over the horizon

# 8th International TRI Tinnitus Conference

10 - 13 March 2014
Auckland, New Zealand

# Handbook

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# Contents

E nga iwi o te ao
Haere mai, haere mai, haere mai

# Welcome

To the peoples of the world
Welcome, welcome, welcome

On behalf of the Tinnitus Research Initiative it is a great pleasure to welcome you to the 8th International Tinnitus Research Initiative Conference "Over the Horizon".

The organizers would like to thank you all for travelling to Auckland. We hope that your visit will be both educational and enjoyable. It is wonderful that so many prominent tinnitus researchers and clinicians have travelled to New Zealand to share their expertise. Auckland and its surrounds has much to offer visitors, from the wild west coast beaches to the serenity of Waiheke vineyards in the East, from the vibe of the city's bars and restaurants to the vistas of the Waitakere ranges and our magnificent harbours.

The host university, the University of Auckland, was founded in 1883 and is New Zealand's largest university with 38 000 students. The Centre for Brain Research at the University of Auckland is a partnership between scientists, clinicians and the community. Working together in the laboratory, clinic, and community, the CBR strives to provide a brighter and better future for people and families living with brain disease and injury. Tinnitus is an important topic for multidisciplinary research; successful partnerships and innovation begins with networking, this meeting is a perfect opportunity for researchers, clinicians and community organizations to learn from each other, to network and forge collaborations that will provide meaningful benefits to tinnitus sufferers across the globe. The poster sessions are very important for this purpose and so have a prominent part to play here. The posters will be up throughout the meeting, please attend the scheduled poster sessions to hear the presenters, they deserve your attention.

Thank you to all who have contributed to organizing this meeting. We are very grateful for the support of our sponsors and exhibitors. Please take the time to visit the exhibitors and enquire about their services and products.

To cure tinnitus we must: embrace new methodologies, challenge convention, and look over the horizon.

He rangi tā matawhāiti, he rangi tā matawhānui.
*The person with a narrow vision sees a narrow horizon; the person with a wide vision sees a wide horizon. Maori Proverb*

**Grant D Searchfield**
*Chair of Organising Committee*

# Programme

## Monday 10 March

| | |
|---|---|
| 0830 – 1710 | Pre conference workshop |
| 1710 – 1930 | Welcome Reception |

## Tuesday 11 March

| | |
|---|---|
| 0830 – 0900 | Conference opening |
| 0900 – 0945 | Guest Speaker<br>Bioengineering and the Physiome Project<br>Prof Peter Hunter |
| 0945 – 1015 | Morning tea |
| 1015 – 1050 | Invited Speaker<br>Better understanding the heterogeneity of tinnitus to improve and develop new treatments - TINNET<br>Dr Berthold Langguth |

**Podium Session 1 / Tahi**

| | |
|---|---|
| 1050 – 1100 | Characterising the psychosocial experiences of chronic tinnitus sufferers<br>Krysta Callander |
| 1100 – 1110 | Seasonal affective disorder in patients with chronic tinnitus<br>Prof Young Ho Kim |
| 1110 – 1120 | The relation between tinnitus loudness, sleep disorders and emotional distress<br>Narges Jangholi |
| 1120 – 1130 | Use of the significant other to gauge tinnitus severity<br>Dr Tricia Sheehan |
| 1130 – 1140 | Validation of the tinnitus functional index in a UK research population<br>Dr Derek Hoare |

| | |
|---|---|
| 1140 – 1215 | Lunch |
| 1215 – 1345 | Poster Session 1 / Tahi – *refer to page 94* |
| 1345 – 1420 | Guest Speaker<br>Metaplasticity: Brake or accelerator for plasticity?<br>Prof Cliff Abraham |

**Podium Session 2 / Rua**

| | |
|---|---|
| 1420 – 1430 | Responsiveness to threatening sounds: A selective attention paradigm<br>Dr Rilana Cima |
| 1430 – 1440 | Noise protection for hyperacusis patients with stress on teachers<br>A case presentation of a new approach<br>Gaby Lux-Wellenhof |
| 1440 – 1450 | Gentle skin stimulation modulates the balance between the sympathetic nerve and the vagal nerve among the normal adult<br>Prof Masafumi Nakagawa |
| 1450 – 1500 | On the perceptual and neuronal variability in chronic tinnitus<br>Dr Winnifried Schlee |
| 1500 – 1510 | Elderly patients benefit from cochlear implantation regarding auditory rehabilitation, quality of life, tinnitus and psychological comorbidities<br>Prof Heidi Olze |

| | |
|---|---|
| 1510 – 1540 | Afternoon tea |
| 1540 – 1700 | Poster Session 2 / Rua – *refer to page 96* |
| 1700 – 1735 | Invited Speaker<br>Multimodality evaluation and treatment of tinnitus<br>Dr Shujiro Minami |
| 1735 – 1810 | Keynote Speaker<br>Are treatments for tinnitus effective?<br>Prof Deborah Hall<br>*Kindly sponsored by the Neurological Foundation of New Zealand* |

# Wednesday 12 March

| | |
|---|---|
| 0830 – 0900 | **Invited Speaker**<br>Plasticity of multisensory processing in the dorsal cochlear nucleus: It's role in tinnitus generation and suppression<br>Prof Susan Shore |
| 0900 – 0945 | **Keynote Speaker**<br>Tinnitus and abnormal processing in the central auditory system<br>Prof Pim Van Dijk<br>*Kindly sponsored by the Neurological Foundation of New Zealand* |
| 0945 – 1015 | Morning tea |

**Podium Session 3 / Toru**

*Kindly sponsored by the Centre for Brain Research*

| | |
|---|---|
| 1015 – 1025 | Parahippocampal - auditory cortex communication in tinnitus<br>Prof Dirk De Ridder |
| 1025 – 1035 | Modulating alpha and beta oscillations within posterior cingulate cortex through real-time source localized neurofeedback and its effect on tinnitus related distress<br>Prof Sven Vanneste |
| 1035 – 1045 | Change in spontaneous cortical activity during tinnitus remediation<br>Ankit Mathur |
| 1045 – 1055 | Tonotopic map changes during tinnitus remediation<br>Ankit Mathur |
| 1055 – 1105 | Changes in resting-state fMRI activity during salicylate-induced tinnitus and sound stimulation<br>Prof Richard Salvi |
| 1105 – 1115 | Auditory-limbic network in tinnitus revealed by resting-state functional connectivity MRI<br>Prof Josef Rauschecker |
| 1115 – 1145 | Lunch |
| 1145 - 1315 | Poster Session 3 / Toru – *refer to page 172* |

**Podium Session 4 / Wha**

*Kindly sponsored by the Centre for Brain Research*

| | |
|---|---|
| 1315 – 1325 | Infusion of GABAB receptor agonists into the cochlear nucleus on tinnitus development following acoustic trauma in rats<br>**Dr Yiwen Zheng** |
| 1325 – 1335 | Stress-associated changes of mitochondrial proteins in auditory cortex<br>**Dr Agnieszka Szczepek** |
| 1335 – 1345 | Evidence for neurogenesis in the cochlear nucleus following acoustic trauma in rats<br>**Prof Paul Smith** |
| 1345 – 1355 | Sound-triggered suppression of neuronal firing in the auditory cortex: Implication to the residual inhibition of tinnitus<br>**Alexander Galazyuk** |
| 1355 – 1405 | Effects of paraflocculus removal on hyperactivity after acoustic trauma<br>**Darryl P Vogler** |
| 1405 – 1415 | Hyperactivity in the inferior colliculus after noise trauma and it's modulation by extra-cochlear electric stimulation<br>**Dr Arnaud Norena** |
| 1415 – 1445 | Afternoon tea |
| 1445 -1615 | **Poster Session 4 / Wha** – *refer to page 174* |
| 1615 – 1650 | **Invited Speaker**<br>Multidisciplinary association for psychedelic studies<br>**Rick Doblin** |
| 1650 – 1725 | **Invited Speaker**<br>MDMA-assisted psychotherapy for tinnitus and PTSD<br>**Amy Emerson** |
| 1725 – 1810 | **Keynote Speaker**<br>Neural plasticity and attention in normal hearing and in tinnitus<br>**Prof Larry Roberts**<br>*Kindly co-sponsored by the Neurological Foundation of New Zealand and NZ Tinnitus and Hyperacusis Network* |
| 1900 – midnight | **Conference Dinner** |

# Thursday 13 March

| | |
|---|---|
| 0830 – 0915 | **Guest Speaker**<br>The body in mind - current concepts in the brain in pain<br>**Prof Lorimer Moseley** |
| 0915 – 0950 | **Invited Speaker**<br>Attention and subjective tinnitus: From a clinical point of view<br>**Dr Alain Londero** |
| 0950 – 1025 | **Invited Speaker**<br>An ENT doctor's journey to the brain: The auditory and non-auditory brain areas involved in tinnitus and tinnitus-related distress<br>**Dr Jae-Jin Song** |
| 1025 – 1100 | Morning tea |

**Podium Session 5 / Rima**

| | |
|---|---|
| 1100 – 1110 | PRISM (Pictorial Representation of Illness and Self Measure) as a new assessment tool for suffering in tinnitus patients<br>**Dr Tobias Kleinjung** |
| 1110 – 1120 | Proportion and diversification of underlying causes of 242 unilateral venous pulsatile tinnitus cases in dual-phase contrast-enhanced CT<br>**Cheng Dong** |
| 1120 – 1130 | The dural sinus wall dehiscience presenting with pulsatile tinnitus: Evaluation with CT venography<br>**Dr Pengfai Zhao** |
| 1130 – 1140 | Deep brain stimulation of the inferior colliculus for treating tinnitus<br>**Sarah Offut** |
| 1140 – 1150 | Impact of spectral notch width on the clinical effectiveness of the tailor-made notched music training<br>**Robert Wunderlich** |
| 1150 – 1200 | Comparison of positioning the cathode in tDCS<br>**Sarah Rabau** |

| | |
|---|---|
| 1200 – 1230 | Lunch |
| 1230 – 1350 | Poster Session 5 / Rima – *refer to page 259* |

## Podium Session 6 / Ono

| | |
|---|---|
| 1350 – 1400 | Mindfulness based tinnitus stress reduction: A new treatment with ancient roots<br>**Dr Jennifer Gans** |
| 1400 – 1410 | Consensus on hearing-aid candidature and fitting for mild hearing loss, with and without tinnitus: DELPHI review<br>**Prof Deborah Hall**<br>*Kindly sponsored by the Neurological Foundation of New Zealand* |
| 1410 – 1420 | Frequencies characteristics of tinnitus and its impact on different sound-related treatment methods<br>**Prof Weijia Kong** |
| 1420 – 1430 | Space: The 3rd dimension of tinnitus<br>**Dr Grant Searchfield** |
| 1430 – 1440 | Total or significant remission of tinnitus what can we learn from patients who have reached this stage?<br>**Dr Tanit Sanchez** |

| | |
|---|---|
| 1440 – 1510 | Afternoon tea |
| 1510 – 1630 | Poster Session 6 / Ono – *refer to page 261* |
| 1630 – 1705 | **Invited Speaker**<br>Tinnitus: Why not stop it before it starts?<br>**Prof William Martin** |
| 1705 - 1730 | **Conference Close**<br>Establishing networks for tinnitus clinicians and researchers, TRI 2015, and farewells<br>**Grant D Searchfield and Berthold Langguth** |

# Social Programme

## Welcome Reception

When: Monday 10 March 2014
Where: Exhibition Area, Viaduct Events Centre
Time: 5.10pm – 7.30pm
Dress: Smart Casual

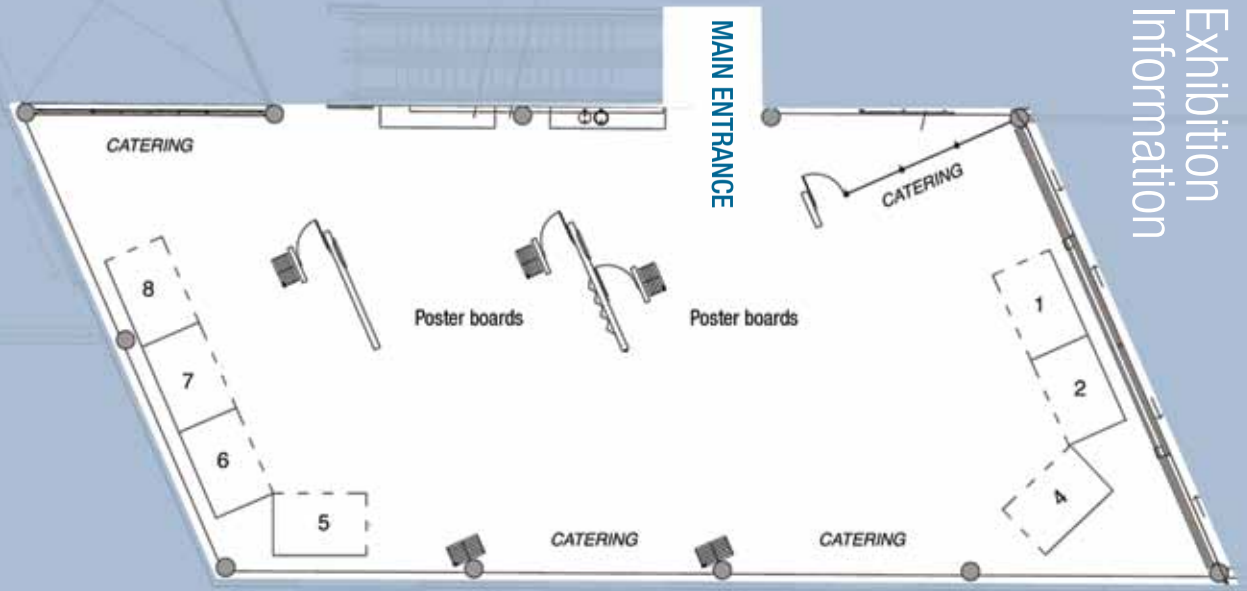
Kick off the social festivities by catching up over wine and cheese. The Welcome Reception will give you the opportunity to sample some of the best local wines from the Auckland region. The winemakers will also be on hand to answer your questions!

## Conference Dinner

When: Wednesday 12 March 2014
Where: Waiheke Room, Viaduct Events Centre
Time: 7.00pm – Midnight
Dress: Smart Casual

Join your colleagues and new conference friends for a night on Auckland's waterfront. A superb venue from which to watch the city transform from day to night, this evening will play on the classic 'kiwi barbeque' with plenty of entertainment and a chance to celebrate after a busy few days.

# Exhibition Information




| Exhibitors | Stand Number |
|---|---|
| MED-EL Implant Systems Australasia | 01 |
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| Cochlear NZ Limited | 04 |
| SIEMENS | 05 |
| The National Foundation for the Deaf | 06 |
| Phonak NZ and Advanced Bionics | 07, 08 |

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# Catering

When planning this conference the organisers were keen to share with you some of the foods that are iconic to New Zealand. Throughout the next few days you will get to sample some of our favourites.

