Special Topic Seminar

Advances in Neuromodulation & Bimodal Stimulation for Tinnitus: From Neural-Networks to Clinical Application

Presenter: R4 張亦愷

Outline

- Epidemiology & Definitions
- Pathophysiology: The Network Model
- Diagnosis
- Treatment
- Bimodal neromodulation
- Conclusion

Executive Summary: The Paradigm Shift

- Historically: Categorized as an *otologic* disorder localized to the cochlea.
- Currently: Redefined as a **complex disorder of neuroplasticity**.
- Scope: Involves distributed neural networks beyond the auditory cortex.
- The therapeutic focus has moved from the *ear* to the *brain*.

> "Tinnitus is not just an ear problem; it is a brain network problem."

Definition & Classification

Tinnitus: The perception of sound in the absence of external auditory stimulation.

Pulsatile Tinnitus

- Rhythmic, often synchronous with heartbeat.
- Source: Vascular or muscular (Somatosound).
- **Action:** Requires distinct diagnostic pathway (rule out tumors/vascular anomalies).

Non-Pulsatile (Subjective)

- **Focus of this report.**
- Phantom auditory perception (ringing, hissing).
- Generated by the nervous system itself.
- Frequently associated with Sensorineural Hearing Loss (SNHL).

Epidemiology: The Global Burden

- **Prevalence:** 10–15% of the adult population globally.
- **Age Factor:** Increases with age, peaking around the 7th decade.
- **Severe Cases:** 1–2% suffer from "bothersome" tinnitus impacting quality of life, sleep, and cognition.

15%

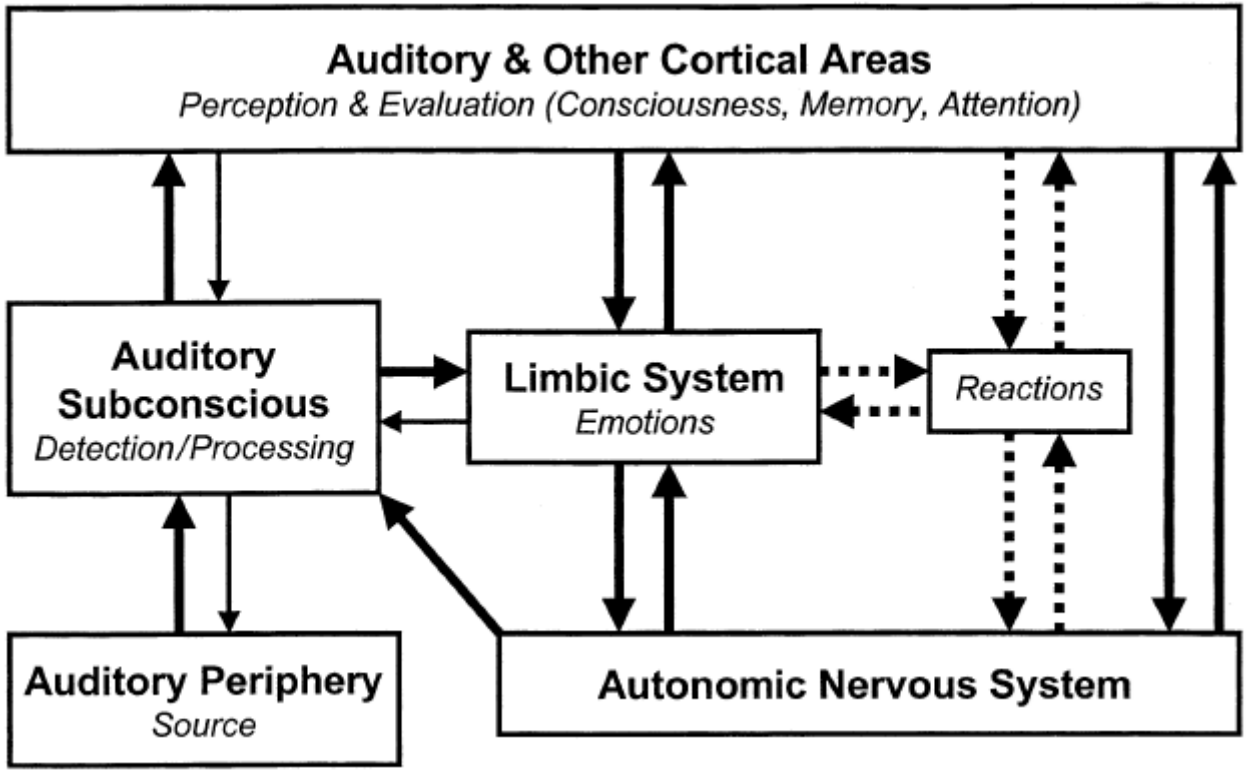
Global Adult Prevalence

Top 1

Service-Connected Disability (Veterans)

Pathophysiology: The Neurophysiological Model

- **Step 1:** Peripheral Deafferentation (The Trigger)
- **Step 2:** Maladaptive Plasticity (The Generator)
- **Step 3:** Network [illegible]



The Trigger: Peripheral Deafferentation

Non-pulsatile tinnitus is almost invariably linked to damage in the auditory periphery.

