Tinnitus pitch matching by residual inhibition and contrast gain control.

Published: 18-12-2018
Last updated: 11-04-2024

The main objective is to improve the existing techniques for measuring the tinnitus pitch in patients, by exploring both the frequency dependence of the residual inhibition and the contrast gain control effect in the auditory system. Behavioral...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hearing disorders
Study type	Observational non invasive

Summary

ID

NL-OMON48700

Source
ToetsingOnline

Brief title
Tinnitus pitch matching

Condition

- Hearing disorders

Synonym
tinnitus

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ESIT

Intervention

Keyword: matching, pitch, tinnitus

Outcome measures

Primary outcome

Part I:

The primary endpoint will be the tinnitus pitch on psychoacoustic responses.

These include the following:

- Difference between audio samples and automatic method for tinnitus characterization.

- Relation between participants* RI function and tinnitus pitch.

Part II:

The primary endpoint of this part will be the difference in contrast gain control between tinnitus patients, hearing loss patients and controls. These include the following:

- Relation between behavioral measures and EEG responses for the three groups.

- Relation between tinnitus pitch and contrast gain control measures for tinnitus patients.

Secondary outcome

Not applicable

Study description

Background summary

Several authors have addressed the relationship between hearing impairment and persistent tinnitus. In the majority of cases, patients' tinnitus percept overlaps the hearing loss frequency region (Tunkel et al., 2014) (Henry 1999) (Norena, Micheyl, Chéry-Croze, & Collet, 2002). Animal studies have shown that after a cochlear damage some changes in the response properties of auditory neurons take place (Noreña & Eggermont, 2003). One of these changes is that neurons in cortical and subcortical auditory structures suffer an increase of their spontaneous firing rates after the input from the ear is diminished. Another change is the temporally synchronous activity of a population of neurons when compared to control animals. The neural synchrony model of tinnitus suggests that these changes might be responsible for generating the tinnitus percept.

There is an increasing interest in sound-based therapies for tinnitus treatment (e.g., Henry et al. 2008; Hobson et al. 2010; McNeill et al. 2012; Shekhawat et al. 2013). Some of these treatments are based on applying a background noise to the hearing loss region, but their effectiveness is still questioned (Davis et al. 2008 positive) (Vanneste et al. 2013 negative). However, the knowledge about neurophysiology of tinnitus is constantly growing and some of the treatments are focused on reversing the changes of maladaptive plasticity, reporting a benefit for the patients. That is the case of the notched music listening approach, aiming at reducing the spontaneous activity in neurons by enhancing lateral inhibition from the frequencies above and below the tinnitus frequency. (Okamoto et al, 2010; Herraiz et al. 2010; Teismann et al, 2011; Pantev et al, 2012). Like other approaches, the goal is to stimulate either the predominant tinnitus frequency or the frequencies around it.

The problem which arises in this context relates to the difficulty of targeting the frequency region of the tinnitus percept, which is crucial for ensuring the correct application of these therapies and is not directly observable. The process of defining the fundamental frequency of the tinnitus percept is known in the tinnitus field as pitch matching (Henry & Meikle, 2000). The most common approach consists of a psychoacoustical task where the patient listens to several pure tones and reports which one is the most similar to the tinnitus percept. The literature is plenty of different approaches to carry out the pitch matching, many of them consisting on several steps of choices where the distance in frequency between the presented tones is narrowed step by step, just as in the case of the two-interval forced choice (2IFC) or the forced-choice double staircase (FCDS). (ref) Despite of the amount of available methods, tinnitus pitch matching is strongly criticized because of its subjective nature. Moreover, some authors claim these are unreliable cause repeated pitch matches often vary over 2 to 3 octaves (Penner 1983; Tyler &

Conrad-Armes 1983; Burns 1984; Henry et al. 2004). Variations might be produced by the reporting difficulties patients have when performing the test or by the tinnitus changes due to the stimulus (Tyler 2000).

