COVER PAGE

Official Title
Clinical Trial of Sound-Based Versus Behavioral Therapy for Tinnitus

NCT number
NCT03022084

Document Date
Last IRB approval date 13 MAR 2018

Research Protocol

Title: Clinical Trial of Sound-Based versus Behavioral Therapy for Tinnitus

Investigators

PI: James A. Henry, Ph.D.
Co-PI: Sarah Theodoroff, Ph.D.

Specific Aims

The purpose of this study is to determine if a customized therapy, Acoustic Coordinated Reset (CR) Neuromodulation (also referred to as Desyncra) reduces tinnitus-related distress with comparable efficacy as for Cognitive Behavioral Therapy (CBT) for people who have bothersome tinnitus.

Inclusion Criteria

- Age ≥18 years
- Primary and persistent tinnitus [defined by AAO-HNSF guidelines (Tunkel et al, 2014); 6 months or longer in duration]
- Tonal tinnitus
- Dominant tinnitus frequency measured between 0.2 and 10 kHz
- Tinnitus Questionnaire (TQ) score ≥30 at screening (to confirm moderate to severe tinnitus)
- No current participation in other tinnitus therapy program
- Willing and able to listen to the acoustic prescription for 4-6 hours daily during the trial
- Able to pass the Tone Audibility Assessment with factor of 1.1

Exclusion Criteria

- Secondary/somatic tinnitus due to a suspected underlying disease (defined by AAO-HNSF guidelines)
- Atonal, pulsatile, intermittent, or occasional tinnitus (determined by self-report and by the Tinnitus Screener)
- Any hearing threshold >70 dB HL from .25-8 kHz, unless subject passes the Tone Audibility Assessment screening with a factor of 1.1
- Any health or other problems that may prevent the person from completing the study procedures as determined by investigator
- Participant reports current (within the past week) suicidal ideation and/or homicidal ideation
- Use of medication that may trigger tinnitus [e.g., quinine derivatives, aminoglycoside antibiotics, daily high dose non-steroidal anti-inflammatory drugs ≥1000 mg, salicylates (when not prescribed as a low dose for cardiac health), loop diuretics and chemotherapy agents like cis-platin] at the discretion of the Principal Investigator
- Conductive hearing loss defined as an air-bone gap of 15 dB or greater at more

than two frequencies in one ear
- Visible congenital or traumatic deformity of the ear
- History of active drainage from the ear within the past 90 days
- History of sudden or rapidly progressive hearing loss within the past 90 days
- Inability to read and respond appropriately to instructions that appear on the computer screen, and/or to perform all of the study procedures

Desyncra Group. Subjects randomized to the Desyncra group will be fit with the devices. The Research Audiologists will be trained by a Desyncra representative to dispense the Desyncra for Tinnitus Therapy System according to company guidelines. The devices are fitted and programmed based on the subject's tinnitus characteristics and hearing ability at the first visit and the subject will use the device for 4-6 hours per day for 24 weeks.

In the case of a subject reporting his/her tinnitus has completely vanished, the subject will be instructed to reduce the amount of time using the therapy device to 1 hour per day. In the event that the tinnitus perception comes back, the subject would increase the amount of time using the device back to 4-6 hours per day.

If a subject's tinnitus characteristics become outside the range where tinnitus is treatable (e.g., too-high or too-low tinnitus pitch), the clinician may stop therapy for up to 2 weeks. Any changes in the therapy schedule will be documented accordingly.

CBT Group. Subjects randomized to this group will receive CBT consistent with best practice guidelines. Subjects will attend 6 CBT therapy sessions over the course of 8 weeks following baseline performed by a psychotherapist as per the recommendations outlined in the AAO-HNSF guideline (Tunkel et al 2014).

Step-by-Step Guidance on Conducting the Study

Recruitment

- Post ads at the VA Portland Health Care System (VAPORHCS; e.g., audiology, primary care, women's health clinics) and in the surrounding community
- Place ads in newspaper (paper and/or online); post online advertising; contact previous participants who consented to contribute their information into data repositories
- Mail recruitment letters to heath care clinics and facilities in Oregon and Washington (USA)

Telephone Screening

- Screen candidates over the phone using screening script; if eligible, gather information from candidate and schedule initial appointment

Visit 1: In-Person Screening/Baseline

- Administer informed consent

- HIPAA authorization
- Administer questionnaires
- Study staff may opt to use the Sound Finder with candidates (classifies tinnitus as tonal vs. noisy perception)
- Audiologic testing
- Tinnitus pitch matching procedure using procedure specified by Desyncra Inc.

