



postponed  
to 2022



# Abstract Book

Local Organizer: Carol and Colin Lau  
Chair Scientific Committee: Prof. Dr. Sylvie Hébert  
Tinnitus Research Initiative Foundation: Prof. Dr. Berthold Langguth

# Content

<b>Content .....</b>	<b>2</b>
<b>Forewords .....</b>	<b>5</b>
<b>Animal Models .....</b>	<b>8</b>
Local cortical changes in primary auditory cortex immediately after noise trauma.....	8
Long-term effects of noise trauma on the intracortical processing in primary auditory cortex .....	9
Decoding Acute Tinnitus by Classifying Dorsal Cochlear Nucleus Spiking-Activity .....	10
Notched noise effect on evoked activites in the primary auditory cortex.....	11
Comparison of Three Methods to Detect Tinnitus on a Rat Salicylate-Induced Tinnitus Model.....	12
Ebselen Can Attenuate Hyperacusis and Tinnitus in A Novel Animal Model of Aminoglycoside Toxicity .....	13
<b>Clinical Management and Clinical Research .....</b>	<b>14</b>
Neurofeedback for tinnitus distress – What are the therapeutic mechanisms? – Preliminary results of a randomized controlled trial.....	14
Long term total remission of tinnitus: fact or myth? .....	15
Prevalence of psychiatric symptoms and the effectiveness of stepped care treatment in tinnitus patients .....	16
T3: Tinnitus Treatment Trends in 2019.....	17
Conceptual Cognitive Model for Tinnitus-Insomnia Comorbidity .....	17
Botulinum toxin injections into bilateral head and neck muscles has major benefit for tinnitus .....	18
Evaluation of Multidisciplinary Tinnitus Pathway introduced in Royal Brisbane and Women's Hospital, Australia .....	19
Tinnitus and caffeine .....	20
A Pragmatic Approach to Treating Tinnitus Patients: The Who, The What, The Why, and The How.....	20
Comparison of Symmetric and Asymmetric Hearing on Tinnitus Distress: Preliminary Study .....	21
Analysing the Relationship Between the Tinnitus Severity and the Sleep Quality .....	22
<b>Computational Modeling .....</b>	<b>23</b>
Stochastic Resonance improved hearing and speech recognition provides a mechanistic explanation of subjective tinnitus .....	23
<b>Education.....</b>	<b>24</b>
Advancing tinnitus research and researcher training: a case study review and future perspectives .....	24
<b>Electrophysiology .....</b>	<b>25</b>
Direct mapping of the cortical tinnitus network.....	25
Identifying Differences in Neurofeedback .....	26
Training Trajectories in the Treat- ment of Tinnitus .....	26
The effect of tinnitus pitch on the N1 .....	26
Late Auditory Evoked Potentials in Chronic Subjective Tinnitus Patients: A Systematic Review and Meta-Analysis .....	27
Multifocal Tomographic Neurofeedback for Treating Chronic Tinnitus in Older People.....	28
Nonlinear (Entropy) Analysis of EEG in Tinnitus .....	29
Does tinnitus fill in the gap? An EEG study on the gap response in tinnitus-matched background noise.....	30

<b>Epidemiology.....</b>	<b>31</b>
Tinnitus and Probiotics: An Open-label Pilot Study .....	31
Prevalence of tinnitus in a large Brazilian city: a health survey in primary health care .....	32
<b>Epidemiology and Prevention.....</b>	<b>33</b>
Tinnitus in Adolescents – a Survey of Secondary School Students .....	33
<b>Help-seekers .....</b>	<b>34</b>
Characteristics of Help-seekers and Non-help-seekers with Tinnitus from a Population-based Sample .....	34
<b>Hyperacusis.....</b>	<b>35</b>
Using psychophysical ratings of natural and artificial sounds to create a new assessment tool for hyperacusis.....	35
An evaluation of the content and quality of hyperacusis information on websites .....	36
The electrophysiological markers of hyperacusis: a scoping review .....	37
Characterization of hyperacusis patients' symptomatology.....	38
<b>Neuroimaging .....</b>	<b>39</b>
Affective learning in chronic tinnitus – behavioral and magnetoencephalographic correlates .....	39
Tinnitus-associated subnetworks are elicited by frequency-specific auditory stimulation: A MEG study .....	40
Reorganization of brain white matter in persistent idiopathic tinnitus patients without hearing loss: Evidence from baseline data.....	41
<b>Neurostimulation .....</b>	<b>41</b>
Modulation of Tinnitus-Related Emotional Processing and Its Effects on Attentional Bias: A model validation study .....	41
Dorsomedial prefrontal cortex rTMS for tinnitus: promising results of a blinded, randomized, sham controlled study.....	42
Combined sound and somatosensory stimulation to treat tinnitus .....	43
Effectiveness of bimodal auditory and electrical stimulation' treatment in patients with tinnitus: A pilot study .....	44
Random Forest Classification to Predict Response to High-Definition Transcranial Direct Current Stimulation Therapy for Tinnitus.....	45
Effectiveness of blinding and occurrence of adverse effects in sham-controlled transcranial direct current stimulation (tDCS) study .....	46
From clinical data to a model accounting for hyperacusis and associated symptoms.....	47
Sound-induced pain in hyperacusis patients from a clinical perspective: the role of Tonic Tensor Tympani Syndrome (TTTS) .....	48
Reliability and validity of oscillatory brain activity changes induced by repetitive transcranial magnetic stimulation.....	48
<b>Tinnitus in Children.....</b>	<b>49</b>
Development of a child-specific questionnaire measure of tinnitus impact .....	49
<b>Pathophysiology .....</b>	<b>50</b>
Strain-specific changes occurring in animal auditory system after stress .....	50
Ventral cochlear nucleus bushy cells contribute to hyperacusis neural coding after noise-exposure.....	51
<b>Pharmacology.....</b>	<b>52</b>
The effects of mirtazapine on tinnitus in patients with panic disorder.....	52
Phase 2b Randomized Double Blind Placebo-Controlled Trial of SPI-1005 for Meniere's Disease.....	52
A Phase II-ready oral drug shows excellent preclinical efficacy for treating blast and noise-induced tinnitus.....	53
<b>Sound Therapy .....</b>	<b>54</b>
Modulation of sound and tinnitus loudness in tinnitus patients with and without hearing loss following three weeks of acoustic stimulation.....	54
Acoustic amplification in case of Single-Side Deafness with residual hearing: an alternative to cochlear implantation to treat tinnitus.....	55
Testing the reliability of psychoacoustic measures of tinnitus.....	56
Investigating the Effect of High-Frequency Amplification as Tinnitus Treatment .....	57
The acute effect of sound therapy on attention for chronic tinnitus patients .....	58
Cochlear implantation for tinnitus – a systematic review.....	59

<b>Specific Forms of Tinnitus.....</b>	<b>60</b>
Effectiveness of dry needling in the annoyance of chronic tinnitus in patients with myofascial trigger points .....	60
Complaints about low-frequency noise: a physical sound or low-frequency tinnitus?	
An overview of noise measurement data .....	61
Physical symptoms in patients with tinnitus .....	62
The effect of orofacial treatment on tinnitus complaints in patients with somatosensory tinnitus: A randomized controlled trial .....	62
Overinterpretation of Research Findings: Evidence of "Spin" in Tinnitus Randomized Controlled Trials .....	63
<b>Systematic Testable Framework.....</b>	<b>64</b>
Neurofunctional Tinnitus Model Validation to investigate cognitive processes causality in clinical distress stage.....	64
<b>Tinnitus Assessment .....</b>	<b>65</b>
Objective correlates of tinnitus and cochlear synaptopathy.....	65
Skarzynski Tinnitus Scale: validation of a brief and robust tool for assessing tinnitus in a clinical population .....	66
Relationship between tinnitus loudness measure by Visual Analogue Scale (VAS) and psychoacoustic matching of tinnitus loudness.....	67
Tinnitus in Brazilian primary health care: perspective of health professionals.....	68
Impact of Choice of Test Stimulus on Pitch Matching Performance: Pure Tone versus Narrow Band Noise.....	68
Differences between post-stimulus suppression of tinnitus and tinnitus-mimicking sound.....	69
Tinnitus Sounds Description by Tinnitus Patients: Preliminary Results .....	70
The Neuroscience of Tinnitus in Humans: A Symposium in Memory of Dr. Larry E. Roberts .....	71
A lot to like: More to tinnitus measurement than pitch matching. – A tribute to Larry Roberts .....	71
Persistence and remission of tinnitus and sound intolerance among adolescents: may hidden synaptic injury repair? .....	71
<b>Citizen Science.....</b>	<b>72</b>
The Power of an Online Community – How Tinnitus Hub Facilitates Citizen Science .....	72
Assessing content validity of concentration instruments for tinnitus clinical trials: a focus group involving patients and researchers .....	73
<b>Physical Symptoms in Patients with Tinnitus: From Subtyping to Cure.....</b>	<b>74</b>
Somatosensory tinnitus: Who gets cured? .....	74
<b>Miscellaneous .....</b>	<b>75</b>
UNITI - a new EU-funded project towards a unification of tinnitus treatments and interventions.....	75
Towards a positive perspective on tinnitus.....	76
Towards a programme theory of tinnitus support group interventions: a systematic review and realist synthesis.....	77
Effect of yoga training on the tinnitus induced distress.....	78
<b>TRI Conference 2021 – Invitation by the Organizers .....</b>	<b>79</b>

# Forewords

**Dear Colleagues and Friends,**



On March 13th we were just about to send notifications of acceptance for abstracts to be presented at the TRI 2020 meeting when confinement for an undetermined period was declared by governments worldwide in response to the COVID-19 pandemic. This planetary public health crisis - from which we are still struggling to recover - prevented us from holding the very first TRI meeting in Canada, from celebrating prominent Canadian figures in the field, and paying homage to our regretted colleague Larry E. Roberts who was still active a few weeks before passing away in the Summer of 2019.

In the tradition of previous TRI meetings, our Scientific Committee had been planning for a fascinating scientific program from the close to 200 abstracts originating from 25 countries representing all continents, as well as from several highly diversified Symposium proposals, that we had received from the TRI community. We were also looking forward to celebrate our precious bonds of friendship in the many informal encounters of a TRI meeting. Fortunately, this was not lost entirely thanks to the TRI International Board and Staff's dedication and generous initiative to offer to our community this Book of Abstracts.

My warm thanks go to my Scientific Committee colleagues, to the TRI International Board, and to Carol Lau and her Vancouver Organizing Committee for their hard work, responsiveness, and collaboration. I am hoping we will work together again in the future.

We will meet again soon!

Sylvie Hébert  
Co-chair of the scientific committee for TRI 2020  
Professor, School of Speech pathology and audiology

Faculty of medicine  
Université de Montréal

**Dear friends, dear colleagues,**



The year 2020 will definitely be a year for the history books – but what history will remember remains to be seen. In the midst of a global pandemic, worldwide health crisis and socio-political upheaval, we were forced to change and adapt to our new “normal”. With new public health protocols set in place to curb the spread of coronavirus, large gatherings were prohibited and our Tinnitus Research Initiative Conference for 2020 (TRI-2020) was forced to cancel. It was with mixed emotions that TRI-2020 was cancelled. On one hand, it was disappointing after all the effort that went into planning the event. But on the other hand, there was relief in knowing that nobody would be put at risk of being infected. While regrettable, the change in status quo reminded all of us to reconsider our priorities and see what was truly important.

And while we were unable to meet in person, the expertise, wisdom and cutting-edge research compiled for our conference are invaluable resources for improving the way we understand and treat tinnitus. In a world changed by the pandemic, we have been given time to reflect on ourselves as a people and to learn a lot about empathy. When faced with any health issues, patients can feel lost and powerless, but they don't need to be.

In the spirit of “From Science to Succour”, TRI has compiled a collection of abstracts from the researchers, clinicians and tinnitus patients whose papers had been accepted for presentation at the conference. With this compilation, we hope to equip those researching and treating tinnitus patients; to empower those suffering and those who care for them. Although the COVID-19 pandemic has left us unable to meet for now, we hope that the knowledge and expertise can still reach you and reinforce that we are all connected and working together to improve the lives of our patients.

Thank you to everyone who contributed to the planning of TRI-2020: to our Scientific Committee Chairs, Dr. Sylvie Hébert and Dr. Paweł Jastreboff, and to Dr Hébert's team for assembling what would have been a very exciting academic program; to the Organizing Committee volunteers for their enthusiastic work which was instrumental in preparing for our event; to our Keynote Speakers for their commitment to our conference and to our sponsors, without whom no conference would exist. Finally, a special thanks to the Tinnitus Research Initiative Executive and Board Members for their always-present support and guidance.

On behalf of TRI, we are pleased to be able to share the knowledge and expertise of our esteemed tinnitus academic community through this TRI-2020 abstract book. We look forward to hearing more about these exciting projects and studies from TRI in the years to come.

Carol Lau

Organizer TRI-2020

**Dear friends, dear colleagues,**



"Social distance", the most efficient defense strategy against the pandemic Covid-19 infection, has turned our lives upside down within a couple of weeks. Nothing is any more, how it was before.

The yearly TRI meeting, a fixed date in the calendar of many tinnitus researchers worldwide could not take place.

Our interactions – even within institutions – are restricted to video-conferences, telephone and E-mail. Even if we may experience that this works better than expected and that video conferences can be a useful tool, we realize more and more the value of face-to-face interactions. We realize that gathering means more than information exchange and we are longing for meeting friends and colleagues.

Unfortunately this is still dangerous and we have to be patient, but I am convinced that this will be possible again. Thus this year, we have no talks and no posters, but we have an abstract book, which provides an impressive overview about the quality and diversity of the tinnitus research field. This abstract book is the best proof, that tinnitus research is alive and more active than ever before.

Particular thanks go to Carol Lau and her team. During the whole preparation period and even in the phase when it became clear, that the meeting may not take place this year, Carol acted with highest personal commitment. I am sure that we would have had a wonderful meeting and that we will have a wonderful meeting in Vancouver 2022.

I wish all of you to stay healthy and to meet you in 2021 in Dublin and in 2022 in Vancouver.

Berthold Langguth

# Animal Models

## Local cortical changes in primary auditory cortex immediately after noise trauma

Parameshwarappa, V1, Pezard, L2, Norena, A3

1,3Aix-Marseille Université and Centre National de la Recherche Scientifique (CNRS)

2Aix-Marseille Université

### Background and Aim

Exposure to loud noise is one of the most common causes of hearing loss and tinnitus (and/or hyperacusis) among the general population. Tinnitus may result from the central changes triggered by the noise-induced hearing loss which can then lead to neural hyperexcitability (increase in spontaneous activity) and/or neural hypersynchrony (increase in spontaneous neural synchrony). The underlying neural mechanisms of tinnitus are however still poorly understood particularly in the auditory cortex (AC), which is a very complex structure with laminar organization and many different inputs and outputs from other cortical regions and sub-thalamic nuclei. Cortical columns can be considered as processing units. . Our study was aimed at investigating the acute effects of noise-induced hearing loss on cortical columns, i.e. on all cortical layers.

### Methods

Local field potentials (LFP) and Multi-unit activity (MUA) were recorded across the cortical columns in the primary auditory cortex from 16 electrodes spaced by 100 µm (i.e., the entire cortical depth was covered by our electrode array) before and after noise trauma (115 dB SPL, 8 kHz tone, 1hour). The neural recordings were divided into two groups: those derived from neurons with characteristic frequency (CF) lower (LF) or higher (HF) than the traumatizing frequency (8kHz) before trauma. Effects of noise trauma were assessed on evoked and spontaneous activity. We also used the current source density (CSD) method on evoked and spike-triggered LFPs to derive the current sources and sinks.

### Results

Following noise trauma, TC was altered differentially in the LF and HF groups. I/O function for the LF group, was increased significantly in the supragranular (layers I –II/III) and granular (layer IV) layers. In contrast for HF group, I/O function was decreased across all layers. Laminar CSD in the LF group reveled enhancement of current sinks at granular and infragranular (layers V-VI) layers. Current sink at supragranular layer was, on the other hand, substantially reduced. In HF group, strong decrease in current sinks was observed at all cortical layers after noise trauma. Immediately after noise trauma, SFR increased significantly in supragranular and granular layers in the LF group, whereas significant increase was found only in the infragranular layer in the HF group. Spectral power increased at low frequency bands (2 – 12 Hz) in the LF group. In the HF group, spectral power was decreased at low frequency bands and increased in gamma frequency band (around 40 Hz). Finally, spike synchrony was increased only in the HF group and was significant at granular and lower infragranular layers.

### Conclusion

Our results are broadly consistent with previous studies which investigated the acute effects of noise trauma on the granular layer. Our study, further shows that noise trauma triggers strong cortical changes that are specific to layers and tonotopy. The observed changes in intracortical processing within the AC can alter the flow of auditory information and potentially disrupt neural activity at sub-cortical and non-auditory structures. Overall these changes may be involved in the mechanisms underlying tinnitus (or hyperacusis).

# Long-term effects of noise trauma on the intracortical processing in primary auditory cortex

Parameshwarappa, V1, Byunghee, C2, Pezard, L3, Norena, A4

1,2,4Aix-Marseille Université and Centre National de la Recherche Scientifique (CNRS),  
3Aix-Marseille Université

## Background and Aim

Chronic noise-induced hearing loss is known to induce neuronal plastic changes, such as enhanced central gain, at virtually all stages of the he central auditory system (CAS), including the auditory cortex (AC). In cortex, these changes have been previously studied at the thalamocortical recipient of the AC, namely at layer IV. However, the AC is a very complex structure with laminar organization and many different inputs and outputs from other cortical regions and sub-thalamic nuclei. It is then still unknown whether chronic hearing loss has layer-specific effects. Given the distinct functional roles of each cortical layer in sensory processing, the long term effects of chronic hearing loss on cortical columns may provide relevant insights into the central impact of chronic hearing loss, including the tinnitus mechanisms. In this context, our study focused on investigating the long-term changes after noise trauma over the different cortical layers.

## Methods

Experiments were conducted on 12 anesthetized guinea pigs (n=4, Control; n=8, Chronic). In chronic study, auditory brainstem responses (ABR) were recorded before and 30 days after noise trauma (115 dB SPL, 8 kHz continuous tone, 4hour), prior to the experiment. Local field potentials (LFP) and Multi-unit activity (MUA) were recorded across the cortical columns in the primary auditory cortex from 16 electrodes spaced by 100 µm (i.e., the entire cortical depth was covered by our electrode array). The neural recordings were divided into two groups: those derived from neurons with characteristic (CF) lower (LF) or higher (HF) than the traumatizing frequency (8 kHz). Effects of noise trauma were assessed on evoked and spontaneous activity. We also used the current source density (CSD) method on evoked and spike-triggered LFPs to derive the current sources and sinks.

## Results

In the LF group, mean I/O function was strongly increased in supragranular and granular layers when compared to control. An increase in evoked activity at high sound levels was found across all cortical layers in the chronic HF group. In the LF group, laminar CSD analysis revealed enhanced current sinks in the granular and infragranular layers with reduced supragranular current sink. In contrast, in the HF group, current sinks in the supragranular and granular layer were enhanced. These results are similar to those observed for acute noise trauma. In LF group, SFR increased significantly across all layers, whereas in HF group SFR increase was limited to the granular layer. Spike synchrony increased at supragranular and granular layer in the LF group, whereas significant increase in granular and infragranular layer was found in the HF group.

## Conclusion

Overall, chronic noise-induced hearing loss was found to have strong effects on cortical columns that are specific to layers and tonotopy. The observed changes in intracortical processing within the AC can alter the flow of auditory information and potentially disrupt neural activity at sub-cortical and non-auditory structures. Overall these cortical changes may be involved in the mechanisms underlying tinnitus (or hyperacusis).



# Decoding Acute Tinnitus by Classifying Dorsal Cochlear Nucleus Spiking-Activity

Calvin Wu<sup>1</sup>, Susan E. Shore

Kresge Hearing Research Institute, Department of Otolaryngology, University of Michigan, Ann Arbor, MI, USA

## Background and Aim

A neural code for tinnitus is first observed in the dorsal cochlear nucleus (DCN), as increased spike synchrony and bursting of the principal neurons. Because noise-exposure does not always result in the phantom sensation of tinnitus, behavioral tests are required to differentiate animals that develop chronic tinnitus from their tinnitus-resilient littermates over the course of several weeks. In acute tinnitus that occurs immediately after noise-exposure, behavioral confirmation is not possible due to the requirement of multiple testing days.

## Methods

We trained a supervised machine-learning classifier to identify an animal's tinnitus status based on features of DCN spontaneous activity with behavioral status established a priori by gap-prepulse-inhibition of the acoustic startle (Wu et al., J Neurosci 2016). The training database was obtained from 1608 single-unit DCN principal neurons from 29 guinea pigs. We applied the trained classifier to naive data in guinea pigs recorded continuously for 12 hours after noise-exposure.

## Results

The machine learning classifier achieved 85% accuracy on a single-unit basis. A Monte Carlo simulation estimated that 20 units were needed to identify tinnitus status of individual animals. While acute noise-exposure induced variable time-courses of DCN spontaneous activity, based on neural population statistics, 75% of guinea pigs developed tinnitus immediately after exposure.

## Conclusion

These results suggest that the highly-distinctive DCN neural activity can be utilized to identify animal's tinnitus status in a time scale unrealistic for behavioral testing. This technique creates the possibility in animal models to examine the development of tinnitus longitudinally from acute to chronic, enabling the examination of exciting questions previously hindered by behavioral testing.

# Notched noise effect on evoked activities in the primary auditory cortex

Choi, B.1 , Parameshwarappa, V1 , Pezard, L.2, Norenä, A.1

1 Aix-Marseille Université and Centre National de la Recherche Scientifique (CNRS), 2 Aix-Marseille Université

## Background and Aim

An auditory illusion called “Zwicker tone” (ZT) can be triggered at the end of a notched noise (NN) exposure, which is a broadband noise with a missing frequency band. The ZT has interesting similarities to tinnitus: pitches in of both “illusory” perceptions correspond to a frequency band with a relative sensory deprivation. The notched noise can be viewed as a stimulus mimicking hearing loss, i.e. a contrast in sensory inputs, similar to the fact that artificial scotoma can be produced by specific visual stimuli. For these reasons, the ZT has been considered as a model of transient tinnitus. Therefore, examining the effect of NN on the auditory system may give insights to the mechanism of tinnitus. The aim of this study is to observe the effects of NN on all six layers of the primary auditory cortex(A1), during and after the presentation of NN.

## Methods

Six anesthetized guinea pigs were tested. Multi-unit activity (MUA) and local field potential (LFP) were recorded by a neural probe covering the entire cortical depth. The neural probe is a 16-channel single shank electrode array with 100 µm distance between each channel. The effects of NN on the cortical activity has been studied using two approaches. First, neural activity has been recorded during and after the simple presentation of the NN or white noise (WN). Second, we documented evoked neural activities during and after NN/WN presentation using multi-tone stimulus. The NN/WN were presented continuously and intermittently (3 s presentation, 1 s silence). The sound pressure level of NN/WN was fixed at 70 dB. The notch width was 1 octave. The center frequency of the NN was chosen to correspond to the best frequency of the cortical column.

## Results

Our preliminary results show that cortical activity evoked by the multi-tone stimuli during simultaneous presentation of a NN is increased within the notch during and shortly after NN presentation. Additionally, we observed offset responses at several layers of the cortical column after NN presentation, but not after WN presentation.

## Conclusion

Our results suggest that NN presentation may trigger fast plastic changes and/or the imbalance between excitation and inhibition in A1, which enhance neural excitability.



# Comparison of Three Methods to Detect Tinnitus on a Rat Salicylate-Induced Tinnitus Model

Dejean C.1, Laboulais A.3, Baudoux V.1\*, Cardoso M.3, Cazals Y.1, Norena A.2, Naert G.1, Goze-Bac C.3 and Pucheu S.1

1CILcare, Montpellier, France, 2Aix-marseille University and CNRS, Marseille, France, 3BionanoNMRI, CNRS, University of Montpellier, France

Tinnitus, the perception of a “phantom” sound in the absence of external stimulation, is a common consequence of damage to the auditory periphery. It affects around 15% of the population and may induce intolerable discomfort. Although there are some drug candidates in the development process, currently no effective treatment exists to cure tinnitus. The biggest challenge till date is to detect tinnitus objectively in animal models, and hence carrying out new quantitative methods becomes the key step in developing new compounds for tinnitus treatment.

## Aim

The objective of this study is to compare three methods on a rat salicylate-induced tinnitus model: a conditioned food reward (CFR) behavioral test, the gap pre-pulse inhibition of the acoustic startle reflex (GPIAS), and a quantitative method, Manganese Enhancement MRI *in vivo* imaging (MEMRI).

## Material and Methods

Nine Long Evans rats were divided in two groups, a control group ( $n=4$ ) and a salicylate group ( $n=5$ ), where all the rats were trained for 3 months to perform a central nose poke for CFR. In order to receive the food, the rats should perform a nose poke on the correct side.

The GPIAS test measures the intensity of the startle reflex to a brief sound with high intensity. If a background acoustic signal was qualitatively similar to the rat’s tinnitus, poorer detection of a silent gap would be expected.

After 3 months of training for the CFR test, the animals were presented to GPIAS & CFR baseline measurements, followed by evaluation of tinnitus 2 hours post salicylate injection (300mg/kg/day; IP). Then rats received a trans-tympanic injection of MnCl<sub>2</sub> (0.2 mmol/kg), 24 h before brain MEMRI imaging, as a contrast agent to follow neuronal brain activity.

## Conclusion

The combination of behavioral tests, and *in vivo* imaging allows to measure putative signs of tinnitus. Similar results were observed in both behavioral tests and MEMRI imaging read-outs after salicylate or vehicle administration. All animal presumed to have tinnitus showed a decrease in the % gap inhibition and proportion of correct responses in the GPIAS and CFR test respectively. Similarly, MEMRI test reported an increase of neuronal activity in the inferior colliculus in animal models with tinnitus. Taken together, these data establish a more robust tinnitus model to accelerate the development of new therapies.

