Reversible Sensorineural Hearing Loss Associated with Off-Label Use of Transcutaneous Vagal Nerve Stimulator

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Transcutaneous vagal nerve stimulators (tVNSs) are available over the counter in Europe, where they are indicated for refractory epilepsy and are known to be used off-label for indications including depression, headache, and insomnia. Previously reported adverse effects from tVNS devices include dizziness and daytime drowsiness but have not been fully studied.1 We present a patient who developed ipsilateral sensorineural hearing loss (SNHL) with use of tVNS for her primary diagnosis of chronic fatigue syndrome and whose hearing improved upon tVNS discontinuation. The Mass Eye and Ear Human Studies Committee granted an exemption for this research.

Case Report
A 58-year-old woman with a history of dysautonomia, chronic fatigue syndrome, and sarcoidosis started using tVNS in her left cymba concha to address chronic fatigue syndrome. Typical daily use was for one 4-hour period, always applied at the cymba concha per instructions included with the device. Of note, this product is not labeled for use under discussion. She had preexisting nonfluctuating SNHL with preserved word recognition and used hearing aids bilaterally (Figure 1A). She noticed a new, gradual decline in hearing in her left ear after several months of using tVNS, and following 14 months of tVNS use, she presented with “muffled hearing” on her left. Interval history was negative for head trauma, ear infections, ear surgery, tick exposure, international travel, otorhea, otalgia, tinnitus, dizziness, or vertigo. She continued to use hearing aids concurrently with tVNS. Her only new medication was pyridostigmine for the past 5 months; all other medications were unchanged. She previously reacted adversely to venlafaxine. She is an entrepreneur. She does not smoke or drink.

Otologic examination was unremarkable. Audiometric evaluation showed decreased word recognition by 20% on the left only, with bilateral increase in pure-tone average (PTA) thresholds of 7 dB compared to 19 months previously (Figure 1B).

The patient brought the tVNS to clinic to demonstrate electrode placement within the cymba concha and provided the device for electrical testing. Device placement in the cymba concha was consistent with manufacturer instructions and previous reports in the literature.1 Output voltages were measured across typical skin impedance using a PXI-4461 Platform (National Instruments, Woburn, Massachusetts) and analyzed in Matlab (Mathworks, Natick, Massachusetts). Testing revealed a 61 nA charge imbalance (Figure 2). She was advised to discontinue tVNS use. Testing for a genetic contribution to hearing loss was ordered.

The patient was scheduled for repeat evaluation in 6 months and was instructed to return sooner if interim hearing changes developed. The patient returned to the otology clinic 5 months after discontinuing tVNS use, reporting improved hearing on the left, now on par with before starting tVNS use. Repeat otologic examination was unremarkable. Audiometry demonstrated improved word recognition on the left of 98% (Figure 1C). Genetic testing for mutations in 87 genes was negative.

Discussion
To our knowledge, this is the first report of SNHL due to a vagal nerve stimulator. Loss and recovery of word
recognition was associated with ipsilateral tVNS use, without change in medications. Threshold shifts, on the other hand, were bilateral and sustained and thus less likely attributable to tVNS use. Several mechanisms may explain the patient’s reversible unilateral SNHL, including inadvertent trigeminal nerve stimulation, autonomic modulation with underlying dysautonomia, or charge imbalance interfering with endocochlear potential.

Trigeminal ganglion stimulation increases vascular permeability of vertebrobasilar and cochlear arteries in guinea pigs. Trigeminal and vagal dermatomes are immediately adjacent in the concha, and inadvertent cross-stimulation may occur with inconsistent electrode placement.

Use of the tVNS may have exacerbated her underlying dysautonomia and cochlear blood flow. Reduced sympathetic activation can protect the cochlea in auditory trauma; however, effects are small and inconsistently reproducible. Targeted stimulation of cochlear autonomic innervation has not been well characterized as for the trigeminal nerve, making comparison difficult.

Finally, tVNS charge imbalance may have influenced endocochlear potential, reducing word recognition. Even with such a small current imbalance of 61 nA, the accumulation of unbalanced charge delivered to the inner ear over time maintains the potential to damage hearing.

Our analysis is limited in that none of these proposed mechanisms definitively explain the patient’s clinical course. Her hearing loss etiology is likely multifactorial, including both chronic bilateral progression and an acutely superimposed component of unilateral reduced word recognition related to tVNS use.

Conclusions
Regardless of mechanism, patients using tVNSs should be warned about the particular risk of SNHL, in addition to broader risks of using the device off-label. Patients should be advised to discontinue use and return to the clinic if hearing changes are noted after starting tVNS use. For tVNS-using patients, clinicians should have a low threshold for audiometry in new-onset hearing loss.

Author Contributions
Samuel Early, concept design, data acquisition and analysis, drafting and revision of manuscript for intellectual content, final approval of submitted manuscript, accountable for accuracy and integrity of work; Konstantina M. Stankovic, concept design, data acquisition and analysis, critical revision of manuscript for intellectual content, final approval of submitted manuscript, accountable for accuracy and integrity of work.

**Figure 1.** Longitudinal audiometry in setting of transcutaneous vagal nerve stimulation use: 5 months before starting (A), after 14 months’ use (B), and 5 months after discontinuing (C). Pure-tone average (PTA) is average of 2 lowest thresholds from 500 to 2000 Hz.
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References

Figure 2. Electrical testing of the patient’s transcutaneous vagal nerve stimulator. Vertical axes in A to C indicate output voltage as measured across typical dry-skin impedance (2 kΩ), and horizontal axes demonstrate progressive magnification of time scale (schematized with a magnifying lens in A and B) to better characterize wave shape.