

Tinnitus and Bimodal Stimulation: How the brain changes its response to tinnitus?

Ali A. Danesh, PhD, FAAA

Farzon Danesh, AuD, CCC-A

Board Certified, American Board of Audiology

Professor, Department of Communication Sciences and Disorders

Clinical Affiliate Professor (Secondary), Integrated Medical Science, College of Medicine

Affiliate Faculty, Department of Psychology, College of Science & Affiliate Professor, Department of Electrical Engineering and

Computer Science, College of Engineering and Computer Science

Voluntary Associate Professor, Department of Otolaryngology, Miller School of Medicine, University of Miami

Audiologist, Labyrinth Audiology, Boca Raton, FL



Ali A. Danesh, PhD

Professor, Department of Communication Sciences and Disorders & Integrated Medical Sciences, Florida Atlantic University

Dr. Ali A. Danesh, Ph.D., CCC-A, FAAA, is currently a Professor at the Department of Communication Sciences and Disorders, and also has a Secondary appointment as Professor of Integrated Medical Sciences in the Charles E. Schmidt College of Medicine, Florida Atlantic University (FAU), Boca Raton, Florida, where he teaches courses in neuroanatomy and neurophysiology of auditory and vestibular systems, audiology, genetics of communicative disorders, and aural rehabilitation. His primary research focus and interest are in the areas of tinnitus, hyperacusis, misophonia, auditory evoked potentials, auditory processing disorders, auditory responses in both normal and pathological populations, vestibular assessment, and diagnostic/rehabilitative audiology. Dr Danesh has affiliate positions in the College of Science, Department of Psychology and Department of Electrical Engineering and Computer Science at FAU. Dr. Danesh obtained his B.Sc. in audiology from Iran University of Medical Sciences, Tehran, Iran, his M.S. in audiology from Idaho State University, Pocatello, Idaho, and his Ph.D. in audiology, with an emphasis on auditory electrophysiology, from the University of Memphis, Memphis, Tennessee. Dr. Danesh is an American Board of Audiology board certified practicing audiologist. His current clinical work concentrates on patients with vertigo, hearing disorders, tinnitus, and decreased sound tolerance disorders (e.g., hyperacusis and misophonia). Dr. Danesh has published more than 40 peer reviewed articles and has presented more than 100 lectures at state, national and international professional meetings.



Farzon Danesh, AuD

- Dr. Farzon Danesh is an audiologist specializing in tinnitus, hearing loss, dizziness, and cerumen removal. His career in audiology began at the age of sixteen with Labyrinth Audiology, where he first honed his expertise. Dr. Danesh earned his Bachelor's degree in Biotechnology from the University of Central Florida and subsequently completed his Doctorate in Audiology at Nova Southeastern University.
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- Following his academic achievements, Dr. Danesh dedicated his professional efforts to serving veterans, addressing their hearing and balance issues, including those resulting from combat-related exposures. This experience provided him with profound insights into the complexities of audiological conditions.
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- Currently, as a valued member of the Labyrinth Audiology team, Dr. Danesh is committed to serving his local community—the very community where he grew up. In addition to his clinical work, Dr. Danesh contributes to the field of audiology through his role as a part-time instructor, teaching audiology courses to master's students at Florida Atlantic University. His dedication to both his patients and his profession underscores his commitment to advancing the field of audiology.



Purpose

- The purpose of this presentation is to introduce and define bimodal auditory and electrical stimulations for tinnitus, analyze recent literature discussing the use of bimodal neuromodulation for the treatment of tinnitus and understand its efficacy and future research recommendations.



What is tinnitus?

- Tinnitus is the perception of sound in the absence of an external stimuli and is commonly described as “ringing in the ears.” (Conlon et al., 2019).
- It is a major health concern that affects roughly 10-15% of the population (Buechner et al., 2022) and approximately 2-3% experience a severe form of tinnitus (Langguth, 2020).

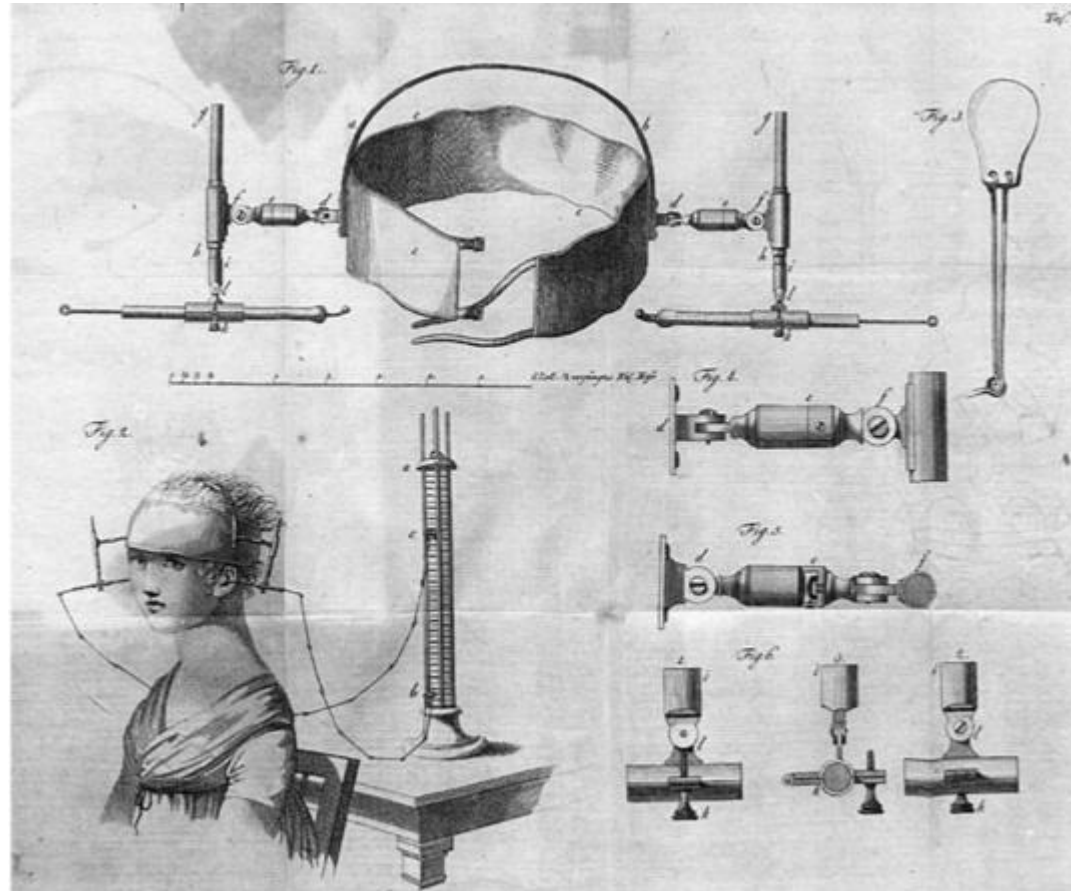
Electrical Stimulation: Where did it all begin?