# Ebselen Can Attenuate Hyperacusis and Tinnitus in A Novel Animal Model of Aminoglycoside Toxicity

Ryan Longenecker, Rende Gu<sup>1</sup>, Jennifer Homan<sup>1</sup>, Jonathan Kill<sup>1</sup>

Sound Pharmaceuticals, Inc. 4010 Stone way North, Suite 120, Seattle, Washington 98103

## Background and Aim

Aminoglycosides (AG) such as amikacin are commonly used in CF patients with recurrent pulmonary infections and those infected with atypical and multi-drug resistant TB. AGs are ototoxic, resulting in auditory dysfunction including hearing loss and tinnitus. Prior studies have shown that ebselen can prevent and treat sensorineural hearing loss in animals and humans. While auditory brainstem response (ABR) has been used to assess hearing loss, behavioral models to assess tinnitus and auditory dysfunction have yet to be established. The Acoustic Startle Reflex (ASR) can assess hearing loss, hyperacusis, and tinnitus making it a powerful tool to assess auditory dysfunction. The goal for this study is to establish an ASR methodology for examining the effect of amikacin on auditory dysfunction and the efficacy of ebselen in reducing amikacin-induced ototoxicity in a clinically translatable mouse model.

## Methods

CBA/CaJ mice three months of age were divided into two groups which both received amikacin (500 mg/kg/ s.c.) daily for 14 continuous days: Group A received injections of ebselen (20 mg/kg/i.p.). Group B received injections of vehicle (DMSO/saline/i.p.). ABRs were performed at baseline, 1 day, 4 and 8 weeks after the end of injections. ASRs were collected at baseline, and 7, 14, 21, 45, and 75 days from the start of injections. ASR tests included input/output functions to assess general hearing and hyperacusis, PPI (Prepulse Inhibition) Audiometry to assess hearing deficits, and GPIAS (Gap-induced Prepulse Inhibition of the Acoustic Startle) to assess tinnitus. Following ASR, hair cell counts were obtained via cochlear histologic analysis.

## Results

Following 14 days of amikacin injections, ABR thresholds increased from baseline over the 8- week recovery period with evidence of fluctuations. Input/output ASRs revealed hyperacusis in response to low level stimulation, which was significantly ameliorated by ebselen treatment. Gap detection deficits, representing tinnitus, were observed in a smaller subset of animals. Cochlear histology did not reveal significant damage to either hair cells or spiral ganglion neurons.

## Conclusion

A behavioral model of AG-induced ototoxicity has been developed and offers a new tool to study ototoxicity and otoprotection involving three forms of auditory dysfunction. We show that a 14-day course of amikacin treatment can cause hearing loss, hyperacusis, and to a lesser extent, tinnitus. Ebselen was able to mitigate the development of amikacin-induced hearing loss and hyperacusis. These data support the clinical testing of ebselen as a potential treatment for the hearing loss, tinnitus, and hyperacusis in patients receiving amikacin.



# Clinical Management and Clinical Research

## Neurofeedback for tinnitus distress – What are the therapeutic mechanisms? – Preliminary results of a randomized controlled trial.

Martin Jensen<sup>1,2</sup>, Eva Hüttenrauch<sup>1</sup>, Cornelia Weise<sup>1</sup>

<sup>1</sup>Division of Clinical Psychology and Psychotherapy, Department of Psychology, Philipps-University of Marburg, Marburg, Germany First Author's Institute, <sup>2</sup>Eriksholm Research Center, Part of the Demant Group, Snekkersten, Denmark

### Background and Aim

Cognitive behavioral therapy CBT) is considered the gold standard of tinnitus treatment. However, not everyone benefits from the treatment. In the past decade, neurofeedback has emerged as treatment with noticeable success for tinnitus related distress. Although the purportedly therapeutic agent in neurofeedback is the redressing of neuronal imbalances, its healing mechanisms are poorly understood. This is mainly because non-specific effects are rarely under investigation. The purpose of the present study was to test the efficacy of a specific neurofeedback training protocol, alpha/delta frequency training (NF-A), which had previously shown promise in the alleviation of tinnitus distress. In a randomized controlled trial, it was tested against a beta/theta neurofeedback control protocol (NF-B) and a Diary control group (DC). We hypothesized, that NF-A would be more efficacious in alleviating tinnitus distress, compared to NF-B and DC, when assessed with the Tinnitus Handicap Inventory (THI).

### Methods

90 tinnitus patients were randomly assigned to NF-A, NF-B and DC. Both neurofeedback conditions consisted of 10 training sessions across four weeks. NF-A participants trained at increasing alpha and decreasing delta oscillatory activity, whereas NF-B participants trained at increasing beta- and decreasing theta activity. DC had two face-to-face consultations and two telephone calls in the four-week intervention period. In the current analysis, 66 participants were included (NF-A: n=31; NF-B: n=27; DC: n=30).

### Results

A 3 x 2 mixed ANOVA with group (NF-A vs NF-B vs DC) as between-subjects factor and time (pre – post intervention THI score) as within-subjects factor, found a significant main effect of time, but no significant interaction between type of intervention and time,  $F(2, 85) = 2.45, p = .09$ , partial  $\eta^2 = .06$ . Subsequent explorative within-group analyses showed that participants in NF-A improved most strongly from pre- to post intervention,  $F(1, 30) = 18,68, p < .001, d = .60$  compared to both NF-B,  $F(1, 26) = 10,06, p = .004, d = .41$  and DC,  $F(1, 29) = 4,93, p < .03, d = .02$ .

## Conclusion

Although the hypothesis was not confirmed in the preliminary analyses, the results are in the expected direction, with participants in NF-A reporting the greatest relief from tinnitus distress. Nevertheless, participants reported significant relief from tinnitus irrespective of allocated type of treatment. This leads to two insights. First, improvement in quality of life following neurofeedback is not specific to training a particular combination of neural targets. Second, the fact that neurofeedback was not superior to the diary control intervention suggests, that factors common to all therapies may account, at least to a large extent, for previously reported relief from tinnitus distress following neurofeedback.

## Long term total remission of tinnitus: fact or myth?

Tanit Ganz Sanchez<sup>1</sup>, Caroline da Cunha Valim<sup>2</sup>, Winfried Schlee<sup>3</sup>

<sup>1</sup>Instituto Ganz Sanchez; University of São Paulo, Department of Otolaryngology, <sup>2</sup>University of São Paulo, Department of Sciences of Rehabilitation, <sup>3</sup>University of Regensburg, Department of Psychiatry and Psychotherapy

### Background and Aim

Tinnitus sufferers wish to be cured, but there is a widespread disbelief among professionals about total remission of tinnitus. Randomized clinical trials with different approaches haven't shown this outcome, but clinical practice reveals that it unexpectedly occurs. This study aims to interview and follow-up individuals who have experienced total remission of tinnitus to identify their common features.

### Methods

Volunteers were included with the following criteria: a) any gender and age; b) past daily perception for at least 3 months (subacute or chronic tinnitus); c) current total remission (lack of tinnitus perception, even with silence and attention) for at least 6 months. Eventual short reappearances that have last maximum 2 days (related to upper airway infections, noise exposure, stress etc) were disregarded. The main exclusion criterion was the comfortable state of habituation or masking by daily sounds. Participants were interviewed about their ex-tinnitus and the current total remission status. Once included, follow-up has been made every 6 months.

### Results

The sample was composed by 105 participants (age 09-89y, average 53.7; 70.4% females). Tinnitus used to be: a) bilateral (53.3%); b) pure tone sound (52.1%); c) annoyance score  $7.24 \pm 2.76$  in 0-10 scale; d) average duration 45.5 months.

So far, total remission: a) last 0.5 - 37 years (average=6.1); b) occurred disregarded of tinnitus duration or subject's age and gender; c) was mostly reached by maximum of 2 treatment attempts (57.1%); d) occurred gradually (75.2%). Follow-up was made for 6 to 30 months after inclusion, and the tinnitus relapse rate was low (7/105; 6.6%).

### Conclusion

Long term total remission of tinnitus is a fact which may be achievable in patients with any age, gender or tinnitus duration, localization, type of sound or degree of annoyance. From the neuroscience perspective, the predominance of gradual disappearance and the low rate of tinnitus relapse after entering the adopted criteria of total remission may suggest that tinnitus-related neuronal activity slowly, but firmly, loses strength in central auditory pathways till the point of no perception.



# Prevalence of psychiatric symptoms and the effectiveness of stepped care treatment in tinnitus patients

Erwin L.J. George<sup>1,2</sup>, Noortje van den Boom<sup>1</sup>, Iris H.L. Maes<sup>1</sup>

<sup>1</sup>Maastricht UMC+, Dept. ENT & Audiology, Maastricht, The Netherlands, <sup>2</sup>MHENS School for Mental Health and Neuroscience, Maastricht, The Netherlands

## Background and aim

Tinnitus is an unsolved neurootological problem, affecting the quality of life of millions of people worldwide. About one in ten tinnitus patients experience severe complaints, with an increasingly acknowledged association with anxiety, depression and sleep disorders. This study's primary aim is to investigate the prevalence of anxiety and depressive symptoms and their relation with tinnitus severity. Secondary aim is to assess the effectiveness of the multidisciplinary stepped care treatment within our tertiary care university medical center.

## Methods

Our tinnitus team provides standardized stepped care for about 650 patients each year, combining diagnostics with treatment specifically fitted to each patient's individual needs. Pre-intervention validated questionnaires were used to assess tinnitus severity (TQ, Tinnitus Questionnaire) and anxiety and depressive symptoms (HADS, Hospital Anxiety and Depression Scale). Follow-up data were collected six months after first consultation.

## Results

Results within the included cohort (n=264) show that 58% experienced depressive symptoms and 21% had anxiety symptoms. The majority (60%) of all patients were referred for consultation with a psychiatrist, and treatment with psychotropic drugs was started in about half of these cases. Based on the follow-up results (n=103), the correlation between anxiety and depression complaints and tinnitus severity was strong ( $r>0.70$ ) for both anxiety and depressive symptoms. The stepped-care treatment was effective in reducing tinnitus severity and comorbid anxiety and depressive symptoms after 6 months of treatment.

## Conclusion

The prevalence of depressive symptoms in tinnitus patients seeking help in a tertiary care setting is high and is strongly correlated with tinnitus severity. Multidisciplinary single team treatment appears to be effective in reducing tinnitus severity. Future research will focus on methods to further distinguish different types of tinnitus complaints, to optimize individually fitted treatment, and to reduce the healthcare and societal costs.

## T3: Tinnitus Treatment Trends in 2019

Tricia Scaglione, AuD1, Lori Zitelli, AuD2, Dave Jedlicka, AuD3

<sup>1</sup>University of Miami Hospital, <sup>2</sup>University of Pittsburgh and UPMC, <sup>3</sup>Pittsburgh VA and University of Pittsburgh

### Background and Aim

Tinnitus evaluation, treatment, and research are continually evolving both inside and outside of audiology. A review of tinnitus literature published in 2019 was conducted with an aim to identify what current trends in tinnitus treatments exist with the intention to educate clinical and research colleagues on the most current evolution of care for tinnitus patients.

### Methods

An extensive literature review across audiological and non-audiological journals was employed. Both peer-reviewed and trade journals were included. Articles and abstracts published in 2019 referencing the term "tinnitus" were retrieved, reviewed, and categorized by treatment type.

### Results

Three hundred and twenty-five tinnitus-focused articles were published in 2019, 80 of which yielded articles with a concentration on treatments with both clinical and research implications. Of the 26 treatment modality approaches publicized over the year, trends were identified in the areas of electrical stimulation, naturopathy, cognitive behavioral therapy (CBT), mindfulness, sound therapy, and surgical treatment approaches. Treatment delivery models ranged from direct patient care to telehealth options.

### Conclusions

Of the 80 treatment articles which were reviewed, clear trends existed in the advancements in tinnitus evaluation and management. Though more research across health-care specialties is warranted, current trends in 2019 demonstrate a promising trajectory in the area of tinnitus treatments.

## Conceptual Cognitive Model for Tinnitus-Insomnia Comorbidity

Z.S. Vaziri<sup>1,2</sup>, I.G. Toostani<sup>1,3</sup>, J.P. Leite<sup>2</sup>, A.C.B. Delbem<sup>1,3</sup>, C.G.C. Barros<sup>4</sup>, M.A. Hyppolito<sup>4,5</sup>, A.A. Oliveira<sup>5</sup>

<sup>1</sup>Neurocognitive Engineering Laboratory, Center of Engineering Applied to Health, Institute of Mathematics and Computer Sciences, University of São Paulo, São Carlos, Brazil; <sup>2</sup>Department of Neuroscience and Behavioral Sciences, Ribeirão Preto Medical School, University of São Paulo at Ribeirão Preto, Brazil; <sup>3</sup>Reconfigurable Computing Laboratory, Institute of Mathematics and Computer Sciences, University of São Paulo, São Carlos, Brazil; <sup>4</sup>Department of Otorhinolaryngology, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; <sup>5</sup>Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, Ribeirão Preto Medical School, University of São Paulo, Brazil.

### Background and Aim

We proposed Conceptual Cognitive Model (CCM) to provide a framework for evaluating the role of emotion dysregulation in promoting tinnitus and insomnia comorbidity. Accordingly, in pre-sleep time, conscious attended awareness perception of tinnitus sound concurrent with failure in falling asleep triggers negative appraisals which in turn cause distress leading to overestimation of tinnitus loudness and sleep deficit. CCM is grounded on the role of evaluative conditional learning mechanism through which the negative cognitive-emotional value related to tinnitus and insomnia reciprocally affect each other resulting in generation and maintenance of tinnitus-insomnia comorbidity. To provide support for the proposed model, we used the data from a running randomized crossover three-session double-blind study investigating under which conditions tinnitus loudness and tinnitus annoyance affect comorbid insomnia.



## Method and Material

Forty-seven (N=47) tinnitus patients referred to the Hospital das Clínicas de Ribeirão Preto in Brazil were recruited to participate in the study. Before each session, the patients responded to Tinnitus Severity, State-Trait Anxiety Inventory, and Mini-Sleep Questionnaires. Questions representing cognitive-emotional symptoms related to tinnitus and insomnia were selected and included in the analysis. To analyze the data, we performed PROCESS macro for SPSS.

## Results

The Durbin Watson test (1.7) exhibited no autocorrelation in the accrued dataset. Within the macro, customized model and 5.000 bias-corrected bootstrap samples were selected. A 95% confidence level was chosen to apply a p-value of 0.05. The Bootstrap analysis was performed in two separate models. The results showed that the indirect effect of negative mood on insomnia was serially mediated by difficulty falling asleep and excessive daily sleepiness. However, in the first model, Tinnitus Annoyance above 4 (TA > 4) and in the second model, Tinnitus Loudness above 6.25 (TL > 6.25) were found to induce Moderated Meditation (MM) upon the effect of negative mood on difficulty falling asleep (TL-MM: 0.544, SE:0.032) (TA-MM: 0.0325, SE:0.021). The bias-corrected bootstrap confidence interval for the indirect effect was entirely measured above zero. Negative mood also had a direct effect on insomnia, independent of its effect on mediators ( $c = 0.862$ ,  $p=0.0009$ ).

## Conclusion

Developing tinnitus-insomnia comorbidity depends on, but not limited to, the adequate value of tinnitus loudness and tinnitus annoyance. Accordingly, CCM delivers clinicians and researchers a novel roadmap for comorbidity rehabilitation.

## Botulinum toxin injections into bilateral head and neck muscles has major benefit for tinnitus

Fady Bou-Malhab, Larry Lockerman, Robert Aaron Levine

Consilia Medicare Clinic, Beirut Lebanon University Massachusetts Medical School Private Practice  
Brookline Massachusetts

## Background and Aim

For more than 85 years it has been appreciated that head myofascial dysfunction can cause tinnitus (Costen 1934). This concept was later extended to cervical muscles by Travell and her colleagues (Travell 1960, Travell and Simons 1983). Animal models and clinical evidence provide strong support for a close connection between the cervical and trigeminal somatosensory systems and the auditory system in general and tinnitus in particular (Levine and Oron 2015). Trigger point injections, dry needling and physical methods have had limited success in treating tinnitus. Botulinum toxin injected to the periauricular area has been reported of minor benefit in one study. We now present our experience of botulinum toxin injected to multiple areas of the head and neck.

## Methods

16 adults (ages 19 to 57) with tinnitus and head/neck myofascial trigger points were injected with botulinum toxin (abobotulinumtoxinA (Dysport)) at one session. Six had a sensorineural hearing loss; ten had the upper crossed syndrome. The masseter (50 units), temporalis (50 units), and trapezius (75 units) muscles were injected bilaterally in all. Twelve with headaches and/or dizziness also received bilateral corrugator (20 units) and occipital nerve (25 units) injections. Loudness was assessed with the 0 to 10 visual analog scale (VAS). Follow-up was for 12 months.

## Results

Prior to receiving botulinum toxin, tinnitus loudness ranged between a VAS score of 7 and 9. At the 12 month follow-up there was no tinnitus in 13 subjects (10 with normal audiometric thresholds and 3 with a sensorineural hearing loss). The other three with sensorineural hearing loss had persistent low-level tinnitus of 1 or 2 on the VAS scale.

## Conclusion

Botulinum toxin applied bilaterally to an array of head and neck muscles appears to have major benefit for tinnitus.

# Evaluation of Multidisciplinary Tinnitus Pathway introduced in Royal Brisbane and Women's Hospital, Australia

Alicja N. Malicka<sup>1</sup>, Alice Pender<sup>2</sup>, Anita Burgess<sup>3</sup>, Joseph Kei<sup>3</sup> and Carla Rose<sup>2</sup>

<sup>1</sup>School of Allied Health, Human Services and Sport, La Trobe University, Australia, <sup>2</sup>Audiology Department, Royal Brisbane and Women's Hospital, Australia, <sup>3</sup>School of Health and Rehabilitation Sciences, The University of Queensland, Australia

## Background and Aim

This study assessed the effect of the multidisciplinary Tinnitus Pathway established and trialled at The Royal Brisbane Women's Hospital (RBWH) on self-reported measures of tinnitus, its impact on everyday life and patients' satisfaction of the service.

## Methods

Initially, 162 adults with tinnitus were identified on the RBWH Ear, Nose and Throat Outpatients waiting list and were offered appointments within the Tinnitus Pathway which was developed according to the contemporary, evidence-based recommendations for tinnitus assessment and rehabilitation. The primary intervention outcome measures were the change in scores on the Tinnitus Reaction Questionnaire (TRQ) and Depression Anxiety and Stress Scale (DASS-21) applied pre- and post-intervention. Additionally, a Patient Satisfaction Survey was administered upon discharge from the Tinnitus Pathway.

## Results

The pre- and post-intervention TRQ and DASS-21 questionnaires were completed by 31% and 26% of 136 patients respectively. The scores significantly decreased following the participation in the Tinnitus Pathway suggesting improvement in tinnitus related distress. The Patient Satisfaction Survey was returned by 22% of participants. All respondents were satisfied with the received service and would recommend it to family and friends. Out of 136 patients enrolled in the pathway, only 16% returned to the ENT waiting list.

## Conclusions

Tinnitus Pathway introduced within RBWH was effective in providing timely and targeted service to patients with tinnitus while greatly shortening the waiting time for treatment.



## Tinnitus and caffeine

Carlos A Oliveira<sup>1</sup>, Alleluia Losno<sup>1</sup>, Fayed Bahmad Junior<sup>1</sup>

<sup>1</sup>Brasília University Medical School-Brasília, D.F. Brasil

Very often Physicians prohibit caffeine consumption for tinnitus patients. The relation of caffeine and tinnitus has been studied by different methods but there is no consensus in the literature.

### Objective

To study the effect of caffeine on tinnitus in a single blinded randomized clinical trial.

### Methods

Eighty patients with chronic significant tinnitus were selected and randomized into two groups with 40 patients each. A caffeine free 24 hours diet was prescribed for both groups. They answered the THI, POMS questionnaires and completed the VAS test. Tonal and high frequency audiometry, transient otoacoustic emissions, (TOAE), distortion product otoacoustic emissions(DPOAE) were applied to all patients. After 24 hours caffeine free the study group (SG) had a 300mg caffeine capsule and the control group had an identical placebo capsule. All the previously mentioned questionnaires and tests were again applied to both groups.

### Results

There was a significant change of mood detected by POMS in both Groups. Tonal and high frequency audiometry as well as TEOAE and DPOAE showed no significant changes after the capsules were ingested. THI and VAS showed lower scores after the capsules in both groups.

### Conclusions

Caffeine (300mg capsules) did not change the psychoacoustic measures, electrophysiologic findings and the degree of discomfort in patients with chronic significant tinnitus.

## A Pragmatic Approach to Treating Tinnitus Patients: The Who, The What, The Why, and The How

Stephen M. Nagler, M.D., FACS

Atlanta Tinnitus Consultants, LLC

### Background and Aim

This paper presents a philosophy of treatment that lends itself to providing tinnitus patients with a practical path towards achieving meaningful lasting relief, a philosophy of treatment that is consistent with the principles of Cognitive Behavioral Therapy, Tinnitus Retraining Therapy, Tinnitus Activities Treatment, and other habituation-based approaches, as well as with tinnitus masking strategies and traditional counseling. The purpose of the paper is three-fold. First, I hope to give tinnitus researchers in the lab a feel for the challenges and frustrations faced daily by tinnitus clinicians in the trenches. Second, I hope to give tinnitus clinicians a tool that will immediately return a sense of power and control to their patients, individuals who have suffered the loss of silence, an entity so near and dear to them that they never recognized its importance until they lost it. And third, I hope to identify an effective weapon that will in a highly practical manner aid tinnitus patients in their efforts to overcome "The Guest from Hell," the amorphous intruder who has taken up residence in their auditory systems.

# **Comparison of Symmetric and Asymmetric Hearing on Tinnitus Distress: Preliminary Study**

Emre Gurses, Songul Aksoy

Hacettepe University, Faculty of Health Science, Department of Audiology, Ankara, Turkey.

## **Background**

It is well documented in the literature that tinnitus and hearing deficit are often related phenomena (1). Even in tinnitus patients with normal hearing are being discussed whether having hidden sensorineural hearing loss (2). However, which types of hearing loss cause more distress, can rarely be determined.

## **Objective**

This study was carried out in order to compare the tinnitus distress of the patients with a symmetrical and asymmetrical hearing with and without hearing loss.

## **Materials and Methods**

A total number of 111 patients (Mean Age:  $47.81 \pm 14.85$ , 57 Female, 54 Male) with tinnitus included in this study. Participants were classified according to hearing status as normal hearing (52.3 %- 10 participants had high-frequency hearing loss  $\geq 8$  kHz), slight (22.5 %), mild (17.1 %) and moderate (8.1 %) hearing loss. Hearing thresholds  $\geq 10$  dB within at least three frequencies, is accepted as 'asymmetric hearing'. Tinnitus duration, pitch and loudness were assessed. Tinnitus Handicap Inventory, Tinnitus Questionnaire Short Form (Mini-TQ) were applied to the participants. Results were compared with independent sample t-test between symmetric and asymmetric hearing status.

## **Results**

Regardless of hearing loss degree, the distress found in asymmetric hearing status in terms of the emotional subscale of Mini TQ ( $p < 0.05$ ), catastrophic subscale of THI ( $p < 0.05$ ) and tinnitus loudness ( $p < 0.05$ ) were all statistically significant. The differences that were found in patients with high-frequency hearing loss  $\geq 8$  kHz were particularly more significant.

## **Discussion**

Asymmetric hearing leads aural preference and eventuate plastic changes (3) which could be more devastated for tinnitus patients. However, these tests should be repeated with larger sample size and health-related quality of life and the results obtained should be assessed as cofactors.

## **Reference:**

- 1) Savastano, M. (2008). Tinnitus with or without hearing loss: are its characteristics different?. European Archives of Oto-Rhino-Laryngology, 265(11), 1295-1300.
- 2) Schaette, R., & McAlpine, D. (2011). Tinnitus with a normal audiogram: physiological evidence for hidden hearing loss and computational model. Journal of Neuroscience, 31(38), 13452-13457.
- 3) Gordon, K., Henkin, Y., & Kral, A. (2015). Asymmetric hearing during development: the aural preference syndrome and treatment options. Pediatrics, 136(1), 141-153.



# **Analysing the Relationship Between the Tinnitus Severity and the Sleep Quality**

Gurbet İpek Sahin-Kamışlı<sup>1</sup>, Songül Aksoy<sup>2</sup>

<sup>1</sup>Gazi University, Faculty of Health Sciences, Department of Audiology, Ankara, Turkey, <sup>2</sup>Hacettepe University, Faculty of Health Sciences, Department of Audiology, Ankara, Turkey

## **Background and Aim**

One of the most common complaints in individuals with tinnitus is the problems they experience during their sleep. These can be specified as: difficulty in falling asleep, waking up from sleep due to tinnitus then not falling asleep again and , exacerbation of tinnitus when they wake up. The sleep characteristics that form the basis of complaints in subjective sleep evaluations in these individuals are as follows: prolonged sleep latency, prolonged moderate sleep and difficulty in waking up in the morning, impaired sleep quality and decreased sleep efficiency. The aim of the study is to investigate the effect of tinnitus severity on sleep quality.

## **Methods**

A total number of 89 (40 F and 49 M) patients with tinnitus were included in this study. Their age range is 24-59 ( $43 \pm 10$ ) years. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index. Tinnitus level was determined by THI. THI and PSQI were applied after performing audiological evaluation and psychoacoustic measurements of tinnitus.

## **Results**

PSQ mean score was  $6.4 \pm 3.4$  and it's well above the cut off value ( $\geq 5$ ). 53 of the participants scored above cut-off point and 36 participants scored below. THI mean score was  $57.2 \pm 23$ . The correlation analysis between sleep quality and tinnitus level was significant but low degree ( $r = 0.275$ ,  $p = 0.009$ ). It was found that as the tinnitus level increased, PSQ scores also increase ( $p = 0.006$ ). Only grade 1 tinnitus level indicated that PSQ mean score was below cut off value.

## **Conclusions**

Sleep quality is an important component for general health. We found that sleep problems in individuals with tinnitus are associated with tinnitus level and sleep quality deteriorates as the severity increases. According to the results of our study: assessment of sleep quality at all other tinnitus levels except Grade 1 was recommended. There is a clear relationship between tinnitus and sleep problems, but longitudinal studies are needed to determine the relationship between the cause and the effect. Sleep problems can be a predisposing factor for tinnitus or comorbid. The sleep assessment should be done on a standard scale. As a result of the assessment, individuals who need the support to sleep should be identified. Advising these individuals for a consultation from specialists, will be effective in breaking the vicious circle of tinnitus and associated symptoms.

# Computational Modeling

**Stochastic Resonance improved hearing and speech recognition provides a mechanistic explanation of subjective tinnitus**

Patrick Krauss, Achim Schilling, Holger Schulze

1Neuroscience Lab, Experimental Otolaryngology, University Hospital Erlangen,  
University of Erlangen-Nuremberg , Germany

## Background and Aim

Cross-modal interactions are common in sensory processing, and phenomena reach from changed perception within one modality to misperceptions like synesthesia. A recent study demonstrated that electro-tactile stimulation applied to the index finger of cochlea implant patients significantly improves speech recognition. We argue that such cross-modal enhancement can be explained in terms of stochastic resonance (SR), a phenomenon that is ubiquitous in nature. SR refers to a processing principle where signals otherwise sub-threshold for a given sensor can, at least partially, be detected anyway by adding noise (i.e. a random signal) of a suitable intensity to the sensor input.

