Research Project Involving Human Subjects, RIPH Type 2

Title: Multicenter Study on the Effectiveness of Sound Therapy Using Hearing Aids in Tinnitus Patients with Mild Hearing Loss

Short Title: Study on the Effectiveness of Sound Therapy in Tinnitus Patients

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Scientific Background and Rationale

A subjective tinnitus is defined as an auditory sensation without external sound stimulation or meaning, identifiable by its subjective characteristics: location, intensity, frequency, and timbre. It reflects a dysfunction of the auditory system and/or other structures that may interfere with it (Noreña et al., 2020). It is therefore hypothesized to result from abnormal neural activity within the auditory pathway (Noreña, 2011). Tinnitus can take various forms, and certain factors may modulate it. It may occur in isolation or be associated with other clinical symptoms, the most frequent being hearing loss. The frequencies that make up tinnitus are very often associated with the frequency regions of hearing loss (Basile et al., 2013; Fournier & Hébert, 2013; Noreña et al., 2002; Sereda et al., 2011). When associated with hearing loss, its severity, audiometric curve shape, and origin vary (Henry et al., 1999). Nevertheless, noise-induced trauma and presbycusis, which cause hearing loss predominantly at high frequencies, are the most common associated circumstances (Langguth et al., 2017).

Tinnitus also varies in the impact it has on patients, leading to sleep disturbances, concentration difficulties, and psycho-emotional consequences including stress, anxiety, and depression (Colagrosso et al., 2018; Deborah Ann Hall et al., 2018; Hébert & Carrier, 2007; Hébert & Lupien, 2007; Langguth et al., 2011). It is estimated to affect 10–15% of the population, with 20% of these individuals experiencing disabling symptoms that negatively affect their quality of life (McCormack et al., 2014, 2016). Assessment of distress and perceived handicap is carried out using validated questionnaires, the most widely used being the **Tinnitus Functional Index** (Meikle et al., 2012) and the **Tinnitus Handicap Inventory** (Newman et al., 1996, 1998). Visual analog scales measuring tinnitus severity and loudness are also widely used (Adamchic et al., 2012; Deborah A. Hall et al., 2017; Schaette et al., 2010).

Clinical management strategies always include, at a minimum, listening, directive counseling, and patient education about tinnitus (Baguley et al., 2013; Langguth et al., 2013; Liu et al., 2018). This approach is referred to as “counseling” in English-language literature; we will use the term **directive counseling** in this document. Furthermore, when tinnitus severity is high and directive counseling alone is insufficient, other approaches may be proposed: psychological approaches and sound therapy approaches. Psychological approaches include cognitive behavioral therapy (Fuller et al., 2020) and sophrology, widely used in France (Grevin et al., 2020; Grevin, 2010). Sound therapy approaches include amplification via hearing aids, noise generators, or combined devices that provide both amplification and noise generator (Sereda et al., 2018). Depending on available resources, tinnitus severity, and patient preferences, the ENT specialist may propose one or more of these combined approaches. Some therapies combine elements of psychological and sound therapy approaches, the most well-known being **Tinnitus Retraining Therapy**, which combines directive counseling, noise generators, and relaxation (Jastreboff & Jastreboff, 2002).

Apart from directive counseling, sound therapy is the preferred approach among audiologists for managing tinnitus patients in most Western countries (Deborah A. Hall et al., 2011). The term **sound therapy**, broadly speaking, generally includes sound enrichment either through amplification using hearing aids (for tinnitus with hearing loss) or through noise generators alone (for patients without hearing loss or with mild loss) (Henry et al., 2019; Hoare, Searchfield, et al., 2014; Ibarra et al., 2018). In practice, both options are now most often integrated into the same hearing aid device. They can be combined—meaning the patient receives both amplification and continuous noise generation—or separated, meaning two programs allow independent use of each option at the patient’s discretion. Hearing amplification increases external sounds, which can act on tinnitus at several levels. First, amplification of external sounds reduces tinnitus salience through informational masking. Second, amplified external sounds help redirect auditory attention away from tinnitus. It may also reduce auditory deprivation by stimulating deafferented frequency regions, thereby reversing certain neural plasticity phenomena responsible for tinnitus generation. Finally, it improves speech perception, which can indirectly enhance well-being and tolerance to tinnitus (Hoare, Searchfield, et al., 2014).

Noise generators, on the other hand, provide energetic masking of tinnitus, reducing its salience and intrusiveness. Like amplification, they help divert auditory attention from tinnitus and, according to some authors, may lead to progressive habituation (Hoare et al., 2014).

However, there is no strong evidence to support or refute the use of sound therapy as a first-line intervention or as an adjunct to directive counseling for tinnitus patients in the literature. Guidelines from the **National Institute for Health and Care Excellence (NICE)** and the **American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS)** both support directive counseling, which includes attentive listening to the patient's complaint, empathetic support from the healthcare professional, and information about tinnitus. This directive counseling approach is strongly recommended and considered the essential first-line management for tinnitus patients.