Alessandro Volta (1745-1827)
Inventor of Battery



Application of Electricity for Hearing

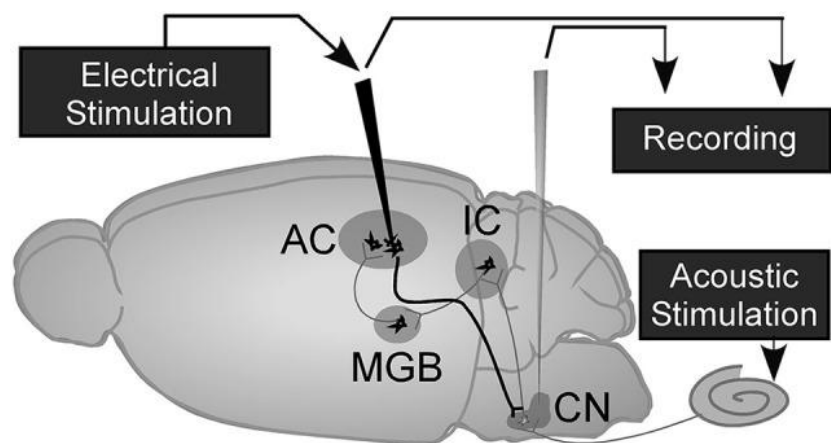
The first application of the Voltaic battery as a cure for deafness, described by Volta himself.





What is bimodal neuromodulation?

- Bimodal neuromodulation for tinnitus treatment combines auditory stimuli with electrical stimulation (Riffle et al., 2021).
- It has been tested and supported by animal studies demonstrating that it can evoke neural plasticity within the auditory cortex (Conlon et al., 2022).



Bimodal vs. Unimodal neuromodulation

“Neurons that fire together, wire together.” (Hebb, 1949)

- Bimodal stimulation may be more effective than unimodal stimulation in inducing neuroplasticity since it can cause long-term potentiation (LTP), (De Ridder et al., 2021).

LTP: “a process that strengthens the connection between neurons, which is thought to be a cellular basis for learning and memory”.

IMPORTANCE OF EXPLORING BIMODAL NEUROMODULATION



“There is a globally recognized clinical need for new treatments for tinnitus because of the lack of effective options for this debilitating condition” (Conlon et al., 2020).

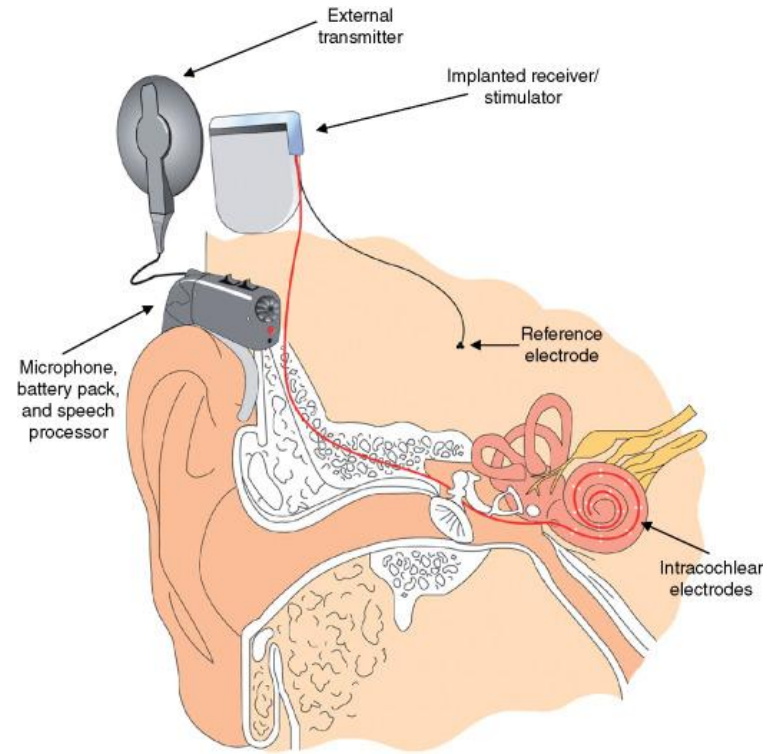


Tinnitus has a major impact on the quality of life and those affected often suffer from sleep disorders, anxiety, and depression (Spencer et al., 2022).



As of today, treatment focuses on reducing tinnitus-related annoyances and no established treatment with supporting evidence from randomized controlled studies for reducing tinnitus loudness exist (Langguth, 2020).

What is the most common electrical stimulator in our field? Cochlear Implant!



For tinnitus treatment, where the electrical stimulations are applied to?

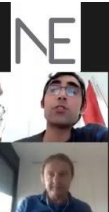
- Skin (surface epidermal)
- Skin/Transdermal/transcutaneous
- External Auditory Canal/Vagus Nerve
- Lobule/Pinna
- Cochlear Stimulation via Cochlear Implants
- Wrist
- Radial nerve
- Skull
- Dorsal Cochlear Nucleus (DCN)/Neck
- Lateral Neck/ Vagus Nerve
- Tongue/Trigeminal Nerve
- Auditory cortex and subcortical nuclei (invasive); Deep Brain Stimulation for Tinnitus??

Electricity is the Language of the Brain!



Instrumentation and set-up

NE
neuroelectric



Electrodes

- 1st gen (traditional): 25-35 cm² saline-soaked sponges.
- Current models: Small (1 cm radius) Ag/AgCl with conductive gel.



Headcap



Cable connectors

Stimulator

- Current controlled.
- 1-4 mA total injected current.
- Multiple channels.
- Different waveforms allowed.