To all our conference guests welcome to 'our place' and we hope you enjoy!

# General Information

**Registration and Information**

Located in the Viaduct Events Centre Foyer the registration and information desk will be open at the following times:

| | |
|---|---|
| Monday 10 March | 0730 - 2000 |
| Tuesday 11 March | 0730 - 1830 |
| Wednesday 12 March | 0730 - 1900 |
| Thursday 13 March | 0730 - 1800 |

**Telephone Directory**

| | |
|---|---|
| Viaduct Events Centre | +64 9 307 5498 |
| Registration and Information Desk | +64 21 918 524 |
| Conference Innovators after hours (Rachel Cook) | +64 21 918 524 |

Hotels

| | |
|---|---|
| Sofitel Auckland Viaduct Harbour | +64 9 909 9000 |
| The Sebel Suites Auckland | +64 9 978 4000 |
| Copthorne Hotel Auckland HarbourCity | +64 9 377 0349 |

Transport

| | |
|---|---|
| Corporate Cabs | +64 9 377 0773 |
| Auckland Coop Taxis | +64 9 300 3000 |
| Blue Bubble Taxis | +64 9 302 6001 |

**Accommodation**

For those delegates who have reserved hotel accommodation through the conference managers (Conference Innovators), please ensure your account is settled in full prior to your departure.

**Airport Transfers**

Auckland International and Domestic Airport is 40 minutes by car from the Viaduct Events Centre (allow 60 minutes in rush hour).

There are a number of companies that provide transport to the airport. Should you wish to pre-book, we suggest the operators below, or ask your hotel reception to book it for you.

| | |
|---|---|
| Super Shuttle | +64 9 522 5100 |
| Airbus Express | +64 9 366 6400 |

| | |
|---|---|
| **Attendance at the Conference and Social Functions** | Please wear your name badge when attending all conference sessions, catering areas and social functions. |
| **Banking and ATM Machines** | Central city banks are open Monday to Friday from 9:00am to 4:30pm. The nearest ATM is located at the ASB building in North Wharf. |
| **Catering** | Catering is available within the Exhibition area located on level 1 of the Viaduct Event Centre. |
| **Luggage Storage** | It is preferable for you to ask your hotel concierge to arrange for luggage storage as there are no storage facilities at the conference venue. |
| **Medical and Pharmacy Assistance** | Auckland City Medical Centre, located at 8 Albert Street is the closest medical centre to the conference venue (a 12 minute walk). They can be contacted on +64 9 377 5525.<br><br>The closest pharmacy is Radius Pharmacy, located at 7 Queen Street (a 10 minute walk). |
| **Messages** | Should you need to send a message to another delegate, please visit the registration desk. |
| **Mobile Phones** | Please ensure mobile phones are switched off prior to the start of conference sessions. |
| **Name Badges** | Please wear your conference name badge when attending conference sessions and within the venue. |
| **Parking** | No parking is available at the conference venue, however street parking is available nearby, as is car parking at Wynyard Quarter Carpark, entrance off Beaumont Street and Madden Street. The first hour is free and $2.00 every hour thereafter. Please note rates are current at time of printing. |

**Smoking**

Smoking is not permitted at the conference venue.

**Speaker Preparation**

The Speaker Preparation Room is located in Kawau Room 2 (level 1). If you are speaking at the conference, please ensure you visit the Speaker Preparation Room at least two hours before your presentation (ideally allow as much time as possible). The technician will load your presentation and ask you to check it before your session.

Speaker Preparation Room hours:

| | |
|---|---|
| Monday 10 March | 0800 - 1800 |
| Tuesday 11 March | 0800 - 1800 |
| Wednesday 12 March | 0800 - 1800 |
| Thursday 13 March | 0800 - 1730 |

**Special Diets**

For those delegates who provided specific details during registration, special dietary meals/options will be available in the main catering area. Venue staff will be available to assist.

**Wi-Fi**

Complimentary wireless access is available to all conference delegates. Please visit the registration desk for the Wi-Fi code.


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## BIOENGINEERING AND THE PHYSIOME PROJECT

Hunter, P.

*Auckland Bioengineering Institute, University of Auckland, New Zealand*

Multi-scale models of organs and organ systems, based on model encoding standards, are being developed under the umbrella of the IUPS Physiome Project and the Virtual Physiological Human (VPH) project funded by the European Commission. These computational physiology models deal with multiple physical processes (coupled tissue mechanics, electrical activity, fluid flow, etc) and multiple spatial and temporal scales. They are intended both to help understand physiological function and to provide a basis for diagnosing and treating pathologies in a clinical setting. A long term goal of the project is to use computational modelling to analyse integrative biological function in terms of underlying structure and molecular mechanisms. Web-accessible databases, based on the standards (which include SBML, CellML and FieldML), have been established for models and model-related data at the cell, tissue, organ and organ system levels. This talk will discuss recent developments in the VPH/Physiome Project and the application of these multi-scale modelling approaches to several physiological systems including the cardiovascular system, the respiratory system, the musculo-skeletal system and the digestive system.

## BETTER UNDERSTANDING THE HETEROGENEITY OF TINNITUS TO IMPROVE AND DEVELOP NEW TREATMENTS – TINNET

Langguth, B.

*University Hospital Regensburg, Department of Psychiatry and Psychotherapy*

Tinnitus is the perception of sound in the absence of a corresponding acoustic stimulus. In Europe over 70 million people experience tinnitus and for 7 million it creates a debilitating condition. Established therapeutic approaches are limited and better treatment is urgently needed.
Brain research has demonstrated that tinnitus is the consequence of altered neural activity in specific brain areas. This has prompted the development of new therapeutic approaches but their further development is hampered by the heterogeneity of tinnitus and limited knowledge about the neuronal correlates of the different tinnitus subtypes.

The COST-Action will foster the establishment of a pan-european multidisciplinary network with the major goals to identify clinically relevant tinnitus subtypes, their neurobiological underpinnings and their relevance for response to treatment. This will substantially speed up the clinical investigation of new treatments and their translation into marketable products.

## CHARACTERISING THE PSYCHOSOCIAL EXPERIENCES OF CHRONIC TINNITUS SUFFERERS

**Callander, K.J**.; McLachlan, N.M.; Wilson, S.J.

*Melbourne School of Psychological Sciences, University of Melbourne, Victoria, Australia*

Chronic tinnitus is highly subjective, both in terms of the sound experienced, and an individual's reactions to the sound. While some people are able to "tune out" their tinnitus, others report that their experience of tinnitus has a substantial negative impact on their psychosocial functioning. This commonly includes feelings of low mood, high anxiety, and decreased engagement in, and enjoyment of, daily routines. As such, an important step in understanding the tinnitus experience, and thus helping sufferers, is the characterisation of the factors contributing to the observed decline in psychosocial functioning. Thus, the aim of this study was to characterise these factors, as well as identify those that predict an individual's ability to adjust to the presence of their tinnitus from both a psychological and daily functioning perspective.

### Method

37 tinnitus sufferers (15 male) were recruited for this study with a range of tinnitus experiences from chronic non-bothersome tinnitus, to chronic bothersome tinnitus. Participants were asked to complete a series of questionnaires assessing mood, thinking strategies, health attitudes and coping styles to capture their broader psychosocial experiences. In addition, participants were assessed for the impact their tinnitus had on their emotion regulation and general daily functioning.

### Results

Preliminary analyses indicate an important distinction between tinnitus sufferers who experience a significant functional impairment and those who experience significant emotional dysregulation in response to their tinnitus. Contributing factors to these distinct psychosocial outcomes will be explored, in particular, the role of different coping strategies, attitudes towards illness, mood, and subjective tinnitus variables, to characterise these groups and determine the predictors of each. These results will form the basis of a model outlining the psychosocial factors influencing differences in the tinnitus experience to inform more targeted treatment strategies and thus assist in improving the experiences and coping abilities of tinnitus sufferers, and ultimately facilitation of their ability to "tune out" their tinnitus.

## SEASONAL AFFECTIVE DISORDER IN PATIENTS WITH CHRONIC TINNITUS

Kim, Y.H.

*Department of Otolaryngology, Seoul National University Boramae Medical Center, Seoul, Korea*

### Objective

Seasonal affective disorder (SAD) is one type of depressions presenting in area with a big seasonal difference, especially showing recurrent depressive symptom in winter. The aim of this study is to investigate incidence of SAD, degrees of anxiety/depression/sleep disturbance, and characteristics of tinnitus in chronic tinnitus.

### Methods

From December 2012 to November 2013, seventy-five patients with chronic persistent or intermittent tinnitus were enrolled in this study. Exclusion criteria were pulsatile tinnitus, tinnitus by temporal bone trauma or ear surgery, history of tinnitus treatment more than 3 months previously, history of neuropsychological disease or depression, abuse history of alcohol or drug, cognitive dysfunction (brain lesion or surgery), and severe illness making regular follow-up and treatment difficult. Audiometry, tinnitogram, and questionnaire for anxiety/depression/sleep disturbance/ SAD were performed in all patients.

### Results

Among total 75 chronic tinnitus patients enrolled in this study, male to female ratio was 42:33 and mean age was 55.3 years. Number of patients suggesting SAD and subclinical SAD (S-SAD) was 7 (9.3%) and 9 (12.0%), respectively. The favorite season was autumn in most cases and most patients disliked winter. There were 7 patients showing catastrophic score more than THI 76 and the proportion was 2/7 (28.6%) in SAD group, 2/9 (22.2%) in S-SAD group, and 3/59 (5.1%) in control group suggesting the significant correlation between SAD and THI. There was no significant difference among audiogram and tinnitogram results in three groups. Anxiety/ depression/sleep disturbance tests showed more abnormal findings in SAD and S-SAD groups. In particular, the possibility of depression in SAD/S-SAD groups was significantly higher compared to that of control group (BDI>16: 7/16 (43.8%) vs 10/59 (17.0%); BDI>30: 3/16 (18.8%) vs 1/59 (1.7%), respectively).

### Conclusion

In the present study, SAD and S-SAD were suspected in about 20% of chronic tinnitus patients and this disease entity may be considered to manage tinnitus effectively.

## THE RELATION BETWEEN TINNITUS LOUDNESS, SLEEP DISORDERS AND EMOTIONAL DISTRESS

**Jangholi, N.**[1]; GhodratiToostani, I. [2,3]; Maurice Erna Claessens, P. [1]

[1] *Universidade Federal do ABC, Center of Mathematics, Computer and Cognition, São Paulo, Brazil*
[2] *Research and Development department of Fannavaran Gostaresh Salamat (FGSco), Tehran, Iran*
[3] *Research and Development department of Neurophoneme, LA, USA*

### Introduction

Subjective tinnitus is a common hearing disorder in which patients suffer from ringing, buzzing and other perceived noises without external source, due to a number of different possible peripheral and central causes. Tinnitus often leads to cognitive impairment and emotional distress, and, among other complaints, a variety of sleep disturbances. Among standard exams applied to tinnitus patients are an audiometric exam to estimate the intensity of the phantom sound – tinnitus loudness matching (LM) – and internationally validated questionnaires to assess the level of psychological suffering induced by tinnitus, such as the Tinnitus Questionnaire (TQ) and Tinnitus Handicap Inventory (THI). Sleep disturbance is one of the factor dimensions of the TQ for which a score can be determined based on a subset of the items. The objective of this study is to investigate the relation between tinnitus loudness as measured by the LM procedure, sleep disturbance, and measures of other cognitive, emotional, perceptual and somatic stress symptoms.

### Materials and Methods

Complete data were gathered from 134 male and female adult tinnitus patients obtained from test reports of FGS and Neurophoneme R&D departments. Associations between loudness, THI and total and subscales of the TQ in their Iranian versions were calculated using Pearson and Spearman rank order correlations and Pearson chi-squared tests.

### Results

Only the Spearman correlation results will be reproduced in this abstract, with two-sided p-values. Rank order correlations between different dimensions of TQ, and THI and TQ, are, in general, moderate to high (>0.2) and statically significant (=0.05), as expected. Sleep disturbance is particularly correlated with emotional distress ($\rho$= 0.28, p=0.001), but, more surprisingly, the correlation with subjective loudness is negative rather than positive, and slightly significant ($\rho$=

-0.18, p=0.036). Subjective loudness as measured through LM also hardly has any correlation with emotional and cognitive symptoms in tinnitus patients.

### Conclusion

These results indicate that, while there seems to be a positive association between sleep disturbance and emotional distress, there is no direct relation with tinnitus loudness. The dissociation between sleeplessness and distress on the one hand, and loudness on the other, goes against earlier studies, and shows the necessity of careful study and modeling of potentially relatively independent systems for sensory experience and suffering due to tinnitus.

## USE OF THE SIGNIFICANT OTHER TO GAUGE TINNITUS SEVERITY

**Sheehan, T.** [1]; Davis, P. [1, 2]

[1] *University of Miami Ear Institute Tinnitus Clinic*

[2] *Scientific Advisor to Neuromonics*

### Aims / Objectives

Tinnitus reaction is notoriously difficult to quantity, and sufferers lack any internal reference to benchmark their tinnitus over time. It is possible that the patient's Significant Other's (SO's) perspective might be helpful in measuring it, given that tinnitus can also greatly impact the SO's quality of life. The Significant Others Tinnitus Questionnaire (SOTQ) was thus developed to assess the severity of the patient's tinnitus disturbance from the SO's perspective and also to more directly involve the SO in the counseling and rehabilitation process.

### Methods

The SOTQ incorporates five key areas of tinnitus disturbance that are also quantified by the patient on the Tinnitus Reaction Questionnaire (TRQ). Three questions that are also important to the effect on the SO were added in addition to two questions on how often the patient spontaneously mentioned their tinnitus as well as how often it appeared that the patient was disturbed by their tinnitus. There were also five questions on whether the SO themselves suffered from tinnitus. The same five-response option system (0-4) from the TRQ was thus utilized for all SOTQ items.

The SOTQ was presented to the SOs as part of routine tinnitus evaluation and counseling sessions on twenty-eight concurrent patients at the University of Miami Tinnitus Clinic. Concurrently, the patient completed the TRQ.

### Results and Discussion

Data on the five common questions from the TRQ was paired with the SO's corresponding SOTQ questions; results were then pooled as grouped data. Two-tailed paired t-tests were calculated on each domain, as well as the composite scores.

Mean results indicated that the SOs rated the patient's avoidance of social situations as a significantly more frequent problem than the patients did. Perhaps this is like hearing loss, where the social situation avoidance might affect the SO's more than the patients themselves.

There was no significant difference between the two groups in terms of tinnitus interfering with the patient's relaxation and sleep, with both domains being rated as quite frequently disturbed. This might be because the SOs can readily determine that the patient has a lot of trouble relaxing or

sleeping.
The SO rated the patient's ability to work as a frequent problem on average, while the patient rated it as more minor. This significant difference doesn't yet have a clear explanation.
Patients rated concentration as a significantly more frequent problem than the SOs. Perhaps this is the one domain that the SO can't readily gauge.