Regarding sound therapy, AAO-HNS guidelines recommend hearing aids only if disabling tinnitus is associated with hearing loss. They also mention the option of noise generator therapy if tinnitus is persistent and disabling (Tunkel et al., 2014). Similarly, NICE (2020 edition) recommends hearing aids for tinnitus management in patients with hearing loss and speech intelligibility issues. NICE also suggests, as an optional approach, trialing amplification when tinnitus is associated with moderate hearing loss without intelligibility problems. Unlike AAO-HNS, NICE does not recommend noise generator therapy alone without amplification, citing insufficient evidence and a lack of high-quality, unbiased studies. European multidisciplinary guidelines also recommend hearing aids for tinnitus patients with hearing loss but do not propose them as an option when no hearing loss is present (Cima et al., 2019).

A Cochrane review analyzed studies on sound therapy effects—whether through hearing aids alone, noise generators alone, or combined stimulation (Sereda et al., 2018). Again, the authors found no evidence suggesting one type of sound therapy is superior to another and reported no adverse effects in the studies included (8 out of 590). These eight studies showed significant improvements in tinnitus severity (measured by THI or TFI) for all three stimulation types. Consequently, recommendations from agencies, scientific societies, and recent Cochrane reviews call for future research focused on sound therapy efficacy using rigorous methodologies emphasizing randomization, blinding, control or waitlist groups, and, if possible, placebo-controlled designs (Cima et al., 2019; Hoare, Edmondson-Jones, et al., 2014; Hobson et al., 2010; Sereda et al., 2018; Tunkel et al., 2014). The CONSORT methodology is strongly recommended for research protocol design and writing. It is also strongly advised to use tinnitus-specific severity questionnaires alongside validated tools for depression, anxiety, sleep disorders, and quality of life. Analysis of side effects such as pain, discomfort, or skin irritation related to hearing aids is also recommended.

In France, the 2019 Health Law modified conditions for hearing aid coverage by health systems. These conditions are based on specific hearing loss criteria described in the decree, relying on pure-tone and speech audiometry in quiet and noise. No specific consideration is given to tinnitus if no associated hearing loss meets these criteria. Coverage criteria include four conditions:

1. Average hearing loss >30 dB according to BIAP method (BUREAU INTERNATIONAL D'AUDIOPHONOLOGIE, 1997), or
2. Speech intelligibility threshold in quiet >30 dB, or
3. Significant degradation of intelligibility in noise with a Signal-to-Noise Ratio >3 dB, or
4. High-frequency hearing loss >30 dB from 2000 Hz and speech intelligibility threshold >30 dB in quiet and/or degraded in noise by >3 dB, as stipulated in Decree No. 2019-21 of January 11, 2019 (J.O., January 12, 2019).

Analysis of a cohort of 295 patients from a specialized tinnitus clinic showed that 53% had normal hearing (<20 dB BIAP criteria) and 61% had normal hearing or mild hearing loss (<30 dB) (Roger, 2018). This group had an average THI score of 55/100, corresponding to moderate handicap, confirming clinical experience that disabling tinnitus can occur with mild or even no measurable hearing loss.

Given these factors, decisions regarding sound therapy management are influenced by ENT and/or audiologist experience or opinion, or by reimbursement systems. Thus, patients with mild hearing loss and highly disabling tinnitus are less likely to receive hearing aids than those with more significant hearing loss—even if their tinnitus is less severe. Since the effectiveness of hearing aids for tinnitus improvement is recognized as a research priority for clinicians and patients (Hall et al., 2013), and given the major inequalities in tinnitus management based on hearing loss rather than tinnitus severity, AFREPA—a French nonprofit association of multidisciplinary teams for tinnitus patients—proposes to conduct a clinical study involving ENTs, audiologists, and tinnitus researchers to establish a research protocol with the rigorous criteria mentioned above for a multicenter, randomized, controlled, double-blind study compared to a placebo-controlled group.

Purpose and objectives

Our study aims to test the hypothesis that acoustic stimulation therapy (noise generator alone or combined with amplification) reduces tinnitus-related distress and improves patients' quality of life compared to a placebo sound therapy (referred to in this document as neutral amplification). The originality of this research project lies in the combination of an initial rigid experimental phase (weeks 0 to 6), during which one of the three therapies (called the monotherapy phase) will be imposed on each participant, typical of randomized, double-blind controlled trials. From week 6 to 12, greater flexibility will be given to participants in the treatment groups, who will be able to choose their therapy at any time of the day—that is, select the stimulation of their choice among the three options—based on their preferences, needs, and daily life circumstances (called the polytherapy phase).

The **primary objective** of the study is to evaluate the specific impact of sound monotherapies and polytherapy on tinnitus-related handicap and distress in patients with mild hearing loss over twelve weeks. The primary measure of tinnitus-related handicap and distress will be the overall score on the **Tinnitus Functional Index (TFI)** questionnaire (Meikle et al., 2012), validated by improvement noted on the **Global Rating of Change Scale (GRCS)** (Kamper et al., 2009).

The **secondary objective** is to assess the overall impact of sound monotherapies and polytherapy in patients with mild hearing loss over twelve weeks, including sleep quality, quality of life, auditory listening improvement, and well-being (including anxiety and depression):

- Quality of life: **SF-12 questionnaire** (Gandek et al., 1998)
- Sleep quality: global scale (Snyder et al., 2018)
- Listening improvement: **SSQ15 questionnaire** (Moulin et al., 2019)
- Anxiety and depression: **HADS** (Zigmond & Snaith, 1983)
- Visual Analog Scales (VAS) for tinnitus distress and loudness (Deborah A. Hall et al., 2017)

The **primary endpoint** is a change of at least 13 points in the total TFI score after 12 weeks of therapy. This value is recommended by the TFI creators, who observed a 13-point improvement after 3 months of treatment—a score corresponding to a "moderate to large" improvement on the GRCS scale (Meikle et al., 2012).

