Neuromodulators for Treatment of Post-Viral Parosmia

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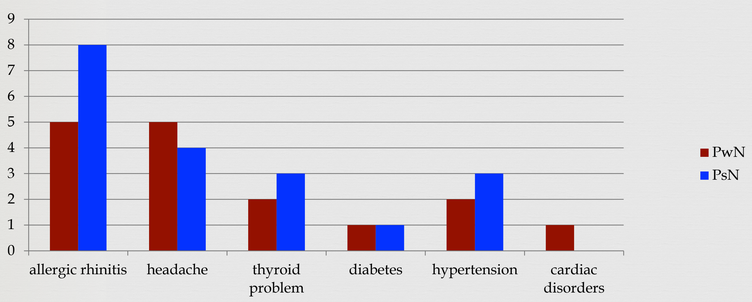
Introduction

Parosmia is defined as a qualitative dysfunction resulting from distorted odor perception in the presence of an odorous medium.[1] This disorder is often associated with negatively perceived changes in odor quality, commonly described as "burnt," "foul," "disgusting" and "fecal".[1–6] Very often, qualitative changes occur in conjunction with quantitative alterations, as distorted sensations can occur any time during the recovery phase, typically 2–3 months after olfactory loss, but can occur even at 1 year out from the initial insult,[7] especially when caused by a viral infection of the upper respiratory tract.[8,9]

Parosmia impacts patient quality of life severely, with a significant proportion of patients reporting symptoms of anxiety and depression, most commonly surrounding food intake.[10–12] Prior to the COVID-19 pandemic, parosmia was noted in patients with post-viral olfactory loss, but the percent of patients with COVID-19 induced olfactory loss associated with parosmia is much higher than previously seen.

Whether the underlying mechanism of parosmia lies within decreased overall number of olfactory receptor neurons or aberrant signaling of the neurons present, or incorrect synaptic connections and signaling more proximally in the pathway at the level of bulb or cortex, or all of the above, will likely determine whether neuromodulating agents will be useful for this group of patients. The purpose of this study was to assess the therapeutic potential of neuromodulators like gabapentin, pregabalin or amitryptiline to treat patients with parosmia.

Figure 1. Comorbidities in all participants



Methods and Materials

In this retrospective analysis, patients presenting to a tertiary care academic smell center with post-viral parosmia that had been **treated with a neuromodulating agent (PwN)** between June 2015 and December 2022 were compared to a cohort of patients with post-viral parosmia who had **not been treated with a neuromodulating agent (PsN).** Duration of parosmia prior to presentation, demographics, medical co-morbidities, UPSIT and SNOT-22 were recorded at presentation.

Follow up was at least 6 months for all patients, and a Visual Analog Scale (VAS) was utilized to assess for subjective score and change over time of smell distortion.

Results

Of 21 patient identified in the PwN group, 18 completed follow up VAS. 18 patients in a controlled, matched cohort of PsN also then completed VAS.

Mean age in the PwN and PsN groups were 44 and 47, respectively. Mean SNOT-22 was 31 and 33, respectively. Mean baseline UPSIT was 24 in both groups. Mean duration of olfactory disturbance was 13.88 months in the PwN group and 19.44 months in the PsN group. There were two active smokers in each group and no patients in either group with chronic rhinosinusitis.

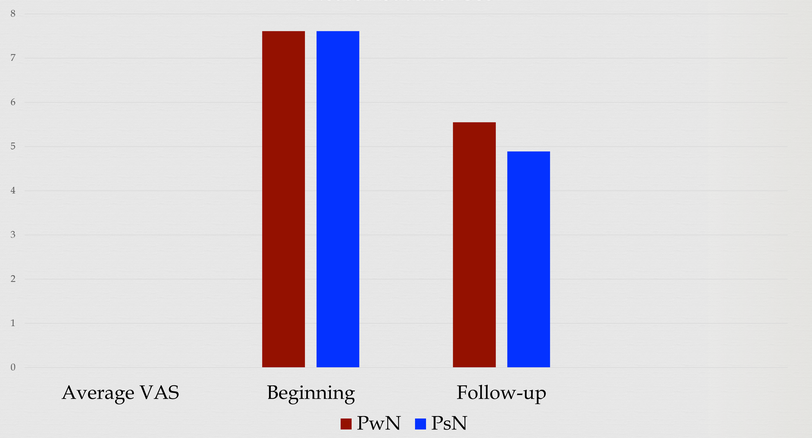
Follow up was at least 6 months with a range of 6-24 months. VAS started at an average of 7.61 in both the PwN group and the PsN, (range 3-10). VAS on follow-up was an average of 5.55 in the PwN group and 4.89 in the PsN group, (range 0-9). 7 patients of the PwN group and 6 patients of the PsN group had a >5 point improvement in the VAS.

There was no significant difference between VAS scores between the two groups (p=0.51), or in duration of parosmia prior to presentation, time to follow-up, co-morbidities, or demographic data.

In the group treated with neuromodulators:

- Gabapentin - 11 cases
- Amitriptyline - 5 cases
- Pregabelin and lamotrigine - 1 case

Figure 2. Change in Parosmia VAS in Patients with and without Neuromodulator Use



Discussion

Although treatment of COVID-19 parosmia with gabapentin was presented only recently by Garcia et al.[13] , the treatment of post-viral parosmia with neuromodulators has been trialed since the 1980s. In the recent small case series, the authors suggest potentially promising treatment effects given the drug's good tolerability in people with post-viral parosmia, achieving subjective improvement of complaints after 3 weeks of treatment in eight of nine patients, although noting the limitation of a small 9-person sample.

In our retrospective study with a larger patient population, we did not observe any significant difference in improvement in the subjective sensation of parosmia. Similarly, the authors of another multicenter longitudinal study of parosmia[14] **show a similar yield of olfactory improvement as the previously mentioned small case series within 3-4 months *without any intervention***, for Covid-19 and non-Covid-19 URIs.

Again, different theories of mechanism underlying parosmia include loss of receptor neurons at the peripheral level by which sensory information is reduced and, consequently, an incomplete olfactory "image" is formed, as well as the theory of central origin, in which there is a distorted perception of odors, which may be due to altered integration and interpretation of odors at the bulb or cortex.[2]

Neuromodulators will likely impact patients with central origins of parosmia but may not impact those with simple loss of receptor cells. **Larger prospective studies are truly needed to delineate whether these medications are an appropriate treatment option for any of these patients, and thus a randomized controlled trial is currently being established to study this question.**

References:

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Conclusions

Direct retrospective comparison of post-viral parosmia treated with and without neuromodulators did not show a significant effect on the outcome of smell distortion. Limitations of this study are its small number and retrospective nature, and the question will have to be answered in a larger scale randomized controlled trial. Until then, there does not appear to be good evidence supporting use of neuromodulators, such as gabapentin, pregabalin or amitriptyline to treat post-viral parosmia.