Overall, the composite score mean differences indicated a trend where the SO rated tinnitus as more disturbing than the sufferer did, although this difference was not significant. As the SOs and the patients each rated various domains more highly than the other, the composite score tended to average out those differences.

**Conclusion**

This data indicated that the SO's perspective is useful in quantifying a patient's tinnitus distress, and they may suffer as a result of the patient's tinnitus. It was an excellent counseling resource that empowered the SOs to help in the rehabilitation process, particularly in maintaining realistic expectations.

## VALIDATION OF THE TINNITUS FUNCTIONAL INDEX IN A UK RESEARCH POPULATION

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### Background

Chronic tinnitus is a common and sometimes disabling condition yet there is no standardized approach to measuring its impact in either the clinical setting or research. For clinical assessment of tinnitus the preferred questionnaire in the UK is the Tinnitus Handicap Inventory1. This was developed as a diagnostic tool to measure tinnitus severity. Although it lacks sensitivity to treatment-related changes in tinnitus it is also often used as an outcome measures in both clinical practice and research. Current alternatives to the THI equally only measure severity, or are good measures of change, but not both. In contrast, the Tinnitus Functional Index (TFI)2 was developed to be used as both a diagnostic measure of severity and to be a sensitive measure of treatment-related change. We are currently validating this questionnaire for use in the UK.

### Methods

The present study evaluates the TFI as a diagnostic tool for the assessment of tinnitus in a research population. Questionnaire data was obtained from a multi-site clinical trial. As part of the initial screening, 294 participants completed six screening assessment questionnaires; the TFI, the Beck's Depression Inventory (BDI), the Beck's Anxiety Inventory (BAI), the World Health Organisation Quality of Life Bref (WHOQOL-BREF) the Tinnitus Handicap Inventory (THI), and the Tinnitus Handicap Questionnaire (THQ). 100 tinnitus participants completed the TFI at a second visit before the research intervention. We evaluated discriminant and convergent validity of the TFI with this large cohort (N= 247) comparing the six assessment questionnaires. Test-retest reliability and agreement (N=94) of the TFI were evaluated using Intra-class correlation coefficients (ICC). Confirmatory factor analysis in progress uses the eight subscales identified by Meikle et al. (2012) during TFI development.

### Results

Convergent and discriminant validity of the TFI revealed high correlations with the THI ($r = 0.82$) and THQ ($r = 0.82$) and moderate to low correlations with the BDI ($r = 0.56$), BAI ($r = 0.38$) and WHOQOL ($r = -0.48$). Test-retest reliability for the TFI global score was extremely high, with the

ICC (95% CI) showing strong correlations between two administrations (ICC = 0.86, p< .001, 95% CI = 0.8-0.9). Ongoing CFA to be presented is predicted to demonstrate the TFI has a multidimensional questionnaire structure.

**Conclusion**

We can confirm that the TFI is a reliable measure of tinnitus for use in evaluating a research population. The TFI demonstrates high discriminant and convergent validity and extremely high test-retest reliability. It is expected that confirmatory factor analysis will show eight separate domains.

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## TINNITUS PRECEDED DEPRESSIVE SYMPTOMS IN COMMUNITY-DWELLING OLDER JAPANSES: A PROSPECTIVE COHORT STUDY

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### Objective

Depression has a strong negative impact on well-being in older adults, so primary prevention of depression is desirable from a public health point of view. Given the association of tinnitus with depression and the availability of treatment for tinnitus, it is important to establish whether the association is a causal one, namely whether tinnitus is a risk factor of depression. However, most studies of the association between tinnitus and depression have been cross-sectional, making it difficult to draw any conclusions about the directionality of the association. This study aimed to clarify whether tinnitus precedes the development of depressive symptoms in a general older population.

### Methods

We performed this study in Kurabuchi town, Gunma prefecture, Japan (approximately 100 km north of Tokyo). For the present study, we selected only those who had no depressive symptoms (GDS5 ≤ 1) at baseline. We performed health examinations of 535 residents (239 men; 296 women) aged 65 years or older without depressive symptoms (year: 2005-2006). Information on tinnitus was obtained via a questionnaire “Have you ever had any ringing, buzzing, or other sounds (tinnitus) in your ears within the past year?” The response options were “Yes” or “No”. Depressive symptoms were assessed according to the Geriatric Depression Scale 15-item version (GDS15) in face-to-face home visit interviews carried out once in 2007 and once in 2008. In the present study, participants with scores of 6 or more in either 2007 or 2008 were considered depressed.

## Results

During the average follow-up period of 2.5 years, a total of 27 men and 56 women were newly identified as having depressive symptoms (GDS15≥6), giving an overall incidence of depressive symptoms of 11.3% in men and 18.9% in women. Among the men, the incidence of depressive symptoms was higher in those with tinnitus than in those without (20.5% vs. 9.5%). In the multi-adjusted model, tinnitus was significantly associated with an increased risk of depressive symptoms (relative risk=2.07; 95% confidence interval=1.01-4.25). On the other hand, no association between tinnitus and depressive symptoms was observed in the women.

## Conclusion

In the present study, We observed a sex-specific association between tinnitus and depressive symptoms: the men with tinnitus had approximately twice the risk of developing depressive symptoms compared with the men without tinnitus, but no apparent association was found in the women. Our study is the first to present data on the temporal association between tinnitus and depressive symptoms in a general older population. We believe primary care providers and public health staff should recognized tinnitus as a risk factor for depressive symptoms. Because tinnitus is a common complaint in older adults, effective screening and management are, if tinnitus is confirmed as a risk factor of depression, expected to be important for preventing depression.

## VALIDATION OF THE TINNITUS FUNCTIONAL INDEX IN NEW ZEALAND

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### Aims and objectives

The subjective nature of tinnitus necessitates the use of self-report questionnaires in order to assess tinnitus severity and evaluate the outcomes of treatments. The limitations of existing tinnitus questionnaires have led to the development of a new questionnaire, the Tinnitus Functional Index (TFI), in the United States. The aims of this study were to determine if the TFI is a reliable and valid measure of the negative impacts and severity of tinnitus in New Zealand, and to find out whether the TFI needs to be modified for use in the New Zealand context.

### Methods

Secondary data from two studies conducted at the University of Auckland were used. Principal components factor analysis with varimax rotation to an eight-factor solution was undertaken to investigate the internal structure of the TFI. Internal consistency reliability was examined by computing the Cronbach Coefficient Alpha for the TFI and its subscales. Intraclass Correlation Coefficients were computed to assess the test-retest reliability of the TFI and its subscales. To evaluate convergent validity, Pearson correlations between the TFI scores and scores on the Tinnitus Handicap Questionnaire (THQ) and Tinnitus Severity Numerical Scales (TSNS) were computed. Pearson correlations between the TFI scores and scores on the Hearing Handicap Inventory (HHI) were computed to evaluate divergent validity.

### Results

The internal structure of the TFI remained unchanged from the USA. The Cronbach Alpha and Intraclass Correlation Coefficients were greater than 0.7 for the TFI overall and for each of the 8 subscales, indicating high internal consistency reliability. There was high test-retest reliability. Strong Pearson correlations with the THQ and TSNS, and a moderate correlation with the HHI, indicated strong convergent and divergent validity.

### Conclusions

These findings indicate that this new questionnaire is a reliable and valid measure of tinnitus

severity in New Zealand and can therefore be used for assessing tinnitus patients in the clinical context. The unchanged factor structure indicates that the TFI does not need modification for use in New Zealand. It also indicates that the results of clinical trials evaluating the effectiveness of treatment interventions, that use the TFI as an outcome measure, can be compared between the United States and New Zealand, as the questionnaire items measure the same dimensions of tinnitus severity in both countries.

## ARE PEOPLE WITH TINNITUS SATISFIED WITH THEIR INTERACTION WITH THE HEALTHCARE SYSTEM?

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### Background

There is limited research on people with tinnitus and their interaction with the healthcare system. Research shows that people who seek healthcare for tinnitus report low satisfaction with diagnosis and treatment (Redmond, 2010). There is much scope to improve diagnostics and treatment for people with tinnitus (Hoare & Hall, 2011).

### Aims

To examine whether people with tinnitus are satisfied with the interaction with the healthcare system, considering factors such as severity of tinnitus and health status.

### Methods

Two cohorts were used: (i) Cohort 1: Volunteers from the community, presenting with tinnitus, aged 18 years and over from the metropolitan area of Perth, Western Australia and (ii) Cohort 2: Those self-reporting tinnitus in an epidemiological study of people born between 1946 to 1964 from the Shire of Busselton, Western Australia. A five part questionnaire was administered: Tinnitus Sample Case History Questionnaire – Adapted (TSCHQ), Tinnitus Reaction Questionnaire (TRQ), Glasgow Health Status Inventory – all purpose (GHSI), Patient Satisfaction with Communication (PSC) and the Functional Assessment of Chronic Illness Therapy - Treatment Satisfaction - General (FACIT-TS-G).

### Results/Discussion

Of the 332 people who participated (Cohort 1 n=180 and Cohort 2 n=152), 281 completed the survey: Cohort 1 (n=150; mean TRQ score: 19.09, SD: 17; mean age: 58.94, SD:13.24) and Cohort 2 (n=131; mean TRQ score: 11.83, SD:14.85; mean age: 59.74, SD:5.04). TRQ<17 indicated sub-clinical tinnitus. Analysis showed a significant relationship between TRQ>=17 score and Cohort 1, age category, and lower health status (GHSI total score). Seeking healthcare was significantly associated with TRQ>=17, Cohort 1, self-report hearing loss, those on medication and lower health status. For those who sought healthcare (Cohort 1 n=90 and Cohort 2 n=57)

few were offered treatment (Cohort 1 n=27 and Cohort 2 n=6). Mean satisfaction rating for initial diagnosis had no significant relationships with cohort, gender, self-report of hearing loss or age. The mean satisfaction rating for initial treatment was significantly related with gender, with males more likely to be less satisfied and more likely to have treatment offered. Mean diagnosis and mean treatment satisfaction ratings were low. Seeking more than one treatment was significantly related to Cohort 1 and TRQ>=17, although the number of people who sought more than one treatment was low.

## Conclusion

The study shows that those who sought healthcare tended to report dissatisfaction with the healthcare they received and those who reported greater tinnitus interference and lower health status were more likely to seek healthcare. More research and improvements in healthcare for tinnitus are required.

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## TINNITUS IN NEW ZEALAND

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### Aims and objectives

There is the lack of population data for tinnitus in New Zealand. It is often presumed that tinnitus prevalence in New Zealand is the same as North America or the United Kingdom, however New Zealand has a large Maori, Pacific and Asian community. The aim of this study was to determine the characteristics of tinnitus in the New Zealand population.

### Methods

As part of a household survey Roy Morgan Research questionned 69,976 people across New Zealand between August 2007 and July 2013, of whom 4,771 (6.8%) responded 'yes' to having tinnitus. The data was explored with regard to gender, age, ethnicity, region, and income along with other health and lifestyle factors.

### Results

The adjusted prevalence of tinnitus was 6.0% for the total population. The prevalence was higher among men (6.5%) compared to women (5.5%). Men are 16% more likely to have tinnitus compared to women. The prevalence of tinnitus increased with age affecting 13.5% of people age ≥65 years; this age group accounts for over one-third of all people with tinnitus. The prevalence of tinnitus was highest among NZ European (7.1%), accounting for 86% of all tinnitus in the total population. Three-quarters of all cases of tinnitus occurred in the North Island. The mean prevalence of tinnitus across all major centres was 6.0%, although nearly one-third (27.2%) of all tinnitus cases occurred in Auckland. There was no significant difference in tinnitus prevalence between people earning $50,000 or more, and people earning $49,999 or less.

### Conclusions

This survey data provides some insight into tinnitus in New Zealand. Further analysis will explore the relationship between tinnitus, other heath related factors, and technology use by people experiencing tinnitus, so as to assist in the development and planning of new treatment solutions for tinnitus.

## CLINICAL CHARACTERISTICS OF PATIENTS WITH TINNITUS EVALUATED WITH TINNITUS SAMPLE CASE HISTORY QUESTIONNAIRE IN JAPAN

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### Background

At the Tinnitus Research Initiative in Regensburg, Germany in 2006, an attempt was made to gain a consensus for patient assessments. Through workshops, Tinnitus Sample Case History Questionnaire (TSCHQ) was determined as a standardized questionnaire to obtain a patient's case history and to characterize candidates into subgroups [1]. In this study, we developed a Japanese version of TSCHQ for evaluating clinical characteristic of patients with tinnitus in Japan. This will be available for comparing among tinnitus research centers and evaluating treatments for tinnitus.

### Aims / Objectives

To evaluate clinical characteristic of patients with tinnitus in Japan using a newly-developed Japanese version of TSCHQ.

### Methods

The subjects were patients with subjective tinnitus who were examined at the otolaryngology departments of two university hospitals, five general hospitals and six Ear-Nose-Throat private clinics between August 2012 and December 2012 in Japan. In this study, 336 patients were included: 159 males and 177 females; and age ranging from 18 to 91 years old (mean age, 61.2 years). Eighty-nine patients visited university hospitals, 177 patients visited general hospitals, and 70 patients visited clinics.

### Results

The Japanese version of TSCHQ showed high availability to obtain various patients' information; such as background, tinnitus history, influences affecting tinnitus, and accompanying conditions.

## Discussion

We compared our statistics to data from other countries, and found some difference in our samples. For example, a number of patients with tinnitus generated from an acoustic trauma were fewer than reported in western countries. One of the possible reasons is that there is no conscription system in our country. Patients with tinnitus who visited university hospitals demonstrated more serious symptoms than patients who visited other institutions, although patients can directly access any medical centers because of universal coverage health insurance system in Japan. In order to standardize set of data of tinnitus patients over the world, we should be care about subtle difference when TSCHQ is translated to different languages especially outside western countries.

## Conclusion

The Japanese version of TSCHQ is a useful tool to evaluate patients with tinnitus at any institutions in Japan. Results of this multicenter study reflect an attribute of patients with tinnitus who require medical care in Japan. Our data can be a basis of an international comparison of tinnitus epidemiology in different centers and countries.

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## CLINICALLY RELEVANT CHANGES ON THE PRIMARY TINNITUS OUTCOME MEASURES; NORMS AND RELIABLE CHANGE ANALYSES

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### Aims / Objectives

Tinnitus is a subjective experience and therefore difficult to measure and quantify, and several tinnitus measures for the assessment of the impact of tinnitus on cognitive, emotional, physical, and auditory functioning, have been developed over time. The most frequently used measures for tinnitus distress are the tinnitus questionnaire (TQ) and the tinnitus handicap inventory (THI). Although both have their merits, they are also conceptually hybrid in that they assess a combination of different constructs at the same time. A valid and reliable measure to assess more general functional disability, i.e. the interference of tinnitus with performance on major daily life activities, is the Tinnitus Disability Index (TDI). A first psychometric examination supported that the Tinnitus Disability index (TDI), introduced as a novel unitary brief index, is a valid measure for assessing tinnitus-related disability in daily life. The TDI was found to be a brief and easily administered index, with good test retest reliability, capturing a unitary construct, namely tinnitus disability. Given for the TQ and the THI no norms exist for determining clinically relevant changes, or for indicating sub-groups of patients, and that TDI is a newly developed assessment instrument, more work is needed not only in the replication of these first findings, but also in establishing norms, such that for each individual a meaningful level of disability can be identified.

