

Multiscale Computational Modeling of Nociceptive Responses to Biomechanical Loading in TMJ Disc Displacement

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INTRODUCTION: Temporomandibular joint (TMJ) disc displacement (DD), a structural change, significantly affects oral function and quality of life, with pain during jaw movement being one of the most prevalent symptoms. Currently, few approaches exist to quantitatively characterize the relationship between TMJ structure, function, and pain, limiting our understanding of pain mechanisms and the identification of therapy targets. This study aims to develop a multiscale computational model that integrates biomechanical and neural electrophysiological simulations to analyze the nociceptive signals at the trigeminal ganglion region during clenching and mouth opening in healthy and TMJ DD conditions.

METHODS: Strain distributions of the TMJ disc during clenching and mouth opening were obtained using rigid body dynamics combined with finite element analysis in ArtiSynth Modeling Toolkit for healthy and DD conditions (Fig. 1A). TMJ disc nerve density and morphological characteristics were obtained through 3D nerve mapping of a pig TMJ disc, providing the anatomical basis for developing a reconstruction of peripheral nociceptive nerve fibers in the human TMJ disc using NEURON (Fig. 1B), which integrated ion channels and membrane properties (Fig. 1C). The strain distributions were then mapped onto the membranes of reconstructed nociceptors, activating mechanosensitive ion channels and generating ionic currents. The resulting currents depolarized the membranes, producing receptor potentials that transmitted signals to the trigeminal ganglion region.

RESULTS SECTION: Finite element analysis revealed similar maximum strain (~0.30) during clenching in both conditions but located centrally in healthy joints and posteriorly in DD joints; during mouth opening, DD joints showed a 22% higher maximum strain with the peak also shifted posteriorly (Fig. 2A). 3D nerve mapping revealed fine neural structures in the TMJ disc, with no innervation in the central region and dense innervation at the anterior, posterior, and lateral regions. Nociceptive analysis showed that DD joints had a broader depolarization area of nociceptor membrane potential during clenching and mouth opening compared with healthy joints. Time analysis further revealed pronounced trigeminal ganglion firing rate in DD joints (47 Hz during clenching and 33 Hz during mouth opening), whereas healthy joints exhibited only sparse activity (0–3 Hz) (Fig. 2B).

DISCUSSION: Our results demonstrate a direct link between altered biomechanical loading and nociceptive activation at TMJ disc nerve terminals. They align with the clinical observations that DD-induced loading elevates nociceptive activation, contributing to increased pain intensity. By integrating macroscopic biomechanical loading with microscopic neural electrophysiology, this study provides a novel quantitative approach to elucidate the relationships between TMJ structure, function, and pain.

SIGNIFICANCE/CLINICAL RELEVANCE: By linking altered biomechanics to increased nociceptive signaling, this study enhances understanding of the underlying mechanisms of TMJ pain and offers potential for targeted treatment strategies. Beyond the TMJ, this approach can be applied to investigate structure-function-pain relationships in other load-bearing joints.

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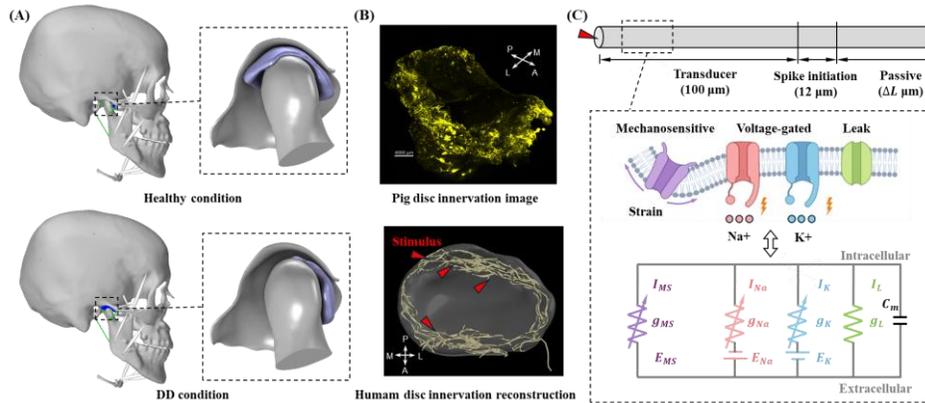


Fig. 1 (A) Finite element model of TMJ. (B) 3D reconstruction of TMJ disc nociceptors. (C) Membrane ion channels of nociceptors.

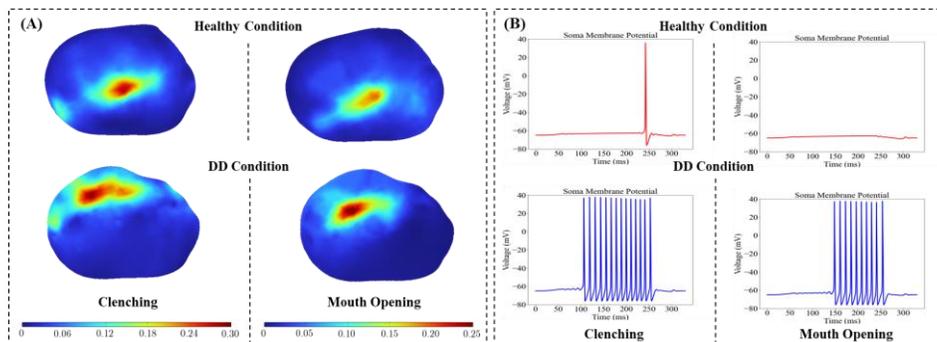


Fig. 2 (A) Strain distribution of TMJ disc. (B) Action potential frequency at trigeminal ganglion.