The "Ignition" Site.

- **Discordant Damage Theory:** Damage to Outer Hair Cells (OHC) with intact Inner Hair Cells (IHC) creates an imbalance, leading to central disinhibition.
- **Calcium Channel Dysfunction:** Intracellular calcium levels in cochlear cells, affected by noise or drugs (salicylates), may trigger firing.
- **Glutamate Excitotoxicity:** Noise trauma causes excessive glutamate release, damaging the synapse (AMPA/NMDA receptors).

Hidden Hearing Loss (Cochlear Synaptopathy)

- **Definition:** Damage to synapses between inner hair cells and spiral ganglion neurons.
- **Clinical Picture:** Normal audiometric thresholds, but reduced neural output.
- **Significance:** Explains tinnitus in patients with "normal hearing."
- **Diagnosis:** Often requires high-frequency audiometry or ABR (Wave I amplitude).

Diagnostic Evaluation: Protocol

Goal: Exclude treatable pathology and phenotype the patient.

1. History

Characterize sound, onset, and modulating factors.

2. Audiology

Pure tone, High-freq, Pitch matching.

3. Questionnaires

Quantify impact (THI, TFI).

4. Imaging

MRI/CT if indicated.

History & Red Flags

Key Questions

- Pulsatile vs. Non-pulsatile?
- Unilateral or Bilateral?
- Sudden or Gradual onset?

⚠ Red Flags

Require immediate medical referral:

- Unilateral tinnitus
- Sudden onset
- Focal neurological signs
- Pulsatile character

Risk: Vestibular Schwannoma, Vascular anomalies.

Somatic Modulation Evaluation

- **Definition:** Ability to modulate tinnitus pitch or loudness via somatic maneuvers.
- **Maneuvers:** Jaw clenching, neck rotation, pressure on cheek/forehead.
- **Physiology:** Indicates connectivity between somatosensory and auditory systems (Dorsal Cochlear Nucleus).
- **Clinical Relevance:** Positive somatic modulation suggests the patient is a prime candidate for **Bimodal Neuromodulation**.

Audiological Assessment

- **Pure Tone Audiometry (0.25 - 8 kHz):** The Gold Standard.
- **High-Frequency Audiometry (up to 16 kHz):**
  - Increasingly utilized.
  - Identifies "hidden" damage in patients with normal standard audiograms.
- **Tinnitus Matching:** Validates patient experience (Pitch/Loudness).
- **Residual Inhibition:** Tests temporary suppression after masking.

Validated Questionnaires

- Subjective distress must be quantified.

Tinnitus Handicap Inventory (THI)

- 25-item survey.
- Quantifies impact on daily living.
- **Score >38:** Often used as inclusion criterion for intervention (e.g., Lenire).

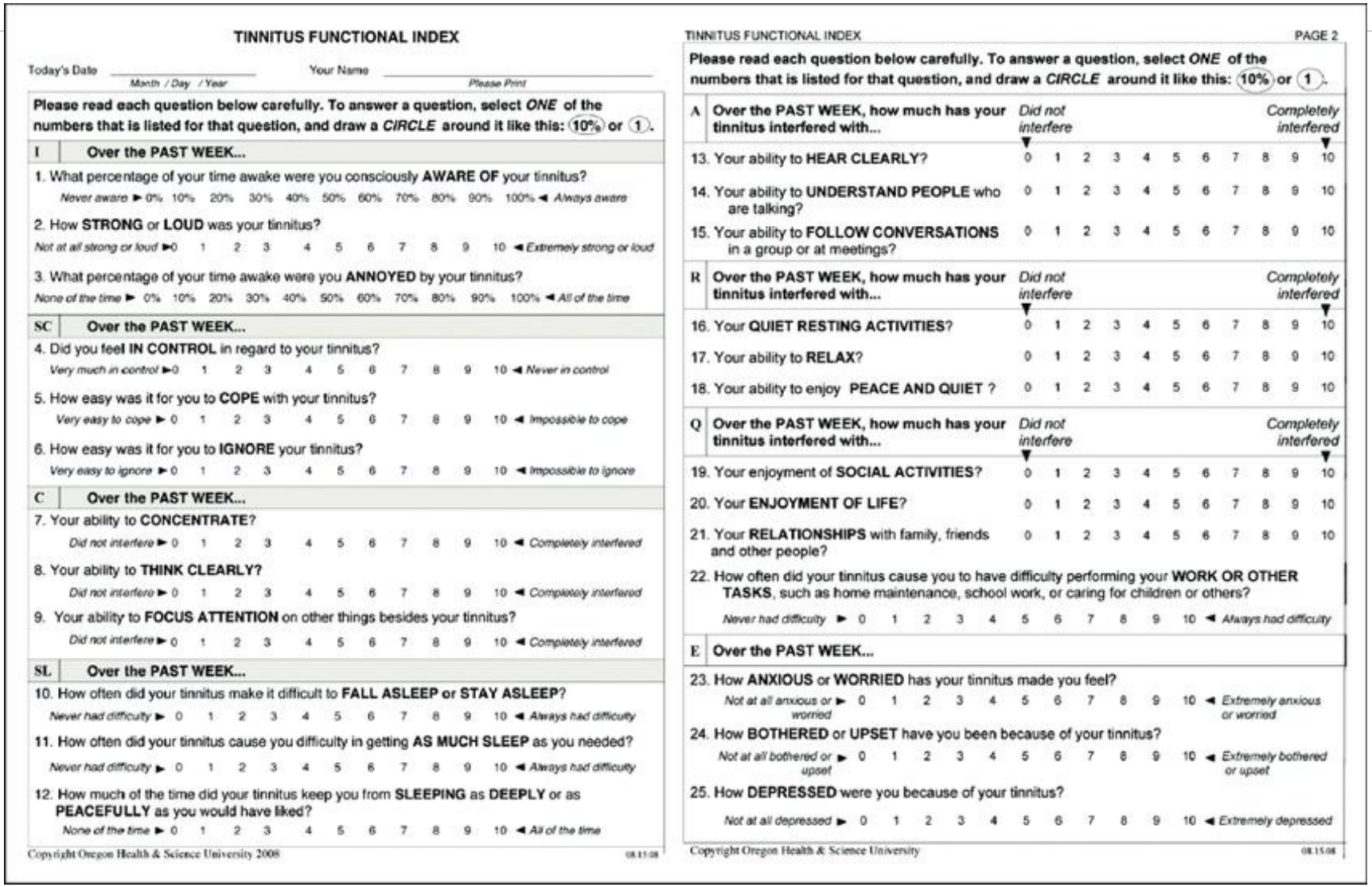
Tinnitus Functional Index (TFI)