Secondary endpoints:

- SF-12v2: significant change in overall score (Gandek et al., 1998)
- Sleep quality: average improvement of 2 points in total score (Snyder et al., 2018)
- SSQ15: average improvement of 1.5 points in total score (Kelsall et al., 2017)
- HADS: average improvement of 1.5 points in total score (Puhan et al., 2008)
- Tinnitus VAS: decrease of at least 2 points on each scale (Hall et al., 2017)

METHODS

Participants : Six multidisciplinary teams in France specializing in tinnitus management—comprising ENT specialists and audiologists, working in hospital or private settings—will recruit patients whose primary complaint is tinnitus. Audiologists involved are senior professionals working in specialized tinnitus centers and responsible for teaching. Patients may be referred by general practitioners or ENT specialists. All patients must sign informed consent and undergo a clinical tinnitus evaluation and audiometric hearing assessment. Specific inclusion criteria: disabling tinnitus with a score above 38 on the French version of the **Tinnitus Handicap Inventory (THI)** (Ghulyan-Bédikian et al., 2010). According to the questionnaire authors, a total score between 38 and 56 corresponds to moderate handicap, 58–76 to severe handicap, and 78–100 to catastrophic tinnitus (Newman et al., 1996).

Table I. Inclusion and Exclusion Criteria for Study Participants

Inclusion Criteria

1. Adults aged 18 years and older
2. Continuous subjective tinnitus
3. Bilateral tinnitus for more than 3 months with mild bilateral hearing loss
4. Patient must present mild bilateral hearing loss, strictly defined by three audiometric profiles:
    - (1) Average thresholds at conversational frequencies (0.5–1–2–4 kHz) >15 dB HL and ≤30 dB HL
    - (2) Average thresholds at high frequencies (3–4–6–8 kHz) >15 and ≤40 dB HL
    - (3) Notched hearing loss defined by thresholds at 3 and/or 4 and/or 6 kHz at least 10 dB HL higher than thresholds at 1 or 2 kHz and at 6 or 8 kHz, and less than 80 dB HL. This definition corresponds to a notched loss per Coles et al. (2000).
      The patient may present the same audiometric profile in both ears or any combination of the three profiles above.
5. Tinnitus handicap score ≥38 on THI

Exclusion Criteria

1. Objective tinnitus
2. Intermittent tinnitus
3. ENT diseases (Ménière's disease, serous or chronic otitis, labyrinthitis, perilymphatic fistula, superior canal dehiscence, vestibular migraine, neurological disorders, ongoing neoplastic pathology treatment, autoimmune hearing loss, or monitored/operated/irradiated schwannoma)
4. Moderate to severe hearing loss in one or both ears, or normal hearing in one or both ears
5. Pregnancy
6. Inability to communicate in written French
7. New medication for anxiety, depression, or sleep within the last 3 months
8. Use of hearing aids, noise generators, or combined devices in the past 12 months
9. Tympanometry result with type B curve (shift >200 daPa) or type C
10. Psychiatric illness: major depression, schizophrenia, bipolar disorder, personality disorder
11. Tinnitus handicap score <38 on THI

Assessment Measures

• Pure-tone and Speech Audiometry

Hearing thresholds will be assessed at frequencies 0.25, 0.5, 1, 2, 4, 6, 8, 10, and 12 kHz for both ears. This is a standard clinical audiology measure. Pure-tone stimuli will be presented at a clearly audible level, then gradually reduced (in 5 dB steps) until no longer perceived. The last perceived intensity is the threshold at a given frequency.

Discomfort thresholds will be measured in both ears using pure tones. Sound intensity will be gradually increased in 5 dB steps until reaching the discomfort threshold—just below the pain threshold. Sound duration will be short (≤3 sec) to ensure safety. This measure is widely used in hearing aid fitting to adjust maximum gain below discomfort thresholds.

Speech audiometry assesses speech intelligibility and discrimination (phoneme recognition). Speech-in-noise audiometry will use the **Vocale-rapide-dans le bruit (VRB) test** (Leclercq et al., 2018), based on lists of sentences from the "Marginal Benefit from Acoustical Amplification" corpus and global speech-shaped noise at varying signal-to-noise ratios. The SNR allowing identification of 50% of keywords (SNR-50) will be determined for each patient.

• Tympanometry

A non-invasive medical test used by ENTs to assess middle ear and tympanic membrane conditions by creating air pressure variations in the ear canal. All tympanometry will use clinically validated equipment. The procedure involves inserting a probe into the external auditory canal—non-invasive, painless, and safe (far from touching the tympanic membrane). Measurements of ear canal volume, middle ear pressure, and compliance (tympano-ossicular chain elasticity) will be recorded.