### Method

A recent and promising method is based on regression models. This approach offers at least 2 advantages. First, multiple regression allows determination of patient-variables which are and which are not relevant to the norming (validity). Second, by using information from the entire sample, multiple regression leads to continuous and more stable norms for any subgroup defined in terms of prognostic variables (reliability). These models will be used to determine patient-variables and prognostic variables in a cross-sectional sample of N = 600, as well as on a sample of a 2-group randomized, repeated measures design (N=492)

### Results

Analyses will reveal relevant norms for interpreting the raw scores of patients. Moreover, result assist in outcome comparisons across scientific patient studies, as well as in clinical and diagnostic decision-making.

### Conclusions

Norms will be established, based on the comparison to the values of scores of a relevant reference population using regression models of raw scores on demographic and other patient variables. Compared with traditional norming methods, this approach offers at least two advantages: first, it allows determination of which patient variables are relevant to the norming and which are not (validity). Second, by using information from the entire sample rather than subgroups based on gender and age, multiple regression leads to continuous and more stable norms for any subgroup that is defined in terms of prognostic variables (reliability).

## ASSESSMENT OF HYPERACUSIS SEVERITY USING QUESTIONNAIRES AND ITS CLINICAL USEFULNESS

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### Backgrounds

Hyperacusis, commonly described as hypersensitivity to sound, is a condition in which some ordinary or well-tolerated sounds to most people are experienced as extremely loud or uncomfortable with distress. Self-report instruments are useful to assess the severity of subjective phenomena such as hyperacusis. There are two major validated questionnaires frequently used for assessing hyperacusis: the Hyperacusis Questionnaire (HQ) devised by Khalfa et al. (2002) and the German questionnaire on hypersensitivity to sound (GÜF) developed by Nelting et al. (2002). However, there is no established Japanese questionnaire for hyperacusis clinically used in Japan.

### Aims

We prepared Japanese-translated versions of HQ and GÜF. The purpose of this study was to examine the clinical usefulness of these two questionnaires by assessing the severity of hyperacusis in the Japanese patients.

### Patients and Methods

Thirty-four Japanese patients visiting our university hospital with a complaint of hyperacusis were included. They underwent the psychoacoustic measurement of hearing thresholds by standard pure-tone audiometry and uncomfortable loudness levels (ULLs) and completed the following questionnaires: the Japanese versions of HQ and GÜF, Self-rating Depression Scale (SDS), and State-Trait Anxiety Inventory (STAI). Several months after the first examination, a second administration of HQ and GÜF was conducted in 18 patients.

### Results

The total scores for HQ and GÜF ranged from 3 to 35 with an average of 18.0 (SD = 7.4) and from 1 to 37 with an average of 16.0 (SD = 8.3), respectively. Both scores seemed to demonstrate normal distribution and were significantly correlated. Neither total HQ nor total GÜF scores significantly correlated with ULL and the dynamic range, which is the difference between the hearing thresholds and ULLs. On the other hand, statistically significant correlations were

observed between the total scores for GÜF and those for SDS and STAI. However, The HQ scores demonstrated no significant correlations with SDS and STAI scores. On the second administration of HQ and GÜF, a change of nine points or more in total scores of both questionnaires was observed in most patients with subjectively clear change (markedly improvement or exacerbation) in hyperacusis, whereas this change was less than 8 points in most patients who subjectively felt no clear changes (slight or no improvement) of their symptom.

### Conclusion

The Japanese versions of HQ and GÜF are considered useful for clinical assessment of hyperacusis severity because of the normal distribution of their total scores and appropriate changes in scores for subjective changes in hyperacusis severity. The results also suggest that the emotional aspects of GÜF are more satisfactory than those of HQ. Large-scale studies should be conducted to confirm the validity and reliability of these two questionnaires.

## EFFECT OF DRINKING ALCOHOL, BATHING, AND EXERCISING ON TINNITUS

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### Background and aims

Tinnitus patients often complain that the severity of their tinnitus changes in some situations in their daily life. This change, although variable, seems to have a somewhat common tendency. The aim of this study was to evaluate the changes in tinnitus while performing common activities of daily living (e.g., drinking alcohol, bathing, and exercising), and to examine the correlations among them.

### Patients and Methods

Two hundred and fourteen patients visiting our university hospital with a complaint of tinnitus answered questions regarding how the severity of tinnitus changed in each of the following situations: drinking alcohol (moderately), bathing (relaxing in a bathtub), and exercising.
According to their responses for each situation, the patients were divided into 3 groups (improved, unchanged, or worsened) and the correlations among these were examined using Pearson's 2 test.

### Results

1. Drinking alcohol: Of the 214 cases, 93 were non-drinkers and were excluded. In the remaining 121 cases, tinnitus improved in 41 (33.9%), remained unchanged in 63 (52.1%), and worsened in 17 (14.0%).
2. Bathing: Tinnitus improved in 89 (41.6%), remained unchanged in 104 (48.6%), worsened in 19 (8.9%), and was obscure in 2 (1.0%) cases.
3. Exercising: Most of the patients were seniors and their exercises varied (e.g., jogging, walking, or playing tennis, golf, or ping-pong), but 8 did not perform any exercise. In the remaining 206 cases, tinnitus improved in 110 (53.4%), remained unchanged in 78 (37.9%), worsened in 16 (22.3%), and was obscure in 2 (1.0%).
4. Correlation between drinking alcohol and bathing: In the drinking-improved group (41 cases), tinnitus improved in 23, remained unchanged in 13, and worsened in 5 on exercising. In the drinking-unchanged group (63 cases), tinnitus improved in 32, remained unchanged in 30, and worsened in 1 on exercising. In the drinking-worsened group (17 cases), tinnitus

improved in 9, remained unchanged in 7, and did not worsen in any case on exercising; 1 patient did not exercise. The correlation was not significant between these two situations.

5. Correlation between drinking alcohol and bathing: In the drinking-improved group (41 cases), tinnitus improved in 24, remained unchanged in 13, worsened in 3, and was obscure in 1 on bathing. In the drinking-unchanged group (63 cases), tinnitus improved in 22, remained unchanged in 39, and worsened in 2 on bathing. The correlation was significant ($p < 0.05$).
6. Correlation between bathing and exercising: In the exercising-improved group (110 cases), tinnitus improved in 68, remained unchanged in 34, and worsened in 8 on bathing. In the exercising-unchanged group (78 cases), tinnitus improved in 16, remained unchanged in 56, worsened in 5, and was obscure in 1. In the exercising-worsened group (16 cases), tinnitus improved in 3, remained unchanged in 8, worsened in 4, and was obscure in 1. No significant correlation was noted between these two situations ($p < 0.01$).

**Conclusions**

The change in tinnitus severity varies while drinking alcohol, bathing, and exercising. However, the changes during bathing and exercising as well as during drinking and bathing were somewhat similar.

## PROPOSAL OF THE CLASSIFICATION OF TINNITUS SEVERITY AND MANAGEMENT

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### Objective

Tinnitus is a sensation that sometimes causes suffering. Generally, tinnitus evaluation have been used by tinnitus questionnaires. Tinnitus Handicap Inventory (THI) by Newman et al. is the major questionnaire in the world. We also use this for tinnitus evaluation. However, many of the tinnitus patient have psychological problem, especially depression and anxiety, it is difficult to evaluate of tinnitus severity by THI only. Since purpose of treatment for chronic tinnitus is to habituate itself, Tinnitus Retraing Therapy(TRT) consists of directive counseling and sound therapy have been useful, but in practice, We have been treated with a combination of antidepressants and psychotherapy for severe tinnitus patients. Therefore we make the classification of tinnitus severity, and plan to treatment along tinnitus severity.

### Method(s)

We analyzed 113 cases of tinnitus patients that were treated by TRT over 6 months at the Department of otolaryngology, Nagoya city university hospital and Kasugai city hospital. Tinnitus severity was evaluated by THI, psychological scale was evaluated by Hospital Anxiety and Depression Scale (HADS), and four catastrophic items were answered. We classified the tinnitus patients by THI scores, HADS and catastrophic items into four categories. To make treatment course of each categories, we investigated that tinnitus patients have been treated of psychotherapeutic drugs and psychotherapy.

### Result(s)

Numbers of grade 1 are 38 patients, and average of THI score is 37.6±12.2 points, average of HADS score is 10.9±4.5 points, catastrophic item are 0 point. Numbers of grade 2 are 24 patients, THI score is 70.6±8.6 points, HADS score is 13.1±3.5 points, catastrophic items are 0 points. Numbers of grade3 are 38 patients, THI score is 64.7±19.3 points, HADS score is 20.9±8.1 points, catastrophic items are 0.87 points. Number of grade 4 are 13 patients, THI score is 73.2±16.8, HADS score is 22.4±3.5, catastrophic items are 2.2 points.

We have just investigated whether received psychotherapeutic drug treatment for each category, 2.6% in grade I, 4.2% in grade II, 44.7% in grade III, 84.6% in grade IV, the medication enough to severe stages was used in combination. Psychotherapy as well, 27.3% were treated at grade III, 53.8% in grade IV.

**Conclusion(s)**

Because it is difficult to evaluate for tinnitus severity only THI, we made a classification for it. We suggested that tinnitus should be treated along severity of tinnitus.

## CHARACTERISING THE PSYCHOSOCIAL EXPERIENCES OF CHRONIC TINNITUS SUFFERERS

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Chronic tinnitus is highly subjective, both in terms of the sound experienced, and an individual's reactions to the sound. While some people are able to "tune out" their tinnitus, others report that their experience of tinnitus has a substantial negative impact on their psychosocial functioning. This commonly includes feelings of low mood, high anxiety, and decreased engagement in, and enjoyment of, daily routines. As such, an important step in understanding the tinnitus experience, and thus helping sufferers, is the characterisation of the factors contributing to the observed decline in psychosocial functioning. Thus, the aim of this study was to characterise these factors, as well as identify those that predict an individual's ability to adjust to the presence of their tinnitus from both a psychological and daily functioning perspective.

### Method

37 tinnitus sufferers (15 male) were recruited for this study with a range of tinnitus experiences from chronic non-bothersome tinnitus, to chronic bothersome tinnitus. Participants were asked to complete a series of questionnaires assessing mood, thinking strategies, health attitudes and coping styles to capture their broader psychosocial experiences. In addition, participants were assessed for the impact their tinnitus had on their emotion regulation and general daily functioning.

### Results

Preliminary analyses indicate an important distinction between tinnitus sufferers who experience a significant functional impairment and those who experience significant emotional dysregulation in response to their tinnitus. Contributing factors to these distinct psychosocial outcomes will be explored, in particular, the role of different coping strategies, attitudes towards illness, mood, and subjective tinnitus variables, to characterise these groups and determine the predictors of each. These results will form the basis of a model outlining the psychosocial factors influencing differences in the tinnitus experience to inform more targeted treatment strategies and thus assist in improving the experiences and coping abilities of tinnitus sufferers, and ultimately facilitation of their ability to "tune out" their tinnitus.

## SEASONAL AFFECTIVE DISORDER IN PATIENTS WITH CHRONIC TINNITUS

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### Objective

Seasonal affective disorder (SAD) is one type of depressions presenting in area with a big seasonal difference, especially showing recurrent depressive symptom in winter. The aim of this study is to investigate incidence of SAD, degrees of anxiety/depression/sleep disturbance, and characteristics of tinnitus in chronic tinnitus.

### Methods

From December 2012 to November 2013, seventy-five patients with chronic persistent or intermittent tinnitus were enrolled in this study. Exclusion criteria were pulsatile tinnitus, tinnitus by temporal bone trauma or ear surgery, history of tinnitus treatment more than 3 months previously, history of neuropsychological disease or depression, abuse history of alcohol or drug, cognitive dysfunction (brain lesion or surgery), and severe illness making regular follow-up and treatment difficult. Audiometry, tinnitogram, and questionnaire for anxiety/depression/sleep disturbance/ SAD were performed in all patients.

### Results

Among total 75 chronic tinnitus patients enrolled in this study, male to female ratio was 42:33 and mean age was 55.3 years. Number of patients suggesting SAD and subclinical SAD (S-SAD) was 7 (9.3%) and 9 (12.0%), respectively. The favorite season was autumn in most cases and most patients disliked winter. There were 7 patients showing catastrophic score more than THI 76 and the proportion was 2/7 (28.6%) in SAD group, 2/9 (22.2%) in S-SAD group, and 3/59 (5.1%) in control group suggesting the significant correlation between SAD and THI. There was no significant difference among audiogram and tinnitogram results in three groups. Anxiety/ depression/sleep disturbance tests showed more abnormal findings in SAD and S-SAD groups. In particular, the possibility of depression in SAD/S-SAD groups was significantly higher compared to that of control group (BDI>16: 7/16 (43.8%) vs 10/59 (17.0%); BDI>30: 3/16 (18.8%) vs 1/59 (1.7%), respectively).

### Conclusion

In the present study, SAD and S-SAD were suspected in about 20% of chronic tinnitus patients and this disease entity may be considered to manage tinnitus effectively.

## THE RELATION BETWEEN TINNITUS LOUDNESS, SLEEP DISORDERS AND EMOTIONAL DISTRESS

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### Introduction

Subjective tinnitus is a common hearing disorder in which patients suffer from ringing, buzzing and other perceived noises without external source, due to a number of different possible peripheral and central causes. Tinnitus often leads to cognitive impairment and emotional distress, and, among other complaints, a variety of sleep disturbances. Among standard exams applied to tinnitus patients are an audiometric exam to estimate the intensity of the phantom sound – tinnitus loudness matching (LM) – and internationally validated questionnaires to assess the level of psychological suffering induced by tinnitus, such as the Tinnitus Questionnaire (TQ) and Tinnitus Handicap Inventory (THI). Sleep disturbance is one of the factor dimensions of the TQ for which a score can be determined based on a subset of the items. The objective of this study is to investigate the relation between tinnitus loudness as measured by the LM procedure, sleep disturbance, and measures of other cognitive, emotional, perceptual and somatic stress symptoms.

### Materials and Methods

Complete data were gathered from 134 male and female adult tinnitus patients obtained from test reports of FGS and Neurophoneme R&D departments. Associations between loudness, THI and total and subscales of the TQ in their Iranian versions were calculated using Pearson and Spearman rank order correlations and Pearson chi-squared tests.

### Results

Only the Spearman correlation results will be reproduced in this abstract, with two-sided p-values. Rank order correlations between different dimensions of TQ, and THI and TQ, are, in general, moderate to high (>0.2) and statically significant (=0.05), as expected. Sleep disturbance is particularly correlated with emotional distress ($\rho$= 0.28, p=0.001), but, more surprisingly, the correlation with subjective loudness is negative rather than positive, and slightly significant ($\rho$=

-0.18, p=0.036). Subjective loudness as measured through LM also hardly has any correlation with emotional and cognitive symptoms in tinnitus patients.

