Orofac Pain* 2005;19:159-167.
5. Spears R, Dees LA, Sapozhnikov M, Bellinger LL, Hutchins B. Temporal changes in inflammatory mediator concentrations in an adjuvant model of temporomandibular joint inflammation. *J Orofac Pain* 2005;19:34-40.
6. Thut PD, Hermansteyne TO, Flake NM, Gold MS. An operant conditioning model to assess changes in feeding behavior associated with temporomandibular joint inflammation in the rat. *J Orofac Pain* 2007;21:7-18.
7. Palla S. A need to redefine chronic pain? [editorial]. *J Orofac Pain* 2006;20:265-266.