## Methods

We demonstrate the plausibility of our hypothesis by computational modeling and provide exemplary findings in animal and human studies that are consistent with our model.

## Results

Our model suggests that SR is a major processing principle of the auditory system and takes place in the dorsal cochlear nucleus (DCN). Following hearing loss, SR serves to lift signals above the increased neuronal thresholds, thereby partly compensating for the hearing loss. The noise necessary for SR to work corresponds to somatosensory input to the DCN leading to increased spontaneous neuronal firing rates in the DCN and subsequent stages of the auditory system. In that view, SR is the primary cause of tinnitus-related neuronal hyperactivity and tinnitus perception.

## Conclusion

Our computational model provides a mechanistic explanation why electro-tactile stimulation improves speech recognition in cochlea implant patients: electro-tactile stimulation increases somatosensory input to the DCN, which is equivalent to increased neuronal noise, which in turn improves detection thresholds for auditory stimuli via SR, and hence also improves speech recognition.



# Education

## **Advancing tinnitus research and researcher training: a case study review and future perspectives**

Dawn Hazle<sup>1</sup>, Derek Hoare<sup>1</sup>, Axel Schiller<sup>2</sup>, Kathryn Fackrell<sup>1,3</sup>, Winfried Schlee<sup>2</sup>

<sup>1</sup>University of Nottingham, <sup>2</sup>University of Regensburg, <sup>3</sup>University of Southampton

### **Background and Aim**

Tinnitus affects one in 10 people, and for many significantly impairs quality of life. Whilst there has been a notable increase in research funding and the number of publications in recent years, this is not keeping pace with other related disciplines. Tinnitus research is also not yet attracting substantial industry funding; because we do not yet understand the biological basis of tinnitus, cannot measure it objectively, and do not yet have any treatment success stories. There is a clear need for increased funding, better-quality studies, increased capacity, and interdisciplinary working in the field.

### **Methods**

The European School for Interdisciplinary Tinnitus (ESIT) research project was a European Union-funded doctoral training programme that brought together a consortium of clinicians, academics, commercial partners, patient organisations, and public health experts, from various European countries with students from across the world.

### **Results**

The programme supported various fundamental science and clinical research projects in order to advance treatments, develop innovative research methods, perform genetic and epidemiological studies, and establish a pan-European data resource. With researchers from such diverse backgrounds, there were challenges in providing relevant and suitable training for all students. These were overcome by providing a comprehensive curriculum designed to address all areas of skill and researcher competency as defined by the Vitae Researcher Development Framework. This approach allowed for systematic identification of strengths and development needs, action planning, and review of individual and group achievements.

### **Conclusion**

There is a general need for increased capacity, as well as coordinated efforts to both improve research quality and address fundamental issues that will attract and retain funding and researchers. ESIT provides an evidenced format for training in the field of tinnitus research.

# Electrophysiology

## Direct mapping of the cortical tinnitus network

Phillip E. Gander, Joel I. Berger, William Sedley, Sukhbinder Kumar, Hiroyuki Oya, Christopher K. Kovach, Kirill V. Nourski, Hiroto Kawasaki, Matthew A. Howard III, Timothy D. Griffiths

### Background and Aim

Tinnitus occurs when peripheral hearing damage leads to secondary changes in ongoing brain activity. These central mechanisms are poorly-understood, partly because relevant experimental evidence is almost entirely indirect, meaning it does not reflect the real-time perception of tinnitus, and/or it does not provide a direct measure of neural activity.

### Methods

Previously we reported on a test of this hypothesis in a human neurosurgical subject, who had an extensive array of electrocorticography and depth electrodes placed for the localization of epilepsy. Tinnitus loudness was modulated with residual inhibition using noise, and quantified with real-time ratings. Here we report an experimental replication in a second neurosurgical subject with broadly comparable tinnitus and intracranial recording.

### Results

Similar findings in both subjects were obtained: 1) Suppression of tinnitus correlated with widespread reductions in delta (1-4 Hz) oscillatory power throughout most of auditory cortex, and large parts of non-auditory cortex in temporal, parietal, limbic and motor areas. These areas also showed changes in inter-regional delta phase coherence with tinnitus suppression. 2) Theta (4-8 Hz), alpha (8-12 Hz), and high beta (20-28 Hz) power was similarly suppressed in most of these areas. 3) Gamma (28-144 Hz) power increased, during tinnitus suppression, throughout auditory cortex and in posterior temporal, inferior parietal, sensorimotor and parahippocampal cortex. In the second subject electrical stimulation of Heschl's gyrus elicited reductions in tinnitus loudness comparable to that induced by sound. The change in tinnitus perception from stimulation occurred without alteration to other external auditory perception.

### Conclusion

These findings support the definition of the brain networks critically involved in tinnitus perception which will be necessary to create effective treatments and possible cures.



## **Identifying Differences in Neurofeedback Training Trajectories in the Treatment of Tinnitus**

Constanze Riha<sup>1,2</sup>, Dominik Güntensperger<sup>1</sup>, Martin Meyer<sup>1</sup>

<sup>1</sup>Chair of Neuropsychology, Department of Psychology, University of Zurich, Zurich, Switzerland,

<sup>2</sup>Research Priority Program "ESIT - European School of Interdisciplinary Tinnitus Research"

### **Background and Aim**

The widespread understanding of chronic tinnitus being a heterogeneous phenomenon has spurred investigations of subject-specific approaches in its treatment. Neurofeedback has become increasingly popular in personalized procedures with a wide range of disorders. Despite the success of neurofeedback on group level, the variability in the efficacy of the treatment on the individual level is high. To reveal who may be more suitable, hence benefit most from a neurofeedback treatment; we classified individuals into unobserved subgroups with similar oscillatory trajectories during the treatment and investigated how these subgroups were predicted by a series of covariates.

### **Methods**

Growth Mixture Modeling was used to identify distinct latent subgroups with similar oscillatory trajectories among 50 individuals over 15 neurofeedback training sessions. We further evaluated the impact of concomitant variables on the identified subgroups and their course of treatment, by including measures of demographics, tinnitus-specific (THI), and depression variables, as well as subjective quality of life subscales (SF-36), and health-related quality of life subscales (WHO-QOL).

### **Results**

A latent class model could be fitted to the longitudinal data with a high probability of correctly classifying distinct oscillatory patterns into three different groups: non-responder (80%), responder (16%), and others (4%). Our preliminary results suggest that some covariates were found to be differentially associated with the three groups. However, due to the small sample size in our responder group, we are not able yet to provide meaningful evidence for a distinct responder profile and therefore try to avoid erroneous generalizations at this point.

### **Conclusion**

Nevertheless, the identification of oscillatory change-rate differences across distinct groups of individuals provides fundamental work to tease apart complex oscillatory processes underlying tinnitus and their modification attempts with neurofeedback. While more work is needed, our results and the analytical approach may bring clarity to some contradictory past findings in the field of tinnitus research and find their translation into clinical practice.

## **The effect of tinnitus pitch on the N1**

Victoria Duda<sup>1,2</sup>, Brandon Paul<sup>3</sup>, Olivia Scully<sup>1,2</sup>, Charlotte Bigras<sup>1,2</sup>, Sylvie Hébert<sup>1,2</sup>

<sup>1</sup>Université de Montréal, Montréal, QC, Canada, <sup>2</sup>Center for Research on Brain, Language, and Music (CRBLM), <sup>3</sup>Sunnybrook Hospital, Toronto, ON, Canada

### **Background and Objective**

The mechanism of tinnitus is still unknown. Previous studies have used EEGs to determine the physiological changes that occur in patients that report tinnitus. However, none of these studies have used stimuli matched to the frequency and intensity of the perceived tinnitus.

## Methods

Participants with reported non-pulsatile, subjective tinnitus ( $n=15$ ) were individually matched based on audiogram, sex and age to non-tinnitus controls ( $n=15$ ). Tinnitus participants underwent a MatLab tinnitus matching procedure which allowed the matching of the pitch and loudness of the tinnitus to a narrowband stimulus presented via ER2a transducers. Three stimuli were presented where the stimulus was (1) at a frequency that matched the perception of the tinnitus, (2) was 1/3rd of an octave above or (3) 1/3rd an octave below the tinnitus pitch. These stimuli were presented for 5 seconds with inserted gaps (see poster 2 for more details on the gap analysis) and an EEG was used to record the response of the auditory cortex. All stimuli were presented at a tinnitus-matched intensity level between 5 to 47 dB above threshold.

## Results

An N1 response peaked at about 120 ms following the onset of the stimulus. It was maximum over the fronto-central sites and declined in amplitude at the lateral sites. It inverted in amplitude at the mastoids. Confidence interval testing was conducted at Fz and Cz where the amplitude was maximal. It showed a significant N1 for the tinnitus group at and below the frequency of the tinnitus, however it was not significant at any of the frequency conditions for the control group. Frontal and central data of the individual data was entered into a 2-way ANOVA with repeated measures on group (tinnitus vs. controls), frequency (below, at, above tinnitus). Although the N1 was larger in the tinnitus group at and below tinnitus frequency, the between- and within-subjects effects failed to reach significance.

## Conclusions

These results show that the larger N1 found in the tinnitus group may be associated with reorganization of the auditory cortex. Tinnitus may thus be related to a cortical overrepresentation of frequency regions distal to the dominant frequency of the tinnitus.

# Late Auditory Evoked Potentials in Chronic Subjective Tinnitus Patients: A Systematic Review and Meta-Analysis

Cardon E.<sup>1,2</sup>, Joosse I.<sup>2</sup>, Vermeersch H.<sup>2</sup>, Jacquemin L.<sup>1,2</sup>, Mertens G.<sup>1,2</sup>, Topsakal V.<sup>1,2</sup>, Vanderveken O.M.<sup>1,2</sup>, Van de Heyning P.<sup>1,2</sup>, Van Rompaey V.<sup>1,2</sup>, Gilles A.<sup>1,2,3</sup>

<sup>1</sup>Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, Antwerp University, Wilrijk, Belgium, <sup>2</sup>University Department of Otorhinolaryngology and Head & Neck Surgery, Antwerp University Hospital, Edegem, Belgium, <sup>3</sup>Department of Education, Health & Social Work, University College Ghent, Ghent, Belgium

## Background and Aim

Subjective measures such as questionnaires are typically used to diagnose tinnitus and assess its severity. Late auditory evoked potentials (LAEPs), cortical electrophysiological responses to auditory stimuli, might be considered as a potential candidate for objectively measuring tinnitus burden, an achievement which would greatly advance qualitative tinnitus research. This review systematically and quantitatively assesses LAEP differences between tinnitus patients and controls.

## Methods

Major databases were searched for articles concerning the measurement of LAEPs in tinnitus patients and controls. Title and abstract screening and subsequent full-text screening were performed by at least three independent authors. After data extraction, data were pooled for meta-analysis as standardized mean differences. A multivariate model was constructed in R using the Metafor package. Risk of selection bias, concerning differences in baseline characteristics between tinnitus patients and controls, was rated as low, high or unclear. Publication bias was assessed using funnel plots and Egger's regression tests.



## Results

A total of 695 records were identified, out of which 43 full-text papers were assessed for eligibility. The final systematic review considered 32 studies, with a subset of 21 papers included for meta-analysis. A multivariate model revealed that latency of the P300 component was significantly longer in tinnitus patients than controls ( $p = 0.002$ ), while the amplitude of this component was significantly lower in tinnitus patients ( $p = 0.009$ ). Risk of selection bias regarding hearing levels was generally high or unclear. No evidence of publication bias was found.

## Conclusion

This meta-analysis revealed a specific difference in LAEP components between tinnitus patients and controls, with both latency and amplitude of the P300 component being perturbed in the tinnitus group. As this component reflects conscious cognitive neural processing, these findings provide further support for the current hypothesis that the perception of tinnitus is largely maintained by the central nervous system.

## Multifocal Tomographic Neurofeedback for Treating Chronic Tinnitus in Older People

David Talaska<sup>1,4</sup>, Tobias Kleinjung<sup>4</sup>, Nicole-Peter Siegrist<sup>4</sup>, Patrick Neff<sup>5</sup>, Dominik Güntensperger<sup>1,2</sup>, Martin Meyer<sup>1,2,3</sup>

<sup>1</sup>Department of Psychology, University of Zurich, Zurich, Switzerland, <sup>2</sup>University Research Priority Program ‘Dynamics of Healthy Aging’, University of Zurich, Zurich, Switzerland, <sup>3</sup>Tinnitus Centre, Charité University Medicine Berlin, Berlin, Germany, <sup>4</sup>ENT Department, University Hospital Zurich, Zurich, Switzerland, <sup>5</sup>Tinnitus Centre, University of Regensburg, Regensburg, Germany

## Background & Aim

Prevalence of chronic subjective tinnitus is rising with age and associated with maladaptive oscillatory changes in auditory as well as non-auditory regions of the brain. In the context of a recent longitudinal study in which participants with chronic tinnitus have been trained via tomographic neurofeedback (ToNF) in order to alter these maladaptive changes (alpha/delta ratio) in the auditory cortex, improvements in electroencephalographic (EEG) oscillations have been shown (Güntensperger et al. 2019). However, this oscillatory change did not show an effect in perceived tinnitus loudness- or distress in every participant. As chronification of tinnitus also involves maladaptive oscillatory changes in non-auditory regions such as the insula and the anterior cingulate cortex (low theta, high beta) which are known to be key points within the salience and distress networks of the brain, we are conducting a new clinical trial by additionally implementing the mentioned non-auditory regions into the ToNF-protocol.

## Methods

Prior to 12 EEG-based (32 electrodes) tomographic NFB-trainings á 21 minutes with 36 participants between the age of 50 and 80 years with normal age-related hearing loss (<50 dB) and normal cognitive function (MoCA & no other neurological disorders) using standardized Low Resolution Electromagnetic Tomography Software (sLORETA, Pascual-Marqui 2002), participants' brains will be measured using structural magnet resonance imaging (sMRI) in order to identify potential structural markers for training success (e.g. cortical thickness).

## Results

Training success will be measured by oscillatory change (EEG, 64 electrodes) before, between and after the training period as well as by means of follow-up (three and six months after the final training) measures. Furthermore, a comprehensive battery of behavioral and psychometric standardized self-report questionnaires (e.g.THI, TSCHQ, WHOQOL-BREF.) will be applied.

Preliminary results are pending.

## Conclusion

Based on this multifocal (Insula, dorsal anterior cingulate cortex & auditory cortex) ToNF we expect oscillatory changes resulting in decreased tinnitus symptoms such as perceived loudness, duration and distress.

## Nonlinear (Entropy) Analysis of EEG in Tinnitus

Akram Pourbakht<sup>1</sup>, Maryam Sadeghijam<sup>1</sup>, Samer Mohsen<sup>2</sup>, Saeed Talebian<sup>3</sup>, Mehdi Akbari<sup>1</sup>

<sup>1</sup>Department of Audiology, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran, <sup>2</sup>Department of Otolaryngology, Faculty of Medicine, Damascus University, Damascus, Syria, <sup>3</sup>Department of Physiotherapy, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran

### Background and Aim

Subjective tinnitus is a common clinical symptom and a comprehensive understanding of the underlying mechanisms is needed. Brain regions are related through neuronal effective connections and time-varying EEG is considered as an appropriate technique to explore tinnitus network function. Comparing to methods that summarize neural activities with linear relationships, non-linear methods might be better in describing how tinnitus network acting. In this regard, we studied Shannon Entropy in EEG raw data obtained from normal subjects and compared it to data from chronic tinnitus subjects. We aimed to find out the differences in EEG Entropy between tinnitus subjects before and after the sound therapy intervention and normal controls.

### Methods

From the qEEG database of Iran University of Medical Sciences, the School of Rehabilitation Sciences, we have selected 23 qEEGs of healthy and 23 qEEGs of chronic tinnitus subjects. QEEGs were measured with a 27-channel EEG amplifier in the sitting position with the eyes closed for 5 minutes. Shannon entropy was investigated for all electrodes separately and compared between groups using a one-way ANOVA statistical test. 17 subjects of the tinnitus groups had benefited from a complete course of sound therapy (Binaural Beat was used for a month), therefore their pre- post- intervention differences were also studied.

### Findings

Our results revealed a significant difference between normal and tinnitus subjects ( $p<0.05$ ). Post- hoc comparisons using the Bonferroni test showed increased entropy in the tinnitus group for all electrodes ( $p=0.00$ ). After the intervention, there was a significant decrease in entropy ( $p<0.05$ ) for all electrodes; that is, the values decreased to levels near and somehow above normal control levels. Such results were in accordance with clinical improvement after the intervention.

## Conclusion

Nonlinear methods in EEG studies (Entropy) could be of great importance in understanding the tinnitus neurophysiology and might be potentially used as suitable indices for clinical purposes.



# Does tinnitus fill in the gap? An EEG study on the gap response in tinnitus-matched background noise

Brandon Paul<sup>1</sup>, Victoria Duda<sup>2,3</sup>, Olivia Scully<sup>2,3</sup>, Charlotte Bigras<sup>2,3</sup>, & Sylvie Hébert<sup>2,3</sup>

<sup>1</sup>Sunnybrook Hospital, Toronto, ON, Canada, <sup>2</sup>Université de Montréal, Montréal, QC, Canada,

<sup>3</sup>Center for Research on Brain, Language, and Music (CRBLM)

## Introduction

One common animal model of tinnitus is predicated on the notion that the perception of tinnitus can mask or „fill-in“ short silent gaps within a continuous background sound. However, behavioural studies on humans with tinnitus have not corroborated the view that gap detection is impaired by the tinnitus perception. Here, we test this „gap masking“ hypothesis by measuring neuroelectric potentials (e.g., N1 responses) evoked by silent gaps in sounds in a cohort of tinnitus sufferers and in a control group. We took the important step of using a novel psychophysical resampling procedure to estimate acoustical properties of each participant’s tinnitus, including loudness, pitch, and bandwidth, which were used as test stimuli. The hypothesis was that gap-evoked N1 potentials would be reduced or absent in individuals with tinnitus when probing at their tinnitus pitch and loudness level compared to pitches higher or lower than this frequency, and compared to the control group.

## Methods

Participants with reported non-pulsatile, subjective Tinnitus ( $n=15$ ) were individually matched based on audiogram, sex and age to non-tinnitus Controls ( $n=15$ ). Tinnitus participants underwent a MatLab tinnitus matching procedure that allowed the matching of the pitch and loudness of the tinnitus to a narrowband stimulus presented via ER2a transducers. Three stimulus types were presented, which were either at a frequency that (1) matched the perception of the tinnitus, (2) was 15% of an octave above or (3) was 15% of an octave below the tinnitus pitch. Each stimulus was presented for 5 seconds with inserted gaps and an EEG was used to record the response of the auditory cortex. All stimuli were presented at a tinnitus-matched intensity level between 5 to 47 dB above threshold.

## Results

Gap-N1 responses of the tinnitus group were lower in amplitude, but not significantly different from the control group. No interaction was observed between condition and group, indicating there was no evidence that changes in gap-N1s depended on the pitch of tinnitus. Assessment of group differences separately for each condition suggested that gap-N1s were lower in amplitude at frequencies above the tinnitus pitch, but not at the tinnitus pitch or below it.

## Conclusions

Results were inconsistent with the hypothesis that the perceived tinnitus pitch „filled in“ the silent gap. Despite descriptively lower gap-N1 amplitudes in the tinnitus group, these reductions were not significant, and importantly, were not specific to the pitch most closely matching the tinnitus perception. Rather, qualitative gap-N1 amplitude reductions may be interpreted as poorer temporal processing in the tinnitus group. Overall, these observations invite a reconsideration of the notion that tinnitus can mask silent gaps.

# Epidemiology

## Tinnitus and Probiotics: An Open-label Pilot Study

Ricardo R. Figueiredo<sup>1,2</sup>, Andréia A. Azevedo<sup>2</sup>, Jorge A. Simões<sup>3</sup>, Winfried Schlee<sup>3</sup>

<sup>1</sup>Centro Universitário de Valença (UNIFAA), Valença, RJ, Brazil, <sup>2</sup>Otorrinolaringologia Sul-Fluminense (OTOSUL), Volta Redonda, RJ, Brazil, <sup>3</sup>Department for Psychotherapy and Psychotherapy, University of Regensburg, Germany

### Introduction

Tinnitus is frequently associated with psychiatric disorders, specially anxiety and depression. In the last decade, an extensive bidirectional communication network between the gastrointestinal tract and the central nervous system, the “gut-brain axis”, has been unveiled, and the microbiome became a potential target for novel antidepressant therapies.

### Aim

To analyze the potential benefits of probiotics to treat tinnitus in a pilot study.

### Method

Twenty-three tinnitus patients were selected, and treated with *Bacillus clausi* spores for 16 weeks. Patients were evaluated with the Tinnitus Research Initiative protocol (case report forms) and the main outcome measures were the Tinnitus Handicap Inventory (THI) and the Clinical Global Impression (CGI). Results Thirteen patients completed the trials. Among these, five patients improved (THI score reduction equal or greater than 7 points), and the responders also improved in the CGI. Average THI score reduction of the responders was 22 points, significantly higher than the non-responders ( $p=0.04$ ).

### Discussion

Open pilot studies are useful to establish potential candidate therapies to treat tinnitus. In this case, the responders represent 38.46% of the sample. Although these results were modest, the THI scores reduction was noticeable and corroborated by the CGI changes. No side effects were observed. Conclusion Probiotics may represent a safe option to treat tinnitus in some patients, and these effects should be further evaluated in larger controlled subtyping studies.



# **Prevalence of tinnitus in a large Brazilian city: a health survey in primary health care**

Carla Salles Chamouton, Helenice Yemi Nakamura

University of Campinas (UNICAMP)

## **Background and Aim**

Tinnitus is a health problem characterized as the perception of sound in the absence of a sound source, affecting over than 15% of the world population. The high prevalence and negative impact on quality of life, determine it as a public health problem and, therefore, a relevant and necessary topic in the organization of health services. Hearing issues are still considered to belong to specialized care, with no approach in primary care. This is still a context little addressed within the theme, containing incipient data and practically non-existent in the Brazilian scenario.

The aim of the study was to estimate the prevalence and characterize the profile of people living with tinnitus in a health district of a large city in the state of São Paulo.

## **Methods**

The sample calculation was made based on the flow mapping of each primary health unit and on the population over 18 years, resulting in a sample of 1,720 people. The survey was carried out through the application of a questionnaire about the health and tinnitus profile of the individuals. The periods were drawn among services, according to the singularity of each unit. The data collection happened from September to December of 2018.

## **Results**

1,569 questionnaires were applied, having 151 refusals. Of these, 496 reported tinnitus, with a prevalence of 31.6%. Most were women and the average age was 59.24 years. 73.59% reported having a chronic disease, the most common being high blood pressure with continuous use of some medication. Regarding hearing, 56.25% answered that they think they do not hear well. Tinnitus complaint time ranged from one month to 50 years. The most frequent tinnitus was reported as acute, unilateral and intermittent. 76.82% of people reported that tinnitus disturbs their lives, with an average of 7.74 degree of discomfort on a scale from zero to 10. Of the total respondents, 52.62% sought for treatment, having the private professional as the most accessed service. From zero to 10, the average improvement in tinnitus reported after treatment was 2.24.

## **Conclusion**

The prevalence of 31.6% is close to the world literature. The profile of having comorbidities, using continuous medication and with hearing complaints, shows the multifactorial etiology of tinnitus. The degree of discomfort reinforces the negative impact that may have on the individual's life. More studies are needed in the Brazilian scenario and mainly, in the context of primary health care.

# Epidemiology and Prevention

## Tinnitus in Adolescents – a Survey of Secondary School Students

Anna C.S. Kam<sup>1</sup>, Chelton C.T. Ho<sup>2</sup>

<sup>1</sup>Department of Special Education and Counselling, The Education University of Hong Kong, <sup>2</sup>Integrated Centre of Wellbeing (I-WELL), The Education University of Hong Kong, <sup>2</sup>Student Health Service, Department of Health, Government of the Hong Kong Special Administrative Region

### Background and Aim

The prevalence and risk factors of tinnitus have been extensively studied in adults but only a few population studies have been performed in children or adolescents. The reported tinnitus prevalence in children and adolescents ranges from 6 to 36%. There is a large inter-study variability due to the difference in study population, definition of tinnitus, and methodologies employed. This study aims to investigate the prevalence and risk factors of tinnitus in a sample of adolescents.

### Method

In this cross-sectional study, 276 secondary students were surveyed for the presence of tinnitus and its impact, health factor, recreational noise exposure, psychological factor, and socioeconomic status. Tinnitus impact was measured by the Tinnitus Functional Index. All students were screened for possible hearing loss with pure-tone audiometry. Audiological information on pure-tone thresholds, tympanometry, otoacoustic emission and otoscopy were obtained in respondents who have experienced tinnitus that last more than 5 minutes in the past 12 months.

### Results

91 out of 276 students (33.0%) reported that they have experienced tinnitus. Only 6 of them (2.2% of the total sample) reported that they have experienced tinnitus that last more than 5 minutes in the past 12 months. Recreational noise exposure, ear disease, and family history are significantly associated with tinnitus.

### Conclusion

The results suggest that the prevalence of tinnitus in adolescents may be over-estimated. Further study in a larger sample size is needed.



# Help-seekers

## Characteristics of Help-seekers and Non-help-seekers with Tinnitus from a Population-based Sample

Ms Natalie Carmody

Ear Sciences Centre, School of Medicine, The University of Western Australia

### Background and Aim

Little is known about those who seek help for tinnitus in the general population and only a few tinnitus studies exist that use population-based samples on this topic. Using a sample of tinnitus-affected individuals from an epidemiological study of health and ageing, this study examines the characteristics of help-seekers and non-help-seekers.

### Methods

Individuals who reported tinnitus ( $n=200$ ) in a population-based sample of older individuals ( $n = 1004$ ; born 1946 to 1964) were invited to complete three surveys: a) a short adaptation of the Tinnitus Sample Case History Questionnaire, b) the Tinnitus Reaction Questionnaire and c) the Glasgow Health Status Inventory. This sample was categorised according to whether they sought help ( $n = 57$ ) or did not seek help for their tinnitus ( $n = 74$ ).