### Conclusion

These results indicate that, while there seems to be a positive association between sleep disturbance and emotional distress, there is no direct relation with tinnitus loudness. The dissociation between sleeplessness and distress on the one hand, and loudness on the other, goes against earlier studies, and shows the necessity of careful study and modeling of potentially relatively independent systems for sensory experience and suffering due to tinnitus.

## USE OF THE SIGNIFICANT OTHER TO GAUGE TINNITUS SEVERITY

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### Aims / Objectives

Tinnitus reaction is notoriously difficult to quantity, and sufferers lack any internal reference to benchmark their tinnitus over time. It is possible that the patient's Significant Other's (SO's) perspective might be helpful in measuring it, given that tinnitus can also greatly impact the SO's quality of life. The Significant Others Tinnitus Questionnaire (SOTQ) was thus developed to assess the severity of the patient's tinnitus disturbance from the SO's perspective and also to more directly involve the SO in the counseling and rehabilitation process.

### Methods

The SOTQ incorporates five key areas of tinnitus disturbance that are also quantified by the patient on the Tinnitus Reaction Questionnaire (TRQ). Three questions that are also important to the effect on the SO were added in addition to two questions on how often the patient spontaneously mentioned their tinnitus as well as how often it appeared that the patient was disturbed by their tinnitus. There were also five questions on whether the SO themselves suffered from tinnitus. The same five-response option system (0-4) from the TRQ was thus utilized for all SOTQ items.

The SOTQ was presented to the SOs as part of routine tinnitus evaluation and counseling sessions on twenty-eight concurrent patients at the University of Miami Tinnitus Clinic. Concurrently, the patient completed the TRQ.

### Results and Discussion

Data on the five common questions from the TRQ was paired with the SO's corresponding SOTQ questions; results were then pooled as grouped data. Two-tailed paired t-tests were calculated on each domain, as well as the composite scores.

Mean results indicated that the SOs rated the patient's avoidance of social situations as a significantly more frequent problem than the patients did. Perhaps this is like hearing loss, where the social situation avoidance might affect the SO's more than the patients themselves.

There was no significant difference between the two groups in terms of tinnitus interfering with the patient's relaxation and sleep, with both domains being rated as quite frequently disturbed. This might be because the SOs can readily determine that the patient has a lot of trouble relaxing or

sleeping.
The SO rated the patient's ability to work as a frequent problem on average, while the patient rated it as more minor. This significant difference doesn't yet have a clear explanation.
Patients rated concentration as a significantly more frequent problem than the SOs. Perhaps this is the one domain that the SO can't readily gauge.

Overall, the composite score mean differences indicated a trend where the SO rated tinnitus as more disturbing than the sufferer did, although this difference was not significant. As the SOs and the patients each rated various domains more highly than the other, the composite score tended to average out those differences.

**Conclusion**

This data indicated that the SO's perspective is useful in quantifying a patient's tinnitus distress, and they may suffer as a result of the patient's tinnitus. It was an excellent counseling resource that empowered the SOs to help in the rehabilitation process, particularly in maintaining realistic expectations.

## VALIDATION OF THE TINNITUS FUNCTIONAL INDEX IN A UK RESEARCH POPULATION

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### Background

Chronic tinnitus is a common and sometimes disabling condition yet there is no standardized approach to measuring its impact in either the clinical setting or research. For clinical assessment of tinnitus the preferred questionnaire in the UK is the Tinnitus Handicap Inventory1. This was developed as a diagnostic tool to measure tinnitus severity. Although it lacks sensitivity to treatment-related changes in tinnitus it is also often used as an outcome measures in both clinical practice and research. Current alternatives to the THI equally only measure severity, or are good measures of change, but not both. In contrast, the Tinnitus Functional Index (TFI)2 was developed to be used as both a diagnostic measure of severity and to be a sensitive measure of treatment-related change. We are currently validating this questionnaire for use in the UK.

### Methods

The present study evaluates the TFI as a diagnostic tool for the assessment of tinnitus in a research population. Questionnaire data was obtained from a multi-site clinical trial. As part of the initial screening, 294 participants completed six screening assessment questionnaires; the TFI, the Beck's Depression Inventory (BDI), the Beck's Anxiety Inventory (BAI), the World Health Organisation Quality of Life Bref (WHOQOL-BREF) the Tinnitus Handicap Inventory (THI), and the Tinnitus Handicap Questionnaire (THQ). 100 tinnitus participants completed the TFI at a second visit before the research intervention. We evaluated discriminant and convergent validity of the TFI with this large cohort (N= 247) comparing the six assessment questionnaires. Test-retest reliability and agreement (N=94) of the TFI were evaluated using Intra-class correlation coefficients (ICC). Confirmatory factor analysis in progress uses the eight subscales identified by Meikle et al. (2012) during TFI development.

### Results

Convergent and discriminant validity of the TFI revealed high correlations with the THI ($r = 0.82$) and THQ ($r = 0.82$) and moderate to low correlations with the BDI ($r = 0.56$), BAI ($r = 0.38$) and WHOQOL ($r = -0.48$). Test-retest reliability for the TFI global score was extremely high, with the

ICC (95% CI) showing strong correlations between two administrations (ICC = 0.86, p< .001, 95% CI = 0.8-0.9). Ongoing CFA to be presented is predicted to demonstrate the TFI has a multidimensional questionnaire structure.

**Conclusion**

We can confirm that the TFI is a reliable measure of tinnitus for use in evaluating a research population. The TFI demonstrates high discriminant and convergent validity and extremely high test-retest reliability. It is expected that confirmatory factor analysis will show eight separate domains.


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4. *Meikle MB, Henry JA, Griest SE, Stewart BJ, Abrams HB, McArdle R et al. Ear Hear, 2012; 33(2):153-76.*

## DEVELOPMENT OF OBJECTIVE MEASUREMENT FOR TINNITUS

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### Aims / Objectives

No objective test is available for most tinnitus cases, and diagnosis is made on the basis of medical history. In this study, we develop the novel device to objectively detect tinnitus.

### Methods

We developed the portable electroencephalography (EEG) device and measured at their left side of FP1 of EEG alone. FP1 is located on forehead area and is reflected by higher cognitive processes including attention and relaxation algorithms. The patients group with chronic tinnitus and no tinnitus (healthy volunteers) group were tested and analyzed by our device. IRB was approved in Keio University Hospital.

### Results

There are three EEG patterns at FP1 we obtained; pattern A (lower spectrum at higher EEG frequencies), pattern B-1 (8-9Hz at EEG peak), B-2 (10-11Hz at EEG peak), pattern C (alpha and beta waves at peaks). In no tinnitus group (N=25), twenty subjects presented pattern B-2, four for pattern B-1, one for pattern A. On the other hand, in tinnitus group (N=25), 11 people for pattern A, 7 for pattern B-1, 4 for B-2, 3 for pattern C. The typical pattern in tinnitus group is B-2 (peak frequency 10-11Hz) . Five subjects of no tinnitus group presented B-2 pattern, suggesting false positive.

### Conclusion

This study indicated that this measurement device of FP1 we developed can detect tinnitus objectively (sensitivity; 84%, specificity;80%). FP1 may reflect anxiety of patients with tinnitus. The further study of analyzing pathophysiological background will be necessary.

## METAPLASTICITY: BRAKE OR ACCELERATOR FOR PLASTICITY?

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Synaptic plasticity is a fundamental mechanism of learning, and thus critical for all cognition. Too much or too little plasticity, however, can lead to abnormal levels of neural activity and thus dysfunctional networks. Mechanisms must be present therefore that can homeostatically regulate plasticity capability to help keep neural activity within safe limits. On the other hand, there are times, for example during learning, when plasticity may need to be temporarily up-regulated. The general ability of prior neural activity to regulate future plasticity is termed "metaplasticity". Understanding of specific homeostatic and non-homeostatic metaplasticity mechanisms may help with identifying mechanisms and potential treatments of conditions where neural activity is unusually sustained or reduced.

## RESPONSIVENESS TO THREATENING SOUNDS: A SELECTIVE ATTENTION PARADIGM

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### Aims / Objectives

The impact of tinnitus on cognitive resources has scarcely been studied experimentally. We presently hypothesize that responsiveness to tinnitus is determined by the perceived harmfulness of the tinnitus, i.e. the threat- appraisal of the sound, leading to lower tolerance to sound and depletion of cognitive resources. The influence of perceived threat value of neutral tones on responsiveness was studied in a selective attention paradigm with healthy individuals. It was hypothesised that performance on a primary decision task is negatively influenced by increased perceived threat of distracting neutral tones.

### Method

First and second year psychology and speech pathology students of the KU Leuven were recruited (N=70). Individuals with a hearing loss (cut-off at a pure tone average on 1, 2 and 4 kHz of 35 dB hearing level), or chronic tinnitus complaints, were excluded. Participants were randomly assigned to one of two threat conditions, high-threat (HT) versus low-threat (LT). Both groups were exposed to both pure tones (4kHz, 70 dB) and warbles (4 kHz, 70 dB, modulated by 100 Hz, moderation frequency of 20 Hz) while performing a cognitive decision task. In the threat-condition either the pure tone or the warble was manipulated to increase threat-value of the tone (counterbalanced). A mixed model ANCOVA with 'threat' (high vs. low) as the between subjects factor and 'Tone' (warble vs. pure tone) as the within subjects factor was conducted, with response times on the decision task as the outcome variable.

### Results

The expected interaction between threat and tone-type reached significance, $F(1, 113)$ $p = .03$. Analyses showed a main effect of threat $F(6.04)$ $p = .02$, $\eta^2 = .16$ and not tone type $F(.38)$ $p > .05$, $\eta^2 = .01$.

### Conclusions

Exposure to an (initially neutral) tone, which is manipulated to have increased threat-value, will deplete cognitive resources. Exposure to threatening tones has detrimental effects on cognitive task performance in normal subjects. These results shed light into the mechanisms underlying tinnitus and its interruptive effects on daily tasks.

## NOISE PROTECTION FOR HYPERACUSIS PATIENTS WITH STRESS ON TEACHERS

### A CASE PRESENTATION OF A NEW APPROACH

**Specific aspects of noise protection for patients with hyperacusis with particular stress on teachers.**

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**Aim**

It is a challenge for every acoustician and ENT-doctor to provide noise protection for tinnitus- and hyperacusis patients. The problem is even more difficult for teachers who work in class rooms with background noise and reverberation and at the same time their work necessitates good speech understanding.

Understanding of speech in a classroom could be difficult even for a person with normal hearing, but it is especially challenging for those with hearing disorders. These people need better acoustic conditions for understanding.

We developed noise protection for different professional groups working in noisy surroundings with special emphasis on persons with tinnitus and hyperacusis. Apart from improving the quality of life for these patients, these new possibilities of noise protection help to prevent loss of working hours.

Out of 110 patients we treated successfully over the last 3 years we present one case which is exemplary as teachers in classrooms are exposed to disturbing noises from the children andon the other hand have to understand them clearly.

**Method**

Case: A 36 year old teacher with sound-speech audiograms differing on both sides, hyperacusis approx. 70 – 75 dB, not able to continue her teaching job. In January 2013 we supplied her with a combination of sound generators and a frequency amplifier which enhances sound in the speech range and/or compensates for hearing loss.

The challenge in providing noise protection for hyperacusis patients is keeping the balance of

noise protection. Too much protection is not helpful, because it increases the gain within the auditory system consequently increasing hyperacusis. Too little protection could annoy the patient and consequently increase hyperacusis. Our patient wears dynamic noise protection, a "sound brake", which produces a defined noise level, the so called "digital sound separating technology". This means an instrument with a sound manager for disturbing noises (sound cleaning) which suppresses disturbing noises and enhances speech. We chose an instrument with automatic directional microphones and wireless function so that both instruments can be adjusted at the same time.

### Result

Sound generator, frequency amplifier and "sound brake" are matched and can be adapted to the respective sound situation. Symptoms of hyperacusis are relieved, leading to relaxation of body and psyche, decrease of stress level and lasting improvement.
Our patient is teaching again since August 2013.

### Conclusion

This method proves very effective in many of our patients. It is a good way to reintegrate patients in their working lives, thus being beneficial for the patients and for the community.

## GENTLE SKIN STIMULATION MODULATES THE BALANCE BETWEEN THE SYMPATHETIC NERVE AND THE VAGAL NERVE AMONG NORMAL ADULT

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### Background

There is a simple method for measuring heart rate variability called “Standing Up test” that is a very easy examination. When a subject sits on the chair, one has a low resting heart rate. But after standing up one’s heart rate will be greater than the resting state. When one is healthy, it will get into flat smoothly. But some researchers alarm that it will be some prediction for the mortality. On the other hand, the Standing Up test based heart rate variability is an actual physiological phenomenon caused by the autonomic nervous system. This system consists of sympathetic system and Cardiac vagal nervous system. This present study, we evaluates whether the skin stimulation can modulate the balance between the sympathetic nerve and the vagal nerve in human subjects using Micro Cone.Lux

### About Micro Cone

The adhesive plaster called “Micro Cone” is produces in Japanese markets as a substitute of painkiller medicine by Toto Resin Inc. It possesses a 376 of nano-sized cone on 1cm diameter of the plastic disk with the plaster. The efficacy of the Micro Cone for the neuropathic pain in human was reported. As the results of the modulation of the neural transmission of A- delta fiber and C fiber, threshold of pain will be reduced in the same manner of the Gate Control Theory. In the anesthetized animal study, the neural transmission was restrained regardless of attention and recognition by somatic sensation and the usability test of the cardiac sympathetic nerve reflection by mechanical skin stimulation. These means that Micro Cone Skin Stimulation has the capability of the influence for a sympathetic nerve and the interaction of the vagal nerve.

### Subjects and Methods

21 healthy normal adult subjects are employed in the study. 3 types of the skin stimulation were taken for the study; Real plaster (SC-II), Sham-1 plaster (plaster only) and Sham-2 plaster (disc

without the micro-cone). When the subject put the plaster under the double blind condition, one performed a Standing Up test and was checked the pNN50 during the standing state. pNN50 was calculated with RR interval of one's plethysmogram (Stress Checker 2, Azumio Inc). Subject performs all types of plaster at random (NN50 is the number of interval differences of successive NN (RR) intervals of heart rate greater than 50 msec. pNN50 is the proportion derived by dividing NN50 by the total number of NN intervals).

### Results

The grand averaged score of pNN50 is significantly different among these plaster: 44.9%(ave.) in Sham-1, 41.0% in Sham-2 and 26.4% in Real Plaster (SC-II). The differences among the GA score were confirmed with the statistical meaning of Student t-test.

### Conclusion

It is confirmed that the under threshold Skin Stimulation modulates the Balance between the sympathetic nerve and the vagal nerve using Micro Cone. As the same meaning of vagal nerve stimulation or Galvanic SCM electrical stimulation, this skin stimulation technology can be applied for the tinnitus treatment.

