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Real-world clinical experience with bimodal neuromodulation for the treatment of tinnitus - A case series

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Dear Editor:

Tinnitus is a major health issue in our society that affects 10–15% of the population with bothersome or debilitating symptoms associated with phantom auditory sensations [1]. Bimodal neuromodulation combining sound stimulation with electrical stimulation of non-auditory peripheral nerves including trigeminal, vagus, and other somatosensory nerves can drive neural plasticity relevant for tinnitus treatment and significantly improve tinnitus symptoms [2–5]. Trigeminal nerve activation, such as non-invasive electrical stimulation of the tongue or face, can access neurons throughout the auditory pathway and modulate the reticular activating system of the brain that mediates emotional, attentional, and cognitive functions [6,7]. Therefore, bimodal stimulation using sound paired with stimulation of tongue or face regions may treat tinnitus symptoms, including the affective and bothersome components of the condition.

A recent large-scale clinical trial (TENT-A1) with 326 tinnitus participants investigated the efficacy and safety of bimodal neuromodulation using a device known as Lenire (Neuromod Devices, Ireland) [2]. Lenire is a CE-marked Class IIa device that delivers sound stimulation through wireless headphones and electrical stimulation to the tongue via an intra-oral device. 12-weeks of treatment with Lenire's PS1 stimulation setting significantly reduced tinnitus severity by 14.6 points on a commonly used and validated outcome instrument, the Tinnitus Handicap Inventory (THI) [2]. The minimum clinically important difference (MCID) for the THI is 7 points [8], in which Lenire achieved more than double the MCID. 86.2% of treatment-compliant participants across different bimodal stimulation settings obtained improvements in their THI scores [2].

Although these results were quite encouraging, real-world data are still needed to assess how the Lenire treatment will perform in a realistic clinical setting. Here, we present real-world data for the Lenire treatment at HörSys GmbH, a tinnitus treatment provider in partnership with the Hearing Center Hanover (DHZ) at Hannover Medical School in Germany.

Between November 2019 to May 2021, 20 patients consented to our standard of care procedure for Lenire treatment and in providing their THI scores for evaluation at the screening visit, fitting visit and at the 6-to-12-week follow-up visit. All patients commenced treatment with the PS1 stimulation setting, which consists of pure tones presented to the ears that are synchronized with electrical pulses presented to the top surface of the tongue (details of the stimulation parameters are presented in Ref. [2]). The Hannover Medical School Ethics Committee approved the retrospective analysis of the data for publication in anonymized form. The main indication for Lenire prescription is subjective tinnitus over a period of at least 3 months. Contraindications included those who are under 18 years of age; have a pacemaker, defibrillator, or any other active implantable device; are pregnant; have epilepsy or other conditions which may cause loss of consciousness; have conditions that cause impaired sensitivity in the tongue; or have lesions, sore or inflammation of the oral cavity. All patients were initially assessed by an otolaryngologist and fitted with the device by an acoustician. During fitting, electrical tongue stimulus intensity was calibrated to a comfortable sensation level for the patient and sound stimulus was adjusted to comfortable levels based on the audiogram of each patient. They were also provided comprehensive training with the device and the Lenire User Manual. They were instructed to use the device for up to 60 minutes per day for at least 10 weeks. Patients were asked to return after 6–12 weeks for a follow-up visit, which included assessing their tinnitus with the THI and in updating their stimulation settings as needed. Additional follow-up visits were also scheduled for patients opting to return for further clinical support.

Across the 20 patients, the mean age was 49.6 ± 14.8 years with a mean tinnitus duration of 9.3 ± 9.9 years. Eighteen of the 20 patients were males. The baseline THI score was 46.3 ± 4.8 points, which was based on the averages of the THI values from the screening and fitting visits across all patients. The mean improvement (i.e., decrease) in THI score was 10.4 points (Fig. 1A). Furthermore, as shown in Figs. 1B and 85% of patients achieved an improvement in THI score, which is similar to the 86.2% outcome in the TENT-A1 study. THI improvements ranged from one to 50 points, with ten patients (50%) achieving clinically significant benefit exceeding the MCID. These outcomes are relatively consistent with the positive benefits observed from the TENT-A1 study, though the mean THI improvement and clinically significant responder rate was higher in the TENT-A1 study (i.e., 14.6 points and 72%, respectively). The TENT-A1 results were based on 12 weeks of Lenire treatment, whereas the clinical data presented

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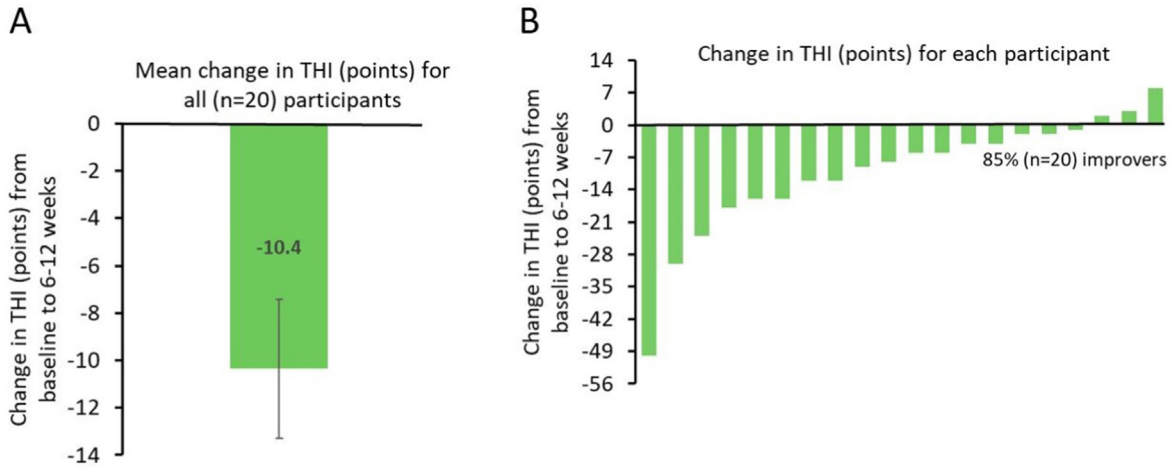

Fig. 1. (**A**) Mean improvement in THI score in 20 patients who received Lenire treatment at HörSys GmbH. Negative value corresponds to improvement in tinnitus symptoms; SEM error bar is shown. (**B**) Change in THI score for each patient with 85% of patients showing improvements in their score.

here were based on a shorter duration of treatment. Also, the larger heterogeneity for the real-world patient population compared to the narrower inclusion criteria for the TENT-A1 study can contribute to these outcome differences, supporting the need for further subtyping of patients to enhance Lenire treatment. In terms of safety, there were no device related issues reported.

These results from 20 patients treated with the Lenire device support the efficacy and safety of bimodal neuromodulation for treating tinnitus in a real-world clinical setting. As more patients are treated with the Lenire device across multiple tinnitus centers, a large population of patient data will become available to further reveal the potential and relative efficacy of bimodal neuromodulation across different subtypes of patients and to help identify the most effective stimulation setting for each patient. At present, only cognitive behavioral therapy is consistently recommended as a clinically validated treatment for tinnitus [9], in which significant improvements in tinnitus symptoms can take 8–12 months through various forms of counselling, education, psychotherapy, and behavioral interventions [10]. The Lenire treatment provides a device-based at-home approach to treat tinnitus symptoms within 6–12 weeks of treatment. This at-home approach offers a potential clinical solution to a larger patient population than is possible with current treatment methods.

Declaration of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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