

## Review of: "Stellate ganglion block for anosmia and taste disturbance due to Long-COVID"

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This article discusses a case report of a patient receiving bilateral ultrasound guided stellate ganglion block (SGB) for loss of smell and taste associated with COVID-19 infection. The study's findings suggest that SGB may be an effective therapeutic modality for ameliorating long COVID symptoms related to smell/taste dysfunction.

In this review, I raise several points that the authors may consider:

1. The article discussed how SGB can restore smell/taste function by resetting the tone of the autonomic nervous system. However, the discussion section can benefit from a more detailed overview of the potential mechanisms of SGB. For instance, although the effects of the local anesthetic are temporary, why was taste sensation resolved a few days after the second block? Would SGB be targeting central brain regions related to olfactory and gustatory function? Exploring these papers would be helpful in discussing SGB's effects on both peripheral and central nervous systems: <a href="https://doi.org/10.1016/j.mehy.2022.110833">https://doi.org/10.1016/j.mehy.2012.08.019</a>. The discussion section can also benefit from an explanation on how SGB can affect key cranial nerves (CN) related to smell/taste function i.e., CNs 1, 7, 9, and 10 and how blocking the superior cervical ganglion would affect those anatomic structures.

Further, the paper discussed how COVID-19 can lead to hyperinflammation, disturbance in autonomic dysfunction, and thus loss of taste/smell. However, it would be helpful if there is also a more detailed discussion on how SGB may affect COVID-19 related inflammation, facilitate immunomodulatory effects, and thus restore of smell/taste function. Several prior studies have explored SGB's effects on the immune response and they can be further discussed: <a href="https://doi.org/10.1016/j.autneu.2021.102903">https://doi.org/10.1016/j.autneu.2021.102903</a>, <a href="https://doi.org/10.1016/j.autneu.2021.102903">https://doi.org/10.1016/j.autneu.2021.102903</a>, <a href="https://doi.org/10.1016/j.autneu.2021.102903">https://doi.org/10.1016/j.autneu.2021.102903</a>, <a href="https://doi.org/10.1016/j.autneu.2021.102903">https://doi.org/10.1016/j.autneu.2021.102903</a>, <a href="https://doi.org/10.1016/j.autneu.2021.102903">https://doi.org/10.1016/j.autneu.2021.102903</a>, <a href="https://doi.org/10.1016/j.autneu.2021.102903">https://doi.org/10.1016/j.autneu.2021.102903</a>.

2. The study should mention how specifically smell/taste were assessed. As self-reported perceptions of smell/taste can be highly subjective, any exploration of more objective parameters, such as functional neuroimaging of key olfactory/gustatory regions, would be informative. Functional neuroimaging would also be helpful in validating the paper's discussion of SGB's effects on cerebral blood flow: "The increase in CBF leading to improved perfusion of cortical areas associated with the sense of smell or the peripheral receptors in the facial region might be responsible for an immediate resolution of anosmia seen with SGB."

In conjunction to their discussion on SGB's effects on blood flow, further explanation on cerebral blood flow's effects on



neurogenesis of olfactory/gustatory brain regions would be informative. For instance, prior studies have proposed that neurogenesis in the olfactory bulb affect smell function (<a href="https://doi.org/10.1523/JNEUROSCI.22-07-02679.2002">https://doi.org/10.1002/jnr.21455</a>) and that blood flow is closely associated with the migration of newborn cells (<a href="https://doi.org/10.1016/j.gde.2003.08.012">https://doi.org/10.1016/j.gde.2003.08.012</a>.

- 3. The possibility of placebo effect should not be ruled out, and the authors may consider discussing this. As the study was a case report, it is not known whether only a positive finding is being reported and whether there were other patients suffering from COVID-19 related smell/taste dysfunction who did not benefit from SGBs. Further study on a larger cohort of patients and with a control group would be beneficial. Additionally, providing a radiographic picture of successful injection into the targeted site would be informative. The authors should also report whether Horner's syndrome was present after the procedure to confirm successful block.
- 4. COVID-19 associated smell/taste dysfunction has been attributed to dysautonomia. It would be worth mentioning whether the patient suffered from other symptoms related to autonomic dysfunction (i.e. heart rate variability, bowel/bladder dysfunction, fatigue, sleep disturbances) and whether SGB was effective in ameliorating them. Did the patient try any other therapeutic modalities i.e., steroids, to help alleviate autonomic disruption or inflammation?
- 5. In contrast to several SGB procedures that are performed unilaterally, this study reports restoration of taste and smell function after the block was performed bilaterally. Was the decision to perform the block bilaterally due to inefficacy of the block unilaterally? The second block was performed after 72 hours of the first block. What was the rationale for that specific time frame? Would outcomes have been different if the second block was performed a week after the first block? A more detailed explanation of why a bilateral block was more effective than the unilateral block would be beneficial and whether there is a mechanistic difference in blocking the left versus right stellate ganglion.
- 6. The study's findings align well with previous findings on the potential of SGB to treat long COVID symptoms (<a href="https://doi.org/10.1016/j.jneuroim.2021.577784">https://doi.org/10.1016/j.jneuroim.2021.577784</a>). Other studies have also found that SGB can ameliorate smell dysfunction not associated with COVID-19 (<a href="https://doi.org/10.3344/kjp.2013.26.1.57">https://doi.org/10.3344/kjp.2013.26.1.57</a>). Despite progress in accumulating results on the efficacy of SGB to treat smell/taste dysfunction, further study with a larger sample size is needed for validation.

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