Visit 2 (1 week after screening completed, approximately ±1 week)

- All subjects will complete the pitch matching procedure and questionnaires
- Subjects in the Desyncra group will have their device adjusted according to manufacturer guidelines
- Subjects in the CBT group will complete their 1st CBT session
- Subjects are paid $40 for attending the visit

Follow-up to Visit 2 for subjects randomized to the Desyncra arm

- An audiologist will call subjects randomized to the Desyncra arm approximately 1 to 2 weeks after Visit 2 to follow-up and see how the subject is doing with the sound-based therapy

Visit 3 (4 weeks after screening completed, approximately ±1 week)

- All subjects will complete the questionnaires
- Subjects in the Desyncra group will complete the pitch matching procedure and have their device adjusted according to manufacturer guidelines
- Subjects in the CBT group will complete their 4th CBT session
- Subjects are paid $40 for attending the visit

Visit 4 (8 weeks after screening completed, approximately ±2 weeks)

- All subjects will complete the pitch matching procedure and questionnaires
- Subjects in the Desyncra group will have their device adjusted according to manufacturer guidelines
- Subjects in the CBT group will complete their 6th and final CBT session
- Subjects are paid $40 for attending the visit

Visit 5 (16 weeks after screening completed, approximately ±2 weeks)

- All subjects will complete the questionnaires
- Subjects in the Desyncra group will complete the pitch matching procedure and have their device adjusted according to manufacturer guidelines
- Subjects are paid $40 for attending the visit

Visit 6 (24 weeks after screening completed, approximately ±2 weeks)

- All subjects will complete the pitch matching procedure and questionnaires
- All subjects will complete an exit interview
- Subjects in the Desyncra group will discontinue use of the device
- Subjects are paid $40 for attending the visit

Visit 7 (28 weeks after screening completed, approximately ±2 weeks)

- All subjects will complete the pitch matching procedure and questionnaires
- Subjects are paid $40 for attending this final visit
- Desyncra group will have the opportunity to keep their devices
- CBT group will have the opportunity to be fit with and receive the Desyncra device
- Any participant who keeps the Desyncra device will be given information on how to receive assistance from a local provider or company representative for device-related concerns

Statistical Analysis Plan

A Bayesian approach to the analysis of outcome data will be used. Based on simulations across several conditions, we anticipate requiring a total of no more than 200 subjects to have at least 80% power to identify a significant benefit of Desyncra therapy compared to CBT.

Data from this study will be provided to the NCRAR Data Manager who will develop and maintain a database with all study data. Either the Data Manager or other study personnel (e.g. Research Assistant) will enter the data. The Data Manager will perform double entry of the data and check for any errors, which will be remediated. After the study is complete and all data are entered and verified, the Data Manager will conduct preliminary analyses of the data to determine if there are any differences in outcomes between groups. These analyses will be overseen by the NCRAR Biostatistician who will conduct further analyses as necessary.

A preliminary analysis will be conducted after a total of ~30 subjects have been randomized and completed the 16 week follow-up visit. The first formal interim analysis will be conducted after a total of ~30 subjects have been randomized and completed the 24 week follow-up visit or ~16 subjects per treatment arm. A second formal interim analysis will occur after a total of ~72 subjects have been randomized (~31 subjects per treatment arm) and completed the 24-week follow-up. The primary endpoint of this study occurs 24 weeks after being dispensed the Desyncra device at which time the primary outcome measure, the TQ, is repeated.

The efficacy of Desyncra will be assessed by contrasting the Desyncra and CBT subjects' change from baseline on the TQ outcome. The δ parameters describe the overall change from baseline common to both treatment arms. The φ parameters describe the benefits of Desyncra over CBT in this study. We assume that the TQ observations are Gaussian random variables with population mean defined above plus a subject-specific random intercept θ_i, and with residual standard deviation σ.