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Redefining burning mouth syndrome: A nociplastic pain disorder?

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Burning mouth syndrome (BMS) is a complex chronic pain condition characterized by a persistent burning sensation in the oral mucosa without visible lesions. Despite advances in understanding BMS, its etiology remains elusive, likely involving an interplay between peripheral and central mechanisms.[1] We propose that the concept of nociplastic pain may offer a novel framework to explain the pathophysiology of BMS, considering its dual etiology.

Nociplastic pain, as defined by the International Association for the Study of Pain (IASP), arises from altered nociception without clear evidence of tissue damage or inflammation that would typically explain the pain intensity.[2] This is relevant to BMS, which presents with chronic burning pain despite the absence of identifiable causes. Emerging evidence indicates that BMS patients often exhibit features of central sensitization, such as allodynia and hyperalgesia, common in nociplastic pain disorders.

Peripheral mechanisms in burning mouth syndrome[3]

Peripheral nerve dysfunction is a significant factor in BMS. Many patients show signs of small fiber neuropathy (SFN), involving damage to thinly myelinated (Aδ) or unmyelinated (C) sensory nerves. Reduced intraepidermal nerve fiber density in BMS patients suggests a loss of peripheral nociceptors. Impaired nerve conduction in these fibers may contribute to abnormal pain signaling and spontaneous sensations.

Altered ion channel expression, particularly transient receptor potential vanilloid 1 (TRPV1), plays a key role in sensitization. TRPV1 upregulation in BMS increases nociceptive neuron sensitivity to stimuli, leading to exaggerated pain responses. Sodium channel dysregulation (e.g., Nav 1.7) may enhance neuronal excitability, contributing to spontaneous pain.

Neuroimmune interactions may exacerbate sensitization. Elevated levels of pro-inflammatory cytokines (e.g., IL-6, IL-8, TNF-α) in BMS patients indicate a pro-inflammatory state sensitizing peripheral nerve endings. These cytokines can activate TRP channels, enhancing pain transmission and reinforcing peripheral contributions to pain in BMS.

Central mechanisms and nociplastic pain[4]

Central sensitization, a hallmark of BMS, involves enhanced synaptic plasticity and hyperexcitability in trigeminal pathways. NMDA receptor upregulation and increased glutamatergic transmission may lead to sustained neuronal hyperactivity, perpetuating chronic pain independent of

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peripheral input. Additionally, dysfunction in descending pain modulatory pathways with reduced GABA activity and increased facilitatory signaling (e.g., substance P) may amplify pain.

Neuroinflammatory processes involving microglial and astrocytic activation may play a role in maintaining central sensitization in BMS. Elevated cytokines (e.g., IL-1β) can activate Toll-like receptors, promoting pro-nociceptive mediator release that enhances neuronal excitability and pain perception.

Conclusion

In conclusion, we propose that recognizing BMS as a nociplastic "chronic pain continuum"[5] condition aligns well with its clinical presentation and underlying pathophysiology. The defining features of nociplastic pain absence of clear tissue damage, central sensitization, and altered pain modulation—are evident in BMS, highlighting its dual etiology involving both peripheral nerve dysfunction and central sensitization. This perspective may provide a more comprehensive framework for understanding BMS, guiding future research, diagnosis, and treatment strategies aimed at addressing both peripheral and central mechanisms of pain. We encourage further studies to validate this classification and explore novel therapeutic approaches to improve outcomes for patients with BMS.

Declaration of competing interest

The author has no conflicts of interest relevant to this article.

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