## ON THE PERCEPTUAL AND NEURONAL VARIABILITY IN CHRONIC TINNITUS

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Subjective tinnitus is defined as an auditory perception in the absence of any physically identifiable source for it. About 5-10% of the population report an ongoing and chronic perception of the tinnitus sound – but how chronic is this perception? Is the tinnitus constantly "on", or are there also periods were the tinnitus is perceived less? Indeed, more than 60% of the chronic tinnitus subjects report a variability of the tinnitus perception between days, but to date we don't understand where this variability comes from and if this is an important indicator for the treatment response of the subjects. In order to measure this within-person variability of tinnitus perception, we developed an experience sampling application running on smartphones that is able to track the individual tinnitus perception and distress during the day under real world conditions. In the first part of the talk, we want to present preliminary results of this study.

With the second part of the talk we want to concentrate on the variability of neuronal activity in the auditory cortex. Chronic tinnitus is usually associated with a decrease of the alpha frequency oscillatory power in temporal areas. Here we show, that also the moment-to-moment variability of the alpha activity is largely reduced in chronic tinnitus. Most importantly, it can be shown that this neuronal variability is associated with the tinnitus duration. Subjects with a longer history of tinnitus show less alpha variability in auditory regions. Whether these changes in neuronal variability relate to the perceptual variability remains to be seen.

## ELDERLY PATIENTS BENEFIT FROM COCHLEAR IMPLANTATION REGARDING AUDITORY REHABILITATION, QUALITY OF LIFE, TINNITUS AND PSYCHOLOGICAL COMORBIDITIES

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### Aims / Objectives

To evaluate the effect of cochlear implantation (CI) on the health related quality of life (HRQoL), speech understanding, tinnitus impairment, perceived stress and depressive and anxiety disorders in the 70+ years old, postlingually deafened patients and to compare the results to these obtained from a group of younger patients.

### Methods

Fifty-five postlingually deafened adults at least 6 months after CI were included in this study (20 patients ≥70 years/ 35 patients <70 years. Using 5 validated questionnaires, we have evaluated the quality of life (NCIQ), tinnitus impairment (TQ), perceived stress (PSQ), depressive (ADSL) and anxiety symptoms (GAD-7). In addition, speech perception in quiet and noise (Freiburg monosyllables, HSM sentences, Oldenburg Inventory) was determined.

### Results

Cochlear implantation significantly increased the HRQoL in both age groups, as measured by the NCIQ and its six subscales. The speech perception after CI did not differ from that of the younger patients. Of the 55 patients, 48 (87%) reported having chronic tinnitus before CI. Among the older patients, tinnitus-induced distress had a tendency to decrease following CI. In patients who had a high severity level of tinnitus, the TQ score decreased significantly in the older and younger group. Similarly, patients with high severity level of perceived stress, the PSQ scores decreased significantly in both age groups. Nearly 30% of patients had depressive disorders prior to CI. Number of these patients decreased to 11% in the younger and 1% in the older group. Furthermore, 20% of the younger and 36% of older patients had severe or moderate anxiety disorder prior to CI. Older group of patients had no longer anxious symptoms after cochlear implantation

**Conclusion**

The present study provides evidence that cochlear implantation represents a very successful procedure of auditory rehabilitation, also for patients over 70. In addition, elderly patients benefit from CI with increased quality of life and a reduction in tinnitus, stress and psychological comorbidities.

## TINNITUS: A SEMINAR IN THE LANCET

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There has been significant progress in tinnitus research in recent times, which has led to a deeper understanding of causes, impacts, and effective treatment strategies. Much of this has been published in specialist journals, and not readily available to the wider clinical and scientific communities. We recently published a major review in The Lancet - a journal that is hugely well respected. These peer-reviewed 'seminars' as they are known are commissioned by Lancet editors. The purpose of each seminar is to provide a state-of-the-art, broad-ranging overview of a disease, covering epidemiology, pathogenesis, diagnosis, treatment, and prevention, while highlighting relevant clinical controversies. The seminars are relevant to doctors and other medical professionals anywhere in the world, ideal for exam preparation, and invaluable as teaching tools for clinical tutors worldwide.

Our review summarises present knowledge from clinical and auditory neuroscience perspectives for all interested scientific and clinical readers. Whilst a treatment to abolish tinnitus completely continues to elude us, this is an indication of the tinnitus field coming of age, and troublesome tinnitus being recognised as an issue that requires urgent research and appropriate resources. This poster summarises the main themes contained within our review and provides an ideal opportunity to disseminate to the wider tinnitus community.

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

*Reference*

*Baguley D, McFerran D, Hall DA. The Lancet, 2013; 382:9904:1600-7.*

## IS GENTLE SKIN STIMULATION MODULATING TINNITUS DISTRESS AMONG TINNITUS PATIENTS?

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### Introduction

As the result of posture change (i.e., standup and standstill condition), it causes the pressor reflex. This physiological change is based on the autonomic balance between sympathetic nervous system and vagal nerve system. However this response can be modulated with gentle skin stimulation, that Dr. Nakagawa discovered and have presented on this 8th TRI meeting. HRV is dynamically changed when the gentle skin stimulation plaster (Micro Cone, Toyo Resin Inc.) sticks on the hallucal area (ball of the thumb).

This technique might be applied for the neural modulation for the autonomic nervous system instead of other invasive methods (i.e., electrical vagal nerve stimulation).

In the present study, we evaluate whether gentle skin stimulation modulates tinnitus and related distress with the gentle skin stimulation as the results of the neural modulation for the balance between the sympathetic nerve and the vagal nerve in human subjects.

### Subject and Method

Fourteen severe and moderate tinnitus suffer participants were recruited among our out door patients. Subjects undergo 3 months course of Micro Cone absorbed plaster treatment. Their tinnitus severity was assessed with the questionnaires before the gentle skin stimulation therapy (GST) and after 3 month.

Several questionnaires were taken as follows: Tinnitus Handicap Inventory-12 (THI-12), visual analog scale (VAS) for TSSw and TRSw and etc. This study is designed with the sham controlled double blind condition.

### Results

There was no statistical significant change among all subjects between before and after 1 month. Final results after 3 months data will be presented on the site.

### Conclusion

Among total 14 patients with severe and moderate chronic tinnitus, some patients felt the improvement of symptoms after 1 month without statistical confirmation. GST might have some potential to be considered management modality for tinnitus even with distress as severe.

## MULTISENSORY CONTRIBUTORS TO TINNITUS: HEARING, PAIN, TASTE AND SMELL

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### Aims / objectives

The literature demonstrates that tinnitus can be modulated and elicited through stimulation of the somatosensory system. This phenomenon is still not well understood, and other aspects of the somatosensory system and tinnitus have not been explored. The aim of this study is to investigate multisensory contributors to tinnitus perception and to subtype tinnitus into auditory/non auditory contributors. Subtyping tinnitus is crucial for both research into the underlying mechanisms and the development of treatment for tinnitus.

### Methods

Questionnaires were sent to participants from the University of Auckland Hearing Clinic Database. Analysis involved using Chi-squared and one-way ANOVA tests, and a cluster analysis, using Ward's method, to subtype tinnitus into separate groups of non-auditory sensory tinnitus and auditory tinnitus.

### Results

Statistically significant relationships were found between tinnitus severity and spontaneous taste ($p<0.001$), spontaneous smell ($p<0.001$), unexplained pain ($p=0.001$), hearing impairment in the left ear ($p=0.028$), hearing impairment in the right ear ($p=0.020$), sensitivity to loud noise ($p=0.004$) and pain with tinnitus ($p<0.001$). The cluster analysis revealed three clusters of participants with tinnitus; (1) participants who experience tinnitus rarely, (2) participants who experience tinnitus constantly, (3) participants who have hearing impairments and tinnitus.

### Conclusions

These findings support the hypothesis that different sensory systems may contribute to tinnitus. These findings take research another step closer to understanding tinnitus and the developing of more targeted treatment.

## MULTISENSORY TRAINING FOR TINNITUS

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### Aims and objectives

This is a proof-of-principle study to investigate the viability of a home-based computerised programme involving tinnitus training with multiple sensory modalities. Two training paradigms were trialled. Integration theory suggests if tinnitus is paired with visual and tactile features that fit with gestalt principles of good continuation, an object can form involving the tinnitus that no longer violates auditory scene analysis. Such integration may assist in adaptation to tinnitus. Alternatively, attention-diversion theory suggests if attention is trained away from the tinnitus side, decreases may be observed in tinnitus related distress. The aims of the study were to determine if multisensory training was a possible treatment for tinnitus by combining auditory, visual and tactile stimuli and if the sensory-integration paradigm or attention-diversion paradigm was a superior method for unilateral tinnitus treatment.

### Methods

A randomised study included 18 participants, aged between 41 to 75 years, with predominantly unilateral tinnitus (11 right, 7 left). Psychophysical and subjective measures of tinnitus formed the outcome measures. Participants were randomly allocated to one of two groups, with auditory, visual and tactile stimuli presented in either a sensory-integration or attention-diversion training paradigm developed specifically for the study. Participants were provided with laptop computers and trained on a home-based computerised programme over 20 consecutive days for 20-30 minutes per day.

### Results

The multisensory training on average resulted in reduced tinnitus perception as evaluated by the TFI ($F2,32 = 5.254$, $p = 0.011$), with reduced scores reflecting improvements in the negative impact of tinnitus severity and changes that occurred due to treatment. The TSNS also revealed improvements ($F2,32 = 4.787$, $p = 0.016$) suggestive of a reduction in perception of tinnitus loudness, discomfort, annoyance, ignorability, and unpleasantness experienced by the individual. The THI revealed improvements but was not statistically significant ($F2,32 = 2.116$, $p = 0.151$). The results did not show any reliable difference between the sensory-integration and attention-diversion groups. The pitch of participant's tinnitus decreased ($F1,16 = 11.209$, $p = 0.004$) over the training period.

## Conclusions

This preliminary study revealed how a novel home-based computerised perceptual training programme, involving multiple sensory modalities, lead to improvements in tinnitus. Some trends but no statistically signifant differences were found between training types. Improvements in both the subjective impact of tinnitus and the psychophysical characteristics were recorded which may reflect plastic changes within a short time frame. Further research is required to confirm these findings and may involve techniques to enhance plasticity and investigate the neural correlates of improvements observed.

## MULTISENSORY TINNITUS TREATMENT AND SACCADIC EYE MOVEMENTS

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### Aims / Objectives

Tinnitus is the conscious awareness of sound without an external, driving sound source. Recent evidence indicates that cortical and subcortical regions associated with memory, emotion and attention may be involved in tinnitus' pathophysiology. In addition, it has been shown that numerous interventions including attentional perceptual training and oculomotor and somatosensory manipulations can modulate tinnitus perception. In the present study, we developed a novel multisensory treatment for tinnitus relying on audio, visual, and somatosensory stimulation. Two approaches were adopted, whereby the stimuli were used to either divert attention from tinnitus (attention diversion) or to integrate tinnitus with other sensory modalities (integration). Saccadic eye movements were analyzed as a probe to multisensory interactions in tinnitus and to assess the effects of the multisensory training.

### Methods

Eye tracking data were collected before and after multisensory treatment in a group of 16 participants (59.3 years ± 10 SD) with predominantly unilateral tinnitus. Participants received 20 days of either integration (N = 9) or attention diversion training (N = 7), whereby the groups were matched for age and Tinnitus Functional Index. Saccades were assessed in terms of their error rate, latency (the time between stimulus onset and the beginning of the saccade), accuracy (the endpoint of the saccade in respect to the target) and peak velocity. Saccadic data for the tinnitus-dominant and opposite side were compared between the attention diversion and multisensory integration groups.

### Results

No differences were found for saccadic measures between the two sides and groups before the training. The multisensory training significantly altered the error rate of the trials directed to the tinnitus side by 9.5% ± 2.8 SEM ($t8 = 3.409$, $p = 0.009$), whereby this effect was specific

only to the integration group ($F1, 14 = 6.662$, $p = 0.022$). In addition, the treatment resulted in significantly shorter latencies ($F1, 14 = 29.047$, $p < 0.001$), with comparable effects on both sides and groups ($F1, 14 = 0.448$, $p = 0.514$). No other measures were reliably affected by the training.

## Conclusion

These preliminary results show that the novel multisensory treatment can affect oculomotor function in tinnitus patients, as manifested by task-specific decrease of saccadic latency. Specifically, the integration multisensory training altered the saccadic error rate in favor of the non-tinnitus side. This finding suggests that multisensory interventions may be effective in reducing tinnitus salience and emerge as a viable treatment intervention.

## A NONINVASIVE NEUROMODULATION APPROACH FOR TREATING TINNITUS UTILIZING MULTIMODAL ACTIVATION AND PLASTICITY

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### Objectives

Tinnitus affects approximately 250 million people worldwide and has been linked to abnormal activity across the auditory system. We propose a new noninvasive neuromodulation approach for treating tinnitus which we call Multimodal Stimulation Therapy (MST). An underappreciated organization of the brain for treating neurological disorders is the dense and topographic interconnectivity among sensory, motor, cognitive, and limbic centers. Through appropriately-timed activation of different multimodal pathways, we hypothesize that MST can target and modulate aberrant neuronal populations to suppress the tinnitus percept. We initially investigated the effects of combined auditory and somatosensory stimulation to induce auditory plasticity that could be relevant for treating tinnitus.

### Methods

We positioned 32-site electrode arrays throughout the inferior colliculus (IC) and primary auditory cortex (A1) in ketamine-anesthetized guinea pigs and compared spontaneous and acoustic-driven activity in both regions before and after MST. Subcutaneous needle electrodes were used to electrically stimulate different body locations, including the left and right legs, back, left and right shoulders, neck, left and right mastoids, and tongue. Each body region was paired with a broadband noise or pure tone stimulus with varying delays. We also performed several control conditions, including acoustic stimulation alone, body stimulation alone, and no stimulation.

### Results

In IC and A1, MST induced greater changes in spontaneous and acoustic-driven activity compared to the control conditions. More significantly, the delay between somatosensory and acoustic stimulation elicited differential neural effects. Body stimulation before acoustic stimulation evoked vast inhibition of IC activity while the reverse order caused more facilitation of IC activity. Similarly, there was more facilitation of A1 activity at one delay that was not the case for another delay. These changes in activation based on timing differences are consistent with spike-timing

dependent plasticity results shown via invasive neural stimulation protocols. Furthermore, MST could cause differential effects by varying the location of body stimulation. Stimulation of right side body sites induced more inhibition than facilitation in the right IC and A1, while the reverse trend occurred for stimulation of left side body sites. Stimulation of upper body sites also induced more inhibition than facilitation in IC, while the reverse trend occurred for stimulation of lower body sites. Particularly for MST with pure tones, stimulation of left body sites caused A1 neurons to become more sensitive to the frequency of the presented pure tone.

### Conculsion

MST can induce differential changes in firing patterns and sensitivity to acoustic stimuli across the auditory system by varying stimulation parameters. We still need to investigate if MST can systematically reverse neural features linked to tinnitus, such as hyperactivity and hypersynchrony, as well as behavior in a tinnitus animal model. Since MST is noninvasive, we have the opportunity to test MST with different parameters and pathways (e.g., auditory, somatosensory, visual, motor, and limbic) directly in tinnitus patients that are guided by the animal findings.