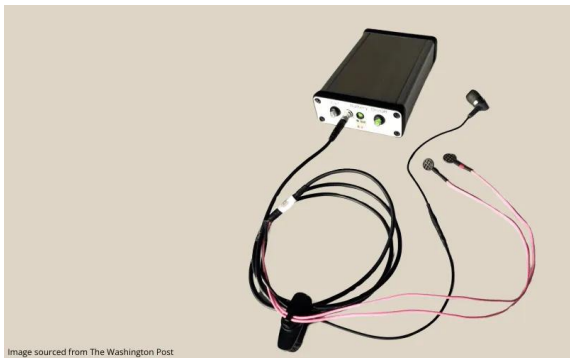
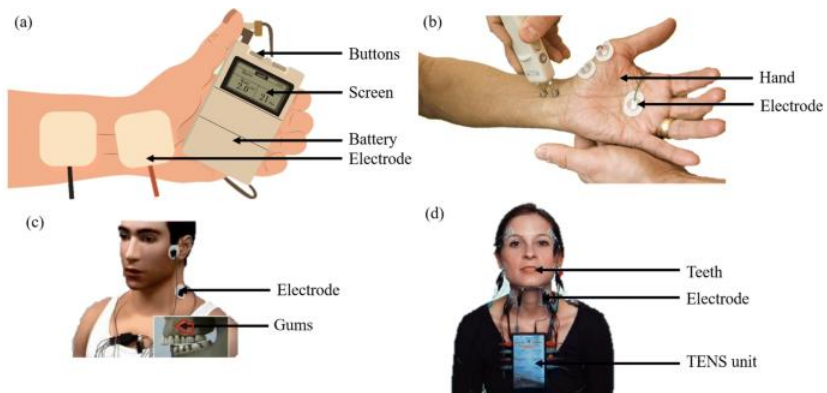
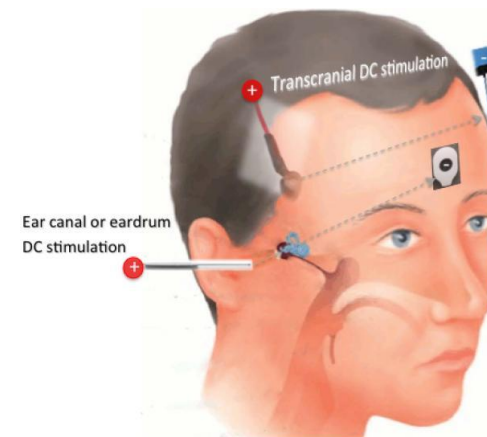
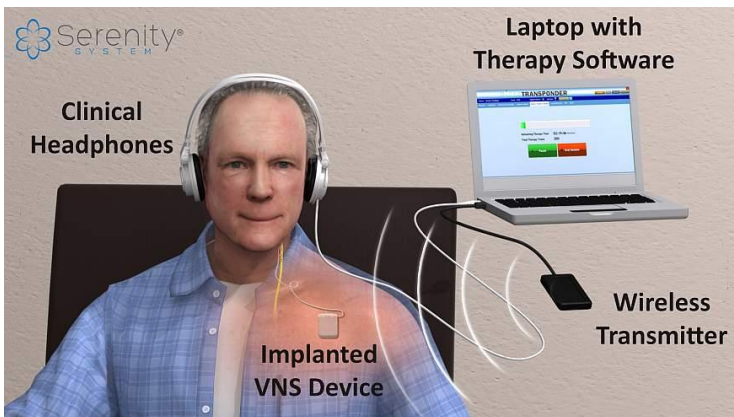
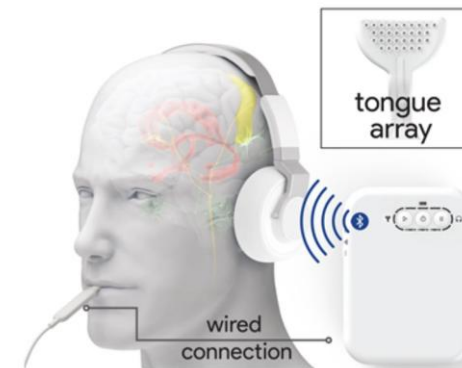
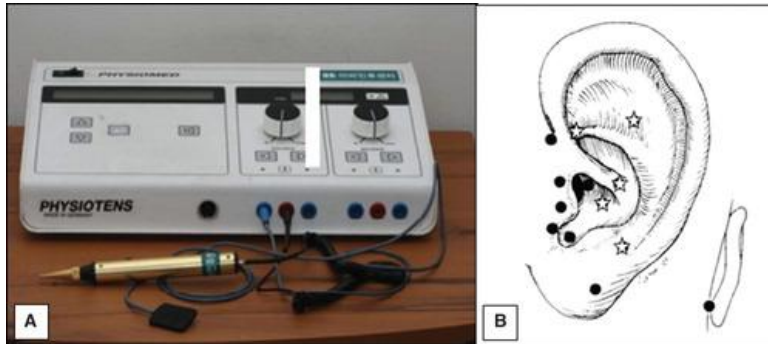
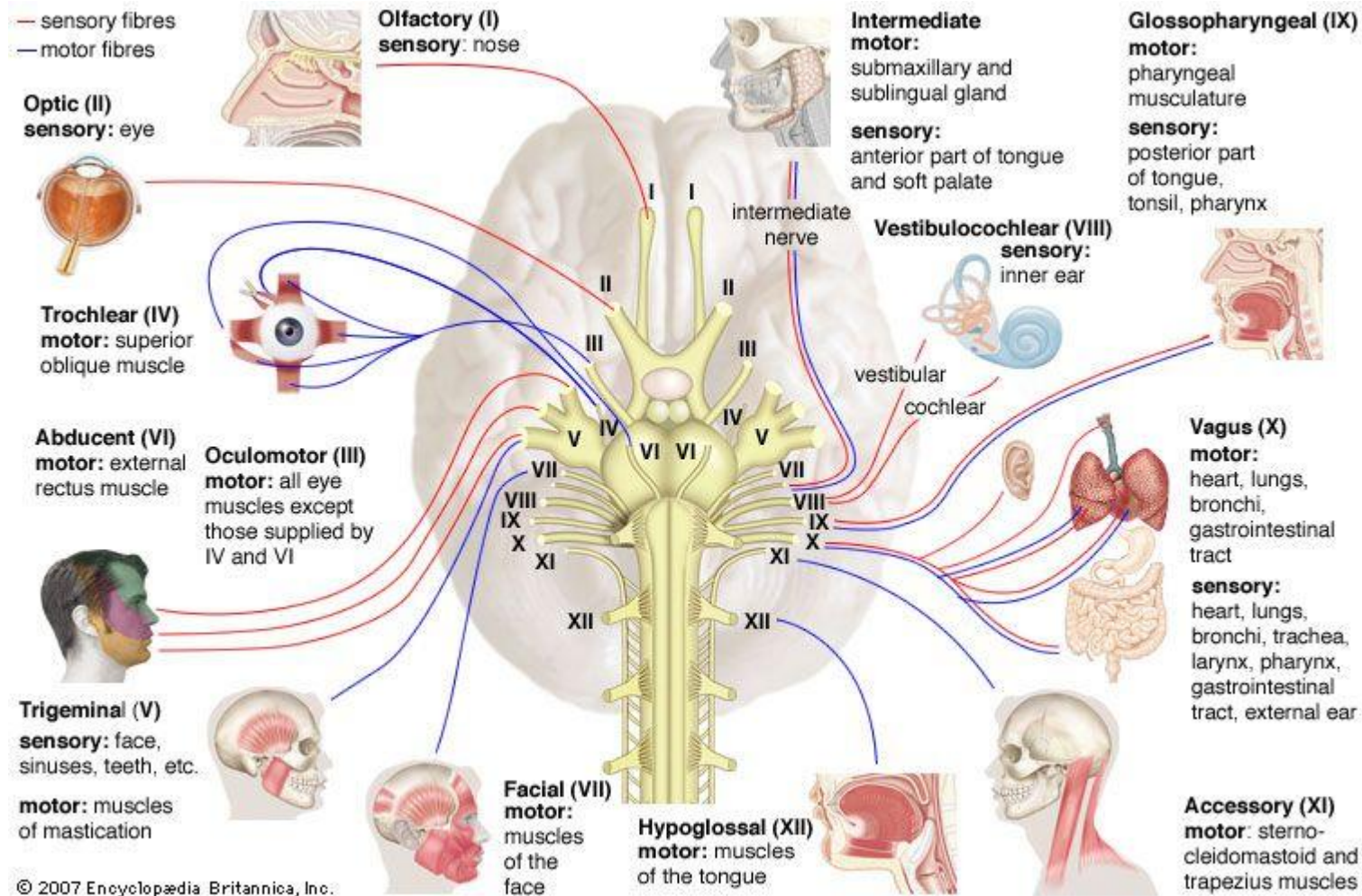