### Results

Help-seekers reported higher tinnitus distress (this included the general distress, interference, severity and avoidance subscales) compared to non-help-seekers and their average TRQ scores were subclinical ( $TRQ < 17$ ). Help-seekers also reported lower health status compared to non-help-seekers (this included general and physical subscales except for social support which was higher for help-seekers).

Help-seekers who reported clinical tinnitus ( $TRQ \geq 17$ ) also reported significantly lower health status (including general subscale). Non-help-seekers who reported subclinical tinnitus distress ( $TRQ < 17$ ) had a significant association with non-ringing tinnitus, tinnitus occurrence (intermittent) and not having depression. Non-help-seekers with subclinical tinnitus ( $TRQ < 17$ ) had significantly higher health status (including general subscale) and significantly lower social support subscale).

Non-help-seekers with depression had significantly higher levels of tinnitus distress (including general distress, interference and severity subscales) and poorer health status (including general subscale); their scores on these variables were similar to those of help-seekers.

Help-seekers with hearing loss reported significantly more tinnitus distress in terms of TRQ interference and significantly poorer health status (including the general subscale). Non-help-seekers with hearing loss reported significantly more tinnitus distress in terms of TRQ avoidance.

### Conclusion

Previous research has found marked differences between help-seekers and non-help-seekers with tinnitus in terms of tinnitus distress and accompanying complications, psychological symptoms, hearing loss and health status.<sup>1-3</sup> In this study help-seekers suffered more tinnitus distress burden and poorer health than their non-help-seeker counterparts. Non-help-seekers with depression faced similar handicap with tinnitus distress and poorer health however chose not to seek medical intervention. Education through health promotion may be required to reach those people with tinnitus and mental health barriers to healthcare to ease the burden of tinnitus.

## Literature

1. Attias J, Shemesh Z, Bleich A, et al. Psychological profile of help-seeking and non-help-seeking tinnitus patients. Scandinavian audiology. 1995;24(1):13-18.
2. Hallberg LR, Erlandsson SI. Tinnitus characteristics in tinnitus complainers and noncomplainers. British journal of audiology. 1993;27(1):19-27.
3. Scott B, Lindberg P. Psychological profile and somatic complaints between help-seeking and non-help-seeking tinnitus subjects. Psychosomatics. 2000;41(4):347-352.

# Hyperacusis

## Using psychophysical ratings of natural and artificial sounds to create a new assessment tool for hyperacusis.

Falco Enzler, Philippe Fournier and Arnaud J. Noreña

Centre National de la Recherche Scientifique, Aix-Marseille University, France

Hyperacusis is defined as an increased sensitivity to sounds, i.e. sounds presented at moderate levels can produce discomfort or even pain. This condition can dramatically affect the quality of life in severe cases. Existing diagnostic methods, like the Hyperacusis Questionnaire (HQ) and Loudness Discomfort Levels (LDLs), have been challenged because of their variability and lack of agreement on appropriate cut-off values. We propose a novel exploratory approach. Using psychoacoustic ratings of natural and artificial sounds, we aimed to explore differences between populations (hyperacusics and controls) and to extract the most discriminant sounds to create a new metric and assessment tool.

With feedback from subjects reporting hyperacusis, we established a list of their most notable pleasant and unpleasant sound encounters. With this, we created a database of natural and artificial (tone pips, noises) auditory stimuli. Hyperacusics ( $n = 26$ ) and controls ( $n = 21$ ) were presented with these in a controlled environment at four different intensities (60, 70, 80 and 90 dB SPL). Their task was to rate them on a pleasant to unpleasant visual analog scale.

Results show a significant difference between controls and hyperacusics in the rating of pleasant sounds (Wilcoxon rank test, Bonferroni corrected:  $p < 0.01/12$  at each intensity). Unpleasant sounds and artificial sounds do not show any significant differences ( $p > 0.05/12$  at each intensity). We then selected the most optimal subset of sounds that could best discriminate our controls from our hyperacusics. These resulting Core Discriminant Sounds (CDS) were used to elaborate a new metric: The CDS Scores, which evaluate how different ratings are from normative data. They contain diagnostic and severity information of hyperacusis at each tested level.

The lack of differences in artificial sound ratings, suggest that tone pips and noises, that are used in clinics, are sub-optimal in objectifying hyperacusis and that natural sounds might be a better approach. Importantly, the CDS show lower unpleasantness ratings than sounds used for LDL assessment (pure tones and noises). We believe our approach is more relevant to subject complaint's than LDLs and that it could be applied in a clinical environment in a fast and effective way, while minimizing discomfort and biases.



# An evaluation of the content and quality of hyperacusis information on websites

Sandra Smith<sup>1,2</sup>, Ethan Smallwood<sup>3</sup>, Magdalena Sereda<sup>1,2</sup>, Bethany Adams<sup>1,2</sup> and Derek J Hoare<sup>1,2</sup>

<sup>1</sup>Hearing Sciences, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, <sup>2</sup>NIHR Nottingham Biomedical Research Centre, Nottingham, UK, <sup>3</sup>School of Medicine, University of Nottingham, UK

## Background and Aim

Hyperacusis, the intolerance to everyday sounds, is commonly comorbid with tinnitus. It can cause distress, social isolation and in some cases pain, which can impact on a person's quality of life. Hyperacusis is often associated with tinnitus. Whereas there are clinical guidelines available for tinnitus, there are no such guidelines for hyperacusis. Therefore, people with hyperacusis often turn to the internet to seek information and treatment options. It is important that the information available on the internet is good quality, evidence-based and consistent. The purpose of the study was to assess the content and quality of information about hyperacusis found in a typical internet search.

## Methods

A search of the internet using three different search engines identified 15 websites meeting our inclusion criteria. The content of each website was extracted using an excel form designed for this purpose and informed by academic literature. The DISCERN tool was used to assess the overall quality of health information provided. Data extraction and quality assessment of each website was independently performed by two members of the research team.

## Results

There was a wide disparity in the content and quality of hyperacusis information across websites. Whilst most websites described treatments such as hearing aids or other sound devices, only a minority of websites described other treatment options such as self-help, counselling, or cognitive behaviour therapy. The website 'Hyperacusis Focus' achieved the highest average DISCERN score (i.e. highest quality) and contained the most comprehensive information relevant to hyperacusis. However, all websites lacked key information identified in the academic literature.

## Conclusions

Analysis of the most prominent websites in internet searches on hyperacusis indicated that there is room for improvement in the content and quality of the information provided. If they are to provide a valuable resource for people who have hyperacusis and healthcare professionals seeking guidance about the condition, internet sites should ensure the information presented is comprehensive and evidence-based. DISCERN scores can guide specific areas for improvement. Further research could also facilitate development of a bespoke evidence-based resource for people with hyperacusis to provide comprehensive information and/or a self-management programme.

# The electrophysiological markers of hyperacusis: a scoping review

Bérangère Villatte<sup>1,2,3</sup>, Charlotte Bigras<sup>1,2,3</sup>, Victoria Duda<sup>1,2,3</sup> & Sylvie Hébert<sup>1,2,3</sup>

<sup>1</sup>School of Speech-Language Pathology and Audiology, Université de Montréal, <sup>2</sup>International Laboratory for Brain, Music and Sound Research (BRAMS), <sup>3</sup>Center of Research on Brain, Language and Music (CRBLM)

## Background and Aim

Recent studies have observed that certain electrophysiological markers can identify neuronal hyperactivity in people with sensitivities to sound, known as hyperacusis. Electrophysiological recordings could therefore be used to investigate known hypotheses on the origin of hyperacusis while also offering a potential measure for its identification in a population. The aim of this scoping review is to gather and extract electrophysiological data from human and animal literature to inform future research.

## Methods

Published studies from four electronic databases (Medline, Embase, CINAHL, and PsychInfo) were retrieved to answer the question: What are the electrophysiological markers of hyperacusis? Keywords such as 'hyperacusis', 'phonophobia', 'sound intolerance' and 'electrophysiology' were used. Studies were included if they investigated a population with hyperacusis using at least one electrophysiological measurement. Studies recording firing rates with implanted arrays were excluded. Two independent reviewers screened articles and extracted data, and a third reviewer resolved conflicts. The review was conducted using the Arksey and O'Malley (2005) five-step framework, within the Covidence software.

## Results

After importing articles for screening ( $n=2901$ ) and removing duplicates ( $n=1118$ ), 1782 articles were retained and underwent screening based on the inclusion and exclusion criteria. In the first screening 1590 studies were excluded based on their title and abstract. Subsequently, a second full-text screening excluded 168 studies for methodological reasons. This resulted in a final yield of 23 studies, of which 6 were studies on animals and 17 on humans. Several themes were identified: autism ( $n=9$ ), salicylate ( $n=1$ ), noise exposure ( $n=2$ ), stress ( $n=1$ ), multiple sclerosis ( $n=1$ ), Williams syndrome ( $n=2$ ), stroke ( $n=1$ ), synaptopathy ( $n=1$ ), and idiopathic hyperacusis ( $n=6$ ). Electrophysiological measures of hyperacusis were assessed using event-related potentials (ABR, MLR, and LLR), resting-state electroencephalography (cortical and spontaneous oscillations), magnetoencephalography (MEG), electrocochleography (ECochG), and electrocorticography (ECoG). Extracted outcomes were latencies and amplitudes of short (I, II, III, IV, V), middle and long-latency waves (P1, N1, P2, N2, P3a, P3b), MEG potentials (M50, M100, MMF) and oscillatory power spectrum (delta to gamma bands). Studies were compared and discussed based on these population characteristics, methodological parameters and outcomes measured.

## Conclusion

In general, the studies yielded from this review provide evidence of a global hyperactivity of the central auditory system. These findings also provide evidence for the central auditory gain hypothesis. The results of this scoping review and the knowledge gaps revealed a potential for further contributions to our understanding of hyperacusis through electrophysiological measures. Furthermore, it calls attention to the possibility of a clinical objective measurement of this functional disorder.



## Characterization of hyperacusis patients' symptomatology

Philippe Fournier<sup>1</sup>, Marie-Josée Fraysse<sup>2</sup>, Alain Londero<sup>3</sup>, Vincent Loche<sup>4</sup> and Arnaud Norena<sup>1</sup>

<sup>1</sup>Centre National de la Recherche Scientifique, Aix-Marseille University, France. <sup>2</sup>Service d'Oto-Rhino-Laryngologie, d'Oto-Neurologie et d'ORL Pédiatrique, Centre Hospitalier Universitaire de Toulouse, Place du Dr Baylac, <sup>3</sup>Service ORL et CCF, Hôpital Européen G. Pompidou, Paris, France, <sup>4</sup>ORL, CHRU, Service Otoneurologie, 2, avenue Oscar Lambret, 59037 Lille cedex

### Background and aim

Acoustic shock and trauma can result in a cluster of debilitating symptoms, including (but not restricted to) tinnitus, hyperacusis, ear fullness and tension, dizziness, as well as pain in and around the ear. A previous multi-centric study reported that 41% of tinnitus patients and 81% of hyperacusis patients suffer from at least one of the above-mentioned symptoms. The characteristics of each of those symptoms (i.e. frequency of occurrence, intensity, etc.) have not been investigated in a large cohort of hyperacusic patients. This has been documented using an online questionnaire and reported in the present study.

### Methods

An online questionnaire of 58 items pertaining the detailed symptomatology of hyperacusis patients was created. The data collected included demographic information's, medical/otological history and symptoms divided into three main categories: „Hearing & Balance“, „Pain & uncomfortable sensations in and/or around the ear“ and „Pain & uncomfortable sensations outside the ear“. The presence, the frequency of occurrence (never/sometimes/ often/ almost always/ always), the intensity (VAS-scale: 0-100) and the triggers/modulators of each symptom were assessed. A total of 410 francophone participants with self-reported hyperacusis mostly from France (Mean age: 48.3 years, range: 13-87, M/F: 224/186) were recruited through patients' associations' media platform and social media.

### Results

The most prevalent symptoms experienced following the onset of hearing hypersensitivity (loudness hyperacusis) were: 1) Tinnitus (92%), 2) Feeling of clogged ears (50%), 3) Hearing impairment (49%), 4) Headache (40%) and 5) Pain in the area surrounding the ear & Sensation of floating eardrum (28%). From the symptoms that persisted, the „Hearing & Balance“ symptoms had generally a higher frequency of occurrence than symptoms from other categories, with tinnitus having the highest occurrence (88%). However, sensation of clogged ear, sensation of tension in the ear, tension in the neck and headache were also very prevalent among subjects (>70%). Overall, when the symptoms were always/almost always present their mean usual intensity ranged from 63/100, SD: 27 (pain in the jaw) to 86/100, SD: 17 (sensation of electric shock in and/or around the ear). Hyperacusis, tinnitus, sensation of clogged ear, sensation of tension/pressure in the ear, pain in the ear, and headache were more specifically fluctuating in severity than other symptoms. These symptoms could be triggered or aggravated either spontaneously or by loud sounds. Pain and uncomfortable sensations outside the ear were more prone to vary spontaneously than other categories of symptoms.

### Conclusions

Those results confirm that hyperacusis is generally accompanied by a plethora of other symptoms with tinnitus being the most prevalent. Some symptoms (Hyperacusis, tinnitus, sensation of clogged ear, sensation of tension/pressure in the ear, pain in the ear, and headache) are more prone to fluctuate either spontaneously or with loud sounds. These results suggest that these symptoms may result from common pathophysiological mechanisms.

# Neuroimaging

## Affective learning in chronic tinnitus – behavioral and magnetoencephalographic correlates

Christian Döbel<sup>1</sup>, Marleen Kissel<sup>2</sup>, Ralph Huonker<sup>2</sup>, Daniela Ivansic<sup>1</sup>, Christo Pantev<sup>3</sup>, Markus Junghöfer<sup>3</sup>

<sup>1</sup>ENT Department, University Hospital Jena, Germany, <sup>2</sup>Biomagnetic Center, Department of Neurology, University Hospital Jena, Germany, <sup>3</sup>Institute for Biomagnetism and Biosignalanalysis, University of Münster, Germany

### Background and Aim

Tinnitus describes the perception of a phantom sound. Despite appearing on first sight as a sensory phenomenon, chronic tinnitus is characterized by high comorbidity with depression and anxiety. This is evidenced by multiple clinical but also from neuroscientific findings. Investigating the neural correlates of chronic tinnitus, research with various imaging and neurophysiological methods suggested that both sensory and limbic systems represent neural correlates. Their interplay in the development of chronic tinnitus is an open question. Here we aimed at investigating this interplay within an affective learning paradigm. Behavioral and magnetoencephalographic (MEG) measures served as dependent variables for learning.

### Methods

We used a multi CS conditioning paradigm in which one half of multiple and different neutral auditory stimuli (click tones) were repeatedly paired with an aversive transcutaneous electrical stimulation on the wrist while the other half of tones remained unpaired. Participants (N=29 chronic tinnitus patients and N=29 balanced healthy controls) were asked to adjust the stimulation amplitude over the course of the experiment by setting the threshold to "aversive, but not painful". The neutral auditory stimuli were presented before (pre) and after (post) this conditioning phase while event related magnetic fields were measured. MEG data were analyzed in sensor and source space in the time window of the N1m component.

### Results

In the course of the experiment, chronic tinnitus patients, in contrast to controls, required lower stimulation thresholds to classify a stimulus as "aversive, but not painful", i.e. there was a decrease of stimulation amplitude in patients while there was an increase in controls. This finding is mirrored by the neurophysiological results. The N1m in controls decreased from pre-learning to post-learning while in chronic tinnitus patients, no change from pre to post was observable. Both groups responded similarly to negatively conditioned stimuli and unconditioned stimuli.

### Conclusion

Chronic tinnitus patients do not habituate to aversive stimuli and they also do not habituate to neutral sounds. This finding suggests the involvement of dysfunctional affective learning in the generation of chronic tinnitus. We will discuss these results in the light of current theories on anxiety disorders and depression.



# Tinnitus-associated subnetworks are elicited by frequency-specific auditory stimulation: A MEG study

Vasiliki Salvari<sup>\*1</sup>, Daniela Korth<sup>2</sup>, Evangelos Paraskevopoulos<sup>3</sup>, Andreas Wollbrink<sup>1</sup>, Christian Dobel<sup>2</sup>, Christo Pantev<sup>1</sup>

<sup>1</sup>Institute for Biomagnetism and Biosignalanalysis, University of Münster, Malmeyweg 15, P.C. D-48149, Münster, Germany, <sup>2</sup>Department of Otorhinolaryngology, Friedrich-Schiller University of Jena, Bachstrasse 18, P.C. D-07743, Jena, Germany, <sup>3</sup>School of Medicine, Faculty of Health Sciences, Aristotle University of Thessaloniki, PO Box 376, P.C. 54124, Thessaloniki, Greece.

## Background and Aim

The neural changes associated with tinnitus are not restricted to the auditory system, but it seems to comprise additional non-auditory functions (Husain and Schmidt, 2014). However, data supporting this argument derive mostly from neuroimaging studies investigating resting-state. Since those data are not obtained in task-related measurements we can neither precisely relate them to neural interaction with the perception of tinnitus, nor to the auditory processing in general. In addition, we do not know whether the malfunctioning of tinnitus network is related to the tinnitus-sound specifically or to a general reorganization of the auditory system, independent of sound frequency. For this purpose, the present study applied functional connectivity analysis to test for potential different brain sub-networks elicited by auditory stimulation using the individuals' tinnitus sound and a control sound.

## Methods

The auditory evoked fields of 54 patients with tonal tinnitus to their individual tinnitus tone and a 500Hz-control tone (1s duration) were recorded by means of MEG and compared. Source space analysis was performed for different time windows by means of LORETA reconstruction. Whole-head connectivity analysis was then calculated, by means of Mutual Information, to examine for statistically significant differences in the brain networks processing the tinnitus versus control-frequency.

## Results

In 30-60ms time window the source space analysis yielded differential brain activation in left somato-sensory regions for Control vs. Tinnitus contrast. In 80-120ms: bilateral prefrontal, parietal and occipital cortex in Tinnitus vs. Control contrast; bilateral primary auditory and bilateral frontal regions in Control vs. Tinnitus contrast. In 140-220ms: anterior cingulate and right frontal cortex in Tinnitus vs. Control comparison; hippocampus, superior and middle temporal cortex gyrus for Control vs. Tinnitus comparison (FWE corrected,  $p < .005$ ). The functional connectivity analysis revealed differential brain network in Tinnitus vs. Control comparison with highly significant interconnections that comprises mainly connections of the left hemisphere of the temporal cortex to the prefrontal and parietal cortex bilaterally (FDR corrected  $p < .001$ ).

## Conclusion

Complementing previous studies, this study demonstrated increased cortical interactions between the regions of temporal, dorsolateral frontal and parietal cortex (Paraskevopoulos et al., 2019). However, this is the case in relation solely to the processing of the tinnitus-frequency and not to the processing of the control-frequency. This result indicates specifically a stronger contribution of higher cognitive processes in the perception of the tinnitus-frequency. We conclude that in order to gain insights of the tinnitus network, it is not sufficient to investigate only the activated regions in isolation, but rather to understand how these regions interact.

## **Reorganization of brain white matter in persistent idiopathic tinnitus patients without hearing loss: Evidence from baseline data**

Qian Chen<sup>1</sup>, Han Lv<sup>1</sup>, Zhenchang Wang<sup>1</sup>

<sup>1</sup>Department of Radiology, Beijing Friendship Hospital, Capital Medical University: 95 Yong'an Road, Xicheng District, Beijing, PR China, Qian Chen: Email: chenqian8319@163.com or chenqian1122@outlook.com

It remains unknown whether tinnitus or tinnitus-related hearing loss (HL) could indirectly impair or reshape the white matter (WM) of the human brain. We aim to explore the possible brain WM change in tinnitus patients without HL, further to investigate their associations with clinical variables. Structural and diffusion tensor imaging (DTI) of 20 idiopathic tinnitus patients without HL and 22 healthy controls (HCs) were obtained. Voxel-based morphometry (VBM) and tract-based spatial statistics (TBSS) analysis were conducted to investigate the differences in WM volume and integrity between patients and HCs, separately. We extracted WM parameters to determine a sensitive imaging biomarker to differentiate the idiopathic tinnitus patients from the HCs in the early stage. Correlations between the clinical variables and WM indices were also performed in patients. Compared with the controls, the tinnitus patients without HL exhibited significant decreased fractional anisotropy (FA) in the body and genu of corpus callosum (CC), left cingulum (LC) and right cingulum (RC), right superior longitudinal fasciculus (RSLF) and increase in mean diffusivity (MD) in the body of CC in WM. Moreover, the patients also showed decreases in WM axial diffusivity (AD) in LC, left superior longitudinal fasciculus (LSLF), right interior cerebellar peduncle (ICP) and increases in radial diffusivity (RD) in the body and genu of CC and RSLF ( $p < 0.05$ , voxel-level FWE corrected). Furthermore, the increased RD value of the genu of CC is closely associated with the Tinnitus Handicap Inventory (THI) subscale scores. No WMV changes were detected in tinnitus patients. We combined the altered WM integrity index of body and genu of CC and LC and RSLF as a biomarker to differentiate the two groups and reached a sensitivity of 100% and a specificity of 77.3%. Our findings suggested that tinnitus without HL is associated with significant alterations of WM integrity. These changes may be irrespective of the duration and other clinical performance. The combination of diffusion indices of body and genu of CC and LC and RSLF might be used as the potential imaging biomarker for the diagnosis of persistent idiopathic tinnitus without HL in the early stage.

# **Neurostimulation**

## **Modulation of Tinnitus-Related Emotional Processing and Its Effects on Attentional Bias: A model validation study**

Z.S. Vaziri<sup>1,2</sup>, M.M. Neto<sup>1,3,4</sup>, M. Colacique<sup>1</sup>, V.M.M Martins<sup>1,5</sup>, M. Ghahery<sup>1,6</sup>, F. Louzada<sup>7</sup>, I.G. Toostani<sup>1</sup>

<sup>1</sup>Neurocognitive Engineering Laboratory, Center of Engineering Applied to Health, Institute of Mathematics and Computer Sciences, University of São Paulo, São Carlos, Brazil, <sup>2</sup>Department of Neuroscience and Behavioral Sciences, Ribeirão Preto Medical School, University of São Paulo at Ribeirão Preto, Brazil, <sup>3</sup>Department of statistics, UFSCAR, São Carlos, Brazil, <sup>4</sup>Department of applied math and statistics, USP, São Carlos, Brazil, <sup>5</sup>Department of Electrical and Computer Engineering, São Carlos School of Engineering, University of São Paulo, São Carlos, Brazil, <sup>6</sup>Department of Philosophy, Sciences, and Letters of Ribeirão Preto, Brazil, <sup>7</sup>Department of Neuroscience, Institute for Cognitive Science Studies, Tehran, Iran, <sup>7</sup>Institute of Mathematics and Computer Sciences, University of São Paulo, São Carlos, Brazil



## Background and aim

Tinnitus is Conscious Attended Awareness Perception (CAAP) of sound in the absence of an external source. While many people live with the condition, for others, tinnitus perception is highly annoying. Neurofunctional Tinnitus Model (NfTM) proposes that such annoyance relates to negative cognitive-emotional evaluation of tinnitus sound which develops through negative appraisals and Evaluative Conditional Learning (ECL) mechanism. Based on the ECL, frequent co-occurrence of neutral phantom sound with negatively-valenced stimuli changes tinnitus-related valence from neutral to negative. Therefore, tinnitus perception triggers distress ending up with attentional bias to tinnitus valence. Contrarily, NfTM predicts that CAAP of tinnitus concurrent with positively-valenced stimuli may weaken the tinnitus negative valence and associated attentional bias. To evaluate this prediction, we designed and conducted a randomized crossover double-blind study in three sessions:(1) Positive Emotion Induction (PEI) via presenting a set of validated positively-valenced pictures. (2) The Anodal HD-tDCS (20 min, 2 mA) with PEI. (3) Sham HD-tDCS with PEI.

## Method and material

Forty-seven (n=47) tinnitus patients from Hospital das Clínicas de Ribeirão Preto in Brazil participated in the study. Emotional Stroop Task (EST) was used before and after each session. Reaction Time (RT) to the color of emotional words versus neutral was considered as the measure factor for attentional bias. Collected data was preprocessed and the RT from 300ms to 1200 ms was included in the analysis according to correct responses. We developed the survival regression model for testing the repeated measures of semantically different words within patients and between sessions.

## Results

To evaluate attentional bias, we considered RT to tinnitus-related (emotional) words in EST as the measurement factor. We hypothesized that RT to emotional words is longer than RT to neutral words. The results of the proposed survival regression model showed an increased RT (-0.013, p=0.04) to emotional words in comparison with neutral words. The second hypothesis was that HD-tDCS concurrent with PEI is more effective than Sham with PEI and against only PEI in decreasing attention bias related to tinnitus emotional words. Comparing Post-EST results for three sessions, through developed survival regression model showed a significant reduction in corresponding RT to emotional words after applying HD-tDCS (-0.015, p =0.24) and Sham (-0.017, p= 0.009) concurrent with PEI compared with the results of Pre-EST sessions. However, there was not enough evidence to find a similar effect for after the only PEI session.

## Conclusion

In contrast with past studies, our research showed that there is an attentional bias to emotionally-laden words against neutral words. Moreover, HD-tDCS and Sham concurrent with PEI provide promising results for decreasing attentional bias in the subjective tinnitus population, but still, further investigations are required.

## Dorsomedial prefrontal cortex rTMS for tinnitus: promising results of a blinded, randomized, sham controlled study

Patricia Ciminelli<sup>1</sup>, Sergio Machado<sup>2</sup>, Manoela Palmeira<sup>1</sup>, Evandro Silva Freire Coutinho<sup>3,4</sup>, Antonio Egídio Nardi<sup>1</sup>

<sup>1</sup>Laboratory of Panic and Respiration (LABPR), Institute of Psychiatry (IPUB), Federal University of Rio de Janeiro (UFRJ), Brazil. Rua Venceslau Brás, 71 Botafogo, Rio de Janeiro – RJ, Brazil 22290-140,

<sup>2</sup>Physical Activity Neuroscience, Physical Activity Sciences Postgraduate Program, Salgado de Oliveira University, Niterói, Brazil. Rua Mal. Deodoro, 217 - Bloco A - Centro, Niterói – RJ, Brazil 24030-060,

<sup>3</sup>National School of Public Health – Fundação Oswaldo Cruz (FIOCRUZ), Brazil. Av. Brasil, 4036 - Manguinhos, Rio de Janeiro - RJ, 21041-361, <sup>4</sup>Institute of Social Medicine – Rio de Janeiro's State University (UERJ), Brazil. Rua São Francisco Xavier 524 – Maracanã, Bloco D, 7º andar. Rio de Janeiro – RJ – 20550-013, eJuiz de Fora Federal University (UFJF), Juiz de Fora, Minas Gerais, Brazil. Rua José Lourenço Kelmer, s/n - São Pedro, MG, 36036-900

## Background and aim

Tinnitus is the perception of sound in ears or head without corresponding external stimulus. Despite the great amount of literature concerning tinnitus treatment, there are still no evidence-based established treatments for curing or for effectively reducing tinnitus intensity. Sham-controlled studies revealed beneficial effects using repetitive transcranial magnetic stimulation (rTMS). Still, results show moderate, temporary improvement and high individual variability. Subcallosal area (ventral and dorsomedial prefrontal and anterior cingulate cortices) has been implicated in tinnitus pathophysiology. Our objective is to evaluate the use of bilateral, high frequency dorsomedial prefrontal cortex (DMPFC) rTMS in treatment of chronic subjective tinnitus.