## THE TEMPORAL CORTEX AND ITS ROLE IN A TINNITUS NETWORK. AN MEG-STUDY

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### Aims / Objectives

Tinnitus is a phantom auditory percept which affects up to 15% of the population. It most likely originates from maladaptive cortical reorganization and a hypersensitive, hyperactive auditory cortex. Research has shown that brain oscillations – which are thought to account for a major role in neural communication – differ between tinnitus patients and healthy controls (1). The Global Brain Model of Tinnitus (2) draws a broader framework for a brain-wide basis of tinnitus: it proposes that a fronto-parieto-cingulate network exerts top-down influence on the local auditory cortex in special frequency ranges.

### Methods

Using five minutes resting state MEG data, we examined seventeen tinnitus patients (n=17) and sixteen healthy controls (n=16) using the matlab based FieldTrip Toolbox. Data was ICA-corrected and artifacts removed via threshold (2.5pT). Connectivity was measured through Partial Directed Coherence (PDC). To analyze in source space, we used a beamformer approach and created eight "virtual channels" representing areas according to the Global Brain Model. In- and outflow were calculated through node degrees, a summation of PDC values.

### Results

In sensor space we found an enhanced delta activity in the tinnitus group compared to the healthy controls in temporal areas. The global power showed an alpha reduction in the tinnitus group, yet the effect was driven by parietal, not temporal areas. Preliminary analysis in source space hints to an alpha reduction in the left temporal cortex. Furthermore, the inflow from the global network to left temporal areas seems to be reduced and the information outflow out of this area enhanced in tinnitus patients compared to the control group.

### Conclusion

We were able to replicate Weisz et al. findings regarding the enhanced delta power in temporal areas in tinnitus patients. Yet, we could not demonstrate the alpha-reduction in temporal areas in sensor space. Source space analysis indicates a temporally located alpha reduction, though only in the left one. The enhanced outflow could represent the auditory hyperactivity and the prominent

role of the auditory cortex in the tinnitus network, the lack of inflow the simultaneous lack of inhibition exerted on the auditory cortex by other part of the brain, e.g. frontal areas.

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## THE ROLE OF INDIVIDUAL PAIN TOLERANCE AND PAIN TRESHOLD IN BEARING TINNITUS

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Tinnitus is a chronic and disturbing symptom that affects millions of people worldwide.

In this study, the differences (and similarities) between short term and long term tinnitus and pain is evaluated. Pain threshold and pain tolerance of patients with tinnitus were measured three times and the average was recorded.

Forty-five patients attending the Audiology department of Hacettepe University (HU) Hospital were evaluated. Patients consisted of 19 female and 26 male, with an age range between 24 to 79 years, and duration of tinnitus of at least 3 months prior to testing. The results were compared to a control group of healthy (non- tinnitus sufferers) individuals, 20 females and 25 males, with an age range between 21 and 48 years.

Pain threshold and pain tolerance measurements of the patients and control group have been recorded in the Department of Physical Therapy and Rehabilitation of HU. These measurements were taken using electrical stimulation. For pain threshold and tolerance measurement Dimeq Med Module 5 (Bosch) instrument was used.
Measurements were made at room temperature of 22 degrees Celsius, in a sitting position, 90 degrees flexion of the elbow and forearm pronation and Supination, while recorded between the neutral positions. Measurements of the radial side of the forearm, proximal to the right passive electrode, the active electrode was placed at the distal end of the Radius. The patients were asked to respond when they feel pain sensation. Pain threshold and pain tolerance measurements were repeated for three times. The average of these three values obtained and recorded in milliamp's. The results from the patients group and the control group were statistically compared using the Mann-Whitney U test and Student's T-Test.

### Results

There was no statistically significant difference in pain threshold between the study and control groups, the same goes for the pain tolerance results.

### Conclusion

It was possible to endure short-term pain and tinnitus. However, it was not possible to endure the pain and tinnitus when the duration is increased.

Tolerance to tinnitus was associated with cortical familiarization (habituation) or brain plastisite and cortical printmaking (suppression). Research and studies in this direction are expected to give positive results.

## PREVALENCE AND FACTORS ASSOCIATED WITH NECK AND JAW MUSCLE MODULATION OF TINNITUS

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Forceful contractions of neck and jaw muscles have been shown to modulate tinnitus and can be used to screen patient who are responsive to somatic modulation.

To identify the factors associated with somatic modulation of tinnitus, 163 patients underwent 19 neck and jaw maneuvers after a physiological and audiological profile was compiled.

Tinnitus was modulated in 57.1% of ears tested. Neck maneuvers generally decreased tinnitus loudness, whereas jaw maneuvers increased loudness. Female gender and buzzing tinnitus were associated with a high prevalence of modulation.

Use of these characteristics to select optimal candidates for somatosensory based tinnitus therapies.

## NOISE PROTECTION FOR HYPERACUSIS PATIENTS WITH STRESS ON TEACHERS

## A CASE PRESENTATION OF A NEW APPROACH

**Specific aspects of noise protection for patients with hyperacusis with particular stress on teachers.**

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### Aim

It is a challenge for every acoustician and ENT-doctor to provide noise protection for tinnitus- and hyperacusis patients. The problem is even more difficult for teachers who work in class rooms with background noise and reverberation and at the same time their work necessitates good speech understanding.

Understanding of speech in a classroom could be difficult even for a person with normal hearing, but it is especially challenging for those with hearing disorders. These people need better acoustic conditions for understanding.

We developed noise protection for different professional groups working in noisy surroundings with special emphasis on persons with tinnitus and hyperacusis. Apart from improving the quality of life for these patients, these new possibilities of noise protection help to prevent loss of working hours.

Out of 110 patients we treated successfully over the last 3 years we present one case which is exemplary as teachers in classrooms are exposed to disturbing noises from the children andon the other hand have to understand them clearly.

### Method

Case: A 36 year old teacher with sound-speech audiograms differing on both sides, hyperacusis approx. 70 – 75 dB, not able to continue her teaching job. In January 2013 we supplied her with a combination of sound generators and a frequency amplifier which enhances sound in the speech range and/or compensates for hearing loss.

The challenge in providing noise protection for hyperacusis patients is keeping the balance of noise protection. Too much protection is not helpful, because it increases the gain within the auditory system consequently increasing hyperacusis. Too little protection could annoy the patient and consequently increase hyperacusis. Our patient wears dynamic noise protection, a "sound brake", which produces a defined noise level, the so called "digital sound separating technology". This means an instrument with a sound manager for disturbing noises (sound cleaning) which suppresses disturbing noises and enhances speech. We chose an instrument with automatic directional microphones and wireless function so that both instruments can be adjusted at the same time.

### Result

Sound generator, frequency amplifier and "sound brake" are matched and can be adapted to the respective sound situation. Symptoms of hyperacusis are relieved, leading to relaxation of body and psyche, decrease of stress level and lasting improvement.
Our patient is teaching again since August 2013.

### Conclusion

This method proves very effective in many of our patients. It is a good way to reintegrate patients in their working lives, thus being beneficial for the patients and for the community.

## GENTLE SKIN STIMULATION MODULATES THE BALANCE BETWEEN THE SYMPATHETIC NERVE AND THE VAGAL NERVE AMONG NORMAL ADULT

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### Background

There is a simple method for measuring heart rate variability called “Standing Up test” that is a very easy examination. When a subject sits on the chair, one has a low resting heart rate. But after standing up one’s heart rate will be greater than the resting state. When one is healthy, it will get into flat smoothly. But some researchers alarm that it will be some prediction for the mortality. On the other hand, the Standing Up test based heart rate variability is an actual physiological phenomenon caused by the autonomic nervous system. This system consists of sympathetic system and Cardiac vagal nervous system. This present study, we evaluates whether the skin stimulation can modulate the balance between the sympathetic nerve and the vagal nerve in human subjects using Micro Cone.

### About Micro Cone

The adhesive plaster called “Micro Cone” is produces in Japanese markets as a substitute of painkiller medicine by Toto Resin Inc. It possesses a 376 of nano-sized cone on 1cm diameter of the plastic disk with the plaster. The efficacy of the Micro Cone for the neuropathic pain in human was reported. As the results of the modulation of the neural transmission of A- delta fiber and C fiber, threshold of pain will be reduced in the same manner of the Gate Control Theory. In the anesthetized animal study, the neural transmission was restrained regardless of attention and recognition by somatic sensation and the usability test of the cardiac sympathetic nerve reflection by mechanical skin stimulation. These means that Micro Cone Skin Stimulation has the capability of the influence for a sympathetic nerve and the interaction of the vagal nerve.

### Subjects and Methods

21 healthy normal adult subjects are employed in the study. 3 types of the skin stimulation were taken for the study; Real plaster (SC-II), Sham-1 plaster (plaster only) and Sham-2 plaster (disc without the micro-cone). When the subject put the plaster under the double blind condition, one performed a Standing Up test and was checked the pNN50 during the standing state. pNN50 was calculated with RR interval of one's plethysmogram (Stress Checker 2, Azumio Inc). Subject performs all types of plaster at random (NN50 is the number of interval differences of successive NN (RR) intervals of heart rate greater than 50 msec. pNN50 is the proportion derived by dividing NN50 by the total number of NN intervals).

### Results

The grand averaged score of pNN50 is significantly different among these plaster: 44.9%(ave.) in Sham-1, 41.0% in Sham-2 and 26.4% in Real Plaster (SC-II). The differences among the GA score were confirmed with the statistical meaning of Student t-test.

### Conclusion

It is confirmed that the under threshold Skin Stimulation modulates the Balance between the sympathetic nerve and the vagal nerve using Micro Cone. As the same meaning of vagal nerve stimulation or Galvanic SCM electrical stimulation, this skin stimulation technology can be applied for the tinnitus treatment.

## ON THE PERCEPTUAL AND NEURONAL VARIABILITY IN CHRONIC TINNITUS

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Subjective tinnitus is defined as an auditory perception in the absence of any physically identifiable source for it. About 5-10% of the population report an ongoing and chronic perception of the tinnitus sound – but how chronic is this perception? Is the tinnitus constantly "on", or are there also periods were the tinnitus is perceived less? Indeed, more than 60% of the chronic tinnitus subjects report a variability of the tinnitus perception between days, but to date we don't understand where this variability comes from and if this is an important indicator for the treatment response of the subjects. In order to measure this within-person variability of tinnitus perception, we developed an experience sampling application running on smartphones that is able to track the individual tinnitus perception and distress during the day under real world conditions. In the first part of the talk, we want to present preliminary results of this study.

With the second part of the talk we want to concentrate on the variability of neuronal activity in the auditory cortex. Chronic tinnitus is usually associated with a decrease of the alpha frequency oscillatory power in temporal areas. Here we show, that also the moment-to-moment variability of the alpha activity is largely reduced in chronic tinnitus. Most importantly, it can be shown that this neuronal variability is associated with the tinnitus duration. Subjects with a longer history of tinnitus show less alpha variability in auditory regions. Whether these changes in neuronal variability relate to the perceptual variability remains to be seen.

## ELDERLY PATIENTS BENEFIT FROM COCHLEAR IMPLANTATION REGARDING AUDITORY REHABILITATION, QUALITY OF LIFE, TINNITUS AND PSYCHOLOGICAL COMORBIDITIES

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### Aims / Objectives

To evaluate the effect of cochlear implantation (CI) on the health related quality of life (HRQoL), speech understanding, tinnitus impairment, perceived stress and depressive and anxiety disorders in the 70+ years old, postlingually deafened patients and to compare the results to these obtained from a group of younger patients.

### Methods

Fifty-five postlingually deafened adults at least 6 months after CI were included in this study (20 patients ≥70 years/ 35 patients <70 years. Using 5 validated questionnaires, we have evaluated the quality of life (NCIQ), tinnitus impairment (TQ), perceived stress (PSQ), depressive (ADSL) and anxiety symptoms (GAD-7). In addition, speech perception in quiet and noise (Freiburg monosyllables, HSM sentences, Oldenburg Inventory) was determined.

### Results

Cochlear implantation significantly increased the HRQoL in both age groups, as measured by the NCIQ and its six subscales. The speech perception after CI did not differ from that of the younger patients. Of the 55 patients, 48 (87%) reported having chronic tinnitus before CI. Among the older patients, tinnitus-induced distress had a tendency to decrease following CI. In patients who had a high severity level of tinnitus, the TQ score decreased significantly in the older and younger group. Similarly, patients with high severity level of perceived stress, the PSQ scores decreased significantly in both age groups. Nearly 30% of patients had depressive disorders prior to CI. Number of these patients decreased to 11% in the younger and 1% in the older group. Furthermore, 20% of the younger and 36% of older patients had severe or moderate anxiety disorder prior to CI. Older group of patients had no longer anxious symptoms after cochlear implantation

**Conclusion**

The present study provides evidence that cochlear implantation represents a very successful procedure of auditory rehabilitation, also for patients over 70. In addition, elderly patients benefit from CI with increased quality of life and a reduction in tinnitus, stress and psychological comorbidities.

## RESPONSIVENESS TO THREATENING SOUNDS: A SELECTIVE ATTENTION PARADIGM

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### Aims / Objectives

The impact of tinnitus on cognitive resources has scarcely been studied experimentally. We presently hypothesize that responsiveness to tinnitus is determined by the perceived harmfulness of the tinnitus, i.e. the threat- appraisal of the sound, leading to lower tolerance to sound and depletion of cognitive resources. The influence of perceived threat value of neutral tones on responsiveness was studied in a selective attention paradigm with healthy individuals. It was hypothesised that performance on a primary decision task is negatively influenced by increased perceived threat of distracting neutral tones.

### Method

First and second year psychology and speech pathology students of the KU Leuven were recruited (N=70). Individuals with a hearing loss (cut-off at a pure tone average on 1, 2 and 4 kHz of 35 dB hearing level), or chronic tinnitus complaints, were excluded. Participants were randomly assigned to one of two threat conditions, high-threat (HT) versus low-threat (LT). Both groups were exposed to both pure tones (4kHz, 70 dB) and warbles (4 kHz, 70 dB, modulated by 100 Hz, moderation frequency of 20 Hz) while performing a cognitive decision task. In the threat-condition either the pure tone or the warble was manipulated to increase threat-value of the tone (counterbalanced). A mixed model ANCOVA with 'threat' (high vs. low) as the between subjects factor and 'Tone' (warble vs. pure tone) as the within subjects factor was conducted, with response times on the decision task as the outcome variable.

### Results

The expected interaction between threat and tone-type reached significance, $F(1, 113)$ $p = .03$. Analyses showed a main effect of threat $F(6.04)$ $p = .02$, $\eta^2 = .16$ and not tone type $F(.38)$ $p > .05$, $\eta^2 = .01$.