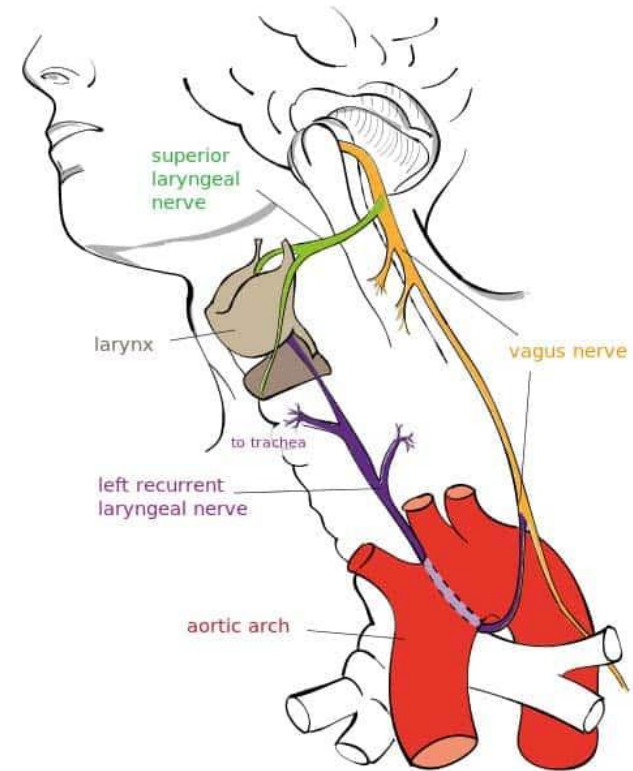
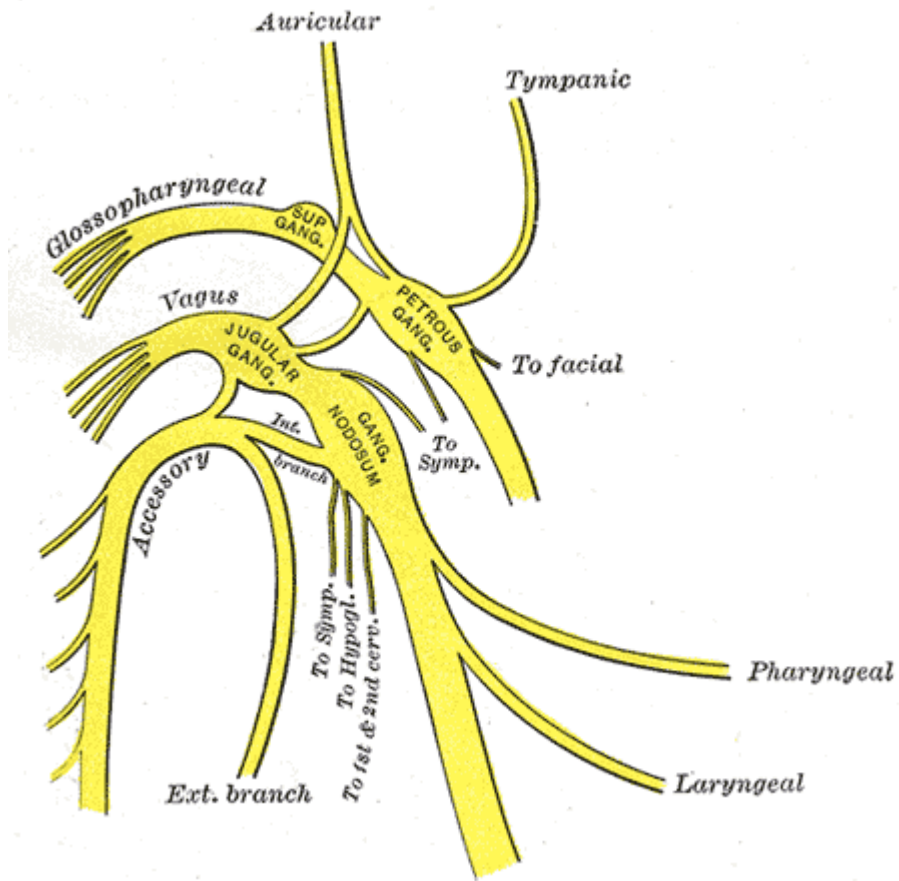
Image sourced from The Washington Post



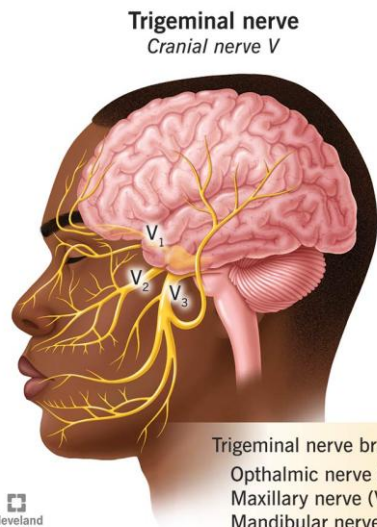
Cranial Nerves



Vagus Nerve and its branches

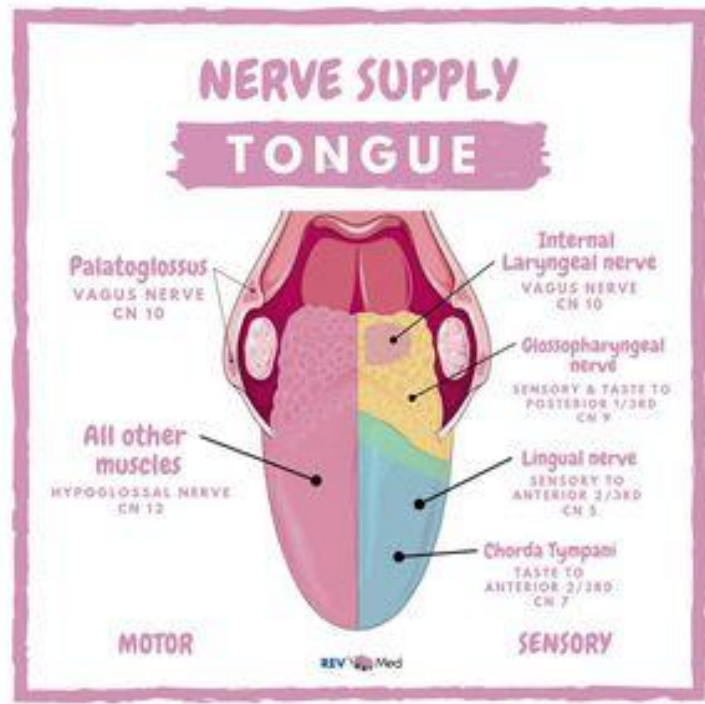
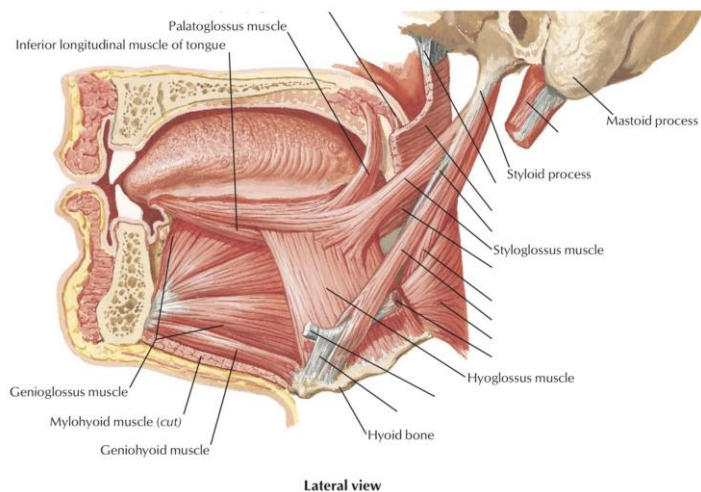
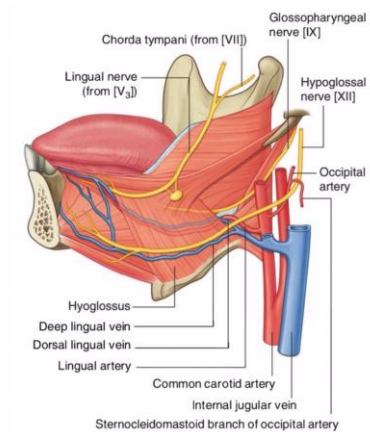