- Preferred tool for clinical trials.
- Highly responsive to treatment effects.
- Domains: Intrusiveness, Control, Cognitive, Sleep.

THI

	SCORE	4	0	2
1.	Because of your tinnitus, do you have difficulties to concentrate?	Yes	No	Sometimes
2.	The volume (intensity) of your tinnitus makes it difficult for you to hear people?	Yes	No	Sometimes
3.	Does your tinnitus make you nervous?	Yes	No	Sometimes
4.	Does your tinnitus make you confuse?	Yes	No	Sometimes
5.	Because of your tinnitus, do you feel hopeless?	Yes	No	Sometimes
6.	Do you complain much of your tinnitus?	Yes	No	Sometimes
7.	Because of your tinnitus, do you have trouble to start sleeping at night?	Yes	No	Sometimes
8.	Do feel as if you could not get rid of your tinnitus?	Yes	No	Sometimes
9.	Does your tinnitus interfere in your capacity to enjoy social activities (such as dinners, going to the movies, etc.)?	Yes	No	Sometimes
10.	Because of your tinnitus, do you feel frustrated?	Yes	No	Sometimes
11.	Because of your tinnitus, do you think you may have some serious disease?	Yes	No	Sometimes
12.	Does your tinnitus make it difficult for you to enjoy life?	Yes	No	Sometimes
13.	Does your tinnitus interfere in your home or work activities?	Yes	No	Sometimes
14.	Because of your tinnitus, do you feel frequently irritated?	Yes	No	Sometimes
15.	Because of your tinnitus, do you have difficulties reading?	Yes	No	Sometimes
16.	Does your tinnitus make you upset?	Yes	No	Sometimes
17.	Do you feel your tinnitus impairs your relationship with family and friends?	Yes	No	Sometimes
18.	Do you find it hard to withdraw your attention from the tinnitus and concentrate in something else?	Yes	No	Sometimes
19.	Do you feel powerless to control you tinnitus?	Yes	No	Sometimes
20.	Because of your tinnitus, do you feel frequently tired?	Yes	No	Sometimes
21.	Because of your tinnitus, do you feel frequently depressed?	Yes	No	Sometimes
22.	Does your tinnitus make you feel anxious?	Yes	No	Sometimes
23.	Do you feel you can no longer withstand your tinnitus?	Yes	No	Sometimes
24.	Does your tinnitus get worse when you are stressed?	Yes	No	Sometimes
25.	Does your tinnitus make you feel insecure?	Yes	No	Sometimes

TFI



TINNITUS FUNCTIONAL INDEX

Today's Date _____ (Month / Day / Year) Your Name _____ (Please Print)

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

I — Over the PAST WEEK...

1. What percentage of your time awake were you consciously **AWARE OF** your tinnitus?
   Never aware ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *Always aware*
2. How **STRONG** or **LOUD** was your tinnitus?
   Not at all strong or loud ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely strong or loud*
3. What percentage of your time awake were you **ANNOYED** by your tinnitus?
   None of the time ► 0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% ◄ *All of the time*

SC — Over the PAST WEEK...

4. Did you **feel IN CONTROL** in regard to your tinnitus?
   Very much in control ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Never in control*
5. How easy was it for you to **COPE** with your tinnitus?
   Very easy to cope ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to cope*
6. How easy was it for you to **IGNORE** your tinnitus?
   Very easy to ignore ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Impossible to ignore*

C — Over the PAST WEEK...

7. Your ability to **CONCENTRATE**?
   Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*
8. Your ability to **THINK CLEARLY?**
   Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*
9. Your ability to **FOCUS ATTENTION** on other things besides your tinnitus?
   Did not interfere ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Completely interfered*

SL — Over the PAST WEEK...