## Methods

Randomized placebo controlled, single blinded clinical trial. Twenty sessions of bilateral, 10Hz rTMS at 120% of resting motor threshold of extensor hallucis longus were applied over the DMPFC. Fourteen patients underwent sham rTMS and 15 were submitted to active stimulation. Tinnitus Handicap Inventory (THI), visual analog scale (VAS) and tinnitus loudness matching were obtained at baseline and on follow up visits. The impact of the intervention on the selected outcomes (THI, tinnitus loudness matching and VAS) was evaluated fitting regression models for longitudinal data (repeated measures) using mixed-effects restricted maximum likelihood (REML) estimation. These models consider the correlation among measures collected from baseline to the end of treatment (1, 2, 4 and 16 weeks) within the same individual. The effect size was calculated by the d-Cohen statistic, and represents the standardized difference between the groups during the follow-up period.

## Results

We found a difference of 11.53 points in the THI score, favoring the intervention group ( $p=0.05$ ). The d-Cohen effect sizes were 0.92, 0.68, 0.86 and 0.88 for weeks 1, 2, 4 and 16, respectively, and can be interpreted as a strong effect. The difference for tinnitus loudness matching was of 4.46 dB also favoring the intervention group ( $p=0.09$ ). The d-Cohen effect sizes were 0.63, 0.70, 1.0 and 1.04 for weeks 1, 2, 4 and 16, respectively, and can also be interpreted as a strong effect. The comparison between active and placebo groups for tinnitus annoyance showed a difference of 0.80 (95% CI: -2.21 to 0.61) in the visual analog scale (VAS). Although this difference favored the active group, this finding was not statistically significant ( $p=0.27$ ).

## Conclusion:

Tinnitus treatment with high frequency (10Hz), bilateral, dorsomedial prefrontal cortex rTMS was effective in reducing tinnitus severity measured by the Tinnitus Handicap Inventory and matched tinnitus loudness when compared to sham stimulation.

## Combined sound and somatosensory stimulation to treat tinnitus

Hubert H. Lim

Department of Otolaryngology, Department of Biomedical Engineering, Institute for Translational Neuroscience, University of Minnesota, USA

## Background and Aim

Over the past decade, new neuromodulation technologies have emerged to treat various brain disorders. A novel paradigm, referred to as bimodal neuromodulation, combines electrical stimulation of peripheral nerves (e.g., vagus, trigeminal or somatosensory nerves) with a sensory input, motor response or behavioral task to drive targeted plasticity within the brain relevant for treating brain disorders such as tinnitus, pain, stroke-related motor deficits, emotional trauma or cognitive impairment. I will present animal findings demonstrating that bimodal neuromodulation can drive extensive plasticity within the auditory brain relevant for treating tinnitus and compare the positive results with those obtained in other human studies using different paradigms of bimodal neuromodulation for tinnitus treatment.



## Methods

In guinea pigs, electrical pulses were presented to different body locations, including the tongue, ear region, neck, back or limbs. Body electrical stimulation was paired with sound stimulation with varying inter-modality delays. Neural responses before and after bimodal neuromodulation were recorded from the midbrain and cortex to analyze the extent and type of plasticity elicited within auditory brain regions. These animal results were assessed together with data obtained from other bimodal neuromodulation studies (i.e., those combining sound with electrical ear, tongue or neck/cheek stimulation) in tinnitus participants who were monitored for changes in tinnitus symptom severity during and after treatment based on Tinnitus Handicap Inventory (THI) or Tinnitus Functional Index (TFI).

## Results

The animal and human results support that bimodal neuromodulation achieves greater auditory plasticity and larger improvements in tinnitus symptom severity compared to acoustic stimulation alone. In the human studies, a majority of participants exhibited improvements in THI and/or TFI. Consistent with our animal findings, bimodal neuromodulation using sound stimulation paired with electrical stimulation of the tongue versus other peripheral nerve pathways appears to drive greater tinnitus therapy that can be sustained out to 12 months post-treatment. Since each human study used a different treatment period, the differences in long-term therapeutic effects may also depend on total duration of bimodal stimulation over time.

## Conclusion

Bimodal neuromodulation is emerging as a promising and safe stimulation approach for tinnitus treatment, which has been supported by several independent studies. Considering that ~10-15% of the population are affected by tinnitus, bimodal neuromodulation can have a major clinical impact in society. Future studies are needed to identify which subtypes of patients can be optimally treated with different paradigms of bimodal stimulation of the auditory and somatosensory systems.

## Effectiveness of bimodal auditory and electrical stimulation' treatment in patients with tinnitus: A pilot study

Spencer Shikha<sup>1</sup>, Mielczarek Marzena<sup>1</sup>, Olszewski Jurek<sup>1</sup>, Sereda Magdalena<sup>2,3</sup>, Joosse Iris<sup>5</sup>, Vermeersch Hanne<sup>5</sup>, Gilles Annick<sup>5,6\*</sup>, Michiels Sarah<sup>4,5,6</sup>

\*Contributed equally

<sup>1</sup>Department of Otolaryngology, Laryngological Oncology, Audiology and Phoniatrics, Medical University of Lodz, Lodz, Poland, <sup>2</sup>Hearing Sciences, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, <sup>3</sup>National Institute for Health Research (NIHR), Nottingham Biomedical Research Centre, Nottingham, UK, <sup>4</sup>Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium, <sup>5</sup>Department of Otorhinolaryngology, Antwerp University Hospital, Edegem, Belgium, <sup>6</sup>Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp.

Tinnitus is a common symptom, affecting about 10–15% of the adult population. When input from somatosensory system can influence and/or elicit tinnitus, this type of subjective tinnitus is called somatosensory tinnitus. Consequently, altering the somatosensory input might be beneficial for patients with tinnitus.

The aim of this study was to investigate the effectiveness of bimodal stimulation (Transcutaneous Electrical Nerve Stimulation (TENS) at C2 or jaw region in combination with auditory stimulation) on reduction of tinnitus symptoms. Thirty chronic subjective tinnitus patients with a baseline score between 25 and 90 points on the Tinnitus Functional Index (TFI) participated in the study.

The TFI was the primary outcome measure. Reduction of 13 points on TFI score was considered as clinically significant. Twenty-seven patients completed the treatment. Immediately after treatment, 3/27 (11%) and 6/25 (24%) patients at follow-up showed a clinically significant reduction in TFI scores. Univariate binary logistic regression analysis showed that the clinically significant decrease after treatment was significantly associated with younger age, higher baseline NBQ-score, higher baseline TMD-pain screener score and lower Fletcher index of the right ear.

## Conclusion

Our study shows significant improvement in TFI score. The results of our study show that bimodal stimulation might be beneficial for tinnitus patients with pain complaints in the neck or jaw area.

# Random Forest Classification to Predict Response to High-Definition Transcranial Direct Current Stimulation Therapy for Tinnitus

Cardon E.<sup>1,2</sup>, Jacquemin L.<sup>1,2</sup>, Mertens G.<sup>1,2</sup>, Van de Heyning P.<sup>1,2</sup>, Vanderveken O.M.<sup>1,2</sup>, Topsakal V.<sup>1,2</sup>, Van Rompaey V.<sup>1,2</sup>, Gilles A.<sup>1,2,3</sup>

<sup>1</sup>Department of Translational Neurosciences, Faculty of Medicine and Health Sciences, Campus Drie Eiken, Antwerp University, Antwerp, Belgium, <sup>2</sup>Department of Otorhinolaryngology – Head and Neck Surgery, Antwerp University Hospital, Edegem, Belgium, <sup>3</sup>Department of Education, Health and Social Work, University College Ghent, Ghent, Belgium

## Background and Aim

Noninvasive brain stimulation techniques such as transcranial direct current stimulation (tDCS) are hypothesized to reduce tinnitus severity by modifying cortical hyperactivity in brain regions associated with tinnitus perception. However, individual response to tDCS has proven to be extremely variable. We employed random forest (RF) classification, a supervised machine learning approach, to predict individual treatment response in a large cohort of chronic subjective tinnitus patients.

## Methods

Ninety-nine tinnitus patients received six biweekly sessions of high-definition (HD) tDCS of the right dorsolateral prefrontal cortex (rDLPFC). Before treatment and at a three-month follow-up time point, patients filled in the Tinnitus Functional Index (TFI), a Visual Analogue Scale (VAS) to assess tinnitus loudness and the Hospital Anxiety and Depression Scale (HADS). Handedness was assessed using the Edinburgh Handedness Inventory (EHI). RF classification with five-fold cross-validation was applied to predict whether an individual responded positively to the treatment, defined as a reduction of at least 13 points on the TFI.

## Results

Thirty out of 99 patients responded positively to HD-tDCS treatment. The RF classifier predicted treatment response with an accuracy of 82.41% and an area under the curve of 0.902, corresponding to a sensitivity of 80.95% and a specificity of 84.71%. Feature importance analysis revealed that patients with higher TFI, VAS and HADS depression scores and negative EHI scores, corresponding to left-handedness, were more likely to respond positively to HD-tDCS treatment.

## Conclusion

Individual response to HD-tDCS treatment may be accurately predicted using easily obtainable questionnaire data. Patients with higher tinnitus burden, concurrent depressive symptoms and/or a preference of the left hand may respond more positively to HD-tDCS of the rDLPFC. Although larger studies are necessary to validate the proposed classifier, our results might provide the basis for better and more personalized guidance towards the right treatment for chronic tinnitus patients.



# **Effectiveness of blinding and occurrence of adverse effects in sham-controlled transcranial direct current stimulation (tDCS) study**

Alex Deng<sup>1</sup>, Bethany Adams<sup>2,3</sup>, Polly Scutt<sup>2,3</sup>, Derek J Hoare<sup>2,3</sup> and Magdalena Sereda<sup>2,3</sup>

<sup>1</sup>School of Medicine, University of Nottingham, Nottingham, UK, <sup>2</sup>Hearing Sciences, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, <sup>3</sup>NIHR Nottingham Biomedical Research Centre, Nottingham, UK

## **Background and Aim**

Transcranial direct current stimulation (tDCS) is a non-invasive neurostimulation technique, which delivers weak (1-2 mA) direct currents to the brain, thereby depolarising or hyperpolarising neurons within the desired region of cortex. It is postulated that tDCS sham stimulation can be applied that in theory should be indistinguishable from the active stimulation. However, currently there is a mixed evidence of blinding effectiveness in tDCS experiments. The aim of the study was to investigate the effectiveness of blinding of both participants and researcher and any adverse effects during sham and active stimulation.

## **Methods**

Twenty health volunteers randomly assigned to receive either active or sham tDCS stimulation. Active tDCS stimulation at 2mA for 20 minutes, with a 10 seconds of ramp-up and ramp-down was delivered via two electrodes placed over right (anode) and right (cathode) dorsolateral prefrontal cortex. Placebo stimulation used the same parameters but reduced the stimulation time down to 40 seconds. After the stimulation participants and researcher indicated whether they thought the stimulation was the active one or sham. Participants were asked to report any sensations they experienced during the stimulation. Effectiveness of blinding was assessed using James' Blinding Index. Strength, duration and onset of adverse effects during active and sham stimulation were compared between active and sham stimulation.

## **Results**

Nine male and 11 female took part in the study (mean age 28, SD=10 years, age range 20-57 years). Five out of ten participants in the sham group and 8/10 participants in the active stimulation group correctly guessed the type of stimulation they have received. Researcher conducting the study correctly guessed the type of stimulation in 8/10 participants in the sham and 6/10 participants in the active stimulation group. Participant James blinding index = 0.35, 95% CI (0.25, 0.46) and researcher James blinding index = 0.34, 95% CI (0.13, 0.54). All participants regardless of whether they received active or sham stimulation reported at least one adverse effect related to the tDCS stimulation. Adverse effects reported were: tingling (n=16), burning (n=14), warmth (n=12), itching (n=11), skin redness (n=11), pain (n=4) and fatigue (n=1). Sensations tended to last longer during the active than sham stimulation.

## **Conclusion**

There was some evidence of unblinding for both participants and researcher, however it was statistically significant only for the participant group. The effectiveness of blinding should be monitored in future tDCS studies and additional measures introduced to avoid unblinding.

## From clinical data to a model accounting for hyperacusis and associated symptoms

Arnaud Noreña

CNRS & University of Aix-Marseille, arnaud.norena@univ-amu.fr

The hypothesis (inspired by clinical data) that the tensor tympani muscle (TTM), the trigeminal nerve (TGN), and the trigeminal cervical complex (TCC) may play a central role in generating hyperacusis and other symptoms will be presented. The TCC is a crossroad structure integrating sensory inputs coming from the head-neck complex (including the middle ear) and projecting back to it. It is suggested that TTM injury can lead to inflammation, thereby activating the TGN, TCC, and the auditory system (tinnitus) and the somatosensory systems (pain). The model suggests that musculoskeletal disorders of the head-neck complex other than those affecting the TTM could also result in hyperacusis and tinnitus.

Characteristics of the Onset and Reoccurring Symptoms of Hyperacusis

Bryan Pollard

Hyperacusis Research

### Background and Aim

The onset and continuing symptoms of hyperacusis are poorly characterized clinically. Hyperacusis patients' initial symptoms can include ear fullness, loud ringing, and pain or burning sensations around the ear. Our aim is to provide the basis for improved clinical intake processes to optimize treatment and clinical research for hyperacusis and hyperacusis symptoms in acoustic shock.

### Methods

A 30 question on-line survey was promoted on six tinnitus and hyperacusis on-line forums and completed by 332 participants with an average completion time of 11 minutes. The results were compared to a more extensive registry assessment of hyperacusis where over 200 participants have completed a 98 question survey with the Coordination of Rare Diseases at Sanford (CoRDS) Registry. A cross over analysis was completed between the two surveys demonstrating similarities on key symptoms of interest.

### Results

The top complaints for participants was ear pain caused by sound and loudness sensation followed increased tinnitus from sound. 89% indicated sound causes discomfort or pain. 88% experience a period of worsening with new sounds often referred to as a setback. 51% experience setbacks daily or weekly. The impact from setbacks included increased pain by 60% of participants which usually included increased ringing and an increase in loudness sensation. By comparison, 77% of participants experienced increased ringing with a setback. 55% indicated that the setback made their condition worse than it ever was. Therefore setback prevention was considered a critical outcome of clinical care. One question that has both clinical and research value was: "Would you say that you experience your hyperacusis symptoms equally in each ear?" A similar question was also asked in the Sanford CoRDS survey. The results of both surveys were statistically matched, revealing that about half have symptom differences between ears. An open ended question asked: "What do you think may explain your symptom differences between ears?" Many could identify specific sources on the impacted side from noises such as a person screaming, a whistle, a loud machine or musical instrument. These single sided exposures and variable impacts have important ramifications for research.

### Conclusion

In summary, multiple surveys suggest that hyperacusis with pain is common among hyperacusis sufferers in addition to an increase in loudness sensation and tinnitus. Also, many sufferers experience setbacks that temporarily or permanently make their symptoms worse. Therefore, setback prevention should be a top priority of clinical treatment programs. Opportunities also exist for researchers to study the physiological mechanism for setbacks and determine what inhibits or enables a quicker recovery.



## **Sound-induced pain in hyperacusis patients from a clinical perspective: the role of Tonic Tensor Tympani Syndrome (TTTS)**

Myriam Westcott

DWM Audiology

Acoustic shock is an involuntary fright/psychological trauma reaction to a sudden, loud, unexpected or unavoidable sound resulting in a characteristic cluster of symptoms consistent with TTTS. These can include a stabbing and/or dull aural pain, tinnitus, aural fullness, pain/numbness/burning around the ear, muffled hearing, tympanic flutter, mild vertigo. This full or partial TTTS symptom cluster has also been identified as strongly prevalent in hyperacusis patients, whether their hyperacusis developed from acoustic shock or from other causes, and shown to be frequently sound-induced.

The clinical presentation, evaluation and effective treatment of TTTS symptoms in over 200 acoustic shock patients, and in hyperacusis patients over a span of 26 years, in a multi-disciplinary setting, has revealed insights into TTTS triggers and hyperacusis mechanisms. In vulnerable patients, TTTS appears to develop involuntarily from a central nociceptive ‘protective’ response to sounds (or other noxious stimuli) subconsciously evaluated as threatening or potentially damaging to the ears/hearing/tinnitus. Other triggers diagnosed to have induced TTTS include aggressive wax removal, water in the ears, wind/cold in the ears, touch in or near the ears. This highlights the importance of thorough history taking and the therapeutic benefit of demystifying these pathways.

## **Reliability and validity of oscillatory brain activity changes induced by repetitive transcranial magnetic stimulation**

Stefan Schoisswohl, Berthold Langguth, Martin Schecklmann

Department of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany

Hyperactivity in auditory and non-auditory brain areas as well as altered oscillatory brain activity was found to be associated with the emergence of chronic subjective tinnitus. A potential approach to reduce this hyperactivity is represented by a non-invasive brain stimulation method referred to as repetitive transcranial magnetic stimulation (rTMS) via e.g. inhibitory low frequency stimulation protocols. However, there is still disagreement with regard to its effectiveness for the treatment of tinnitus. Besides clinical trials of daily rTMS with heterogeneous results, short rTMS sessions demonstrated temporary tinnitus suppression. In addition, neurophysiological experiments were able to reveal power changes in tinnitus related oscillatory brain activity after rTMS. Besides a short background and overview of rTMS in combination with neurophysiological measurement techniques in tinnitus, this talk will focus on the methodological approach and the results of a recent rTMS experiment in combination with electrophysiology. With the aid of an e-field guided rTMS system, tinnitus patients were stimulated with different rTMS protocols over different positions on two different days, while electroencephalography (EEG) was recorded before and after each stimulation in order to investigate valid and reliable neural markers for short-term tinnitus suppression.

# Tinnitus in Children

## Development of a child-specific questionnaire measure of tinnitus impact

Harriet Smith<sup>1,2</sup>, Kathryn Fackrell<sup>1,2</sup>, Veronica Kennedy<sup>3</sup>, Johanna Barry<sup>4</sup>, Lucy Partridge<sup>5</sup>, Claire Benton<sup>4</sup>, Derek J. Hoare<sup>1,2</sup>

<sup>1</sup>NIHR Nottingham Biomedical Research Centre, <sup>2</sup>Hearing Sciences, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, <sup>3</sup>Breightmet Health Centre, Bolton NHS Foundation Trust, <sup>4</sup>Nottingham University Hospitals NHS Trust, <sup>5</sup>The Nuffield Hearing and Speech Centre, Royal National Throat Nose and Ear Hospital, University College London Hospitals NHS Foundation Trust

### Background and Aim

To care for children with tinnitus, health professionals must understand the tinnitus-related problems they experience. Clinical questionnaires are used to assess the severity of tinnitus-related problems in adults and are used to guide decisions regarding treatment. There are currently no tinnitus questionnaires appropriate for use with children and there is a knowledge gap in what is known about the problems that are relevant and critical to measure. The aim of this study was to explore the experiences of children with tinnitus to identify candidate items to include in a new child-specific questionnaire measure of tinnitus impact.

### Methods

Eleven children (aged 8-16) experiencing tinnitus-related problems were interviewed in individual and group sessions. Five parents and eight clinicians caring for children (aged 8-16) with tinnitus-related problems were also interviewed via telephone. Data were analysed to identify all problem domains reported. Problem data were synthesised with several other primary and secondary data sources of children's tinnitus-related problems, to generate a pool of candidate questionnaire items (single questions). Through consultation with an expert panel (clinicians and researchers), critical items were identified, reduced, and refined, and a prototype questionnaire was drafted.

### Results

The initial candidate questionnaire item pool included over 200 unique items. A broad range of problems were identified, including problems related to sleep, learning, emotional health, hearing and communication, participation in everyday activities, and relationships. There were notable differences in problems reported by children compared to what was reported by parents and clinicians. For example, children were more likely to report the impact of tinnitus on conversations, and parents and clinicians were more likely to comment on issues relating to behaviour. The prototype questionnaire included 38-items.

### Conclusion

The prototype questionnaire was designed based on evidence of tinnitus-related problems considered relevant and important to children. The next stages of development will involve cognitive interviews to assess the clarity and usability of the questionnaire. Finally, a validation study will assess the psychometric properties of the instrument in a clinical population. The questionnaire will be the first of its kind and will improve care by supporting health professionals in their assessment and treatment of tinnitus in children.



# Pathophysiology

## Strain-specific changes occurring in animal auditory system after stress

Ewa Domarecka<sup>1</sup>, Heidi Olze<sup>1</sup>, Agnieszka J. Szczepek<sup>1</sup>

Department of Otorhinolaryngology, Head and Neck Surgery, Berlin Institute of Health,  
Charité- Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin,  
Humboldt-Universität zu Berlin, Berlin, Germany

### Background and aim

Clinical data support the association between tinnitus and stress, but the experimental evidence revealing the character of this association (causative or incidental) is minimal. Hence, we studied stress-induced changes in the animal auditory system using three different rat strains: Lewis, Fischer 344, and Wistar. The outbred Wistar rats are commonly used for medical drug testing because of their genetic heterogeneity, whereas the inbred Lewis rats serve as a model of post-traumatic stress disorder (PTSD) and inbred Fischer rats as an anxiety-related model. In humans, PTSD and anxiety often occur as tinnitus comorbidities. We reasoned that the comparative analyses of auditory reactions to stress in Wistar, Lewis and Fischer rats might contribute to a better understanding of the neuronal, immune, and endocrine interplay.

### Methods

We exposed all animals to experimental stress, after which, we measured changes in the function of the auditory system using DPOAE and ABR. In addition, we evaluated the concentration of corticosterone and tumor necrosis factor-alpha (TNF-alpha) in sera of the animals using enzyme-linked immunosorbent assay (ELISA).

### Results

We found that the unstressed Wistar rats had higher ABR thresholds than the unstressed Lewis and Fischer. Also, Fischer DPOAE thresholds measured at 2 kHz were higher than the thresholds of Wistar and Lewis rats.

Immediately after stress, the ABR thresholds of Lewis rats decreased in low frequencies, whereas these of Wistar rats increased and of Fischer rats remained unchanged. At the same time, the DPOAE thresholds measured at 2 kHz decreased in Lewis rats and increased in Fischer and Wistar rats.

We also determined differences in the concentrations of corticosterone between rat strains. The corticosterone serum concentration of unstressed Fischer rats was significantly higher than the levels found in the serum of Wistar and Lewis rats. Immediately after stress, the corticosterone concentration of Fischer and Lewis rats increased, whereas the corticosterone concentration in Wistar rats had decreased. The level of TNF-alpha in the serum of unstressed Lewis rats was higher than this of Wistar or Fischer rats and remained unchanged after stress.

### Conclusion

Here, we demonstrated that in the animal model, the reaction of the auditory system to stress is strain-dependent. Uncovering the biological basis underlying these differences might advance our understanding of hearing disorders, such as tinnitus or hyperacusis.

# Ventral cochlear nucleus bushy cells contribute to hyperacusis neural coding after noise-exposure

David T. Martel and Susan E. Shore

Department of Otolaryngology, University of Michigan, Ann Arbor

## Background and Aims

Psychophysical studies characterize hyperacusis as increased loudness growth over a wide-frequency range, decreased tolerance to loud sounds (Baguley, 2003; Tyler et al, 2014) and reduced behavioral reaction time latencies to high-intensity sounds (Lauer and Dooling, 2007). While commonly associated with hearing loss, hyperacusis can also occur without hearing loss, implicating the central nervous system in the generation of hyperacusis. Ventral cochlear nucleus (VCN) bushy cells (BC) are putative candidates for hyperacusis coding. Compared to other VCN output neurons, BCs show high firing rates as well as lower and less variable first-spike latencies at suprathreshold intensities. Following cochlear damage, BCs show increased spontaneous firing rates (SFR) across a wide-frequency range (Bledsoe et al, 2011), suggesting that they might also show increased sound-evoked responses and reduced latencies to higher-intensity sounds. However, no studies have examined BCs in relationship to hyperacusis. To test the hypothesis that BCs exhibit a neural signature of hyperacusis, we employ noise-overexposure and single-unit electrophysiology.

## Methods

Acoustic startle responses were measured as a behavioral estimate of hyperacusis and tinnitus, which are frequently co-morbid (Turner et al., 2006; Berger et al., 2013). Guinea pigs were then exposed to unilateral narrowband noise twice (Wu et al, 2016), or were non-exposed control animals. Single-unit electrodes were stereotactically inserted into the VCN. BCs were identified by their receptive fields, peristimulus-time-histograms and locations within the VCN (Winter and Palmer, 1990). Spontaneous activity, tone- and noise-evoked rate-intensity functions (RIFs; 0:10:90 dB SPL, 50 ms) were recorded from multiple BCs. For each BC, a Hyperacusis- Index (HI) was computed as the geometric mean of RIF maximum rates and slopes. Synchrony was computed as peak normalized cross-correlation coefficients from sound-evoked and spontaneous firing.

## Results

BCs in noise-exposed animals showed steeper RIFs and reduced first-spike latencies compared to control animals. BCs also showed a correlation between HI and startle amplitude. These findings suggest that BCs contribute to hyperacusis coding. While BC SFR and synchrony were increased over a wide-frequency range, did not correlate with behavioral measures of tinnitus, suggesting that BCs do not contribute to tinnitus.

## Conclusions

Following noise-overexposure, BCs exhibit neural signatures consistent with hyperacusis and not tinnitus. Enhanced BC RIFs are analogous to abnormal loudness growth over wide bandwidths associated with hyperacusis.