• Psychoacoustic Measures of Tinnitus

Tinnitus psychoacoustic characteristics will be assessed using standard, calibrated clinical audiometers:

- Timbre, Pitch, and Loudness of Tinnitus

Timbre will be estimated using pure tones and narrowband noises of varying widths. The subject will indicate which signal most closely matches their tinnitus timbre (spectral quality). The signal matching tinnitus timbre will then be used to estimate dominant pitch by adjusting its center frequency until the subject confirms a match. Loudness will be estimated by comparison to a pure tone at 1000 Hz and at the dominant tinnitus frequency. Intensity will start at threshold and increase in 1 dB steps until the participant reports a match to tinnitus loudness. Minimum masking level will determine the lowest intensity required for a noise to just mask tinnitus. Narrowband noise will start at threshold and increase in 1 dB steps until the participant reports complete masking.

- Questionnaires

▪ Tinnitus Handicap Inventory (THI)

This is the French version of the **Tinnitus Handicap Inventory** developed by Newman and colleagues (Newman, Jacobson, & Spitzer, 1996) (Appendix 1). It includes 25 questions, and the patient must choose one of the following responses for each statement: "Yes," "Sometimes," or "No." The total score is calculated as follows: "Yes" = 4 points, "Sometimes" = 2 points, and "No" = 0 points. The sum of all points corresponds to the final tinnitus handicap score. According to the authors, a total score of 0–16 indicates slight handicap, 18–36 mild handicap, 38–56 moderate handicap, 58–76 severe handicap, and 78–100 catastrophic tinnitus (Newman et al., 1996).

▪ Tinnitus Functional Index (TFI)

This questionnaire was developed to meet three distinct objectives: Provide a broad understanding of all symptoms associated with tinnitus severity, such as sleep or concentration problems; Offer a reliable measure of tinnitus severity on a continuum from "tinnitus is not a problem" to "tinnitus is a very big problem"; Measure changes in tinnitus severity during treatment (Meikle et al., 2012) (Appendix 3). It includes 25 questions, and patients respond using a numeric visual scale from 0 to 10 or 0 to 100 depending on the question. The total score is calculated by summing all question scores (maximum 10 per question) for a maximum of 250, then dividing by 25 and multiplying by 10 to obtain a score out of 100. According to the authors, 10–20 = mild problem, 30–40 = moderate problem, 40–60 = severe problem, and 60–90 = very severe problem. A reduction of 13 points in the total TFI score is considered the minimal clinically significant change.

▪ Speech, Spatial and Qualities of Hearing Scale short version (SSQ15)

The SSQ15 assesses auditory abilities, including sound localization, speech understanding, and listening ease. The short version, validated in French, includes 15 questions (Moulin et al., 2019) (Appendix 4). Questions address participants' hearing and listening experiences in various situations. For each question, participants mark an "X" on a numeric scale from 0 to 10. A mark at 10 means the participant can fully perform the described task; a mark at 0 means they cannot.

▪ Sleep

Sleep questions include a numeric scale assessing overall sleep quality (Snyder et al., 2018) (Appendix 5). Patients rate their sleep quality from 0 to 10, considering factors such as ease of falling asleep and hours slept. Three visual analog scales assess alertness and physical state upon waking: from "very tired" to "very fit" and from "very sleepy" to "very awake." An additional tinnitus-specific question asks patients to rate the impact of tinnitus on sleep quality on a scale from "no impact" to "very significant impact." These questions are similar to those used in previous studies on tinnitus and sleep (Hébert & Carrier, 2007).

▪ SF-12

Perceived health-related quality of life: The SF-12v2, derived from the SF-36 used for over 40 years, explores eight health dimensions: physical activity, physical limitations, pain, social life and relationships, mental health, mental limitations, vitality, and perceived health (Appendix 6). It includes 12 questions, and scores range from 0 to 100. It has been validated in several languages, including French (Gandek et al., 1998).

▪ HADS

The HADS scale screens for anxiety and depressive disorders. It includes 14 items scored from 0 to 3: seven questions for anxiety (total A) and seven for depression (total D), yielding two scores (maximum for each = 21) (Zigmond & Snaith, 1983) (Appendix 7).

▪ GRCS

The GRCS is a simple method for self-assessing therapeutic progress in research and clinical settings. Its face validity is considered high. The scale will include 7 points, as this number offers the best compromise between patient preference, discrimination ability, and test-retest reliability (Bobos et al., 2019). The question will be: "Among the choices below, check the statement that best reflects your overall impression of the effect of sound therapy on your tinnitus and general condition compared to the start of the study. "The scale will include: "Very improved," "Moderately improved," "Slightly improved," "Unchanged," "Slightly worsened," "Moderately worsened," and "Very worsened."

▪ Visual Analog Scales (VAS) for Tinnitus Distress and Loudness

Two VAS will be used: one to assess subjective tinnitus loudness (from "Very loud" to "Very soft") and another to estimate perceived distress (from "Unbearable" to "Bearable"). Patients will draw a line at the point that best represents their perception. These scales are widely used in tinnitus research, particularly for evaluating treatment effectiveness. Some researchers report that a minimal clinically significant change is two points out of 10 (Hall et al., 2017) (Appendix 8).