Residual inhibition

Some authors have tried to shed light on other representations of the tinnitus pitch through different psychoacoustical measurements, such as patients* audiograms (Schaette & Kempter, 2009) or masking levels. The masking intensity of tones or noise throughout the entire frequency range have shown to follow specific patterns that might be related to the tinnitus pitch for some cases (Feldmann, 1971). Some stimuli used in these masking tests have a particular outcome: a temporary suppression of the tinnitus percept can happen even after the cessation of the stimulation. The effect is known as residual inhibition (RI) and its depth and duration can be measured along frequencies, resulting in the residual inhibition functions.
It has been shown that RI functions overlap the tinnitus spectrum and the region of auditory threshold shift (Roberts, Moffat, Baumann, Ward, & Bosnyak, 2008), consistent with the hypothesis of the increased neural synchrony. This difference between responses in the tinnitus frequency region and outside of it during residual inhibition has been also observed in the 40-Hz auditory steady-state response (ASSR) and the event-related potential component N1 (Roberts, Bosnyak, Bruce, Gander, & Paul, 2015). These results suggest that residual inhibition might be a more reliable marker for tinnitus pitch matching. One major problem approaching RI is the time-consuming aspect to measure it. The traditional method consists in measuring the time needed for the tinnitus to reappear after the cessation of a 30s or 60s noise presentation at 10 dB above the Minimum Masking Level (MML), meaning the lowest intensity level required to mask the tinnitus percept. Performing this test with different carrier frequencies to study the frequency dependence and waiting the correspondent recovery times between trials might be impracticable.
A new method has recently been designed, measuring the Minimum Residual Inhibition Level (MRIL) (Fournier & Norena, 2018) for reducing considerably the testing time by using pulsed acoustic stimulation of fixed duration, thus facilitating the study of this feature in depth. Although in this study narrow and wide band noise were used as stimuli, recent evidence has suggested that amplitude modulated tones might reduce the tinnitus loudness even faster (Tyler & Stocking, 2014), specially in the frequencies around the tinnitus pitch (Neff et al., 2017). Therefore, the new method will be used in this project and it will include these stimuli for greater efficiency.

Contrast gain control

Although several neurophysiological models of tinnitus have been proposed, there is still no consensus on the specific mechanisms generating this disorder. One of the most recent proposals is the Central Gain Model of tinnitus. After noise exposure, the neural spontaneous activity is reduced in

the auditory nerve, but the activity in some higher auditory structures, such as the auditory cortex (AC), medial geniculate body (MGB) and inferior colliculus (IC), is increased. The Central Gain Model proposes that tinnitus is caused by an increase in gain or neural amplification in the central auditory system, aimed to compensate the loss of sensory input from the cochlea. In this model, it is important to note the role of *neural noise* in tinnitus generation. Even in silence, the central auditory system is constantly receiving input so there is a minimum level of activity defining this silence or baseline. Central gain enhancement does not only produce an increased sensitivity to sound-evoked activity, but it also amplifies spontaneous activity, resulting in the auditory perception of neural noise. Several behavioral studies with animals suggest a correlation between this central gain enhancement and tinnitus, and moreover, there is some evidence restricting gain enhancement to only the region of hearing loss and tinnitus pitch (Brozoski et al., 2002), which places emphasis on the need for further studies to correlate neural enhancement to the tinnitus pitch (Auerbach, Rodrigues, & Salvi, 2014). One of the most important statistical properties of the auditory system for representing sounds is the spectrotemporal contrast in the auditory environment. Contrast gain control is the property by which neurons adjust their sensitivity to changes in sound level in response to contrast of sound stimuli. As a result, the cortical representation is very robust to the noise increase and invariant to stimulus contrast, which in addition provides a more efficient use of the neural dynamic range. There are few existing studies addressing this feature of the auditory system in ferrets (Rabinowitz, Willmore, Schnupp, & King, 2011) (Willmore, Cooke, & King, 2014), but there is still no behavioral research in humans. In tinnitus patients, an abnormal functioning of the central gain around tinnitus frequencies could be measured by using behavioral test consisting on contrast of stimuli.

Study objective

The main objective is to improve the existing techniques for measuring the tinnitus pitch in patients, by exploring both the frequency dependence of the residual inhibition and the contrast gain control effect in the auditory system. Behavioral measures and EEG responses will be related in order to improve the traditional self-report-based methods for pitch matching and to provide new evidence for the contribution of maladaptive reorganization in tinnitus generation and maintenance.