# Pharmacology

## The effects of mirtazapine on tinnitus in patients with panic disorder

Patricia Ciminelli<sup>1</sup>, Sergio Machado<sup>2</sup>, Antonio Egidio Nardi<sup>1</sup>

<sup>1</sup>Laboratory of Panic and Respiration (LABPR), Institute of Psychiatry (IPUB), Federal University of Rio de Janeiro (UFRJ), Brazil. Rua Venceslau Brás, 71 Botafogo, Rio de Janeiro – RJ, Brazil 22290-140,

<sup>2</sup>Physical Activity Neuroscience, Physical Activity Sciences Postgraduate Program, Salgado de Oliveira University, Niterói, Brazil. Rua Mal. Deodoro, 217 - Bloco A - Centro, Niterói – RJ, Brazil 24030-060

### Background and aim

Tinnitus is described as a sound perceived in the ears or head that is not generated by an outside source. Depression and anxiety are very common in tinnitus patients, prevalence being as high as 80% and antidepressants are commonly prescribed, minimizing comorbid conditions and reducing tinnitus impact. Although tinnitus is a very prevalent symptom and impacts patient's quality of life significantly, there are still no FDA approved drugs to treat tinnitus. The objective of our study is to describe a successful reduction on tinnitus annoyance in patients with panic disorder (PD) and tinnitus treated with mirtazapine. Methods: Fourteen patients with PD and tinnitus were included in our final sample, 7 male and 7 female. Mirtazapine was prescribed with the specific purpose of treating PD and its initial dose varied from 30 to 60 mg per day. Patients were evaluated at baseline, 12 weeks and 3 years after beginning mirtazapine. Scales and outcomes used were the Hamilton Depression Rating Scale (HAMD), the Clinical Global Impression Scale (CGI-S), the Visual Analog Scale (VAS) for tinnitus annoyance and the number of panic attacks. The total treatment with mirtazapine varied from 27 to 36 months (mean SD 32.2/3.7). Results: A statistically significant decrease in the HAMD and CGI scales, in the number of panic attacks, as well as in tinnitus annoyance occurred ( $p=0.001$  for all analysis) and response was sustained after 3 years, even in those patients who discontinued the use of mirtazapine a little before completing the 3 years of medication. Conclusion: Prolonged treatment with mirtazapine in patients with panic disorder and tinnitus could significantly reduce the number of panic attacks and tinnitus annoyance. The results are encouraging and should motivate further studies.

## Phase 2b Randomized Double Blind Placebo-Controlled Trial of SPI-1005 for Meniere's Disease

Jonathan Kill<sup>1</sup>, Shaun A. Nguyen<sup>2</sup>, E. Emily Harruff<sup>1</sup>, Thomas Willcox<sup>3</sup>, Michael Hoa<sup>4</sup>, Hinrich Staecker<sup>5</sup>, Sujana Chandrasekhar<sup>6</sup>, Jeffrey D. Sharon<sup>7</sup>, J. Walter Kutz<sup>8</sup>, Michael Hoffer<sup>9</sup>, May Huang<sup>10</sup>, Gorden McMurry<sup>11</sup>, Paul R. Lambert<sup>2</sup>

<sup>1</sup>Sound Pharmaceuticals, Inc. 4010 Stone Way N, Ste 120, Seattle, WA 98103, <sup>2</sup>Medical University of South Carolina. 135 Rutledge Ave. MSC550, Charleston, SC 29425, <sup>3</sup>Thomas Jefferson University. 925 Chestnut St, 6th Floor, Philadelphia, PA 19107, <sup>4</sup>Georgetown University Medical Center. 3800 Reservoir Rd NW, Washington DC 20007, <sup>5</sup>University of Kansas Medical Center. 3901 Rainbow Blvd, Kansas City, KS 66160, <sup>6</sup>ENT & Allergy Associates, LLP. 18 E 48th St, 2nd Floor, New York, NY 10017, <sup>7</sup>University of California San Francisco. 2233 Post St, Ste 315, San Francisco, CA 94115, <sup>8</sup>University of Texas Southwestern Medical Center. 2001 Inwood Rd, Dallas, TX 75390, <sup>9</sup>University of Miami Miller School of Medicine. 1120 NW 14th St, Ste 581, Miami, FL 33136, <sup>10</sup>Northwest Ear, Inc. 1221 Madison St, Ste 1410, Seattle, WA 98104, <sup>11</sup>Advanced ENT and Allergy. 404 Dupont Cir, Ste 220, Louisville, KY 40207

## Background and Aim

Glutathione peroxidase (GPx) is a critical cytoprotective enzyme in the brain, eye, ear, lung, and kidney. GPx1 is the dominant isoform in the inner ear and is highly expressed within the organ of Corti, spiral ganglia and stria vascularis of the cochlea. Ebselen is a selenorganic compound that mimics and induces GPx1 and has been shown to prevent and treat sensorineural hearing loss in animals (Kil et al., Hear Res 2007). SPI-1005 is an investigational new drug that contains ebselen and was shown to prevent acute noise-induced hearing loss in a Phase2 randomized controlled trial (RCT) (Kil et al., Lancet, 2017) and to treat newly diagnosed Meniere's Disease (MD) in a Phase1b RCT (Kil et al., ARO, 2018). We now report the Phase2b RCT data in active MD where hearing loss, tinnitus, and vertigo are documented and/or patient-reported. FDA has granted Fast Track Designation to SPI-1005 for the Treatment of MD.

## Methods

149 adults with active MD, including hearing loss of  $\geq 30$  dB HL in one of three low frequencies at baseline, were consented, screened, and randomized (1:1:1) to receive either placebo, 200, or 400 mg SPI-1005, twice daily po for 28 days, with follow-ups at 4 and 8 weeks. The pre-specified endpoints were to determine if SPI-1005 could improve hearing by a clinically relevant difference vs placebo, using pure-tone audiometry (PTA). Additional measures of efficacy included the Words-in-Noise test (WINT), and the patient-reported Tinnitus Functional Index (TFI) and Vertigo Symptoms Scale (VSS).

## Results

124 adults (mean age 55 years; range 22-73 years) were in the Intent-to-Treat (ITT) analysis. The primary audiological endpoint ( $\geq 10$  dB gain from baseline in at least one low frequency) showed a significant increase in the 400 mg vs placebo (61% vs 37%,  $p < 0.023$ ), a 65% relative improvement at 8 weeks. The WINT showed significant gains ( $\geq 4$  words improvement from baseline) in the 400 mg vs placebo (60% vs 34%,  $p < 0.017$ ), a 76% relative improvement at 8 weeks. Secondary endpoints showed significant reductions in tinnitus loudness (TFI) in the 400 mg vs placebo (1.4 vs 0.7,  $p < 0.02$ ) at 8 weeks. No SAEs were reported and all AEs were mild to moderate and consistent with other SPI-1005 studies.

## Conclusion

SPI-1005 was safe and effective in improving hearing loss and tinnitus in active Meniere's Disease using PTA, WINT and TFI (ITT analysis). These findings support the advancement of SPI-1005 to pivotal Phase3 RCTs in MD.

## A Phase II-ready oral drug shows excellent preclinical efficacy for treating blast and noise-induced tinnitus

Jianzhong Lu<sup>1</sup>, Matthew B. West<sup>1</sup>, Richard D. Kopke<sup>1,2,3</sup>

<sup>1</sup>Hough Ear Institute, Oklahoma City, Oklahoma 73112, <sup>2</sup>Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma 73104, <sup>3</sup>Departments of Physiology and Otolaryngology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 73104

## Background and Aim

Tinnitus, the phantom perception of sound, is a frequent neuropathological consequence of noise- or blast-induced cochlear injury. This disorder occurs in 14-20% of the population and is one of the most prevalent service-related disabilities among military personnel, representing an especially high-risk demographic for cochlear traumas and comorbidities. In some individuals, the tinnitus percept can become sufficiently debilitating that it leads to psychological distress and loss of situational awareness, negatively impacting health, interpersonal relationships, and job performance. Despite the inherent urgency to develop a pharmacological therapy to address this auditory disorder, no such FDA- approved therapeutic is currently available. Our aim was to test NHPN-1010 as a potential therapeutic in a rat model of blast-induced tinnitus.



## Methods

All procedures regarding the use and handling of animals were approved by the Institutional Animal Care and Use Committee of the Oklahoma Medical Research Foundation (OMRF) or University of Oklahoma School Health Sciences Center (OUHSC). Using a rat model, baseline pre-pulse inhibition (PPI) of the acoustic startle response and auditory brainstem response (ABR) tests were performed. Anesthetized rats were exposed to a single 10psi blast in a shock tube. Blast-exposed rats were treated with NHPN-1010 or placebo beginning at either 1 hour (4 additional doses over 48 h) or four weeks after blast (14-day dosing). PPI and ABR testing were repeated 8-9 weeks after trauma, before animals were euthanized and cochlear and brain tissues collected for histological analysis. CNS biomarkers included Arg 3.1, VACHT, GluR2, GABAR- 1, GAP43 and VR1 in the cochlear spiral ganglion. Cochlear cytograms were also obtained.

## Results

Acute-treated and delayed-treated animals demonstrated a significantly decreased incidence of tinnitus percept and tinnitus index score compared to placebo-treated animals. Additionally, treated animals demonstrated normalization of ABR Wave V/I amplitude ratio and partial normalization of ABR Wave I amplitude, recovery of afferent ribbon synapses and normalization of tinnitus related biomarkers in the cochleae and along the central auditory pathway when compared to placebo-treated animals. The probability of tinnitus percept was highly correlated with normalized ABR Wave V/I ratio, which also correlated highly with afferent ribbon synapse counts but not ABR threshold shifts.

## Conclusion

NHPN-1010 is purposed to be an oral treatment for trauma-induced tinnitus. It is safe and well- tolerated in two-week dosing FDA Phase I safety and tolerability studies. Based on behavioral, biomarker and ABR data, NHPN-1010 is promising therapeutic to advance toward commercialization. Additional chronic tinnitus studies are underway.

# Sound Therapy

## Modulation of sound and tinnitus loudness in tinnitus patients with and without hearing loss following three weeks of acoustic stimulation

Philippe Fournier<sup>1,2,3</sup>, Charlotte Bigras<sup>1,2</sup>, Alexandre Lehmann<sup>2,4</sup>, Arnaud J. Noreña<sup>3</sup> & Sylvie Hébert<sup>1,2</sup>

<sup>1</sup>School of Speech Pathology and Audiology, Université de Montréal, Montréal, Québec, Canada,

<sup>2</sup>International Laboratory for Research on Brain, Music, and Sound (BRAMS), Université de Montréal,

Montréal, Québec, Canada, <sup>3</sup>Université d'Aix-Marseille, CNRS, Marseille, France, <sup>4</sup>Royal Victoria

Hospital, ENT Department, McGill University, Montreal, Quebec, Canada

## Background and Aim

Tinnitus and reduced sound tolerance (a form of hyperacusis) are two debilitating conditions that are highly comorbid. It has been postulated that they may originate from similar pathophysiological mechanisms such as an increase in central gain. Interestingly, sound stimulation has been shown to reduce central gain and is currently used for the treatment of both conditions. This study investigates the effect of sound stimulation on both tinnitus characteristics and sound tolerance in the same patients.

## Methods

Two distinct series of tinnitus participants were tested: one with normal or near-normal hearing (n=16) and one with hearing loss (n=14). A broadband noise shaped to cover most of the tinnitus frequency spectrum was delivered through hearing aids using the noise generator feature (no amplification) and verified through real-ear measurements. The participants were tested before the sound stimulation (baseline), after 1 week, and after 3 weeks of stimulation. There was also a 1-month follow-up after the end of the stimulation protocol. The measurements included self-reported measures of tinnitus and reduced sound tolerance (VAS), validated questionnaires (THI, HQ) and psychoacoustic measurements (tinnitus battery & loudness functions).

## Results

Overall, about 50% of tinnitus participants had a synchronous (either a decrease or an increase) modulation of sound tolerance (ST) and tinnitus loudness (TL) after 1 week and 3 weeks of acoustic stimulation. The decrease of ST and TL was more prevalent in normal-hearing participants. There was a significant increase in tinnitus loudness during and following the stimulation in the group with hearing loss. ST improvement as assessed by loudness function was significantly correlated with the level of acoustic stimulation in tinnitus participants with normal/near-normal hearing thresholds.

## Conclusion

The present findings only partly support the central gain hypothesis and deserve further scrutiny, for instance by better defining tinnitus subtypes in order to circumscribe potential benefits. In addition, in some cases, the stimulation improved one condition but worsened the other. It is thus essential to verify that the acoustic stimulation does not have adverse effects such as reducing sound tolerance in the case of patients consulting for a tinnitus concern and managed with acoustic treatment.

## Acoustic amplification in case of Single-Side Deafness with residual hearing: an alternative to cochlear implantation to treat tinnitus.

Morgan Potier<sup>1,2</sup>, Arnaud Noreña<sup>1</sup>, Philippe Fournier<sup>1</sup>, Nicolas Guevara<sup>3</sup>, Stéphane Gallego<sup>1,4</sup>

<sup>1</sup>IUMR CNRS 7260, Laboratoire de Neurosciences Sensorielles et Cognitives (LNSC) - Aix-Marseille - Université Centre Saint-Charles, 3 Place Victor Hugo, 13331, Marseille, France, <sup>2</sup>Laboratoire d'Audiologie Clinique - 26 Boulevard Marcel Sembat, 11100, Narbonne, France, <sup>3</sup>Institut Universitaire de la face et du cou - Université Côte d'azur - Centre hospitalier de Nice, 31 Avenue de Valombrose, 06100, Nice, France, <sup>4</sup>Institut des Sciences et Technologies de Réadaptation (ISTR) - Université de Lyon, 8 Avenue Rockefeller, 69008, Lyon, France

## Background and Aim

Most patients suffering from Single-Side Deafness (SSD) with residual hearing, and/or with Unilateral Severe-to-Profound Sensorineural Hearing Loss (USNHL) have trouble with speech understanding particularly in noisy environments. They may also suffer from balance disorders and they often complain of disabling tinnitus located in their deaf ear. In these cases, cochlear implantation has been suggested as the best option as it restores hearing abilities and may reduce tinnitus. Regarding amplification there are relatively only a few options available for these patients: bilateral amplification (Stereophonics) and Bilateral Contralateral Routing of Signal (BiCROS) that consist of routing the signal from the poor ear to the better ear. Until recently, the latter option did not allow additional amplification of the poorer ear, but this option is now available in some hearing aids. In this case, the technology combines BiCROS with additional amplification of the poorer ear that we have called StereoBiCROS. The additional amplification of the poorer ear in addition to BiCROS could enhance speech intelligibility and reduce tinnitus. The aim of this study is thus to compare the performance of this new StereoBiCROS stimulation with the effectiveness of conventional acoustic stimulation (Stereophonics and BiCROS) when using them on single sided deaf individuals who also complain of annoying tinnitus.



## Methods

We studied 14 first hearing aid users (mean age 70.7 years  $\pm$  7.9) with a USNHL associated with tinnitus. The tinnitus handicap, discomfort and loudness were assessed using the THI questionnaire and Visual Analog Scales (VAS) before the hearing aid fitting and one month after. During the one-month hearing trial, three different programs were available to the participants: the Stereophonic, the BiCROS and the StereoBiCROS program. The Stereophonic program consisted of conventional bilateral amplification. The BiCROS and StereoBiCROS programs both consisted at rerouting signals from the poorer ear to the best ear. However, the StereoBiCROS program included bilateral amplification to both, the best ear and the poorer ear, while the BiCROS included amplification for the best ear only. During the one-month trial period, participants could switch freely between the three programs. In addition, comparing the VAS when the hearing aids were turned on to when they were turned off at each assessment period assessed the acute effect of amplification.

## Results

The overall daily usage of the hearing aids was of  $11.9 \pm 1.7$  hours per day. The participants mainly used the StereoBiCROS program ( $88.9\% \pm 5.4\%$  of the time), followed by the Stereophonic ( $8.1\% \pm 6.1\%$  of the time) and finally, the BiCROS programs (only  $3.0\% \pm 3.6\%$  of the time). When combining the two programs stimulating the poorer ear, that is the StereoBiCROS and the Stereophonic programs, the poorer ear was stimulated almost  $97.0\% \pm 5.7\%$  of the time. In addition, there was a clear reduction of tinnitus handicap, loudness and discomfort in USNHL participants after the one-month trial period: the average THI total score decreased from  $58.0 \pm 12.9$  to  $18.6 \pm 16.8$  ( $p = 0.008$ ), the VAS-loudness score decreased from  $7.0 \pm 1.2$  to  $2.3 \pm 1.8$  ( $p = 0.002$ ), and the VAS-discomfort score decreased from  $7.0 \pm 1.3$  to  $2.8 \pm 2.1$  ( $p = 0.002$ ).

## Conclusion

StereoBiCROS stimulation strategy seems to offer an effective solution for subjects with USNHL and tinnitus. Amplification of the poorer ear with StereoBiCROS stimulation or conventional amplification is a less invasive and cheaper option than cochlear implantation. We recommend this option to be tried out during at least a month before considering a cochlear implantation, in order to assess the possible benefit for patients with USNHL and annoying tinnitus.

## Testing the reliability of psychoacoustic measures of tinnitus.

Elza Daoud<sup>1</sup>, Falco Enzler<sup>1</sup>, Philippe Fournier<sup>1</sup>, Fabien Paolino<sup>2</sup>, and Arnaud Norena<sup>1</sup>

<sup>1</sup>Centre National de la Recherche Scientifique, Aix-Marseille University, France, <sup>2</sup>Hôpital Privé Clairval, Explorations Oto-Neurologiques et Réhabilitation des Troubles de l'Equilibre, Marseille, France

## Background and aim

Psychoacoustic measures may serve as tools to estimate the psychoacoustic properties of tinnitus for clinical and research purposes. A novel approach was developed in our laboratory to replace the measure of residual inhibition (RI) duration by a measure of RI intensity. This method was proven to provide a minimum masking level (MML) and a minimum residual inhibition (MRIL) in most tinnitus patients. However, the reliability and reproducibility of these measurements need to be verified.

## Methods

A total of 30 patients (mean age: 55) with chronic tinnitus (unilateral: n=5, bilateral: n=25) were recruited for the study. The participants were tested twice over an average one-month period (mean days: 25, min: 5, max: 91). Two independent experimenters tested each participant once (test or retest) and were blinded to previous results. The stimulation used for the measures consisted of pulsed narrowband noises of 3-sec duration and 1-sec silence intervals (between the pulses). MML was obtained by increasing the stimulus intensity (3 dB steps) until the tinnitus was unheard during the noise presentation. MRIL was obtained by further increasing the stimulus intensity until the tinnitus was suppressed during the silence period between the acoustic pulses. The hearing thresholds (HT), and loudness discomfort level (LDL) were also assessed using the pulsed noise. All measures were obtained at seven standard audiometric frequencies (0.25 to 8 kHz).

## Results

MML was obtained at test and retest in 86% of all conditions. For these cases, the mean inter-session MML difference was of 3 dB (SD=12 dB, min= -39 dB, max= 37 dB). The Intra-Class-Correlation (ICC) was 0.83 (95% CI: 0.76-0.87). For MRIL, a similar outcome was obtained at test and retest for 55% of all conditions. When complete RI (20%) was obtained in both sessions, the mean inter-session MRIL difference was of 3 dB (SD=11.2 dB, min= -33 dB, max=19 dB). The ICC was 0.86 (95% confidence interval: 0.77-0.92). For HT measurements, the mean inter-session difference was of 1 dB (SD=9 dB, min=-27 dB, max=27 dB). The ICC was 0.89 (95% CI: 0.86- 0.92). When LDL could be obtained, the mean inter-session difference was of 2 dB (SD=12 dB, min=-39 dB, max=21 dB). The ICC was 0.84 (95% CI: 0.74-0.90).

## Conclusions

MML and MRIL measurements obtained with this method seem to be reliable and stable over time. When similar outcomes were obtained at test and retest (complete MML and MRIL), mean inter-session intensity differences (in dB) were comparable to the difference in HT and LDL.

# Investigating the Effect of High-Frequency Amplification as Tinnitus Treatment

Mie Lærkegård Jørgensen<sup>1,2</sup>, Petteri Hyvärinen<sup>2</sup>, Sueli Caporalil<sup>1</sup>, Torsten Dau<sup>2</sup>

<sup>1</sup>WS Audiology, Lyngé, Denmark, <sup>2</sup>Hearing Systems, Department of Health Technology, Technical University of Denmark, Kgs. Lyngby, Denmark

## Background and aim

More than 80% of people suffering from chronic tinnitus also have hearing loss and earlier studies have found that the tinnitus pitch is often located within the range of the hearing loss. These findings led to the hypothesis that it may be possible to decrease tinnitus loudness by increasing the auditory nerve activity via amplification provided by hearing aids.

## Methods

In this longitudinal crossover study, the effect of amplification is investigated in a randomized double-blinded trial. 20 participants suffering from tinnitus with clinically normal hearing ( $\leq 25$  dB) in the frequency range from 125 Hz to 3 kHz and a hearing loss at high frequencies are included in the study. To assess the possible effect of amplification, tinnitus questionnaires, visual analogue scales for loudness and annoyance, and psychoacoustic measures of the tinnitus likeness and loudness are measured before and after treatment. The study consists of an experimental condition where the participants receive amplification in an extended range of frequencies (125 Hz to 10 kHz) and a control condition where the participants receive amplification in a normal frequency range (125 Hz to 4 kHz).



## Results

We hypothesize that the experimental condition will provide a larger decrease in the tinnitus perception compared to the control condition. Preliminary results at the three-month crossover time point will be presented and discussed.

## Conclusion

The results from the current study will indicate whether tinnitus patients with high-frequency hearing losses benefit from high-frequency (>4 kHz) amplification.

# The acute effect of sound therapy on attention for chronic tinnitus patients

Mie Lærkegård Jørgensen<sup>1,2</sup>, Petteri Hyvärinen<sup>2</sup>, Sueli Caporali<sup>1</sup>, Torsten Dau<sup>2</sup>

<sup>1</sup>WS Audiology, Lyngé, Denmark, <sup>2</sup>Hearing Systems, Department of Health Technology, Technical University of Denmark, Kgs. Lyngby, Denmark

## Background and aim

Over the past 20 years there has been an increasingly focus on the role of cognitive networks and attention in tinnitus patients. Multiple studies have shown an attentional difference between tinnitus patients and controls in behavioral attention tests. Furthermore, electrophysiological differences have been found between the groups for both the P300 and the N100 component. The aim of the current study is to investigate the acute effect of sound therapy on tinnitus patients' attention.

## Methods

In this study, baseline event-related potentials (ERPs) are compared to corresponding ERPs measured after short-term exposure to sound therapy. Tinnitus patients with and without hearing loss and with THI > 18 are included in the study. Participants will be listening to their preferred Widex Zen sound prior to and during the measurement. Furthermore, a silent control condition is included to control for possible learning effects. The ERP measurement consists of the attentional network test in which visual incongruent and congruent arrow trials will be presented. The participants select the direction of the center arrow as quickly as possibly by pressing a keyboard button. During the task, ERPs are recorded using a 32-channel EEG system.

## Results

The results from the current study will indicate whether tinnitus patients experience an acute effect of sound therapy on their attentional resources as measured by the reaction times in the behavioral attention task and the amplitudes of the ERPs.

We hypothesize that the sound therapy will decrease the attention paid to the tinnitus percept and thereby decrease the reaction times in the attention task.

Preliminary results of this study will be presented and discussed

# Cochlear implantation for tinnitus – a systematic review

Assouly KKS<sup>1,2,3</sup>, van Heteren JAA<sup>1,2</sup>, Stokroos RJ<sup>1,2</sup>, Stegeman I<sup>1,2</sup>, Smit AL<sup>1,2</sup>

<sup>1</sup>Department of Otorhinolaryngology and Head & Neck Surgery, University Medical Center Utrecht, the Netherlands, <sup>2</sup>UMC Utrecht Brain Center, University Medical Center Utrecht, the Netherlands, <sup>3</sup>Cochlear Technology Centre, Mechelen, Belgium

## Background and Aim

Tinnitus has a high prevalence in the hearing-impaired. Cochlear implantation (CI) is standard of care for patients with severe-to-profound hearing loss when hearing aids provide limited or no benefit. Studies on this topic reported tinnitus reduction as a common side effect of cochlear implantation. The aim of this review is to assess the effectiveness of electrical stimulation with a cochlear implant in patients with tinnitus as a primary complaint.

## Methods

A literature search was performed using the keywords and synonyms of "tinnitus" and "cochlear implantation". Two independent authors identified studies, extracted data, and assessed risk of bias. Original studies reporting outcomes of electrical stimulation by cochlear implantation for severe or incapacitating tinnitus were included. The pre- and post-implantation tinnitus scores on single- and/or multi-item questionnaires of the included studies were extracted.

## Results

In total, 4091 unique articles were retrieved. After screening titles, abstracts and full texts, we included seven articles (105 subjects in total, range: 10-26). All were prospective cohort studies with a considerable risk of bias. A statistically significant tinnitus distress improvement, based on tinnitus questionnaire scores, was found in every study. All tinnitus patients in the included studies had asymmetrical hearing loss or single-sided deafness.

## Conclusion

Our systematic review reveals that electrical stimulation by cochlear implants in patients with tinnitus has a positive effect on tinnitus distress. Nevertheless, only small sample sizes were found and studies showed high risks of bias. Further research seems essential to investigate severe to incapacitating tinnitus as a primary indication for cochlear implantation.



# Specific Forms of Tinnitus

## Effectiveness of dry needling in the annoyance of chronic tinnitus in patients with myofascial trigger points

Carla Alexandra Campagna, Juliana Anauate Alves de Aguiar, Jeanne da Rosa oiticica Ramalho, Laura Garcia Vasconcelos

### Introduction

Tinnitus can be defined as the perception of sound in the ears or in the head in the absence of an external sound source. A recent study in the city of São Paulo found that the prevalence of tinnitus in this population is of 22%. It is a common symptom that may arises from several different etiologies. The suspicion of somatosensory tinnitus occurs whenever an active or passive contraction of the head's and/or neck's muscles is able to modulate its psychoacoustic characteristics (loudness, pitch, location). The phenomenon arises from a dysfunction in the network of neural connections between the auditory and proprioceptive pathways. The treatment of somatosensory tinnitus can be approached in several ways, including the deactivation of myofascial trigger points (MTP). Dry needling (DN) is one of the therapeutic strategies used to deactivate MTP, even though it hasn't been tested before for tinnitus's treatment.

### Objective

To evaluate the efficacy of DN in the treatment of chronic somatosensory tinnitus patients with MTP.