Sound therapies

The research protocol includes three arms corresponding to two "active" sound therapies and one "placebo" sound therapy called minimal-gain amplification. All participants will receive two hearing aids with open-fit domes, adjusted by an audiologist. Open-fit domes are preferable for high-frequency hearing loss: low frequencies enter the ear naturally, while high frequencies are amplified by the devices. One hundred devices from three different brands will be evenly distributed among the three study arms: Signia Pure 7x**,** Starkey Livio 2400**,** and Phonak Marvel 90, for a total of 300 hearing aids. The characteristics and specifications of these three hearing aids are considered equivalent. The three manufacturers (Signia, Starkey, and Phonak) have agreed to lend all devices for the duration of the research project (see Appendix 9). Devices will be loaned to participants for the study period.

▪ First Arm : Neutral Amplification

Hearing aids in the placebo condition (called neutral amplification) will provide no real amplification; environmental sounds will not be amplified but simply transmitted through the devices. The actual gain of the device is the sum of the natural part and the amplified part: a gain of 0 dB with the device results in a gain of 6 dB from the natural component. The time delay between the natural and amplified parts processed by the hearing aid produces periodic oscillations every 200 Hz due to a processing time of about 5 milliseconds. This phenomenon is noticeable, especially for the first 1500 Hz. The amplitude of these modulations depends on the ratio between the natural and amplified parts. To limit this effect, the absolute difference in level between the natural and amplified parts should be at least 10 dB. Devices will therefore be adjusted with negative gains of -10 dB, with lighter compensation of -5 dB around 3 kHz. The sum of the natural and amplified signals will be neutral but perceptible to the patient at suprathreshold levels (above the perceptual threshold). Additionally, device settings will allow participants to hear their own voice through the device, increasing the credibility of the placebo treatment. Activation alerts and battery charge warnings will also be enabled to further reinforce belief in proper device functioning.

▪ Second Arm : Sound Generator

In this condition, hearing aids will generate noise adapted to each participant's audiogram so that it is equivalent to white noise for an individual with normal hearing (flat audiogram). White noise has equal power spectral density across all frequencies in the bandwidth. To produce white noise adapted to each participant's hearing, audiologists will measure hearing thresholds using in-situ audiometry with the hearing aids. In-situ audiometry follows the same procedure as pure-tone audiometry but reduces interindividual variability and accounts for ear canal specifics, dome insertion effects, and receiver characteristics. Once in-situ audiometry is completed, the noise frequency distribution will be calculated from perception thresholds to obtain individualized white noise. From this point, perceptually, the noise is equivalent to white noise weighted according to the patient's hearing loss. After generating the noise, its perception threshold will be measured by adjusting the overall noise level. The noise will then be increased in 1 dB steps until reaching the "mixing level," where both the noise and tinnitus are perceptible but blend together. Generally, this level is reached at suprathreshold levels a few dB above the perception threshold and below the masking level (where tinnitus is completely masked). If the participant does not reach the mixing level, the noise level will be set arbitrarily at 7 dB above the perception threshold (7 dB SL).

▪ Third arm: Amplification + Sound Generator

In this third arm, the noise generator will be adjusted as described for the second arm. However, amplification tailored to each participant's hearing loss will be added to the noise. For the same reasons mentioned above, in-situ thresholds will be used to adjust amplification gain. The goal is to compensate for hearing loss and balance aided thresholds across frequencies and ears. Ideally, aided thresholds should be identical between ears and across frequencies. To standardize amplification across centers, all audiologists will use the same prescriptive formula: **DSLio method**. This formula was developed to maximize speech intelligibility and is recommended as the most effective for tinnitus treatment (Shekhawat, Searchfield, Kobayashi, et al., 2013; Shetty & Pottackal, 2019). Using a single prescriptive formula ensures standardized amplification for all participants across centers.