10. How often did your tinnitus make it difficult to **FALL ASLEEP** or **STAY ASLEEP**?
    Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*
11. How often did your tinnitus cause you difficulty in getting **AS MUCH SLEEP** as you needed?
    Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*
12. How much of the time did your tinnitus keep you from **SLEEPING** as **DEEPLY** or as **PEACEFULLY** as you would have liked?
    None of the time ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *All of the time*

 08.15.08

Please read each question below carefully. To answer a question, select *ONE* of the numbers that is listed for that question, and draw a *CIRCLE* around it like this: (10%) or (1).

A — Over the PAST WEEK, how much has your tinnitus interfered with...	*Did not interfere* 0 1 2 3 4 5 6 7 8 9 10 *Completely interfered*
13. Your ability to **HEAR CLEARLY**?	0 1 2 3 4 5 6 7 8 9 10
14. Your ability to **UNDERSTAND PEOPLE** who are talking?	0 1 2 3 4 5 6 7 8 9 10
15. Your ability to **FOLLOW CONVERSATIONS** in a group or at meetings?	0 1 2 3 4 5 6 7 8 9 10

R — Over the PAST WEEK, how much has your tinnitus interfered with...	*Did not interfere* 0 1 2 3 4 5 6 7 8 9 10 *Completely interfered*
16. Your **QUIET RESTING ACTIVITIES**?	0 1 2 3 4 5 6 7 8 9 10
17. Your ability to **RELAX**?	0 1 2 3 4 5 6 7 8 9 10
18. Your ability to enjoy **PEACE AND QUIET** ?	0 1 2 3 4 5 6 7 8 9 10

Q — Over the PAST WEEK, how much has your tinnitus interfered with...	*Did not interfere* 0 1 2 3 4 5 6 7 8 9 10 *Completely interfered*
19. Your enjoyment of **SOCIAL ACTIVITIES**?	0 1 2 3 4 5 6 7 8 9 10
20. Your **ENJOYMENT OF LIFE**?	0 1 2 3 4 5 6 7 8 9 10
21. Your **RELATIONSHIPS** with family, friends and other people?	0 1 2 3 4 5 6 7 8 9 10

22. How often did your tinnitus cause you to have difficulty performing your **WORK OR OTHER TASKS**, such as home maintenance, school work, or caring for children or others?
    Never had difficulty ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Always had difficulty*

E — Over the PAST WEEK...

23. How **ANXIOUS** or **WORRIED** has your tinnitus made you feel?
    Not at all anxious or worried ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely anxious or worried*
24. How **BOTHERED** or **UPSET** have you been because of your tinnitus?
    Not at all bothered or upset ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely bothered or upset*
25. How **DEPRESSED** were you because of your tinnitus?
    Not at all depressed ► 0 1 2 3 4 5 6 7 8 9 10 ◄ *Extremely depressed*

 08.15.08

Imaging Protocols

- **MRI with Gadolinium Contrast:**
  - Gold standard for **unilateral** or asymmetric tinnitus.
  - Goal: Rule out retrocochlear lesions (Vestibular Schwannoma).
- **CT Angiography / MR Angiography:**
  - Indicated for **Pulsatile** tinnitus.
  - Goal: Identify vascular anomalies (Glomus tumors, AVMs).

Cognitive Behavioral Therapy (CBT)

- **Target:** The *Distress*, not the Sound.
- **Gold Standard:** Most evidence-based intervention for tinnitus-related quality of life.
- **Technique:** Restructures maladaptive thoughts ("This noise will drive me mad") and safety behaviors.
- **Evidence:** Consistently improves depression/anxiety scores, even if tinnitus loudness remains unchanged.

Tinnitus Retraining Therapy (TRT)

Based on Jastreboff's neurophysiological model.

1. Directive Counseling

Demystifying the sound. Reclassifying it as "neutral" rather than "dangerous."

2. Sound Therapy

Broadband noise at "mixing point" to reduce signal-to-noise ratio.

Hearing Aids

- **First Line of Defense:** For patients with co-occurring hearing loss.
- **Mechanism 1:** Restoring auditory input reverses the "central gain" and deprivation.
- **Mechanism 2:** Passive masking by amplifying ambient noise.
- **Modern Tech:** Integrated sound generators (maskers) often included.

Sound Therapy Strategies

Strategy	Goal	Method
Masking	Immediate relief	Cover the tinnitus completely (White noise).
Mixing Point (TRT)	Habituation	Sound set *just below* tinnitus perception. Brain learns to ignore both.
Enrichment	Reduce contrast	Environmental sounds (water, nature) to reduce silence.

Pharmacological Interventions

- **Systemic Drugs:**
  - Antidepressants/Anxiolytics: Treat comorbidities only.
  - Anticonvulsants (Gabapentin): Failed in RCTs for idiopathic tinnitus.
- **Exception:** Carbamazepine for rare "typewriter tinnitus" (vascular compression).

Reality Check: No FDA-approved drug exists for tinnitus.

Intratympanic Therapies

Local delivery to bypass blood-labyrinth barrier.