Trigeminal Nerve Branches and Tongue sensory and motor innervations (V, VII, IX, X, XII).



Cleveland Clinic ©2024

Trigeminal nerve branches
Ophthalmic nerve (V₁)
Maxillary nerve (V₂)
Mandibular nerve (V₃)



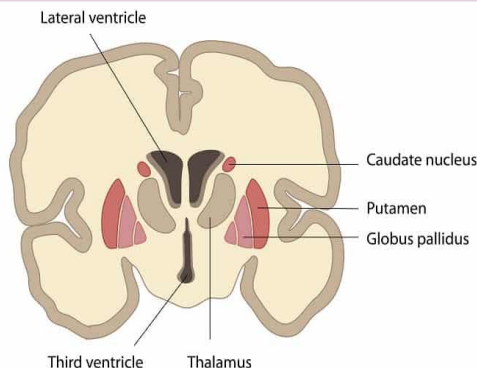
Neuromodulatory Interventions for Tinnitus

Invasive:

- **Auditory cortex**
 - Therapeutic effects depend on electrode placement and patient-specific factors.
- **Deep Brain Stimulation**
 - Targeting the caudate nucleus has been found to reduce tinnitus severity in some patients.

Non-invasive:

- **Transcranial magnetic stimulation (TMS)**
 - Recent studies have shown that rTMS may be beneficial for improving the suffering, but not the tinnitus loudness.



De Ridder et al. (2021)

“Tinnitus and Brain Stimulation”

De Ridder et al. (2021)

Bimodal (Somatosensory and auditory) stimulation approaches:

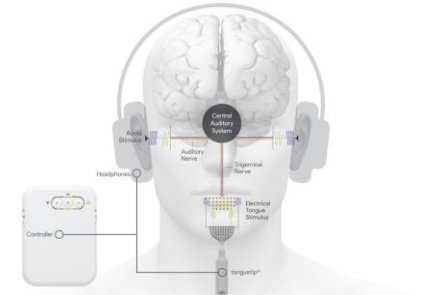
Sound + tES of the C2 nerve

- Modulate activity in the central auditory system by inhibiting activity in the dorsal cochlear nucleus.
- This treatment can improve tinnitus loudness and distress, but its effects were found to be short-lasting.



Sound + tES of the trigeminal nerve

- Provide stimulation over the somatosensory system to compensate the auditory deafferentation that is thought to cause tinnitus.
- Electrical stimulation via the tongue paired with sound, was found to deliver positive long-lasting effects on tinnitus distress.



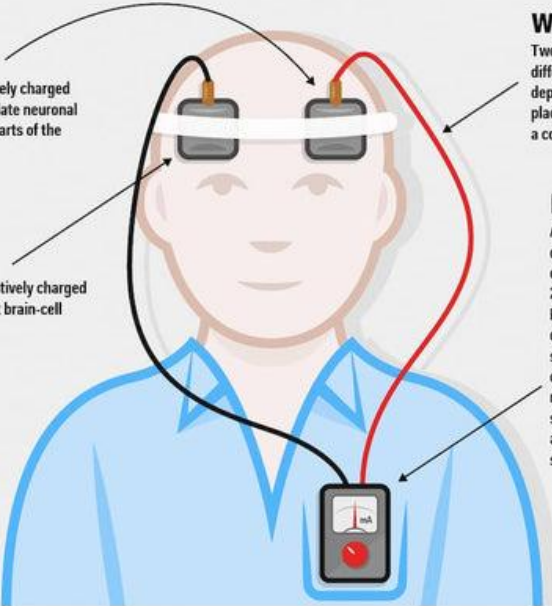
tDCS

vs

direct cortical stimulation

TRANSCRANIAL DIRECT CURRENT STIMULATION

Some studies show that stimulating the brain with electricity can immediately boost memory, focus, energy, and vigilance. Researchers say that it also shows promise as a means of treating drug-resistant mental illness like depression, as well as conditions like epilepsy and chronic pain. Here's how it works:



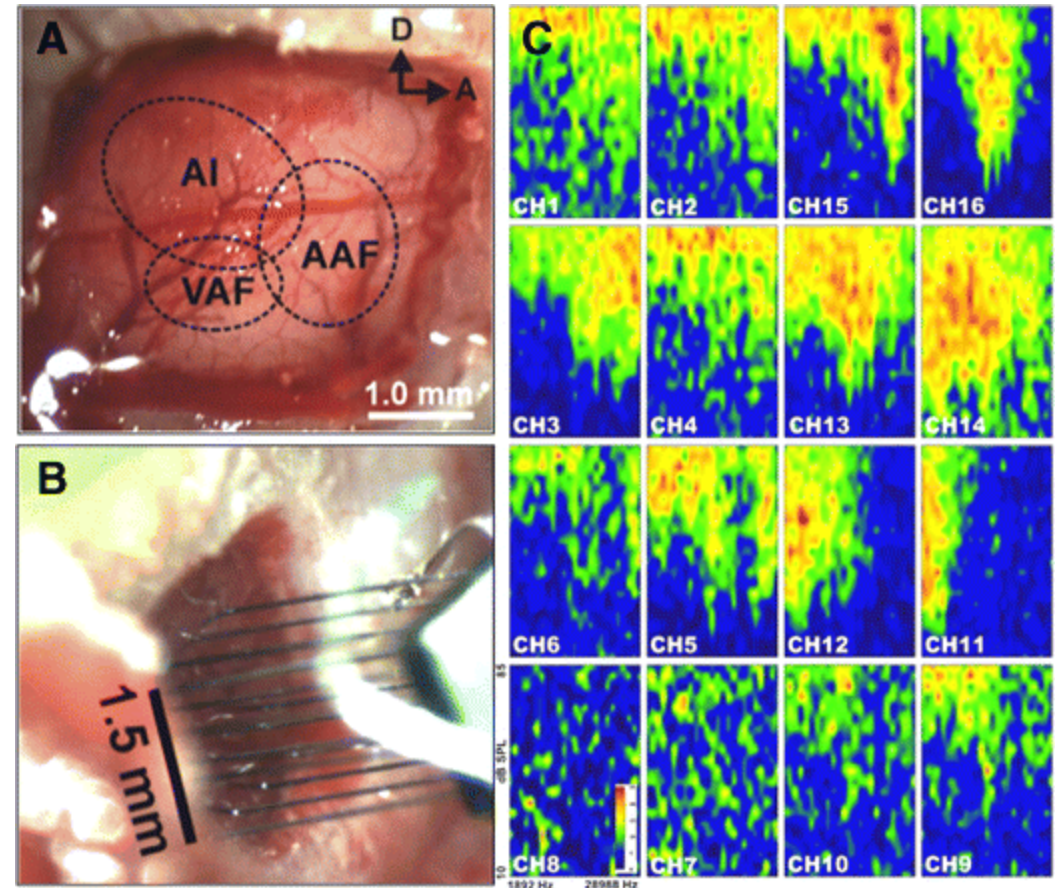
ANODE
The anode, or positively charged electrode, can stimulate neuronal activity in different parts of the brain.