▪ Addition of different options at Week 6

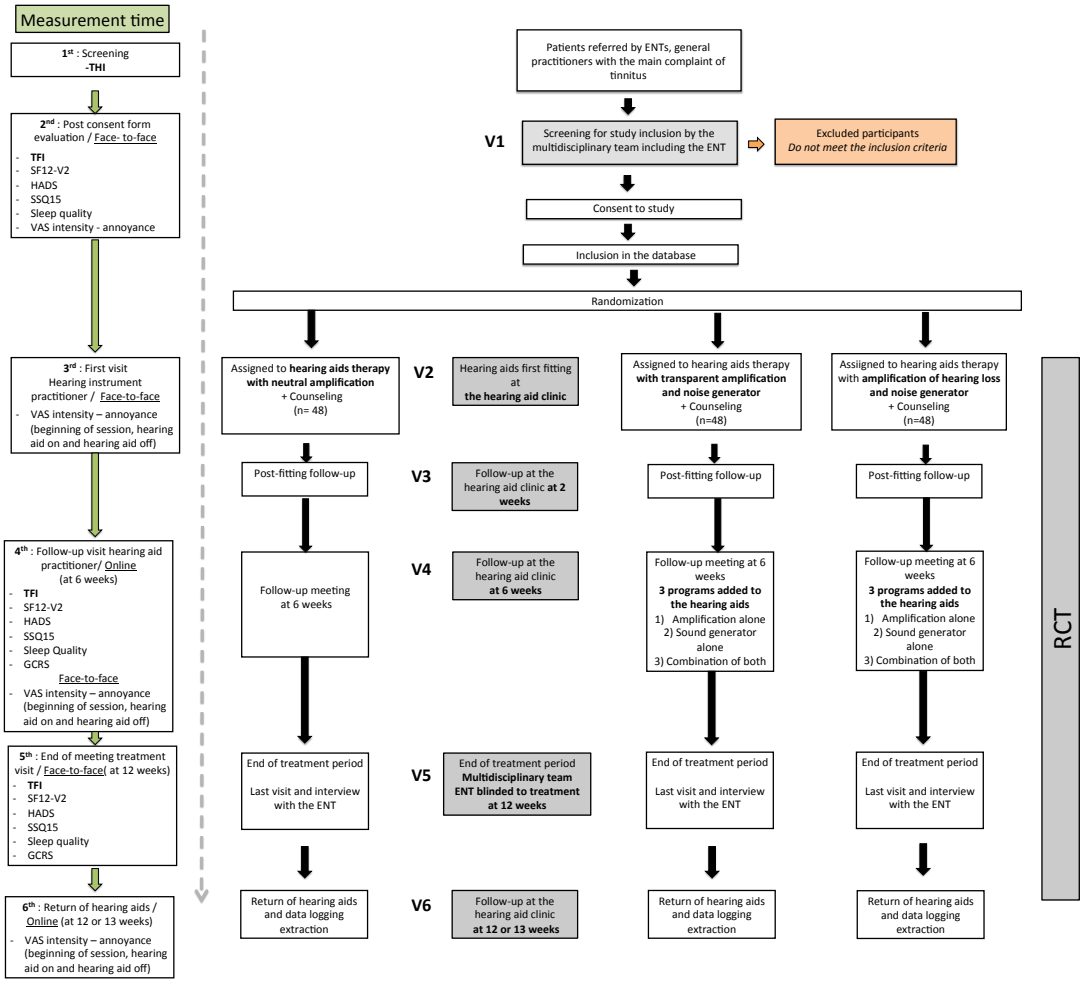
The originality of this research project lies in combining an initial rigid experimental phase (weeks 0 to 6), typical of randomized double-blind controlled trials where treatments are imposed on participants, with a second, more flexible phase (weeks 6 to 12) that allows participants to choose the treatment that best suits their preferences and daily life circumstances. Rigid protocols in double-blind randomized controlled trials are well suited for pharmacological treatments but less adapted for evaluating the effectiveness of technological aids such as hearing aids and/or noise generators. The usefulness of a hearing aid or noise generator may fluctuate depending on patient needs, different sound environments, and circumstances. For example, a noise generator may effectively reduce tinnitus distress and salience in a quiet environment (e.g., library) but have a detrimental effect on speech perception during a work

meeting. We believe that a rigid approach reduces the expected benefit because it only partially meets patient needs. Therefore, this necessary approach has been combined with a more flexible one, giving participants the choice to select the most appropriate treatment day by day.

By offering a choice at six weeks, we apply only a variant of the same initial treatment. Furthermore, we will analyze, using **datalogging** (device data recording), which programs are most frequently used and in what circumstances (e.g., in noise or in quiet). We estimate that giving participants control and flexibility to choose the most appropriate sound therapy based on their preferences and usual life circumstances will enhance the effect of sound stimulation therapy and empower participants. Starting at week 6, the noise generator, amplification, and combined approach (noise generator and amplification simultaneously) will be integrated into three distinct programs on the hearing aid. Participants will be able to switch between these programs using a push button. They may also choose to use only one of the three programs throughout the second phase. Amplification and noise generator settings for groups 2 and 3 will remain as described in previous sections. Group 1 (placebo group) will continue with the same treatment throughout the study.

Procedure :

Figure 1. Flow of the RCT study. The assessments for each measurement time point are shown on the left (green arrow). The six different visits made by participants during the study are labeled V1 to V6.



The initial consultation, tinnitus and hearing loss evaluation, audiological assessment, informed consent signing, and collection of baseline data for referred patients will take place at the ENT center by the investigator ENT specialist. A description of all initial assessment measures is provided in **Table II**. The ENT specialist will explain the study protocol and obtain consent after providing the patient with the information sheet, allowing time for consideration. Once consent is signed, the ENT will perform all evaluations, including pure-tone and speech audiometry, tympanometry, tinnitus assessment using a standardized questionnaire (Appendix 10), and administration of all other questionnaires. Directive counseling considered standard for tinnitus management will then be provided: explaining the different types of tinnitus, the presumed simple pathophysiology, and factors that may worsen or improve tinnitus, with attentive listening and empathy for all patients without distinction. Directive counseling will be standardized so that all ENT specialists across the six centers deliver the same advice (Appendix 11).

Table II. Initial Patient Evaluation and Measurements

Evaluations and Measurements

1. Audiometric thresholds including frequencies: 250, 500, 1000, 2000, 3000, 4000, 6000, 8000, 10,000, and 12,000 Hz for both ears
2. Response to the Tinnitus Functional Index questionnaire
3. Rapid Speech-in-Noise Test (VRB)
4. Standardized questionnaire for tinnitus evaluation
5. Tympanometry for both ears
6. Otoscopy
7. ENT evaluation of patient symptoms to rule out known pathologies that may cause tinnitus (e.g., Ménière's disease)

After the ENT consultation, the patient will be referred to the senior audiologist of each specialized team for tinnitus management within a maximum of 14 working days. Randomization into one of the three study arms will use an algorithm that minimizes:

1. Disparities in tinnitus severity between arms (severe tinnitus cases must be evenly distributed),
2. Disparities in intervention across sites (all sites will perform the same number of treatments per arm), and
3. Hearing aid brand distribution (all sites will use the three brands equally).