- **NMDA Receptor Antagonists (Esketamine/AM-101):**
  - Target: Cochlear excitotoxicity.
  - **TACTT Trials:** Promise for *acute* tinnitus (post-trauma), but failed for *chronic* tinnitus.
  - **Implication:** A "therapeutic window" exists before central plasticity takes over.
- **Steroids:** Standard for Sudden Sensorineural Hearing Loss (SSNHL), but no efficacy for chronic tinnitus.

Non-Invasive Brain Stimulation (NIBS)

rTMS (Magnetic)

- Target: Auditory Cortex or Prefrontal Cortex.
- Evidence: Statistically significant but clinically small/transient effects.
- Status: Research tool; high heterogeneity in protocols.

tDCS (Electrical)

- Weak electrical currents to modulate excitability.
- Evidence: Low-to-moderate certainty.
- Status: Less focal than rTMS. Short-term benefits only.

Dietary Supplements

- **Common Supplements:** Arginine, Beta carotene, Ginkgo, Melatonin, Zinc, B Vitamins, Magnesium, etc.
- **Prevention:** B Vitamins may help defend cochlea against noise trauma. Antioxidants (D-met) also investigated.
- **Conclusion:** No convincing evidence they treat *established* idiopathic tinnitus.

The Zinc Controversy

- **Fact:** Cochlea has body's highest Zinc concentration.
- **Hypothesis:** Deficiency = Tinnitus?
- **Evidence:** Mixed. Paaske et al. showed no correlation. RCT in elderly (>60) showed **no benefit**.

Low-Level Laser Therapy

- **Application:** Transmeatal (ear canal) or Mastoid process.
- **Context:** Used successfully in some forms of chronic pain (mechanism remains contentious).
- **Evidence Base:**
  - Some initial studies reported good results.
  - **Current Status:** [illegible] from placebo.

Review

Efficacy of photobiomodulation in the management of tinnitus: A systematic review of randomized control trials

S. Talluri [a], S.M. Palaparthi [b], D. Michelogiannakis [c], J. Khan [a,*]

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Surgical Intervention

Otosclerosis

Stapedectomy improves or eradicates tinnitus in **80–88.3%** of cases.

Cochlear Implantation (CI)

Effective for profound loss. Tinnitus improvement in:

- **86%** of implanted ears.
- **67%** of contralateral ears.

Complementary Therapy

BOX 61.1 Some of the complementary medicine therapies and exercise regimes that have been used in the management of tinnitus

Acupuncture	Hypnotherapy
Alexander technique	Massage
Aromatherapy	Meditation
Black cohosh	Osteopathy
Chiropractic	Reflexology
Craniosacral therapy	Reiki
Herbal medicine	St John's wort
Ginkgo biloba	Shiatsu
Homeopathy	Tai Chi
Ear candles	Yoga

Therapeutic Revolution

Bimodal Neuromodulation

Targeting the convergence of auditory and somatosensory pathways.

Mechanism: Multisensory Intergration

- **Concept:** The Dorsal Cochlear Nucleus (DCN) receives both Auditory and Somatosensory inputs.
- **Plasticity:** Paired stimulation (Sound + Body) can induce Long-Term Depression (LTD) to suppress hyperactivity.
- **Modalities:**
  - Sound + Tongue (Lenire / Mute Button)
  - Sound + Vagus Nerve (VNS)
  - Sound + Cheek/Neck (Experimental)

The Lenire System

First FDA De Novo approved bimodal device.

1. **Headphones:** Delivers customized sound sequences (Auditory).

2. **Tonguetip:** Intra-oral device delivering mild electrical stimulation (Somatosensory/Trigeminal).

3. **Controller:** Coordinates timing.

a

TENT Clinical Development Program

- Three major studies defining the evidence base.

Trial	Focus	Participants
TENT-A1	Safety & Efficacy (Proof of Concept)	326
TENT-A2	Parameter Optimization	191
TENT-A3	Controlled Pivotal Trial (FDA)	112

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

TINNITUS

Bimodal neuromodulation combining sound and tongue stimulation reduces tinnitus symptoms in a large randomized clinical study

Brendan Conlon[1,2,3], Berthold Langguth[4,5], Caroline Hamilton[1], Stephen Hughes[1], Emma Meade[1], Ciara O Connor[1], Martin Schecklmann[4,5], Deborah A. Hall[6,7,8], Sven Vanneste[9,10], Sook Ling Leong[1,10], Thavakumar Subramaniam[3], Shona D'Arcy[1], Hubert H. Lim[1,11,12]*

Study Design

Experimental Design

This study was a large-scale **randomized, double-blind, exploratory clinical trial**.

The primary objective was to evaluate the safety and efficacy of bimodal neuromodulation and to compare different stimulation settings among patient groups.

Study Sites

The research was conducted across two major international medical centers:

- **St. James's Hospital** (Dublin, Ireland)
- **University of Regensburg** (Germany)

Participants

Inclusion Criteria

- **Chronic Subjective Tinnitus:** Duration between 3 months and 5 years.
- **Severity:** THI score between 28 and 76.
- **Age:** Between 18 and 70 years.
- **Masking Level:** Minimum Masking Level (MML) between 20 and 80 dB HL.