CATHODE
The cathode, or negatively charged electrode, can inhibit brain-cell activity.

WIRES
Two electrodes can provide different types of stimulation, depending on where they are placed. Together, they make a complete circuit.

DEVICE
A battery-powered device delivers a constant electrical current of up to 2 mA (milliamperes). Researchers have demonstrated that it's safe to apply this much current for up to 30 minutes a day. DIY brain stimulators frequently use a 9-volt battery as a power source.

Source: Wright State Research Institute, Johns Hopkins Medicine



Auditory Cortex Electrical Stimulation Suppresses Tinnitus in Rats

Where the electrical stimulations are applied to?

The use of electrodes on TM!

- The tympanic membrane is that closest place in the head, to which noninvasive electric stimulation can be applied.
- Tympanic membrane electrode is four times more efficient than ear canal electrode and 10 times more than scalp electrodes in terms of electrically evoked auditory responses.
- Tympanic membrane electric stimulation is more effective in tinnitus suppression than ear canal and scalp-based electric stimulation.

Source: Electric hearing and tinnitus suppression by noninvasive ear stimulation (Sue et al., 2021)
<https://www.sciencedirect.com/science/article/pii/S0378595522000028>

A. Ear canal electrode



B. Tympanic membrane electrode



Bimodal neuromodulation study

“Auditory-somatosensory bimodal stimulation desynchronizes brain circuitry to reduce tinnitus in guinea pigs and humans”

Marks et al. (2018)

i. OBJECTIVE:

- i. This study aimed to explore auditory-somatosensory bimodal stimulation to induce long-term depression in fusiform cells of the dorsal nuclear complex (DNC) to alleviate tinnitus first in animals and then translate it to human subjects.

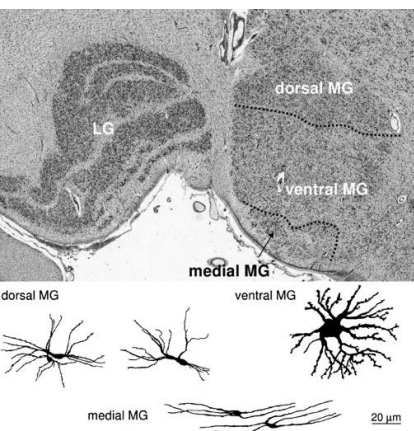
i. METHODOLOGY:

i. Guinea pigs:

- i. Auditory-somatosensory stimulation 30 minutes daily for 25 days.

ii. Human subjects:

- i. 20 participants participated in a double-blinded, sham-controlled, cross-over study and weekly self-reported questionnaires were obtained.



Bimodal neuromodulation study

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Marks et al. (2018)

i. FINDINGS:

- i. In **human subjects'** bimodal stimulation produced a statistically significant decrease in tinnitus loudness after 28 days. 50% of subjects had a clinically significant reduction in TFI scores.
- ii. In **guinea pigs'** bimodal stimulation reduced physiological and behavioral evidence of tinnitus after 25 days was observed.
- iii. Bimodal stimulation demonstrated to be more beneficial than unimodal stimulation

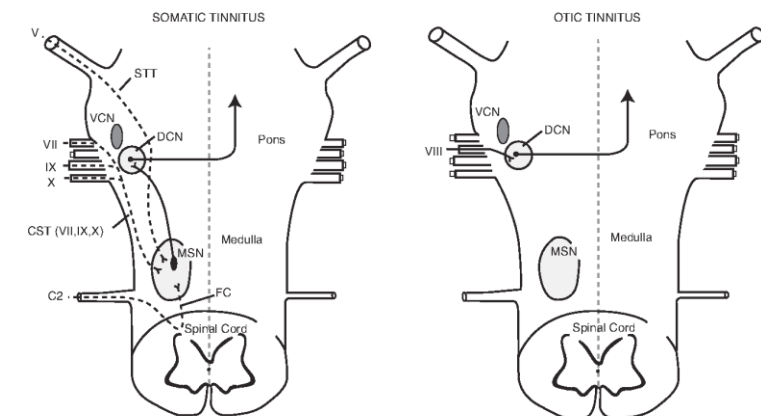
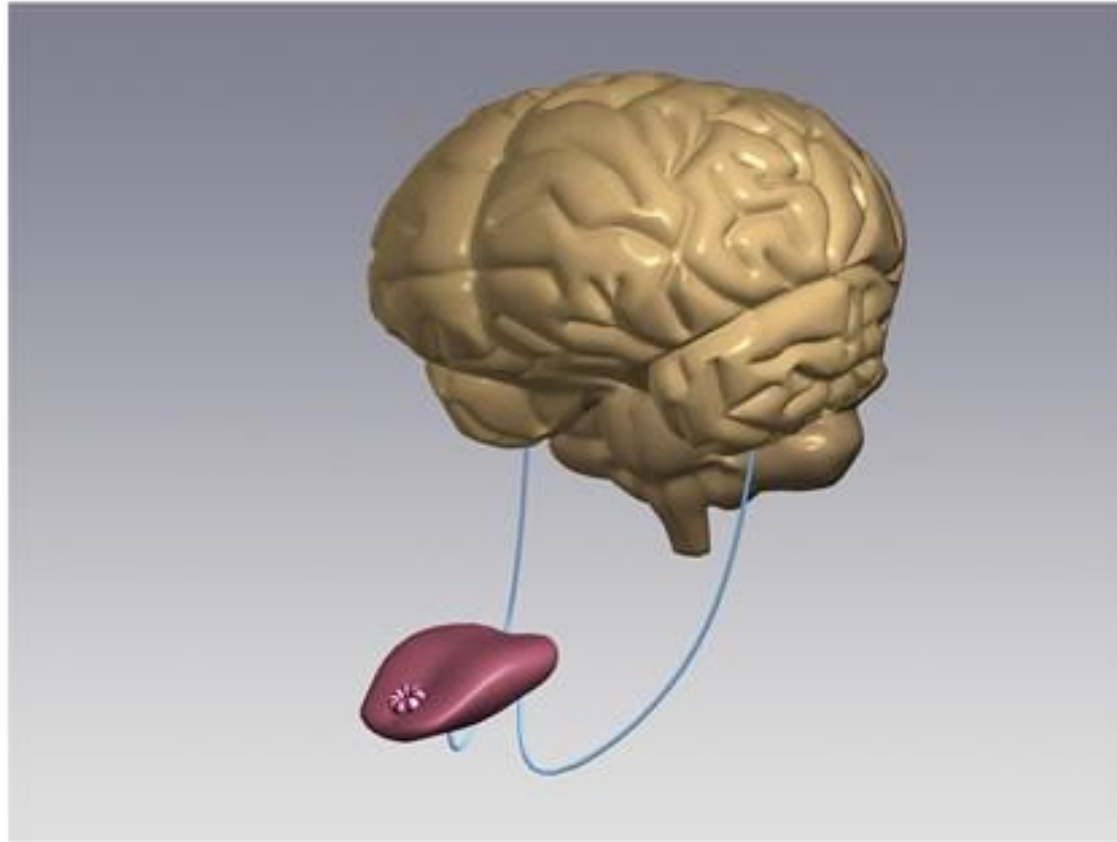


