

# Safety and Efficacy of Vagus Nerve Stimulation Paired With Tones for the Treatment of Tinnitus: A Case Series

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**Objective:** Classical neuromodulation applies current to the nervous system in an attempt to alter ongoing activity. However, classical neuromodulation interferes with activity but does not drive it in a controlled way. Recently, an animal study demonstrated it is possible to drive plasticity in a controlled way by using stimulation of the vagus nerve paired with tones. This reversed the tinnitus percept and pathological neural plasticity in noise-exposed rats with behavioral characteristics of tinnitus. The aim of the current study was to translate this innovative neuromodulation method to humans suffering from tinnitus.

**Materials and Methods:** Ten patients with severe chronic tinnitus were implanted with electrodes on their left vagus nerve. Two and a half hours each day for 20 days, the patients heard tones, excluding the tinnitus-matched frequency, paired with brief electrical stimulation of the vagus nerve.

**Results:** The therapy was well tolerated, and no patient withdrew from the study due to complications or side-effects. Four of the ten patients exhibited clinically meaningful improvements in their tinnitus, both for the affective component, as quantified by the Tinnitus Handicap Inventory, and for the sound percept, as quantified by the minimum masking level. These improvements were stable for more than two months after the end of therapy. Of the ten patients, five were on medications that included muscarinic antagonists, norepinephrine agonists, and  $\gamma$ -amino butyric acid agonists, thereby possibly interfering with acetylcholine and norepinephrine release induced by vagus nerve stimulation (VNS) and essential for inducing plasticity. These patients had no improvement in contrast to medication-free patients.

**Conclusion:** VNS paired with tones excluding the tinnitus-matched frequency is safe and feasible. It seems to exert a beneficial effect in nonmedication-taking patients, both with regard to the perceived sound and the distress. Further studies are therefore mandated.

**Keywords:** Tinnitus, vagal nerve stimulation

**Conflicts of interest:** Drs. De Ridder and Vanneste have no conflicts of interest. Dr. Engineer is working for Microtransponder. Dr. Kilgard is a consult for Microtransponder.