Exclusion Criteria

- **Specific Types:** Objective tinnitus or somatic tinnitus caused by head/neck injury.
- **Hearing Loss:** Substantial sensorineural loss (>40 dB HL at low freq or >80 dB HL at high freq).
- **Implants:** Use of pacemakers or cochlear implants.
- **Comorbidities:** Severe TMJ disorder or high anxiety (STAI >120).

Sample Selection

A rigorous selection process screened 5,826 individuals to ensure high data quality.

5,826
Assessed
Screened for eligibility online

333
Randomized
Met all clinical criteria

326
Enrolled
Fitted with device & started treatment

Treatment Arms (Randomized)

Arm 1 (PS1)
Synchronized

High-frequency tones + broadband noise.

Synchronous delivery with electrical tongue stimulation.

Fixed frequency-to-place mapping.

Arm 2 (PS2)
Async (Short)

Similar to PS1 parameters.

Random delay (30-50 ms) between sound and tongue stimulation.

Randomized mapping.

Arm 3 (PS3)
Async (Long)

Low-frequency tones (100-500 Hz).

Longer delay (550-950 ms) between stimuli.

Randomized mapping.

Procedure Timeline

Week 0: Baseline

Enrollment, device fitting, and initial THI/TFI assessment.

Week 0-12: Treatment

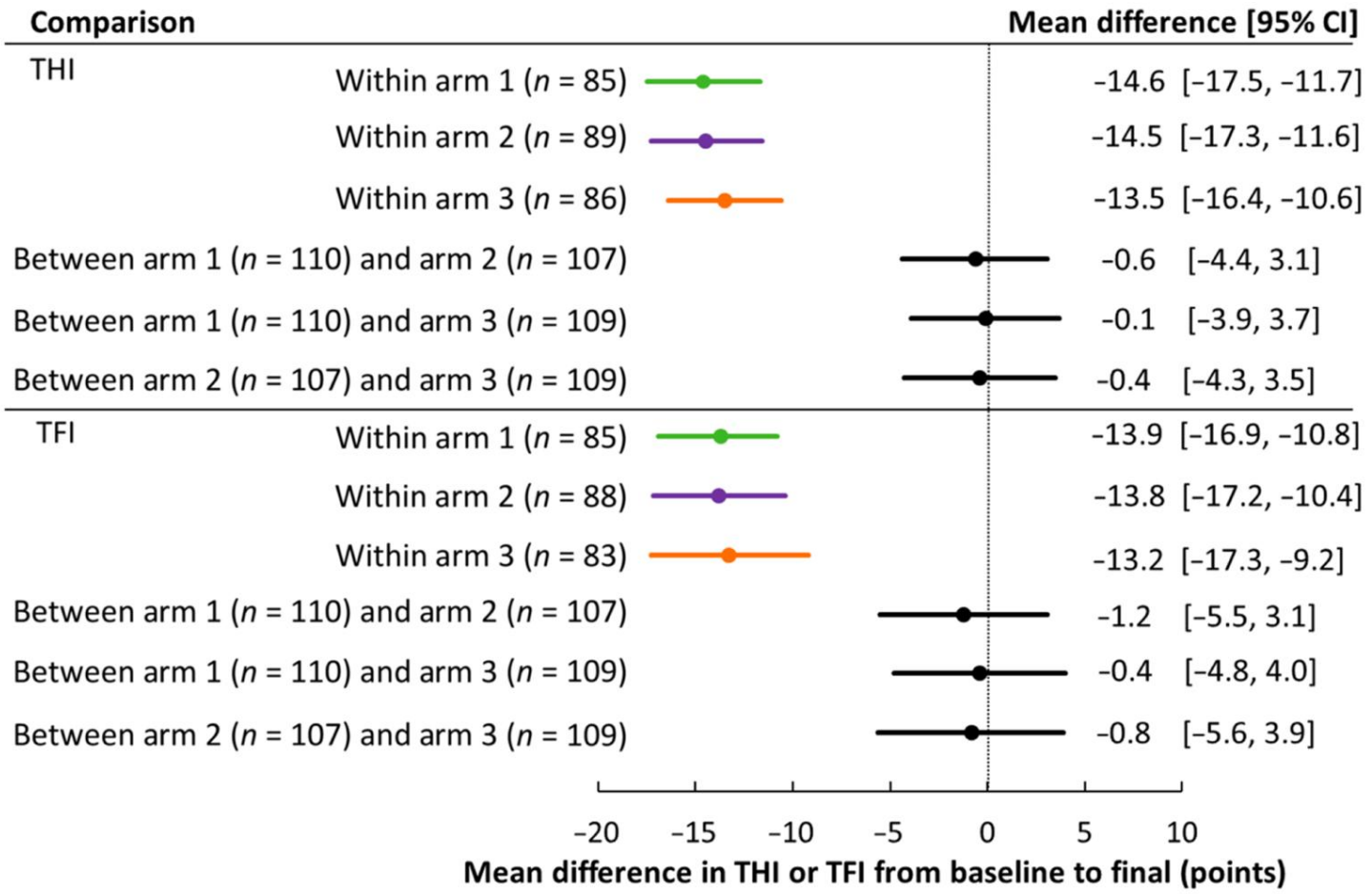
60 mins/day self-administered home treatment.