Study design

The current study has two parts. Part I will be a series of behavioral experiments with the ultimate goal of finding correlation between residual inhibition and the tinnitus pitch, in order to shed light on whether it is a reliable measure for matching the pitch. Part II will consist on a behavioral and ERP study on contrast gain control in tinnitus patients, aimed to

investigate the relation between this feature and the tinnitus pitch. Both parts and the corresponding experiments are described below:

Part I: Residual inhibition

Exp. 1: Tinnitus pitch matching by audio samples and automatic method
Subjects will fill out questionnaires and undergo audiometry testing. In this first session of this experiment, subjects will perform an active listening to a list of tinnitus synthesized audio samples, previously labelled and categorized. Participants will relate their tinnitus percept to one or more of these audio samples by means of a forced-choice procedure, providing relevant information about their tinnitus such as timbre and pitch.
A non-supervised automated tinnitus pitch-matching procedure (also known as bracketing method) will be carried out in a second session. There will be a training session before this procedure starts, in order to familiarize the participants with the task. In this session, participants will perform a forced-choice test using pure tones as stimuli (Vernon, 1983).
Additionally, participants will undergo the regular pitch matching procedure that is currently used in the KNO clinic for assisting tinnitus patients.
The overall duration of the experiment is about 1 hour and a half. Blinding, randomization, placebo-control, or cross-over are not applicable in this study design. Between the two measurements, the participants will be asked to take a break in. The study will be carried out in the tinnitus lab at the Otorhinolaryngology Department at UMCG. The participants will be placed in front of a computer monitor in a sound proof chamber.
Once the participants finish the experiment, a second appointment will be scheduled within one week for repeating the same experiment, in order to test the reproducibility of these methods and to check the variability of their tinnitus.

Exp. 2: Minimum Residual Inhibition Level and tinnitus pitch
In the second experiment, the Minimum Residual Inhibition Level (MRIL) will be measured for several frequencies by means of stimulus sequence consisting of amplitude modulated tones at increasing intensity levels. Subjects will be asked, before, after and between the assessment, to rate the loudness of their tinnitus. For each carrier frequency, the trial finishes when a complete suppression of the tinnitus is achieved or the maximum intensity level of the stimulus is reached. A paradigm similar to Fournier & Norena (2018) will be used, obtaining the MRIL for several frequencies as it is usually done in audiometries. This experiment will explore the relationship between patients* RI measures and tinnitus pitch, expecting to find lower values of RI in the frequencies around the tinnitus pitch.
The overall duration of this experiment is about 20 or 30 minutes. Blinding, randomization, placebo-control, or cross-over are not applicable in this study design.
We will conduct a pilot study in which 10 participants will perform the same test by using narrow band noise as stimulus. The objective is to compare the RI

curves obtained by both amplitude modulated tones and narrow band noise stimuli. Same duration will be needed for this pilot study.
The study will be carried out in the tinnitus lab at the Otorhinolaryngology Department at UMCG. The participants will be placed in front of a computer monitor in a sound proof chamber.

Part II: Contrast gain control

Exp. 3: Loudness discrimination in background noise
In the third experiment, differences in gain enhancement and contrast gain control between normal hearing, tinnitus and hearing loss patients will be investigated.
Participants will perform a psychoacoustic experiment consisting of stimulus discrimination in masking and no-masking conditions with different intensity levels by using a forced-choice task. On the neuronal level, discrimination capacity will be measured by means of ERP responses. The overall duration of this experiment is about 1 hour.

Study burden and risks

Neither risks nor benefits are known with participation.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Tinnitus group (A, n=20):
- No reported neurological or psychiatric disorders (excluding tinnitus and hearing loss);
- Chronic tinnitus (lasting more than 6 months);
- Adult, 18-75 years of age;
- Symmetric hearing loss with PTA (average threshold 1000-2000-4000 Hz) >= 30 dB;
- Written informed consent;
Hearing loss group (B, n=20):
- No reported neurological or psychiatric disorders (excluding hearing loss);
- Adult, 18-75 years of age;
- Symmetric hearing loss with PTA (average threshold 1000-2000-4000 Hz) >= 30 dB;
- Written informed consent;
Control group (C, n=20)
- Healthy subjects (i.e., excluding tinnitus, no medical, neurological, or psychiatric disorders);
- Adult, 18-75 years of age;
- Normal hearing thresholds or mild hearing loss (average threshold <=20 dB @ 500-2000 Hz);
- <=30 dB difference between both ears for all the standard audiometric frequencies;
- Written informed consent;

Exclusion criteria

- All subjects who cannot fully understand the experimental task.
- Non-conformance to any of the inclusion criteria stated above.

Study design

Design

Study type: Observational non invasive

Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2020
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	18-12-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-11-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL66367.042.18
Other	UMCG Research Register, number 201800489