FIGURE 9-1 Schematic diagram of the brainstem and upper cervical part of the spinal cord, depicting the anatomic basis

Bimodal Stimulation for tinnitus using Neuromod



What makes up Lenire?



TONGUETIP®

A proprietary intra-oral device, ergonomically designed to sit comfortably in the closed mouth. Tiny electrodes on the Tonguetip deliver mild and safe energy pulses to activate nerves from the tongue.



CONTROLLER

A lightweight handheld device that controls the timing and intensity of the treatment. Patients can start, pause and resume the treatment session, adjust the volume of the sound, and adjust the level of the tongue stimulation.



HEADPHONES

A set of Bluetooth wireless headphones for use specifically with the controller are provided as part of the Lenire package. They are paired to the controller and deliver customized sounds to activate the auditory nerve.

How does Lenire work?

Lenire's bimodal neuromodulation delivers mild electrical pulses to the tongue combined with sound played through headphones to drive changes in the brain to reduce tinnitus severity.



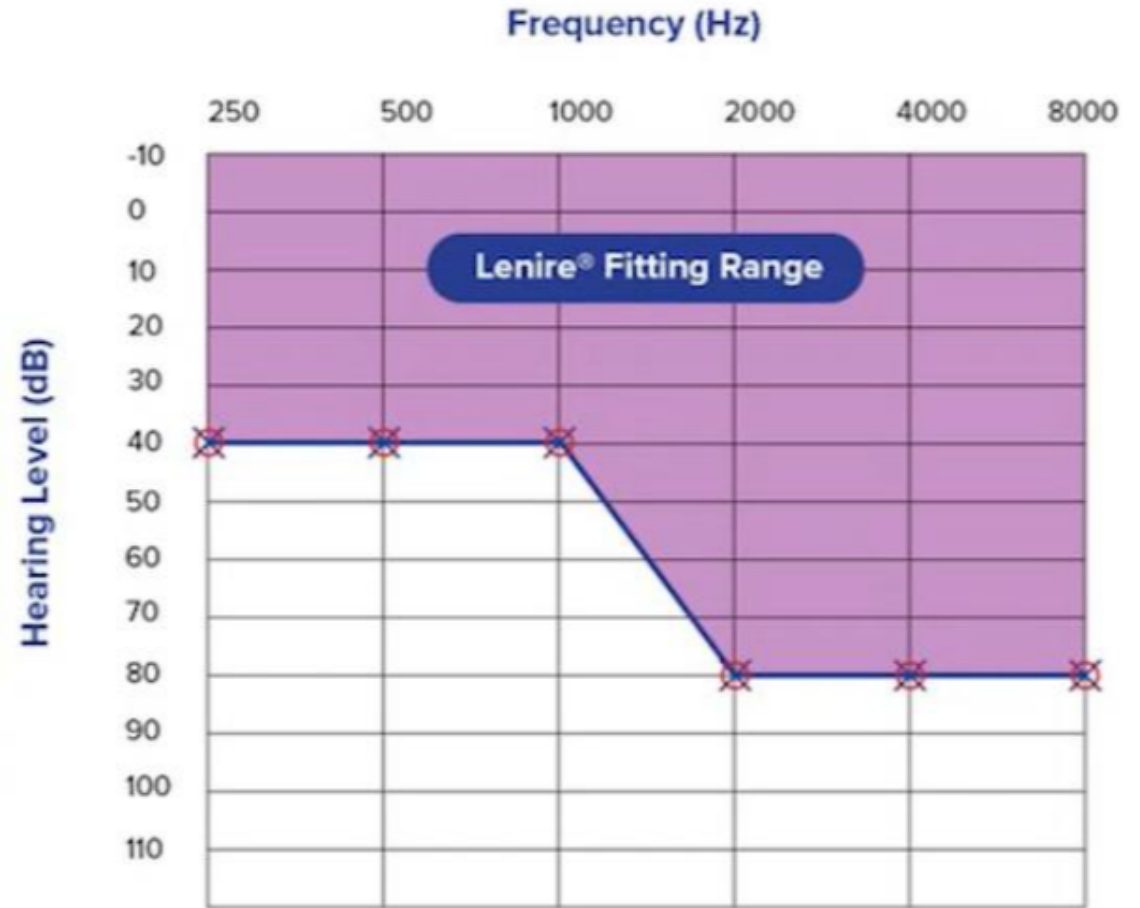
Lenire Fitting Range

Considerations

Compensation of the patient's hearing loss is limited to hearing thresholds up to

- 40 dB HL at 250 - 1k Hz
- 80 dB HL at 2k - 8k Hz

- Not a contraindication for the treatment with Lenire
- No additional risk for the patient
- Lower perception of the loudness of audio



Are there any contraindications for Lenire?

Lenire is intended to treat patients 18 years of age and older suffering from at least moderate, subjective tinnitus

Lenire is not suitable if:

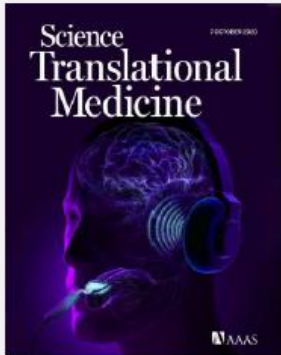
- You have a pacemaker, defibrillator or any other active implantable device.*
- You are pregnant.*
- You suffer from epilepsy or any other condition that may result in loss of consciousness.*
- You suffer from any condition that causes impaired sensitivity of the tongue.**
- You have oral cavity inflammation, sores or lesions that may contact the Tonguetip.**
- You are suffering from any intermittent or chronic neuralgia in the head and neck area.*
- If you have Meniere's disease.* Lenire use has not been evaluated for Meniere's disease.
- If you have objective source tinnitus.
- In the presence of oral piercings.

*Unless directed by a physician.

**Unless directed by a physician or dentist.

Summary of Three Large-Scale Trials

Neuromod devices have undertaken several clinical studies involving a bimodal neuromodulation device (Lenire) to assess safety and the therapeutic effects of bimodal stimulation on tinnitus, which have been published in scientific journals.