Interim check at Week 6.

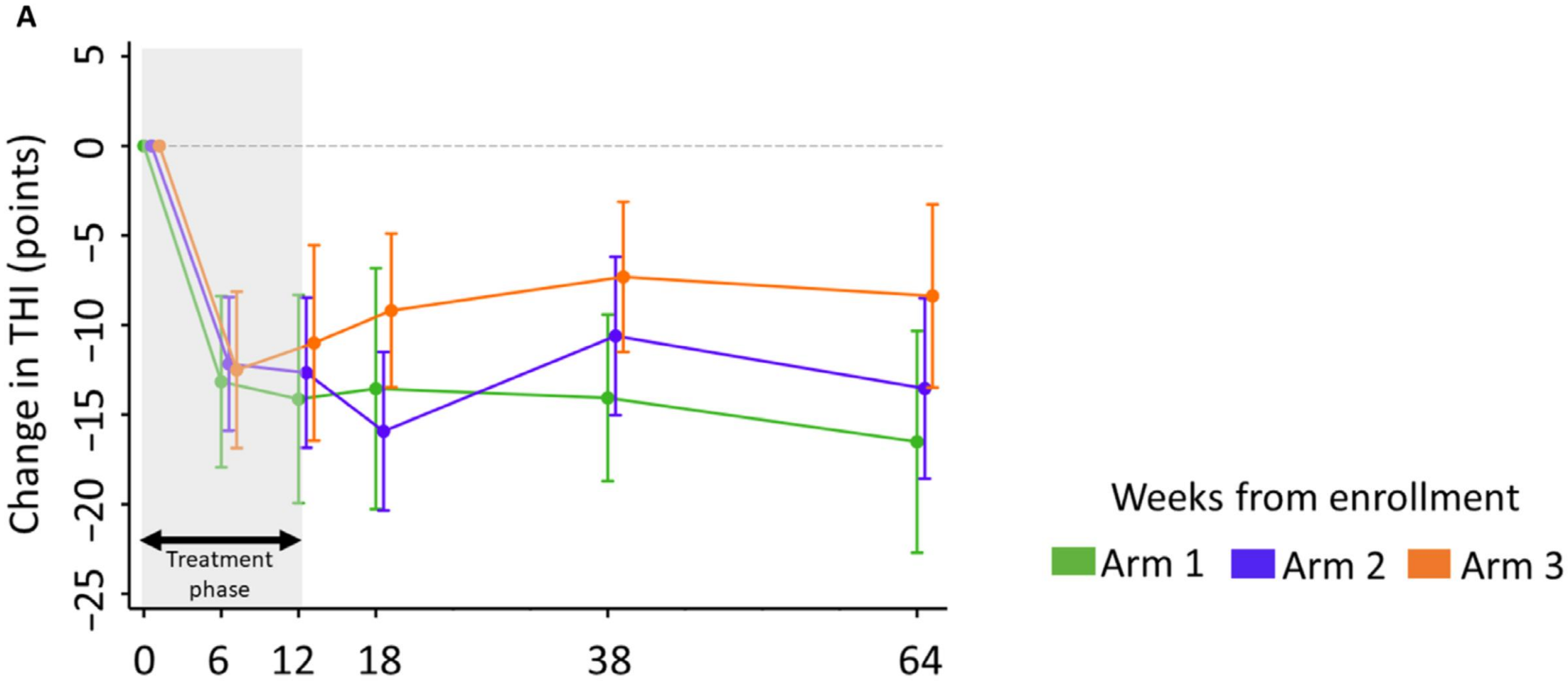
Week 18-64: Follow-up

Post-treatment assessments at Week 18, 38, and 64 (up to 12 months).

Results-12 weeks



Results-Long Term



Safety & Compliance

- **No Serious Adverse Events:** No treatment-related SAEs were reported during the trial.
- **Safe for Home Use:** The study confirmed the device is safe for self-administration.
- **High Compliance:** Participants adhered to the 60 min/day regimen (defined as >36 hours total).
- **High Satisfaction:** Positive feedback reported across all treatment arms.

www.nature.com/scientificreports

scientific reports

Check for updates

OPEN

Different bimodal neuromodulation settings reduce tinnitus symptoms in a large randomized trial

Brendan Conlon[1,2,3], Caroline Hamilton[1], Emma Meade[1], Sook Ling Leong[1], Ciara O Connor[1], Berthold Langguth[5,6], Sven Vanneste[4,7], Deborah A. Hall[8,9,10], Stephen Hughes[1] & Hubert H. Lim[1,11,12]✉

TENT-A2: Importance of Variation

- **Question:** Can we prevent habituation?
- **Method:** Stimulation settings (sound/delay) were altered after 6 weeks in active arms.
- **Findings:** Participants with changed parameters showed **additional** reduction in severity during the second half of treatment.
- **Significance:** The brain habituates to static signals. "Refreshing" parameters re-engages neuroplasticity.

TENT-A2: Long-Term Durability

- Improvements in THI and TFI were sustained at 12-month follow-up.
- **Implication:** Suggests long-term neuroplastic change, not just a transient masking effect.