During the first audiologist visit (V2), participants will undergo measurements necessary for proper hearing aid fitting, including in-situ hearing thresholds and discomfort thresholds. Devices will then be adjusted according to randomization and assigned treatment: minimal-gain amplification, noise generator only, or combined noise generator and amplification.

At this visit (V2), participants will receive usage instructions, including device handling and maintenance, as well as standardized directive counseling specific to audiologists. The minimum required daily usage for the study (at least 6 hours per day) will be explained. At the end of the session, visual analog scales (VAS) measuring tinnitus distress and loudness will be administered with the hearing aid turned off and then on. This simple measure assesses the direct effect of amplification and noise generation on tinnitus and is considered an important marker of hearing aid success: tinnitus easily masked by an open device is more likely to reduce long-term distress (McNeill et al., 2012).

A first follow-up visit with the audiologist is scheduled at 2 weeks (V3) after therapy initiation to check device maintenance, functionality, settings, and patient comfort. Treatment adherence will also be verified using **datalogging** (device usage recording): participants not meeting the average 6-hour daily usage will be asked about reasons for underuse and encouraged to comply.

After six weeks of treatment, participants will complete all primary and secondary outcome questionnaires via an online portal. At the 6-week audiologist visit (V4), device maintenance and handling will again be checked, and adherence verified via datalogging. Participants failing to meet the 6-hour daily usage requirement will be excluded from primary effect analysis but included in separate analyses. They will continue treatment and follow-up with the study audiologists and ENT specialists.

Three programs will be added to the hearing aids for arms 2 and 3: Amplification only, Noise generator only, Combination of amplification and noise generator. Each program will be explained to the patient, who will be free to choose the program(s) they wish to use based on their preferences and daily life circumstances for the next six weeks. Patients may continue with the same therapy used during the first

six weeks or vary their initial approach by combining other types of acoustic stimulation. The therapy period ends at 12 weeks.

At that point, a final visit (V5) is scheduled with the team's ENT specialist to evaluate the primary and secondary treatment effects and gather participants' impressions. The ENT will remain blinded to the type of treatment the participant received. Finally, an additional visit between weeks 12 and 13 (V6) is scheduled with the audiologist to return the hearing aids and extract certain device data, including usage time via **datalogging**. This step constitutes unblinding for the patient, who will be informed of the treatment group they were in during the study. Participants in the placebo group will be offered the opportunity to try the most effective active treatment or the treatment of their choice for 12 weeks if they wish. Additionally, all participants will be allowed to keep the hearing aids free of charge at the end of the study, as manufacturers Signia, Phonak, and Starkey have agreed to invoice the devices at a preferential rate corresponding to the standard "100% Santé" pricing.

MANAGEMENT OF ADVERSES EFFECTS

Participants may contact the audiologist and/or ENT responsible for the study at each site by phone at any time. Minor events, such as discomfort related to the hearing aid, can be managed via a telephone consultation. Major events, such as worsening tinnitus or any other event considered major by the participant, will be managed through an in-person visit with either the audiologist or the ENT, depending on the nature of the event: if the major event is related to the hearing aid, the audiologist will be contacted; if it concerns the participant's health, the ENT will be contacted. Any serious event interfering with the study, such as a major emotional shock (e.g., death of a loved one) or diagnosis of a severe illness requiring intensive medical treatment (e.g., chemotherapy), will lead to exclusion of the participant's data from the primary analysis. However, the participant may continue the study if they wish and will remain under follow-up by the research team.

SAMPLING AND SAMPLE SIZE

The three-arm study is based on an interaction between an intragroup time factor (Start / Midpoint / End of treatment) and an intergroup treatment factor (Placebo / Noise Generator / Amplification + Noise Generator). A literature review reported that most studies on tinnitus treatment with amplification show therapy effects with moderate to large effect sizes (Shekhawat, Searchfield, & Stinear, 2013). However, these studies lacked proper controls, such as a placebo condition. In this context, we adopt a conservative hypothesis that the effect size for this study will be small (Eta-squared = 0.02), and we calculated the sample size accordingly. Using G*Power software (Faul et al., 2007), the calculation revealed that for a small effect size, there is a 90% chance of rejecting the null hypothesis (no interaction between therapy and time factors) with a total sample of 129 participants, i.e., 43 per group. Considering a 90% retention rate, we plan to add 5 extra participants per group (approximately 10% of each group), for a total of 48 participants per group and 144 participants overall.

DATA COLLECTION

The timing of data collection and its modality (in-person or online) is shown in **Figure 1** (see green box on the left). To maximize the number of measurements while reducing the workload for ENT specialists and audiologists, we opted for a combination of direct measures performed by clinicians and indirect measures completed online, referred to as "in-person" and "online" in Figure 1, respectively. Primary measures (**TFI** and **GRCS**) and secondary measures (**SF-12**, **SSQ15**, **HADS**, and sleep questionnaire) will be administered by ENTs during the initial patient evaluation and at the end of the study. All these same measures will be administered by the same ENT at the start of therapy and at the end of the twelve-week therapy period. The ENT will remain blinded to the treatment received.