### Methods

After the patients' physical evaluation and determination of the muscles that needed to be treated, the DN was done by the insertion of a long and fine intramuscular needle in the affected area. The needle's mechanical stimulation was used as a physical agent for deactivation of MTP. All patients underwent one weekly session of placebo DN for 4 consecutive weeks, followed by a 15-day washout, and then one weekly session of therapeutic DN for 4 consecutive weeks. The measurement variables used to assess the degree of tinnitus annoyance included the Visual Analogue Scale for tinnitus (VAST) and the THI questionnaire („Tinnitus Handicap Inventory“). The Visual Analogue Scale for pain (VASp) and the Neck Disability Index (NDI) were used to evaluate muscle pain. The Neutone® device was used to measure muscle tension.

### Results

Patients with somatosensory tinnitus and MTP presented a significantly greater decrease in the total THI score and in THI's emotional domain after therapeutic DN when compared with placebo DN. The VAST showed a significantly decrease comparing after with before therapeutic DN; although no difference were observed between placebo and therapeutic DN, there was a tendency of statistical significance for the second.

### Conclusion

The DN therapy technique for MTP in patients with somatosensory tinnitus was effective to reduce THI (total score and emotional domain), as well as VAST.

# Complaints about low-frequency noise: a physical sound or low-frequency tinnitus? An overview of noise measurement data

Berdien De Herdt<sup>1</sup>, Michel Schellens<sup>2</sup>

<sup>1,2</sup>Department Environmental Research, Provincial Institute of Hygiene, Antwerp, Belgium

## Background and Aim

Complainants who are annoyed by a low-frequency sound in their home end up at environmental services demanding to perform low-frequency measurements. The sound is often only perceived by one person and is not audible to the rest of the household. The question raises if it is a physical sound that causes the annoyance. Therefore, the present study investigated eight cases of low-frequency noise complaints by measuring the amount of the unweighted equivalent pressure levels in the low-frequency spectrum. The results were tested against a reference curve of audibility in order to objectify a complaint of low-frequency noise.

## Methods

Sound recordings and measurements were performed in the home of each subject (N=8) and assessed in accordance with the Dutch 'NSG-Low-Frequency Sound Directive (Delft:1999)' using a sound level meter Class 1 (IEC 61672:2013 standard). Calibration took place before each measurement. The measurement position was located at the point where the complainant was annoyed the most. The duration of the measurement consisted of one week. The complainant updated a logbook with the timing of the appearance of the annoyance. After excluding external noises, the amount of the unweighted equivalent pressure levels in the low-frequency spectrum from 20 Hz to 100 Hz were assessed in accordance with the reference curve which is based on the hearing thresholds of a group of normal hearing persons in the age category of 55 years.

## Results

The results show that in one case the complainant was annoyed by a physical sound caused by an environmental source, while in the other cases the measurements were not able to show any sound that could be causing annoyance because the sound levels were situated beneath the reference curve of audibility. A remarkable finding is that the levels of background noise dropped back to very low levels (e.g. 18,1 dB(A)) caused by a lack of ambient noise in the home. The complainants didn't report any hearing impairment based on hearing tests.

## Conclusion

This study showed that in most cases no apparent sound sources causing low-frequency noise were found. Although, as described in literature, the perception of low-frequency noise causes feelings of distress. In order to find a solution it is important to objectivate cases of extraordinary hearing in complainants who live in environments with very low levels of ambient noise, or that the existence of low-frequency tinnitus is examined and recognized by health care professionals.



## Physical symptoms in patients with tinnitus

Sarah Michiels<sup>1,2</sup>

<sup>1</sup>University of Antwerp, Department of Rehabilitation Sciences and Physiotherapy and Department of ENT, head and neck surgery and communication disorders, <sup>2</sup>Antwerp University Hospital, Department of Department of Otorhinolaryngology

### Background and Aim

Many patients with tinnitus indicate that the perception of their tinnitus is not constant and can vary from moment to moment. This tinnitus fluctuation is one of the diagnostic criteria for somatosensory tinnitus (ST), a tinnitus subtype that is influenced by cervical spine or temporomandibular dysfunctions, although various factors have been reported to cause fluctuations in tinnitus, such as stress, anxiety, and physical activity. The aim of this study was to investigate the prevalence of physical symptoms in patients with tinnitus and their influence on the tinnitus perception.

### Methods

A Web-based survey, questioning the presence of physical symptoms in a convenience sample of participants with tinnitus, was launched on the online forum, Tinnitus Talk, managed by Tinnitus Hub. After a general analysis of the physical symptoms present in our survey population, we further analysed the group of participants who were diagnosed by a physician (n=1262). This subgroup was divided into 2 groups, one group diagnosed with ST and another group diagnosed with other types of tinnitus.

### Results

In total, 6115 participants with a mean age of 54.08 years (SD 13.8) completed the survey. Physical symptoms were frequently present in our sample of participants with tinnitus: 4221 participants (69.02%) reported some form of neck pain, 429 (7.01%) were diagnosed with temporomandibular disorders, 2730 (44.64%) indicated they have bruxism, and between 858 and 1419 (14.03%-23.20%) participants were able to modulate their tinnitus by voluntary movements. ST was diagnosed in 154 out of 1262 (12.20%) participants whose tinnitus cause was diagnosed by a physician. Symptoms referring to the known diagnostic criteria were evidently more present in the ST group than in the non-ST group. Additionally, participants with ST more often indicated a negative effect of a bad night's sleep ( $P=.01$ ) and light intensity exercise ( $P=.01$ ).

### Conclusion

Physical activity and movement (disorders) frequently affect tinnitus severity. Head-neck related symptoms are more frequently reported in the ST group, as is the ability to modulate the tinnitus by head or jaw movements. Additionally, participants with ST more often report fluctuations of their tinnitus and reaction to sleeping difficulties and low intensity exercise.

## The effect of orofacial treatment on tinnitus complaints in patients with somatosensory tinnitus: A randomized controlled trial

Annemarie van der Wal, Sarah Michiels, Annick Gilles, Laure Jacquemin, Vedat Topsakal, Vincent Van Rompaey, Paul Van de Heyning, Marc Braem, Corine M. Visscher, Willem De Hertogh

### Background

Subjective tinnitus can be influenced by the somatosensory system, then called somatic or somatosensory tinnitus (ST). ST is pathophysiologically explained by activity in connecting fibers between the dorsal cochlear nucleus (DCN) and the somatosensory nuclei which are located in the medulla. This mechanism can explain the greater prevalence of tinnitus in patients with temporomandibular disorders (TMD) (30.4%-64%), compared to the prevalence in the general population (10-15%), and suggests that TMD treatment might be beneficial for patients with ST.

## Objective

To investigate the additional effect of non-invasive orofacial treatment on tinnitus annoyance in patients with tinnitus and co-existing temporomandibular disorders (TMD) and/or oral parafunctions.

## Methods

Adult patients with a combination of moderate to severe subjective tinnitus (Tinnitus Functional Index (TFI) score: 25 – 90 points) and TMD and/or oral parafunctions such as clenching and bruxism were recruited from the tertiary tinnitus clinic of the Antwerp University Hospital. All patients received information and advice about tinnitus and conservative orofacial treatment consisting of physical therapy. In case of grinding, night time use of occlusal splints were applied by the dentist. Patients were randomized in an early-start therapy group ( $n= 40$ ) and a delayed-start therapy group ( $n=40$ ). In the first 9 weeks, the early-start group received the orofacial treatment, while the delayed-start group entered a wait-and-see period. After 9 weeks, the delayed-start group started with the orofacial treatment.

The effect of the treatment on tinnitus was investigated using the Tinnitus Questionnaire (TQ) and TFI that were documented at baseline, after the wait-and-see period in the delayed-start group, after treatment and after 9 weeks follow-up.

## Results

In total 80 patients were included. In week 9 of the study, the early-start group showed a decrease of 4,1 points in the TQ-score, compared to 0,2 points in the delayed start group. This change in TQ-score was not significantly different between both groups ( $p=0,099$ ). On the other hand, the change in TQ-degree in week 9 of the study was significantly larger in the early start-group compared to the delayed-start group ( $p=0,006$ ). On TFI, a significantly larger decrease (13,8 points) was found in the direct-start group compared to the delayed-start group (5,0 points)( $p=0,042$ ).

## Conclusion

A multidisciplinary non-invasive orofacial treatment was able to reduce tinnitus severity and annoyance in patients with temporomandibular related somatosensory tinnitus.

## Overinterpretation of Research Findings: Evidence of “Spin” in Tinnitus Randomized Controlled Trials

Velde HM<sup>1</sup>, Smit AL<sup>2</sup>, Stegeman I<sup>3</sup>

<sup>1</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Department of Ophthalmology, University Medical Center Utrecht, <sup>2</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Department of Ophthalmology, University Medical Center Utrecht, <sup>3</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Department of Ophthalmology, University Medical Center Utrecht

## Background and Aim

“Spin” refers to reporting practices that could distort the interpretation and mislead readers by being more optimistic than the results justify, thereby possibly changing the perception of clinicians and influence their decisions. Because of the clinical importance of accurate interpretation of results and the evidence of spin in other research fields, the aim of this study was to identify the nature and frequency of spin in published reports of RCTs in tinnitus studies and to assess possible determinants of spin.

## Methods

We searched PubMed systematically for RCTs with tinnitus related outcomes published from 2015 to 2019. Two researchers assessed spin according to predefined criteria for actual and potential spin, concerning the interpretation of results and conclusions in abstracts and full texts of the included papers. A sensitivity analysis for the importance of the items was done.



## Results

Our search identified 628 studies, of which 97 were eligible for evaluation. Spin occurred in all of these articles. The most frequent forms of actual or potential spin identified were (1) no reporting of the point estimate of the outcome in the abstract (59; 61%); (2) no confidence intervals around point estimates in the full text; (3) conclusion not reflecting the reported point estimate of outcome (32; 33%) and no study limitations discussed (32; 33%). Sensitivity analyses of preliminary results showed that type of primary outcome, type of experimental intervention, statistical significance of primary outcome and the use of a report guideline were possible determinants of spin.

## Conclusion

Our results show that spin is an important obstacle for the interpretation of tinnitus studies. Reports of interventions should focus on diminishing spin and there is a necessity to create awareness of the possibility of spin in clinicians.

# Systematic Testable Framework

## Neurofunctional Tinnitus Model Validation to investigate cognitive processes causality in clinical distress stage

I.G. Toostani<sup>1,2</sup>, Z.S. Vaziri<sup>3,1</sup>, E.A.P. Gomes<sup>4,1</sup>, A.C.B. Delbem<sup>1,2</sup>, C.G.C. Barros<sup>5</sup>, J.P. Leite<sup>3</sup>

<sup>1</sup>Neurocognitive Engineering Laboratory, Center of Engineering Applied to Health, Institute of Mathematics and Computer Sciences, University of São Paulo, São Carlos, Brazil; <sup>2</sup>Reconfigurable Computing Laboratory, Institute of Mathematics and Computer Sciences, University of São Paulo, São Carlos, Brazil; <sup>3</sup>Department of Neuroscience and Behavioral Sciences, Ribeirão Preto Medical School, University of São Paulo at Ribeirão Preto, Brazil; <sup>4</sup>Department of Electrical and Computer Engineering, São Carlos School of Engineering, University of São Paulo, São Carlos, Brazil; <sup>5</sup>Department of Otorhinolaryngology, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil;

## Background and aim

Neurofunctional Tinnitus model (NfTM) delivered a testable framework which hypothesized that Conscious Attended Awareness Perception (CAAP) of sourceless sound is necessary to promote tinnitus valence. The model also highlights that frequent co-occurrence of tinnitus perception with negatively-valenced stimuli as well as negative appraisals can increase the negative cognitive-emotional value of the sound leading to distress and annoyance. We performed a numerical data model based on NfTM cognitive processes using the data of a running randomized crossover three-session double-blind study to investigate the mechanisms by which tinnitus loudness results in tinnitus handicaps.

## Method and Material

Forty-seven (N=47) tinnitus patients referred to Hospital of Ribeirão Preto, Medical Faculty-University of São Paulo (HCRP-FMRP-USP) in Brazil participated in this study. Each session, the patients responded to the Tinnitus Severity Questionnaire, Tinnitus handicap inventory, and Major Depression Inventory. The questions related to the cognitive process in the clinical distress stage were selected and included in the analysis. To analyze the data, we performed PROCESS macro for SPSS.

## Results

The Durbin Watson test(1.7) exhibited no autocorrelation in the collected data. Additionally, multicollinearity was not detected in accrued data within the macro, customized model and 5.000 bias-corrected bootstrap samples were selected. A 95% confidence level was chosen to apply a p-value of 0.05. The Bootstrap analysis showed that the indirect effect of tinnitus loudness on tinnitus handicap was respectively mediated by attention, bothersome, and parallel mediators of emotional and cognitive values. In this projected data model, we indicated the bilateral mediatory effects of the cognitive-emotional values on attention and bothersome. The bias-corrected bootstrap confidence interval for the indirect effect was measured entirely above zero. Based on the integrated serial and parallel mediation model, tinnitus loudness mediates there was no evidence that tinnitus loudness had a direct effect on tinnitus handicap ( $c = 0.149$ ,  $p=0.9$ ).

## Conclusion

In the clinical distress stage, the relationship between tinnitus loudness and tinnitus handicap mediates with attention and bothersome affecting cognitive-emotional value. Reciprocally, the cognitive-emotional value can mediate attention and bothersome as well. Additionally, tinnitus loudness alone would not result in tinnitus handicaps. Eventually, the proposed numerical data model provides support for NfTM prediction.

# Tinnitus Assessment

## Objective correlates of tinnitus and cochlear synaptopathy

Chiara Casolani<sup>1,3,4</sup>, James Harte<sup>2,3</sup>, Bastian Epp<sup>1</sup>

<sup>1</sup>Hearing Systems section, Department of Health Technology, Technical University of Denmark,

<sup>2</sup>Eriksholm Research Centre, <sup>3</sup>Interacoustics Research Unit, <sup>4</sup>Oticon

## Aim/background

The aim of this study was to find objective correlates between tinnitus and cochlear synaptopathy, and thereby to be able to identify a specific group of tinnitus sufferers. It is hypothesized that loud sound exposure results in a disruption of the synapses between IHC and AN, which then triggers the degeneration of SGN and the development of tinnitus. To this end, a test battery was developed that combines tinnitus characterization and measures thought to be sensitive to synaptopathy. The test battery was improved in terms of speed to reduce testing time. Preliminary results show that the extensive test battery can be conducted in reasonable time.



## Methods

Twenty sufferers of subjective, chronic and non-pulsatile tinnitus with normal audiometric hearing (tinnitus group) will be compared to an equally sized age and hearing loss-matched control group. The test included in the battery were: high frequency audiometry (HFA), tinnitus likeness (pitch and loudness matching), psycho-physical tuning curve (PTC), tinnitus masking curve (TMC), wideband tympanometry, middle ear muscle reflex (MEMR), and adaptive categorical loudness scaling (ACALOS). A Bayesian procedure was adopted to reduce measurement time for the HFA, PTC and TMC.

## Results

Preliminary results show a high variability across listeners in the tinnitus group, besides similar, audiometrically normal audiograms. Results of the optimized HFA were comparable to classical HFA. The PTC showed a variability across listeners similar to results found in the literature with sharp tuning for some and broad or no tuning for other listeners. The MEMR was found to be a fast and robust measure in almost all listeners. Overall, the preliminary results are consistent with results reported for each of the included measures in literature.

## Conclusions

The test battery, despite the high number of tests, can be completed in less than 2 hours, thanks to the application of the Bayesian procedure. Collection of these measures, in the light of recent developments within the field of synaptopathy seems to be a promising step towards identification of a subgroup of tinnitus sufferers. If successful, this will aid in the development of specific tinnitus treatment procedures for this group of tinnitus sufferers.

## Funding

„This project has received funding from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (grant agreement n° 764604)”

## Skarzynski Tinnitus Scale: validation of a brief and robust tool for assessing tinnitus in a clinical population

Skarżyński Henryk<sup>1</sup>, Raj-Koziak Danuta<sup>1</sup>, Gos Elżbieta<sup>1</sup>, Kutyba Justyna<sup>1</sup>, Skarżyński Piotr Henryk<sup>1,2,3</sup>

<sup>1</sup>World Hearing Center, Institute of Physiology and Pathology of Hearing, <sup>2</sup>Heart Failure and Cardiac Rehabilitation Department, Second Faculty, Medical University of Warsaw, Warsaw, Poland, <sup>3</sup>Institute of Sensory Organs, Warsaw, Poland.

## Background and Aim

Tinnitus is an auditory sensation generated by abnormal activation within the auditory system when no external sound is present. It is commonly described by the sufferers as “ringing in the ears”, but it can take many forms, such as buzzing, hissing, chirping, and others. Many tinnitus scales are available, but according to systematic reviews not all of them meet the criteria of good measures. In Poland, cross-cultural adaptation and validation have been made for three tinnitus questionnaires: the Tinnitus and Hearing Survey (THS-POL), Tinnitus Handicap Inventory (THI-POL), and Tinnitus Functional Index (TFI-PI); in the current literature these three have been found to be the most robust among the available tools. However, all these questionnaires also have certain limitations. The aim of the current study was to present a psychometric data of a new brief and reliable questionnaire that could be conveniently used for evaluating tinnitus complaint in adults (either with normal or impaired hearing)—Skarzynski Tinnitus Scale (STS).

## Methods

The study included 125 participants with at least 1 month of tinnitus duration. All participants were asked to complete the STS, Tinnitus and Hearing Survey (THS), Tinnitus Functional Index (TFI), Tinnitus Handicap Inventory (THI), and Beck Depression Inventory.

## Results

As a whole, the STS has excellent reliability ( $ICC=0.94$ ) and good internal consistency ( $\alpha=0.91$ ). The results of EFA and content analysis of wording of the items justified the three-factorial structure. The convergent validity was proven by a significant positive correlation with THI, TFI and THS Subscale A scores. Additionally, the authors proposed norms dividing the results into four tinnitus severity grades.

## Conclusions

Statistical analysis shows that STS is a brief but robust tool well-suited to clinical practice. A feature of STS is that it takes into account the impact of tinnitus on the patient's psychological (emotional, cognitive) and functional domains as well as their ability to cope with tinnitus-related distress.

## Relationship between tinnitus loudness measure by Visual Analogue Scale (VAS) and psychoacoustic matching of tinnitus loudness

Raj-Koziak Danuta<sup>1</sup>, Gos Elżbieta<sup>1</sup>, Kutyba Justyna<sup>1</sup>, Karpiesz Lucyna<sup>1</sup>, Niedziałek Iwona<sup>1</sup>, Włodarczyk Elżbieta<sup>1</sup>, Skarżyński Henryk<sup>1</sup>, Skarżyński Piotr Henryk<sup>1,2,3</sup>

<sup>1</sup>World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw/Kajetany, <sup>2</sup>Heart Failure and Cardiac Rehabilitation Department, Medical University of Warsaw, Warsaw, <sup>3</sup>Institute of Sensory Organs, Warsaw/Kajetany

## Background and Aim

The difficulty with subjective tinnitus is that there are no objective measures, and so the patient's description of their symptoms is the only source of information. The clinical value of the psychoacoustic method of matching of tinnitus pitch and loudness is rather equivocal, but is still used as a counseling tool to assess tinnitus numerically. A patient's own description rating of tinnitus loudness measured on a Visual Analog Scale (VAS) is another possible approach to estimate either the patient's tinnitus perception (loudness). The aim of the study was to check correlation between measurements of tinnitus loudness based on Visual Analogue Scales (TL-VAS) and tinnitus loudness matching psychoacoustically (TL-AM) in three patient groups: with normal hearing and with either unilateral or bilateral hearing loss.

## Methods

140 adult patients in mean age  $M=50.01(SD14.24)$  with chronic tinnitus (46.4% women, 53.6% men) were included into the study. All participants first completed a Visual Analogue Scale measurement of tinnitus loudness. The psychoacoustic loudness and frequency of each patient's tinnitus was also evaluated.

## Results

Correlation between TL-AM and TL-VAS in all the patients was statistically significant but weak ( $r=0.17$ ;  $p=0.039$ ). There was no significant relationship in the group of patients with unilateral hearing loss ( $r=0.06$ ;  $p=0.733$ ) or in the patients with bilateral hearing loss ( $r=0.14$ ;  $p=0.270$ ). In normal hearing patients the correlation was statistically significant ( $r=0.46$ ;  $p=0.001$ ).

The regression model was statistically significant in the group of subjects with normal hearing where nearly 23% of the variability in TL-VAS was explained by TL-AM. Standardized regression coefficient was significant only in this group ( $b=0.46$ ;  $p=0.001$ ). A high level of tinnitus loudness measure by VAS could be predicted from a high level of tinnitus loudness measure by psychoacoustic matching, but only in the case of subjects with normal hearing.

## Conclusion

Measurements of tinnitus loudness based on Visual Analogue Scale could be a useful tool in diagnosing patients and measuring effects of treatment only in normal hearing patients.



## **Tinnitus in Brazilian primary health care: perspective of health professionals**

Carla Salles Chamouton, Helenice Yemi Nakamura

University of Campinas (UNICAMP)

### **Background and Aim**

The Brazilian National Attention to Hearing Health Policy previses activities in primary care, once it is the basis of Unified Health System and includes actions from health promotion to the assistance itself. However, hearing issues are still concentrated in the specialized services. Among the hearing disorders, tinnitus affects over 15% of the general population and negatively affects the individuals' lives, requiring its approach to a complete line of health care. The objectives of this study were to investigate the knowledge of tinnitus, the perception of the actions and the care network from the perspective of primary health care professionals.

### **Methods**

This is a quantitative and qualitative research, with a sample of 170 health professionals, including doctors, nurses and nursing technicians of the primary health care of the city of Campinas, in the state of São Paulo. The data were collected by semi-structured interviews transcribed for analysis. The depositions were categorized according to the repetition and relevance criteria. For the analysis, it was used the Discourse of the Collective Subject data processing technique, and the results were obtained by data organization operations in text form.

### **Results**

The results show that primary health care professionals do not consider the hearing related disorders in their daily basis, still have little knowledge about tinnitus and do not consider possible to include tinnitus or hearing related activities in their routine.

### **Conclusion**

It is necessary to invest in the professionals' continued education due to the lack of knowledge that was shown by the results, and complaints, such as tinnitus, still need a more broad treatment, especially in the primary health care.

## **Impact of Choice of Test Stimulus on Pitch Matching Performance: Pure Tone versus Narrow Band Noise**

Andreas Wollbrink<sup>1</sup>, Christian Dobel<sup>2</sup>, Christo Pantev<sup>1</sup>

<sup>1</sup>Institute for Biomagnetism and Biosignalanalysis, University of Münster, P.C. D-48149, Germany,

<sup>2</sup>Department of Otorhinolaryngology, University Hospital Jena, Friedrich-Schiller-University of Jena, P.C. D-07740 Jena, Germany

### **Background and Aim**

Recent electrophysiological studies indicate that in the case of tonal tinnitus a population of neighbouring neurons is involved in the generation process of the sensation. Typically, patients perceive their tinnitus as a sound having a prominent centre frequency with some spectral extent. Currently, the tinnitus frequency is assessed via pitch matching procedures including pure tones as test stimuli. The question arises, why not to use narrow band noise (NBN) instead of that? To investigate this, we first evaluated the pitch matching performance of healthy subjects.

## Methods

Thirty participants (13 females) suffering from chronic tinnitus performed the frequency-matching tasks. In a recursive two alternative choice testing, driven by a computer based automated procedure, the subjects were asked to adapt the pitch of two sounds being delivered via headphones. In a crosswise design, NBNs and pure tones served both as target and as test stimuli. To evaluate participants' performance, we used the difference between center frequency of test and target sound as a measure.

## Results

A one-factorial ANOVA applied to group pitch-matching results with four levels (all combinations of pure tone or NBN being test and target sound) was significant ( $F(3, 87) = 5.031; p=.003$ ). Thus, in general the pitch matching performance differed depending on the signal type of target and test sound. Based on preplanned comparisons matching two sinusoidal sounds produced the smallest errors (estimation of contrast: .947; standard error: .322;  $p=.006$ ) whereas matching a sinusoidal sound to an NBN resulted in the largest errors (estimation of contrast: -1.064; standard error: .342;  $p=.004$ ) in comparison to all other matching conditions. Subjects' performance did not differ when matching an NBN to either a pure tone or an NBN.

## Conclusion

We were able to demonstrate, in a group of healthy subjects, that the performance in pitch matching of two sounds strongly depends on the spectral characteristic of the signals to be compared. According to the widely accepted neurophysiological basics underlying tinnitus, it is rather unlikely that tinnitus sensation is a pure tone but is characterized by a spectral content of different extent which properties are featured best by an NBN. With regard to the outcome of this study we therefore consider an NBN as the more valuable test sound to be used in pitch matching in tinnitus patients. This could enable researchers and clinical investigators to measure the tinnitus pitch and its spectral contents more reliably (Henry, 2016).

## Differences between post-stimulus suppression of tinnitus and tinnitus-mimicking sound

Pierre Bourez, Philippe Fournier & Arnaud Noreña

UMR CNRS 7260, Laboratoire de Neurosciences Sensorielles et Cognitives (LNSC) - Aix-Marseille – Université, Centre Saint-Charles, Marseille, France

## Background and Aim

Tinnitus masking (TM) and residual inhibition (RI) of tinnitus are two methods to investigate how external sounds interact with tinnitus: TM provides insight on the fusion between the external sound activity and the tinnitus related activity while RI provides insight on how the external sound might suppress the tinnitus related activity for a period of time. Differences in the level of masking between tinnitus masking and the masking of an external tone with characteristics similar to tinnitus (pitch and loudness) have previously shown a high level of heterogeneity. The difference in post-stimulus suppression between the two, that is, residual inhibition for the former, and forward masking for the latter, has never been explored.

## Methods

This study aimed to investigate differences in minimum masking levels (MMLs) and in minimum residual inhibition levels (MRILs) for two different targets: tinnitus and an external tone mimicking tinnitus. Pulsed white noise and pulsed narrow-band noises (1 kHz, frequency of the hearing loss slope, tinnitus frequency) were randomly presented diotically and dichotically to 20 tinnitus participants and 20 controls.



## Results

The MML values obtained when the tinnitus was the target were slightly higher than when the mimicking tone was the target, for both within and between group comparisons (mean MML diff: 5 dB, SD: 7; 1.4 dB, SD: 10 respectively). The MRILs were significantly lower when the tinnitus was the target compared to the mimicking tone, for both within and between group comparisons (mean MRIL diff: 15 dB, SD: 12; 25 dB, SD: 10, respectively). The results showed no significant differences between the diotic and dichotic conditions.