12 Months

Sustained Improvement Post-Treatment

nature communications

Article

https://doi.org/10.1038/s41467-024-50473-z

Combining sound with tongue stimulation for the treatment of tinnitus: a multi-site single-arm controlled pivotal trial

Received: 24 August 2023

Accepted: 8 July 2024

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Check for updates

Michael Boedts[1,2], Andreas Buechner[3,4], S. Guan Khoo[5,6], Welmoed Gjaltema[7], Frederique Moreels[1], Anke Lesinski-Schiedat[3,4], Philipp Becker[4], Helen MacMahon[8], Lieke Vixseboxse[7], Razieh Taghavi[7], Hubert H. Lim[9,10,11] & Thomas Lenarz[3,4]

Sample Selection

Participants

N = 112

Enrolled across 3 clinical sites (Belgium, Germany, Ireland).

Inclusion Criteria

Subjective chronic tinnitus.

THI ≥ 38

(Moderate or worse severity).

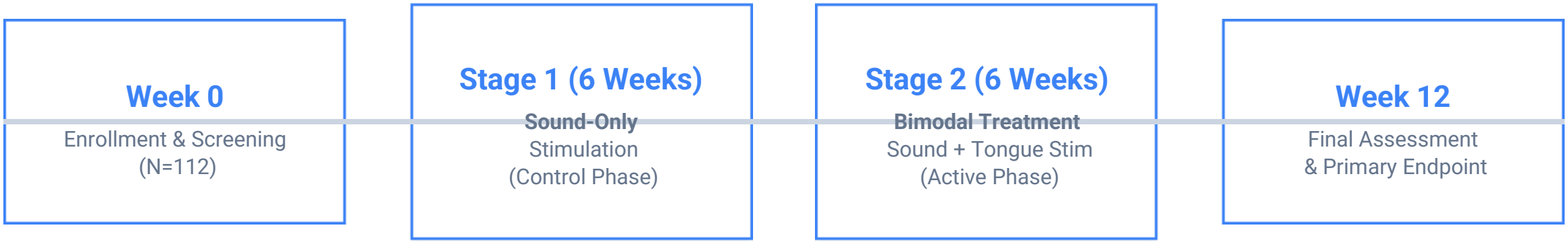
Hearing Profile

Max hearing loss ≤ 40 dB HL (low freq) or ≤ 80 dB HL (high freq).

Device fitted to audiogram.

Study Design

Prospective, single-arm, repeated measures design where participants serve as their own control.



Result-The "Floor Effect"

Sound-Only Performance

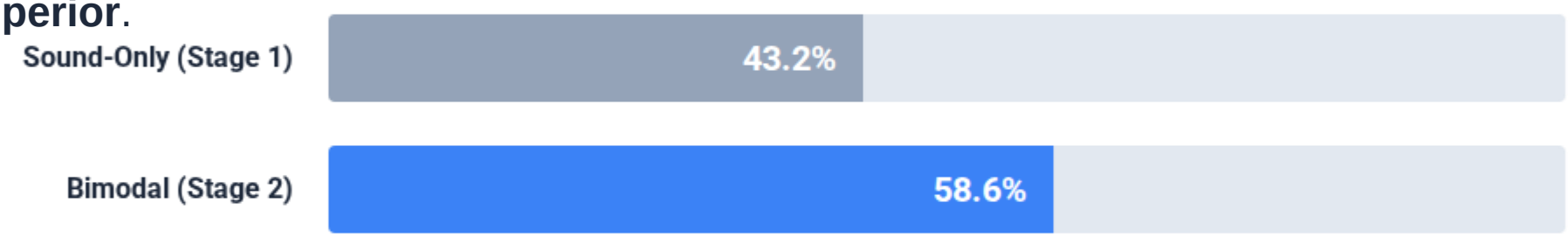
In Stage 1, sound therapy alone was surprisingly effective, with a **63.3%** responder rate. This meant many participants had already improved significantly before starting bimodal treatment.

Full Cohort Outcome

Due to the high baseline set by Stage 1, the additional benefit of Stage 2 (43.3%) did not statistically exceed Stage 1 for the *entire* group. However, a specific subgroup showed clear superior benefit.

Result-Moderate or Worse Tinnitus

In participants who remained bothered by tinnitus (THI ≥ 38) at the start of Stage 2, bimodal treatment was **clinically superior**.



Statistically Significant: *p = 0.022*

Adding tongue stimulation provided benefit above and beyond sound therapy.

Conclusion & Take Home Message

1. **Paradigm Shift:** Tinnitus is no longer just a cochlear issue; it is a **Neuroplasticity Disorder** of the brain. Treatment now targets central networks.
2. **Bimodal Neuromodulation:** Combines Sound + Tongue stimulation to drive **Multisensory Integration** in the DCN, inducing LTD to reduce neural hyperactivity.
3. **Evidence & Durability:** Large-scale trials (TENT-A1/A2) prove the Lenire system is safe, with effects lasting up to **12 months**.
4. **Clinical Superiority:** For patients with **moderate or worse** tinnitus, bimodal stimulation is significantly more effective than sound therapy alone (TENT-A3).

Reference

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