Finally, two visual analog scales will be used to measure the direct effect of amplification and noise generation on tinnitus. These scales will be administered by the audiologist, who will compare tinnitus intensity and distress when amplification is turned off versus on, and when the noise generator is on versus off. This quick measure will be performed at the end of device fitting and adjustment during the first audiologist visit, at the six-week follow-up, and when hearing aids are returned at the end of the study. This simple measure helps distinguish the immediate effect of amplification from its long-term effect on tinnitus and has been reported as an important marker of hearing aid success: tinnitus easily masked by an open device is more likely to reduce long-term distress (McNeill et al., 2012).

DISAVANTAGES AND RISKS

The disadvantages of the study are related to the number of visits patients will need to make throughout the study, either to the ENT specialist or the audiologist. Additionally, continuous use of hearing aids may cause discomfort. Potential risks of the intervention include intolerance to the hearing aid or worsening of tinnitus. Follow-up visits with the audiologist at 2 and 6 weeks will serve as contingency measures to address any potential negative effects related to wearing the hearing aids.

DATA ANALYSIS

Our study aims to test the hypothesis that acoustic stimulation therapy (noise generator alone or combined with amplification) reduces tinnitus-related distress and improves patients' quality of life compared to a placebo sound therapy at 6 weeks. Furthermore, we hypothesize that a sound therapy allowing participants to choose daily between amplification alone, noise generator alone, or the combined approach (noise generator + amplification) will be even more effective in reducing tinnitus-related distress than any single imposed therapy. Statistical tests will be used to compare results across the three groups, first after six weeks of treatment and then after an additional six weeks of sound therapy. We hypothesize an interaction between therapy and time.

The primary variables studied are tinnitus-related handicap and distress as measured by the **TFI questionnaire**, and secondarily, improvements in associated comorbidities such as quality of life, sleep quality, depressive and anxiety symptoms, and auditory comprehension—all assessed through questionnaires. We will check whether the data follow a normal distribution; if so, parametric tests (**mixed ANOVA with repeated measures by time and group**) will be performed. If not (non-normal distribution), non-parametric tests will be used (**Mann-Whitney tests for non-repeated measures**). One of the strengths of the study lies in **within-subject comparisons** (imposed treatment from 0 to 6 weeks vs. flexible treatment between 6 and 12 weeks) and **between-group comparisons** (placebo vs. noise generator alone vs. combined approach at 6 weeks, and placebo vs. choice-based sound therapies at 12 weeks).

ETHICAL CONSIDERATIONS

All sounds presented to participants (in terms of intensity and duration) are safe for the auditory system, i.e., presented at levels below the regulatory limit. The current limit in France is 102 dB(A) for 15 uninterrupted minutes (Decree No. 2017-1244 of August 7, 2017, on the prevention of risks related to amplified sounds). Participants may contact the principal investigators and withdraw from the study at any time. If participants are concerned that their symptoms seem worsened by the experiment or sound presentation (even at moderate levels) and fear they may not return to baseline, they may stop participation. In the unlikely event of adverse effects such as increased tinnitus, patients can quickly meet with the study's ENT investigator or a team member if they wish. Participants will be supported by the ENT or audiologist throughout the study. All professionals involved have several years of experience in tinnitus management. All equipment used complies with standard clinical practice in ENT and audiology. It is worth noting that only one published study using acoustic stimulation for tinnitus treatment reported a significant increase in symptoms. Moreover, sound stimulation is commonly used

in tinnitus management, and several controlled randomized studies show that sound stimulation reduces tinnitus severity.

All participant data will be entered into a digital database hosted on a secure server. Data will be pseudo-anonymized using a secret-key cryptography system, so only the principal investigators will have access to the key linking data to individual participants. Participants may keep the hearing aids at the end of the study if they wish. Additionally, placebo group participants will be offered the option to try active sound therapy after the study and keep the hearing aids at the end of their trial.

SPECIAL CONSIDERATIONS DUE TO COVID-19

We believe that the potential benefits of this project for individuals with disabling tinnitus and mild hearing loss outweigh the risks related to COVID-19. Recent studies have highlighted that the current pandemic situation has led to an increase in tinnitus-related distress symptoms (Anzivino et al., 2020; Xia et al., 2020). Furthermore, one study reported that hearing loss and tinnitus are among the symptoms that can develop post-hospitalization due to COVID-19 (Munro et al., 2020). We therefore consider it important that research on therapeutic options for tinnitus, particularly acoustic therapies, continues even during the COVID-19 pandemic.

To minimize the risk of virus transmission, all ENT physicians will strictly follow the health protocols implemented by their healthcare institutions and comply with the guidelines of the French Society of ENT (SFORL) regarding sanitary protocols in the context of the COVID-19 pandemic. Similarly, all collaborating audiologists on the project commit to adhering to current health regulations and implementing the recommendations of the National College of Audiologists (CNA) regarding sanitary protocols during the pandemic. The SFORL and CNA rules and recommendations are included in the appendix of this document (Appendix 12).

TIMELINE

- **Study Start:** First quarter of 2021
- **Recruitment Period:** 1.5 years
- **Analysis Period:** 4 months

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