## Conclusion

Overall, it was much easier to produce a post-stimulus suppression for tinnitus than for a real sound with similar psychoacoustic properties. These results corroborate other findings suggesting that the tinnitus-related neural activity is very different from the stimulus-related neural activity. The consequences of these findings will be discussed.

# Tinnitus Sounds Description by Tinnitus Patients: Preliminary Results

Emre Gurses, Songul Aksoy

Hacettepe University, Faculty of Health Science, Department of Audiology, Ankara, Turkey

## Background

Patients often tend to express their tinnitus complaints in different ways. One of these ways is the use of a metaphor to describe the frequency they perceive. For this reason, it will be very useful for the clinician to ask the patients if they resemble any sound they have heard before describing their tinnitus.

## Objective

This preliminary study aims to determine metaphors used to describe tinnitus by tinnitus patients and classify them according to tinnitus pitch.

## Materials And Methods

A total number of 45 participants (21 Male -20 Female), mean age:  $46.78 \pm 13.11$  (Min: 20, Max:72), with tinnitus (Tinnitus Handicap Inventory:  $58.73 \pm 21.95$ ) were included in this study. 10 participants had normal hearing, 9 participants had flat hearing loss, 10 participants had high-frequency hearing loss, 7 participants had low-frequency hearing loss, 5 participants had very high-frequency hearing loss, 4 participants had single-sided deafness. Tinnitus sounds description classified with and without hearing status.

## Results

Regardless of hearing status the most described sounds were whistle, bell, firefly and buzzing. Buzzing, cricket, signal, bell, and whistle were the most stated sounds for low frequency, flat, high frequency, very high-frequency hearing loss and normal hearing respectively. For SSD, completely complex sounds such as cicada, wave sounds, washing machine were described.

## Discussion

Currently there are more than 50 apps for tinnitus masking therapy (1). Natural and artificial sounds are mostly stated in these apps. However low stated sounds weren't found in these apps. Therefore, besides the assessment of tinnitus, all sounds descripted by tinnitus patients in this study, should be added to the apps.

## Reference:

- (1) Sereda, M., et al., Mobile Apps for Management of Tinnitus: Users' Survey, Quality Assessment, and Content Analysis. JMIR mHealth and uHealth, 2019. 7(1): p. e10353.

## The Neuroscience of Tinnitus in Humans: A Symposium in Memory of Dr. Larry E. Roberts

Phillip E. Gander, Brandon Paul

Tinnitus is a complex phenomenon with many different presentations, multiple possible causes, and a variety of ways in which a person reacts to it. Research on tinnitus mirrors this complexity by attempting to pinpoint neural mechanisms and etiologies, obtain reliable measurement, and discover effective treatments and therapies. Larry Roberts was a voice that united these perspectives. He strived to paint a more complete picture of the manifestation of tinnitus from the research that emerged over the last 20 years. This interdisciplinary symposium will honor Larry by covering a breadth of topics that were influenced by his work. Speakers will present on neural correlates and potential neural markers of tinnitus, the difficulty and necessity of psycho-physical and subjective measurement, risk factors and epidemiology, the use of sound and music training to understand the neural plasticity behind tinnitus, and current hurdles and breakthroughs in clinical translation. In particular, the speakers will identify and prioritize gaps in our current knowledge, highlight potential new avenues for human research, and consider parallels between human and animal studies. The expected outcome of the symposium is to achieve a better alignment of the diverse perspectives on tinnitus research in humans, and to celebrate the life of Larry Roberts.

### A lot to like: More to tinnitus measurement than pitch matching. – A tribute to Larry Roberts

Grant D Searchfield

Director Hearing and Tinnitus Clinic, Deputy Director Eisell Moore Centre: research into hearing and balance disorders, Faculty of Medical and Health Sciences, University of Auckland, New Zealand.

Larry Roberts understood the complexity of tinnitus. He recognised that understanding how tinnitus sounded was important to unravelling the pathophysiology of tinnitus. The psychoacoustics of tinnitus had fallen somewhat to the periphery of tinnitus research by the early 2000's. New developments in electrophysiology and neural imaging had displaced tinnitus matching as the primary "objective" research tool. Larry recognised the importance of linking peripheral changes demonstrated in the audiogram with the perception of tinnitus as a sound. Larry was an early advocate for a likeness approach to measuring the tinnitus spectrum and pioneered the concept of residual inhibition functions related to the tinnitus spectrum. He was a leader in a movement towards more complex psychoacoustic characterisation of tinnitus. This presentation will focus on the role of ecological psychoacoustics in the evaluation of tinnitus and the role of pitch matching, likeness measures and matching of perceived location in assessing tinnitus. The role of psychoacoustics in a precision approach to sound-based treatments of tinnitus will be introduced. Persistence and remission of tinnitus and sound intolerance among adolescents: may hidden synaptic injury repair?

### Persistence and remission of tinnitus and sound intolerance among adolescents: may hidden synaptic injury repair?

Tanit Ganz Sanchez<sup>1</sup>, Larry Evans Roberts<sup>2</sup>

<sup>1</sup>University of São Paulo School of Medicine; Institute Ganz Sanchez, São Paulo, Brazil, <sup>2</sup>McMaster University, Ontario, Canada

#### Background and Aim

Tinnitus may reflect hidden cochlear synaptic injury that does not express in the audiogram, but leads to neuroplastic changes in auditory pathways that, in turn, reduce tolerance to sounds. Such injury may follow the exposure to loud sounds. The aim of this presentation is to resume the relevant results of 2 sequential studies performed in collaboration with Larry Roberts to estimate the prevalence of tinnitus and reduced tolerance to sounds among adolescents and to observe them one year later.



## Methods

In Study 1, 170 adolescents were evaluated by using a questionnaire about tinnitus and reduced tolerance to ordinary sounds and by psychoacoustic measurements in a sound booth (audiometry to 16 kHz, Loudness Discomfort Levels - LDL - and tinnitus pitch / loudness matching). Tinnitus perceived inside the booth, not only shown in the questionnaire, was called "confirmed tinnitus". In Study 2, 54 adolescents returned voluntarily one year later to repeat the measurements.

## Results

In Study 1 (n=170):

- a) 93 (54.7%) students reported prior experience with tinnitus by questionnaire, and 49 (28.8%) presented confirmed tinnitus. Pitch / loudness matching corresponded with those reported by adult chronic tinnitus sufferers.
- b) LDL was the single exam to discriminate between adolescents with or without confirmed tinnitus, being 11.3 dB lower in the first group ( $p < 0.00001$ ). Risky listening habits were equally prevalent in both groups.

In Study 2 (n=54):

- c) Out of the 14 subjects with confirmed tinnitus in Study 1 who returned for Study 2, 6 (42.9%) remained with confirmed tinnitus in the booth ("persistent tinnitus") and 8 (57.1%) did not have tinnitus anymore ("remitting tinnitus").
- d) LDL remained reduced by 17.2 dB in cases of persistent tinnitus ( $p < 0.0001$ ) and normalized in remitting cases.

## Conclusions

There was a high prevalence of tinnitus confirmed by audiometric assessment of our adolescents (28.8 %). Tinnitus and reduced sound tolerance could feature early indication of vulnerability to hidden synaptic injury that is prevalent among adolescents, hidden from the audiogram, and expressed following exposure to high level environmental sounds. However, there was a notable remission of confirmed tinnitus one year later (57.1%). LDL decreased in cases with confirmed / persistent tinnitus and returned to normal levels when tinnitus remitted. The strong relationship between the presence of both symptoms poses a challenge for future hearing health. The relationship between their spontaneous remissions may signal a possible synaptic repair, which has been reported in animal models.

# Citizen Science

## The Power of an Online Community – How Tinnitus Hub Facilitates Citizen Science

Hazel Goedhart<sup>1</sup>, Markku Vesala

Tinnitus Hub

### Background and Aim

Online communities are gaining in strength and presence. In particular, patient forums are becoming relevant stakeholders in health research. Tinnitus Hub manages the online support forum Tinnitus Talk. With over 30,000 members and millions of visitors per year, Tinnitus Talk has amazing potential for Citizen Science.

Members of the Tinnitus Talk forum have, over the past years, engaged in research through public discussion threads, working groups/panels, surveys (crowdsensing), funding of research, clinical trial recruitment, and dissemination of research outcomes.

Tinnitus Hub hereby presents its newly launched project Tinnitus Quest, as a means for the Tinnitus Talk community to steer the research field in a direction that fits the community's needs and expectations.

## Methods

As part of Tinnitus Quest, we will organize a recurring online community voting process to identify which published tinnitus research papers are of most value to patients. The outcomes of this voting process will be translated into concrete recommendations for the scientific community regarding which areas of research should take precedence. The project will also offer channels for researchers to directly involve patients in various phases of the research cycle.

## Results

Results are very preliminary at this point. Several researchers have pledged their support to the project, including the TRI staff. A poll has demonstrated that tinnitus patients want to be involved early on in the research cycle and be able to influence research priorities. Furthermore, a first round of online voting on newly published tinnitus research papers has demonstrated sufficient appetite for this kind of patient involvement, with several hundred people casting a vote. The pilot voting round has also made clear the importance of optimizing the online environment to facilitate this type of engagement and presenting the research in an easily digestible way for a lay audience.

## Conclusion

The online patient community Tinnitus Talk holds enormous untapped potential for Citizen Science. Preliminary results demonstrate that community voting on research publications is a viable method of engagement. Tinnitus Hub will – over the course of 2020 – continue to refine its methods for facilitating community voting. Voting results will be analyzed and aggregated and presented to the wider patient and research communities. Through Tinnitus Quest, we hope to transform the tinnitus research field by making it truly patient-driven.

## Assessing content validity of concentration instruments for tinnitus clinical trials: a focus group involving patients and researchers

Maryam Shabbir<sup>1</sup>, Michael A. Akeroyd<sup>1</sup>, Deborah Hall<sup>1,2 3,4</sup>

<sup>1</sup>Hearing Sciences, Division of Clinical Neuroscience, School of Medicine, University of Nottingham, Nottingham, UK, <sup>2</sup>NIHR Nottingham Biomedical Research Centre, Nottingham, UK, <sup>3</sup>Nottingham University Hospitals NHS Trust, Queens Medical Centre, Nottingham, UK, <sup>4</sup>University of Nottingham Malaysia, Selangor Darul Ehsan, Malaysia

## Introduction

The Core Outcome Measures in Tinnitus (COMiT) initiative recently recommended a minimum standard of five outcomes when designing a clinical trial to assess the efficacy of sound-based interventions: ability to ignore, concentration, quality of sleep, sense of control and tinnitus intrusiveness (doi: 10.1177/2331216518814384). A systematic review was carried out to gather existing measurement instruments, that might be appropriate for assessing concentration in adults with chronic subjective tinnitus. The current study assesses the content validity of the two free-of-cost self-report instruments, identified from the systematic review, using the COSMIN guidelines.



## Material and Method

Thirteen cognitive experts and ten members of the public with tinnitus were invited to attend the focus group on 8th October 2019. The COSMIN criteria and rating system for evaluating the content validity of measurement instruments was used for two self-report measurement instruments identified from the systematic review, PROMIS Item Bank v2.0 – Cognitive Function and Dundee Stress State Questionnaire (DSSQ). The content validity criteria were divided in three categories; relevance, comprehensiveness and comprehensibility. Group consensus criteria was set at 80% (e.g. 4/5, 5/6... participants).

## Results

A total of six participants took part in the focus group; three cognitive experts and three members of the public with tinnitus. Group consensus was only reached for 4 out of the 8 criteria for both, the PROMIS and DSSQ questionnaires.

## Conclusion

PROMIS and DSSQ are not valid for our construct (the instruments do not measure our working definition of concentration) and population and therefore we have decided to develop a new questionnaire to assess concentration for adults with chronic subjective tinnitus. The next step will use an online survey to ask the population what various difficulties they face relating to concentration due to their tinnitus to help inform and develop items on the questionnaire.

# Physical Symptoms in Patients with Tinnitus: From Subtyping to Cure

## Somatosensory tinnitus: Who gets cured?

Tanit Ganz Sanchez

University of São Paulo School of Medicine and Instituto Ganz Sanchez

## Background and Aim

For the last few years, we have researched the long lasting total remission of tinnitus in a prime study. It consists of finding and interviewing ex-tinnitus sufferers who consider themselves cured, so as to verify the common characteristics regarding their past history of tinnitus and which treatments favored the remission. The objective of this presentation is to describe the subset of cases with somatosensory tinnitus.

## Methods

Due to lack of definition about total remission of tinnitus, our prime study has included patients with the following criteria: any etiology of tinnitus that had been daily present for at least 3 months and has not been perceived for at least the past 6 months. Such cases were initially selected from our databank and then expanded as we communicated our research to other health professionals from whom we have received their similar cases. All subjects were interviewed by the same team. We excluded subjects who were in a comfortable level

of masking or habituation. From the inclusion on, subjects have been followed-up every 6 months to check whether total remission was kept stable. So far we have found 149 subjects, have interviewed 120 and have selected 108 cases with total remission that were described elsewhere. Out of all the etiologies, 6 fit the criteria for somatosensory tinnitus.

## Results

The subset of patients who had somatosensory tinnitus was composed by 5 females and 1 male, with average age 43.1 years (25 to 58 years). The duration of tinnitus ranged from 6 to 36 months (average 19.6 months), and the extent of total remission varied from 6 to 480 months (average 108.1 months). Localization was equally distributed between uni and bilateral cases. The type of sound was similar to a pure tone (n=4) or narrow band sound (n=1) or rhythmic (n=1). Annoyance with tinnitus was evaluated by using the visual analogue scale, and it averaged 7.1 (5 to 10). Remission occurred gradually in 4 cases and suddenly in 2. Three subjects reached this status by trying up to 2 treatment options.

## Conclusion

The growing sample of subjects that reached the long term total remission of tinnitus so far contains a small sample of cases with somatosensory tinnitus. Analysis of such patients hasn't revealed defined patterns for age, gender, localization, type of sound or degree of annoyance when tinnitus was present. In other words, total remission remains an unpredictable condition for patients with somatosensory tinnitus.

# Miscellaneous

## UNITI - a new EU-funded project towards a unification of tinnitus treatments and interventions

Winfried Schlee<sup>1</sup>, Susanne Staudinger<sup>1</sup>, Stefan Schoisswohl<sup>1</sup>, Berthold Langguth<sup>1</sup>, Myra Spilopoulou<sup>2</sup>, Rüdiger Pryss<sup>3</sup>, Dimitris Koutsouris<sup>4</sup>, Antonio Lopez-Escamez<sup>5</sup>, Ilias Trochidis<sup>6</sup>, and the UNITI team

<sup>1</sup>University of Regensburg, Germany, <sup>2</sup>Otto-von-Guericke-University Magdeburg, Germany,

<sup>3</sup>University of Würzburg, Germany, <sup>4</sup>Institute of Communication and Computer Systems, Greece,

<sup>5</sup>Universidad de Granada, Spain, <sup>6</sup>Vilabs Ltd., Cyprus

The EU is funding a new collaborative project entitled 'Unification of Treatments and Interventions for Tinnitus Patients' (UNITI, grant no. 848261). The overall aim of the UNITI project is to deliver a predictive computational model based on existing and longitudinal data attempting to address the question, which treatment approach is optimal for a specific patient group based on specific parameters. Clinical, epidemiological, medical history, genetic and audiological data, including signals reflecting ear-brain communication, will be analysed from existing databases. Predictive factors for different patient groups will be extracted and their prognostic relevance will be validated in an RCT in which different groups of patients will undergo a combination of therapies targeting both, auditory and central nervous systems.



**Analysis of existing data:** Results of existing clinical studies will be analyzed to identify subgroups of patients with specific treatment responses and to identify systematic differences between the patient groups of the participating clinical centers.

**Genetic and biomarker analysis:** High throughput Whole Exome Sequencing (WES) will be done in well-characterized chronic tinnitus cases, together with Proximity Extension Assays (PEA) for the identification of blood biomarkers for tinnitus.

**Randomized control trial:** A total sum of 500 patients will be recruited at five clinical centers across Europe comparing single treatments against combinational treatments. The four main treatments are: CBT, hearing aids, sound stimulations and structured counseling.

**Decision support system:** A decision support system will be implemented, which integrates all available parameters (epidemiological, medical history, clinical, audiology, genetics and socioeconomic) to suggest specific examinations and the optimal intervention strategy based on the collected data.

**Financial estimation analysis:** A cost effectiveness analysis for the respective interventions will be calculated to investigate the economic effectiveness of the interventions based on quality-adjusted life years.

## Towards a positive perspective on tinnitus

Charlotte Bigras<sup>1,2</sup>, Annelies Bockstael<sup>1</sup>, Nathalie Gosselin<sup>2,3</sup> & Sylvie Hébert<sup>1,2</sup>

<sup>1</sup>School of Speech Language Pathology and Audiology, Université de Montréal, <sup>2</sup>Center of Research on Brain, Language and Music (CRBLM), <sup>3</sup>Department of Psychology, Université de Montréal

### Background and Aim

Recent findings highlight the role of attentional mechanisms in the development and persistence of tinnitus. People with tinnitus generally perform worse than controls in attention-based tests. However, a commonly accepted theory in tinnitus generation is precisely an increased sensitivity for low-level input. We hypothesized that the key aspect for these seemingly contradictory findings in tinnitus is the distinction between foreground/background sounds. Here we investigate whether or not adults with tinnitus are more able than controls to scan auditory information while focusing on a non-auditory (visual) task, in a dual-task paradigm.

### Methods

Thirteen tinnitus participants and 35 control participants without tinnitus were asked to respond to irregularly paced background sounds in four test conditions with increasing difficulty (primary tasks): (1) detecting simple tones, (2) classifying sounds as animal/non-animal sounds, (3) classifying sounds with emotional characteristics, and (4) understanding speech in noise. A visual (secondary) task consisted in the presentation of letters on a screen and participants had to respond to the letter "X" by pressing the space bar. Interstimulus intervals (ISI) were 1 or 2 seconds. The digit span test (forward and backward) and the HADS and THI questionnaires were also administered.

### Results

Participants with tinnitus were less accurate than controls at classifying the „happy“ emotion in the auditory modality on the emotional classification task. No other differences were observed between groups regarding accuracy or reaction times in either modality. Performance was generally better for the auditory task, although a ceiling effect was observed in this modality. Reaction times were on average shorter for the visual modality. An interaction was observed between ISI duration and modality: longer ISIs favoured better performance and shorter reaction time in auditory tasks while shorter ISI favoured shorter reaction time in visual modality. No difference were observed between groups on the digit span test scores and HADS questionnaire.

## Conclusion

Performance of tinnitus participants was worse than controls' at classifying the "happy" emotion, although they were neither slower nor less accurate on other tasks in a dual-task attention paradigm. The ceiling effect on performance may explain the lack of difference between groups. An in-depth investigation of the role of top-down cognitive control mechanisms in the development and persistence of tinnitus, using tasks with higher levels of difficulty, could allow a better understanding of the cognitive difficulties not found here but often reported by tinnitus sufferers.

## Towards a programme theory of tinnitus support group interventions: a systematic review and realist synthesis

Carla Salles Chamouton<sup>1,2</sup>, Helenice Yemi Nakamura<sup>1</sup>, Camila Lima Nascimento<sup>1</sup>, Magdalena Sereda<sup>1</sup>, David M. Baguley<sup>1</sup>, Derek J. Hoare<sup>1</sup>

<sup>1</sup>University of Campinas (UNICAMP), <sup>2</sup>University of Nottingham

## Background and Aim

Tinnitus is the experience of hearing sounds (commonly ringing, hissing, or buzzing) in the ears or head that are not associated with any real external sound source. It is most often linked to hearing loss and affects over 10% of the population. For 1-2% of people it has a significant negative effect on quality of life. Support groups are one management option open to most people with tinnitus. These groups can be led by either clinicians or non-clinical members. Survey data suggests many clinicians refer tinnitus patients to local support and that most people who take part in support groups perceive benefit such as learning (from shared stories and practical ideas for coping) and gaining a sense of reassurance. To date however there has been no theory driven approach to understand how tinnitus support groups work; what the mechanisms are; and how they relate to the outcomes that people report.

We conducted a realist review in order to develop a theoretical model of support group benefit.

## Methods

Electronic database were searched using the terms support group, self-help group, persistent, chronic disease\*, noncommunicable disease\*, non-communicable disease\*, medically unexplained symptom\*, and long-term condition\*. Studies were screened according to inclusion/exclusion criteria, data of interest extracted, and the quality of the included studies was appraised using a mixed methods appraisal tool. Data were subjected to a realist synthesis containing the contexts (C), mechanisms (M) and outcomes (O), and general context-mechanism-outcome configurations (CMOCs) found in the studies.

## Results

Results show individual and group based mechanisms that function regardless of the context in which the group is included and therefore enable individual and group outcomes. Further analyses linking components and interactions with outcomes of support group participation will be presented.

## Conclusion

A support group can be an option for people with long-term health conditions in general and tinnitus in particular, due to the many coping tools that can be developed by the individuals and the group itself. More studies in the topic are needed for further information in specific contexts and mechanisms. This realist review provides a framework for designing and/or evaluating support groups for tinnitus.



## **Effect of yoga training on the tinnitus induced distress**

Niedziąłek Iwona<sup>1</sup>, Raj- Koziak Danuta<sup>1</sup>, Kutyba Justyna<sup>1</sup>, Milner Rafał<sup>1</sup>, Wolak Tomasz<sup>1</sup>, Ganc Małgorzata<sup>1</sup>, Gos Elżbieta<sup>1</sup>, Skarżyński Henryk<sup>1</sup>, Skarżyński Piotr Henryk<sup>1,2,3</sup>

<sup>1</sup>World Hearing Center, Institute of Physiology and Pathology of Hearing, <sup>2</sup>Heart Failure and Cardiac Rehabilitation Department, Second Faculty, Medical University of Warsaw, Warsaw, Poland, <sup>3</sup>Institute of Sensory Organs, Warsaw, Poland

### **Background and Aim**

There is increasing interest in the potential of yoga as an intervention for mental health concerns. Yoga is a multi-dimensional system of health and well-being that focuses on the functioning of the mind, with multiple mind-body practices including physical postures and movements, breathing exercises, relaxation, mindfulness, and meditation. The nervousness, sleep disorders, lack of effective rest, and concentration are symptoms often associated with tinnitus.

The aim of the study was to assess the effect of yoga training on tinnitus-related distress.

### **Methods**

The study addressed the efficacy of 12 weeks of yoga training in treating 25 patients with chronic tinnitus. A control group comprised 13 people reporting chronic tinnitus. All participants were assessed with the Tinnitus Functional Index. Ten of the patients underwent magnetic resonance imaging (MRI) before and after yoga training. MRIs of the subjects were acquired using a 3 T S Tim Trio VB17 whole-body magnetic resonance scanner with a 12-channel head matrix coil. Free Surfer 5.3 was used to derive measurements of individual brain regions. Analysis was carried out with the standard pipeline in Volume Based Stream.

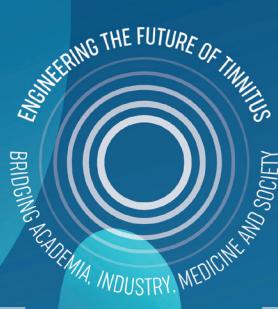
### **Results**

After the 12-week yoga training course the TFI global score had significantly decreased in the study group, while in the control group it was about the same at the initial and follow-up measurements.

The results of segmenting MRI images showed that there were significant changes ( $-5.4\%$ ,  $p < 0.0018$ ) in the thickness of the right anterior circular sulcus of the insula. There was also an increase of white matter volume in the right paracentral area ( $4.57\%$ ,  $p < 0.04$ ) which controls motor and sensory innervation of the contralateral lower extremity.

### **Conclusion**

Yoga training has good potential to improve the daily functioning of patients with chronic tinnitus. Yoga exercises can be considered as one of several supportive therapies for patients with chronic tinnitus.



## 13<sup>TH</sup> TINNITUS RESEARCH INITIATIVE CONFERENCE 8 - 11 JUNE 2021 | TRINITY COLLEGE DUBLIN



TINNITUS RESEARCH INITIATIVE



PLATINUM SPONSOR



Trinity College Dublin  
Coláiste na Tríonóide, Baile Átha Cliath  
The University of Dublin

# TRI Conference 2021 – Invitation by the Organizers

Céad mile fáilte! A hundred thousand welcomes to the 13th Annual Tinnitus Research Initiative Conference at Trinity College Dublin, Ireland from June 8 to 11, 2021. Over the years, the annual TRI conference has attracted scientists, physicians, healthcare professionals and industrialists to influence the tinnitus field. This year we envision a unique and historical extension of this gathering to tinnitus patients and caregivers, inviting them to significantly contribute to shaping the field for the generations to come.

While tinnitus is a common symptom, current-day treatments only reduce the impact of symptoms rather than specifically address the percept itself. Globally, tinnitus sufferers demand a permanent solution to this problem. Although market research demonstrates a strong commercial opportunity, the amount of scientific research and financial investment is small compared to other chronic health conditions. To address these impending issues, TRI 2021 aspires to join hands with experts from emerging scientific fields such as big data science, personalized medicine, neuroinflammation, genetics etc. who can give us insight about their successful translations from bench to bedside. Through this meeting we intend to open new avenues of research, clinical practices, and patient engagement strategies in tinnitus, setting us on a path of disruptive innovation. This led us to title the conference Engineering the future of tinnitus: Bridging Academia, Industry, Medicine & Society (#BridgingAIMS).

TRI 2021 will be held at the Trinity Business School in Trinity College Dublin, the oldest academic institution in Ireland. Established in 1592 as the College of the Holy and Undivided Trinity of Queen Elizabeth in the heart of Dublin city, Trinity College draws more than 400 years of history and houses some of the oldest relics in the world. Complementing its glory is Dublin city itself, weaving centuries of culture and tradition between the modern folds of the third millennium. This year at TRI 2021, along with our vision to #BridgingAIMS, we are honoured to give our delegates a taste of the infamous Irish culture and tradition through our social events.

We would like to thank our platinum sponsor Neuromod and co-sponsor Fáilte Ireland for supporting us in this endeavour. We also would like to introduce our administrative partner, Conference Organisers Limited. We invite you to visit our website [www.tri2021.org](http://www.tri2021.org) and follow us on Twitter (@2021\_tri) for regular updates on the conference.

We look forward to your enthusiastic participation in turning this event into an experience.

Sven Vanneste & the TRI 2021 team





[design.stefanwallner.de](http://design.stefanwallner.de), [design@stefanwallner.de](mailto:design@stefanwallner.de)