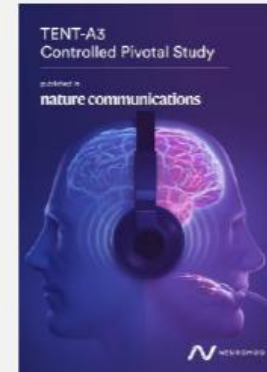


TENT-A1 (Treatment Evaluation of Neuromodulation for Tinnitus) was a randomized, double-blind trial that supported the safety and effectiveness of 12 weeks of bimodal stimulation in 326 tinnitus participants¹.

TENT-A2, which was designed to build on and strengthen the findings from TENT-A1, supported the safety and effectiveness of different stimulation settings of bimodal treatment in 191 tinnitus participants².



Recent **TENT-A3** confirmatory controlled clinical trial (n=112) was completed across 3 sites in Europe and data was submitted to FDA. **Lenire was granted De Novo approval in March 2023 (created new medical device category).**

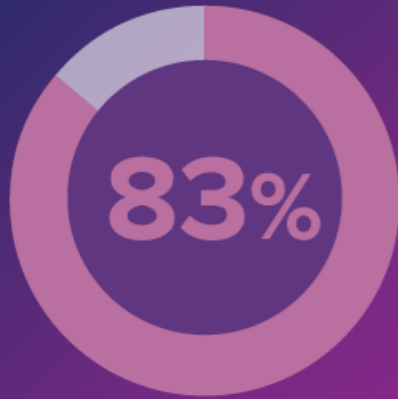


Primary objective was to confirm that bimodal sound and tongue stimulation provides significant clinical benefit beyond sound therapy alone, based on findings from TENT-A2.

1. Conlon B, Langguth B, Hamilton C, Hughes S, Meade E, Conno CO, Schecklmann M, Hall DA, Vanneste S, Leong SL, Subramaniam T, D'Arcy S, Lim HH. Bimodal neuromodulation combining sound and tongue stimulation reduces tinnitus symptoms in a large randomized clinical study. *Science Translational Medicine*. 12: 564, eabb2830 (2020).
2. Conlon B, Hamilton C, Meade E, Leong SL, O Connor C, Langguth B, Vanneste S, Hall DA, Hughes S, Lim HH. Different bimodal neuromodulation settings reduce tinnitus symptoms in a large randomized trial. *Nature Scientific Reports*, 12(1), 10845 (2022).

Is Lenire safe and effective?

Lenire is clinically proven to be more effective at treating tinnitus than sound-only stimulation for people with moderate or worse tinnitus.



of 500+ participants across three large scale clinical trials would recommend Lenire to treat tinnitus.^{1, 2, 3}

7/10

of people with moderate or worse tinnitus had a significant reduction in tinnitus after 6-weeks when 6-weeks of sound-only had little impact.⁴



Zero

serious adverse side effects related to treatment were reported during Lenire's recent large-scale clinical trial.⁴

Lenire in Action!

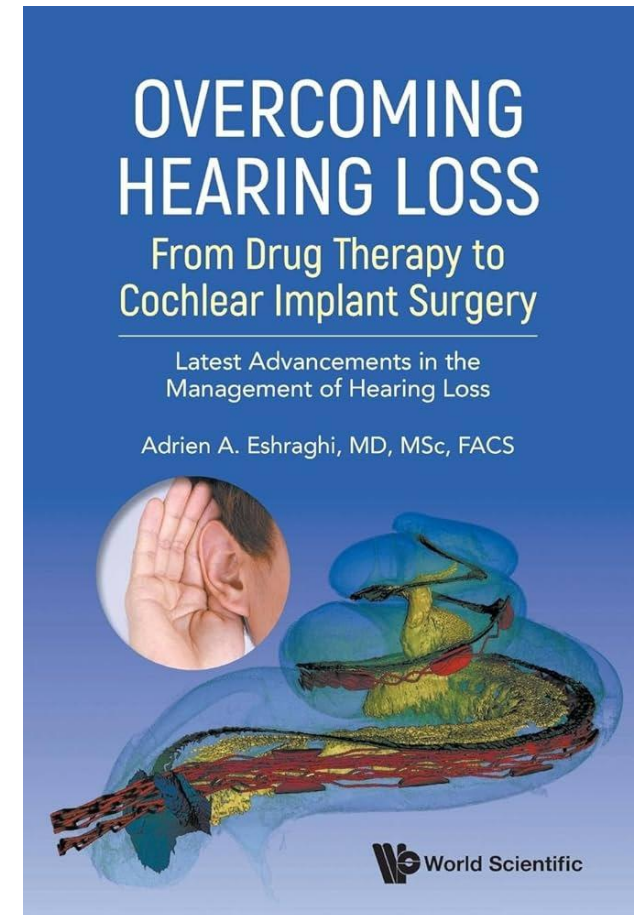
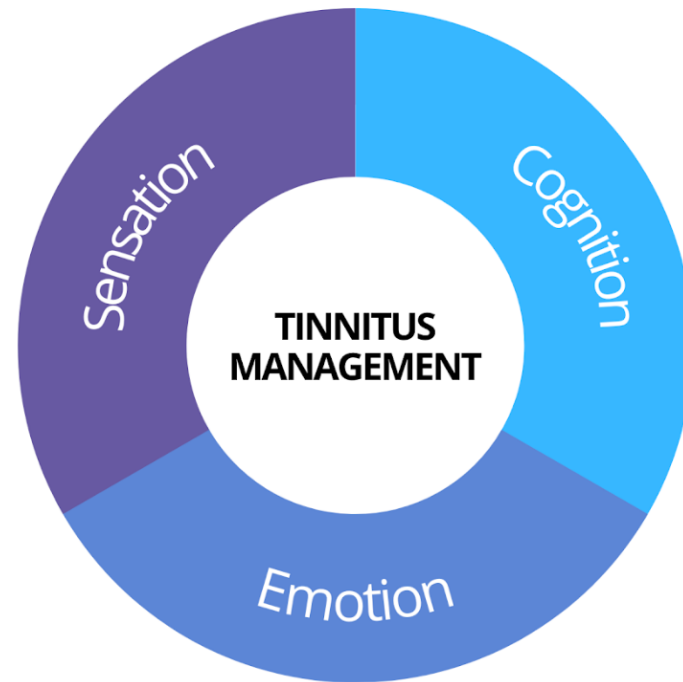


Danesh Model of Tinnitus Management: Got a SEC!

Sensation: includes sound therapy, electrical stimulation or both to alleviate impact of tinnitus.

Emotion: consists of extensive counseling, relaxation techniques and mindfulness and it reduces reaction to tinnitus by controlling ANS response.

Cognition: utilizes direct cognitive behavioral therapy or internet-based CBT to deal with negative thoughts in general.



Take away

- Research is consistent in that non-invasive auditory-somatosensory electrical stimulation has shown to be an effective method to improve tinnitus severity and loudness.
- Non-invasive bimodal auditory-vagus nerve stimulation needs to be further explored and authors recommend more research in large scales with control groups are crucial to validate the efficacy.
- A consistent guideline to evaluate and treat patients with bimodal hearing configuration should be investigated further.
- Overall, after extensive review, it is evident that bimodal neuromodulation yields better results in reducing tinnitus effects than unimodal neuromodulation, but additional analysis is required to make it a routine protocol.
- Remember to address the factors of sensation, emotion and cognition in the management of tinnitus.

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