Peer Review File

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Reviewer A:

Comment 1: Among many types of chronic pain, those without obvious pathology are the most difficult to deal with, thus induce recurring expenses. In this narrative review, the authors discussed the nociplastic component of idiopathic oro-facial pain (IOFP), especially in elderly patients. While the etiologies of IOFP are still under debate, the key idea here is suggesting that certain dysfunction of descending pain inhibition and dopaminergic nervous system plays a major role in these patients. In particular, they are focused on temporal summation (TS) and conditioned pain modulation (CPM). The ideas are interesting and the paper contributes to the current sparse literature of IOFP, thus likely would be of interest to this journal's readership.

Reply 1: Thank you for this generous comment.

Comment 2: However, a few concerns need to be addressed and a major revision might be required before publication. Here I would like to offer some comments as follows:

- My biggest concern is that the lack of a theoretical framework to support the current ideas.
- It would be helpful to describe the context of other published studies in the field on IOFP and nociplastic pain in the introduction, instead of merely mentioning as "It has recently been reported that idiopathic orofacial pain includes an element of nociplastic pain that represents a modulation in somatosensory processing, such as the dysfunction of descending pain inhibition (2)".

Reply 2: Thank you for this suggestion. An addition has been made to the Introduction accordingly.

Changes in text 2:

Traditionally, pain mechanisms have been divided into "nociceptive" and "neuropathic" categories, neither of which adequately describe IOFPs. The term "nociplastic pain" was introduced by the International Association for the Study of Pain (IASP) in 2017 as a third mechanistic pain descriptor (3).… There is growing recognition that not only changes in peripheral neurons but also changes in central neurons may be involved in the development of PIFP, suggesting the presence of neuropathy

components (4–7). Regardless of the generator of peripheral pain, PIFP has been suggested to occur due to a central phenomenon / amplification caused by processes that occur in the periphery. Similar to those shown in fibromyalgia (8), low back pain (9), and peripheral neuropathic pain (10).

4. Woda A. Pain in the trigeminal system: From orofacial nociception to neural network modeling. J Dent Res 2003; 82: 764–768.
5. Woda A and Pionchon P. A unified concept of idiopathic orofacial pain: Pathophysiologic features. J Orofac Pain 2000; 14: 196–212.
6. Woda A. Neuropathic pain. J Orofac Pain 2007; 22: 257–258.
7. Woda A. A ‘‘dysfunctional’’ pain group in addition to the ‘‘neuropathic’’ and ‘‘nociception/inflammatory’’ groups of orofacial pain entities. J Orofac Pain 2009; 23: 89–90.
8. Mhalla A, de Andrade DC, Baudic S, et al. Alteration of cortical excitability in patients with fibromyalgia. Pain 2010; 149: 495–500.
9. Hashmi JA, Baliki MN, Huang L, et al. Shape shifting pain: Chronification of back pain shifts brain representation from nociceptive to emotional circuits. Brain 2013; 136: 2751–2768.
10. Lefaucheur JP. The use of repetitive transcranial magnetic stimulation (rTMS) in chronic neuropathic pain. Neurophysiol Clin 2006; 36: 117–124. Review 2006/10/19.

Comment 3: Of the 5 main parts (intro and discussion not included), the authors discussed in turn about nociplastic pain, nociplastic pain and BMS, dopamine nervous system dysfunction in BMS, nociplastic pain and PIDAP, and other IOFP in elderly (actually only idiopathic TN). The structure was really confused and fragmented. For example, part 1 and 5 are merely a literature review of nociplastic pain and TN (?, not even classified as one of IOFP).

Reply 3: Thank you for this helpful comment. We reorganized the manuscript for improved clarity and flow. We also removed the part 5 which is other idiopathic orofacial pain in elderly patients, since classical trigeminal neuralgia is not idiopathic conditions.

Comment 4: Page 7, line 95-99: not supported by appropriate references.

Reply 4: Thank you for pointing this out. We added a reference:

Changes in the text: “Kosek E, Cohen M, Baron R, Gebhart GF, Mico JA, Rice ASC, Rief W, Sluka AK. Do we need a third mechanistic descriptor for chronic pain states? Pain. 2016 Jul;157(7):1382-1386. doi: 10.1097/j.pain.0000000000000507.”

Comment 5: The abstract and discussion need to be revised. For example, “The idiopathic oral pain syndromes BMS and PIDAP were previously considered to be psychogenic pain, and are now considered to have nociplastic pain components that are part of the chronic primary pain syndrome.” This is not really discussed in the manuscript well.

Reply 5: Thank you for this helpful comment.

Changes in text 5: “Psychological factors such as anxiety and depression may explain some of the individual variability in pain perception and therefore may also play a role in CPM, possibly due to the fact that serotonin and noradrenaline are involved in both anxiety and depression are involved in the CPM response. Recently, Ozasa et al. found a significant positive correlation of CPM47°C with state and trait anxiety in patients with BMS, suggesting that both state and trait anxiety negatively affect the descending pain modulation system”

“Ozasa K, Noma N, Kobayashi M, Takizawa K, Young A, Eliav E, Imamura Y. Association Between Anxiety and Descending Pain Modulation of Thermal Stimuli in Patients with Burning Mouth Syndrome: A Cross-Sectional Study. J Oral Facial Pain Headache. 2022 Winter;36(1):67-77. doi: 10.11607/ofph.3050.”