### Conclusions

Exposure to an (initially neutral) tone, which is manipulated to have increased threat-value, will deplete cognitive resources. Exposure to threatening tones has detrimental effects on cognitive task performance in normal subjects. These results shed light into the mechanisms underlying tinnitus and its interruptive effects on daily tasks.

## THE RELATIONSHIP BETWEEN TINNITUS AND CRANIOCERVICAL MUSCULOSKELETAL DYSFUNCTION

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### Background / Aim

A causal connection between tinnitus and signs and symptoms of craniomandibular disorder in some tinnitus patients has been proposed. Tinnitus sufferers have shown higher prevalence of fatigue/tenderness in jaw muscles, pain on palpation of masticatory muscles, impaired mandibular mobility, signs of parafunctions, and pain upon mouth opening in epidemiologic samples 1,2. A model to explain this causal connection has been proposed that links disinhibition of the dorsal cochlear nucleus with chronic irritation of the craniofacial nerves and the 1st and 2nd spinal nerves. The aim of the present research was to assess the relationship between chronic tinnitus and craniocervical musculoskeletal dysfunction.

### Methods

Twenty participants (mean age 56.3 years) with chronic tinnitus for more than 2 years took part in this pilot study. Participants twice visited the hearing and tinnitus clinic, located at the University of Auckland. The first session built a hearing and tinnitus profile using extended high frequency audiometry, the assessment of tinnitus pitch, loudness, and minimum masking level. Questionnaires were used to collect a tinnitus-related case history, functional index, severity numeric scale, handicap inventory, and a scale of depression anxiety and stress. Information was also collected about participants' self-perception regarding their craniocervical musculoskeletal status. During the second appointment a craniocervical specialist (blind to the participants' data) assessed participants' jaw and cervical spine articular function. Data were analysed by the audiologist and a second independent and blinded craniocervical specialist to assess relationships between tinnitus and musculoskeletal function.

### Results

Of the 20 participants, 5 reported a percept of tinnitus modulation related to craniofacial musculoskeletal (MS) activity, and 15 had evidence of MS dysfunction. Of the 5 reporting tinnitus modulation, clear evidence of mandible and/or upper cervical spine dysfunction was detected. Interestingly in participants with no MS-reported dysfunction the assessor did not detect any evidence of MS dysfunction in 5 participants and MS dysfunction was detected in 10 participants.

## Conclusion

The present study revealed a high incidence of craniocervical dysfunction consistent with the incidence for people who report head and neck pain. We therefore expected to find some participants with evidence of MS dysfunction that did not report an MS-related modulation of their tinnitus. Importantly, all 5 participants reporting an MS-related modulation percept of their tinnitus had evidence of MS dysfunction, but of the 15 who did not report an MS-related modulation, 5 did not have evidence of MS dysfunction. Although our sample size was small, our findings promote the exciting hypothesis that for people who report MS-related modulation and who have evidence of craniocervical dysfunction, restoring normal MS function may improve their tinnitus. We plan to test this hypothesis in a future study.

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## MULTIMODALITY EVALUATION AND TREATMENT OF TINNITUS

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Both the auditory pathway and non-auditory brain are involved in the pathophysiological mechanisms of tinnitus, and therefore both must be treatment targets. Before starting treatment, we have to evaluate both of these in patients. We evaluate auditory pathways by pure tone audiometry, pitch matching, and resting-state fMRI. It is hypothesized that cochlear hearing loss reduces cochlear nerve activity, and this reduced activity within the affected auditory pathwaydown-regulates inhibitory cortical processes, leading to hyperexcitability within central auditory structures, including the primary auditory cortex. We check the functional connectivity (FC) between the left and right auditory cortices by resting-state fMRI. According to our data, FC between left and right auditory cortex in tinnitus patients is significantly reduced as compared to controls. Next, we evaluate the non-auditory brain by the following questionnaires: THI (tinnitus handicap inventory), SDS (self-depression scale), STAI (state-trait anxiety index), HADS (hospital anxiety and depression scale) and PSQI (Pittsburgh sleep quality index), and resting-state fMRI. According to data from our 1424 tinnitus patients, about 40% of severely handicapped patients (THI score $>$ 58) have depressive tendencies (SDS score $>$ 50),80% of severe patients have Grade IV and V state-trait anxiety, and 90% of severe patients have sleep disorders. Based on the results, we propose that tinnitus can be a great distress when aberrant neuronal activity in the primary auditory cortex is connected to a broader cortical “distress network” involving the anterior and the posterior cingulate cortex, the dorsolateral prefrontal cortex, the amygdala, and the hippocampus. Our resting-state fMRI data shows thatFC between the auditory cortex and distress network cortices was elevated in subjects with tinnitus.

Tinnitus treatment that deals with the auditory pathway aims to restore the reduced peripheral auditory activity by hearing aids or cochlear implants or regulate directly the auditory cortex by rTMS (repetitive transcranial magnetic stimulation) or tDCS (transcranial direct current stimulation). For hearing loss that can be improved with hearing aids, sound therapies with hearing aids are the treatment of choice. In our sound therapies, the hearing aid is adjusted following the half-gain rule and the patient wears it all day long. This induces plasticity of the auditory and non-auditory networks. Our 76 tinnitus patients with bilateral hearing loss who received counseling and sound therapy with bilateral hearing aids showed significant reduction of THI score after 6 months (58 ±25 → 14 ±16). The resting-state fMRI shows that FC between left and right auditory cortex returns to normal levels after sound therapy with hearing aids. Treatment for the non-auditory brain is to manage the depression, anxiety, attention, cognition, and memory by counseling, pharmacological treatment (e.g. antidepressants), and psychotherapy. All patients receive counseling to understand the nature and causes of tinnitus and how to manage it.Most tinnitus patients have incorrect negative beliefs concerning tinnitus, such as that tinnitus signals a serious medical problem and that they must monitor changes in the tinnitus tone. We correct the misconceptions through counseling.

We will introduce our multimodality evaluations and treatments of tinnitus and show our data at the presentation.

## ARE TREATMENTS FOR TINNITUS EFFECTIVE?

Hall, D.A.

*Institute for Health Research (NIHR) Nottingham Hearing Biomedical Research Unit*

As resources become increasingly limited, allocations of both research and health care funding are dependent upon high quality evidence. Historically, tinnitus has been the poor cousin of a cinderella science, with low quality clinical research providing unreliable estimates of effect, and with devices marketed for tinnitus without strong evidence for those product claims. However, the field is changing. A number of leading clinical and academic experts on tinnitus have recently made calls to the field to improve the design, implementation and reporting of clinical trials. Since 2008, the NIHR Nottingham Hearing BRU has established itself as the UK's leading centre for early phase clinical trials on tinnitus. This talk enables me to expand on general methodological innovations using specific examples of our own work and that of other groups around the world. Topics include efficacy and effectiveness; multi-disciplinary collaboration; registration of trial protocols; outcome measures; and data analysis and interpretation.

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

## Poster Session 1 / Tahi

*Numbers refer to poster board allocation*

TINNITUS PRECEDED DEPRESSIVE SYMPTOMS IN COMMUNITY-DWELLING OLDER JAPANSES: A PROSPECTIVE COHORT STUDY
**Mizutari, K.**; Michikawa, T.; Nishiwaki, Y.; Saito, H.; Ogawa, K.
01

VALIDATION OF THE TINNITUS FUNCTIONAL INDEX IN NEW ZEALAND
Chandra, N.; Lee, A.; **Searchfield, G**.
07

ARE PEOPLE WITH TINNITUS SATISFIED WITH THEIR INTERACTION WITH THE HEALTHCARE SYSTEM?
Carmody, N.; Eikelboom, R.H
13

TINNITUS IN NEW ZEALAND
**Wu, B.; Exeter, D.; Searchfield, G.D.**
19

CLINICAL CHARACTERISTICS OF PATIENTS WITH TINNITUS EVALUATED WITH TINNITUS SAMPLE CASE HISTORY QUESTIONNAIRE IN JAPAN
**Kojima, T**.; Kanzaki, S.; Oishi, N.; Watabe, T.; Inagaki, Y.; Wakabayashi, S.; Yamada, H.; Ogawa, K.
25

CLINICALLY RELEVANT CHANGES ON THE PRIMARY TINNITUS OUTCOME MEASURES; NORMS AND RELIABLE CHANGE ANALYSES
**Cima, R.**; Vlaeyen, J.
21

ASSESSMENT OF HYPERACUSIS SEVERITY USING QUESTIONNAIRES AND ITS CLINICAL USEFULNESS
**Sakashita, T.**; Kato, S.; Yamane, H.
37

EFFECT OF DRINKING ALCOHOL, BATHING, AND EXERCISING ON TINNITUS
**Kato, S.**; Sakashita, T.; Yamane, H.
43

PROPOSAL OF THE CLASSIFICATION OF TINNITUS SEVERITY AND MANAGEMENT
**Takahashi, M**.; Kabaya, K; Sekiya, Y.; Murakami, S.
49

CHARACTERISING THE PSYCHOSOCIAL EXPERIENCES OF CHRONIC TINNITUS SUFFERERS
**Callander, K.J.**; McLachlan, N.M.; Wilson, S.J.
57

SEASONAL AFFECTIVE DISORDER IN PATIENTS WITH CHRONIC TINNITUS
Kim, Y.H.
63

THE RELATION BETWEEN TINNITUS LOUDNESS, SLEEP DISORDERS AND EMOTIONAL DISTRESS
**Jangholi, N**.; GhodratiToostani, I.; Maurice Erna Claessens, P.
69

USE OF THE SIGNIFICANT OTHER TO GAUGE TINNITUS SEVERITY
**Sheehan, T.**; Davis, P.
75

VALIDATION OF THE TINNITUS FUNCTIONAL INDEX IN A UK RESEARCH POPULATION
**Hoare, D.**; Fackrell, K.; Barry, J.; Hall, D.
80

DEVELOPMENT OF OBJECTIVE MEASUREMENT FOR TINNITUS
Kanzaki, S.[1]; Takayama, K.[2]; Mitsukura, Y.[2]; Oishi, N.[1]; Yamada, H[1]; Inagaki, Y.[1]; Wakabayashi, S.[1]; Kojima, T.[1]; Ogawa, K.[1]
88

## Poster Session 2 / Rua

*Numbers refer to poster board allocation*

TINNITUS: A SEMINAR IN THE LANCET
**Hall, D.A.**; Baguley, D.; McFerran, D.
02

IS GENTLE SKIN STIMULATION MODULATING TINNITUS DISTRESS AMONG TINNITUS PATIENTS?
Tanuma, F.; Nakagawa, M.; Fukasawa, S.; Mori, Y.; Watanabe, S.
08

MULTISENSORY CONTRIBUTORS TO TINNITUS: HEARING, PAIN, TASTE AND SMELL
Kerridge, M.; Searchfield, G.
14

MULTISENSORY TRAINING FOR TINNITUS
Linford, T.; Spiegel, D.; Searchfield, G.D.
20

Multisensory tinnitus treatment and saccadic eye movements
Spiegel, D. P.; Thompson, B.; Petoe, M.; Kobayashi, K.; Linford, T.; Searchfield, G. D.
26

A NONINVASIVE NEUROMODULATION APPROACH FOR TREATING TINNITUS UTILIZING MULTIMODAL ACTIVATION AND PLASTICITY
Markovitz, C.; Smith, B.; Gloeckner, C.; Lim, H.
32

THE TEMPORAL CORTEX AND ITS ROLE IN A TINNITUS NETWORK. AN MEG-STUDY
**Lau, P.**; Pantev, C.
38

THE ROLE OF INDIVIDUAL PAIN TOLERANCE AND PAIN TRESHOLD IN BEARING TINNITUS
**Aslan, S**.; Aksoy, S.; YÄ±lmaz, T.; Keser, I.; Kirdi, N.
44

## PLASTICITY OF MULTISENSORY PROCESSING IN THE DORSAL COCHLEAR NUCLEUS: ITS ROLE IN TINNITUS GENERATION AND SUPPRESSION

Shore, S. E.

Long-term alterations in dorsal cochlear nucleus (DCN) neural firing rates occur following paired somatosensory and auditory stimuli (Dehmel et al., Journal of Neuroscience, 2012). This plastic phenomenon is 'stimulus-timing dependent' in that the strength and direction of the "bimodal" plasticity depends on the order and timing of bimodal stimulation. Hebbian and anti-Hebbian timing rules generated in this way reflect in vitro spike-timing dependent plasticity (Koehler and Shore, PloS One, 2013).

Following noise-exposure and tinnitus induction, stimulus-timing dependent plasticity in tinnitus animals are more likely to be anti-Hebbian than animals that do not develop tinnitus and are broader for those bimodal intervals in which the neural activity was enhanced. Furthermore, units from exposed animals with tinnitus are more weakly suppressed than those without tinnitus. Broadened timing rules in the enhancement phase in animals with tinnitus, and in the suppressive phase in exposed animals without tinnitus would be expected to produce greater neural excitation in animals with tinnitus and reduced excitation in animals without tinnitus (Koehler and Shore, J. Neuroscience, 2013).

These results highlight alterations of stimulus-timing dependent plasticity in the DCN as a new neural correlate of tinnitus opening the way for a therapeutic target for tinnitus.

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## TINNITUS AND ABNORMAL PROCESSING IN THE CENTRAL AUDITORY SYSTEM

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Tinnitus is a multifactorial symptom that may involve mechanisms in het peripheral hearing organ, the auditory brain and non-auditory portions of the brain. Functional magnetic resonance imaging is a method to study the brain mechanisms involved in tinnitus. In particular, it offers the opportunity to test in humans, hypotheses that were developed from experiment in animals. Animal experiments show clear evidence of reorganization of the cortical map with hearing loss, which is possibly associated with tinnitus. In contrast, fMRI experiments show that tinnitus may occur without evidence of cortical remapping. In a study of gaze-modulated tinnitus, the gaze was associated with a decrease in thalamic activity and an increase in cortical activity. In two other studies, subjects with and without tinnitus were compared with respect to the brain's response to sound. In the first study, subjects had normal to near-normal audiogram. In the second study, the subjects had a moderate sensorineural hearing loss. Functional MRI suggested a reduced functional connectivity between the brainstem and the cortex in tinnitus patients, which signifies abnormal auditory processing. Together, these results are consistent with an abnormal role of the thalamus in tinnitus. Future studies must further define this abnormality and may point towards targeted treatments for tinnitus.

## PARAHIPPOCAMPAL-AUDITORY CORTEX COMMUNICATION IN TINNITUS

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### Introduction

The parahippocampal area and auditory cortex are important hubs in tinnitus, as demonstrated by EEG, MEG, fMRI and PET. Furthermore, the functional connectivity between these areas is the only robust finding in resting state fMRI studies in tinnitus.

### Methods and materials

To further explore this critical connection we performed EEGs in 129 tinnitus patients We analyzed the neural correlates of hearing loss and subjective tinnitus loudness (NRS) on a whole brain analysis as well as the functional and effective connectivity between the auditory cortex and parahippocampal area.

### Results

Hearing loss is related to bilateral parahippocampal theta activity and right-sided alpha parahippocampal activity. Tinnitus loudness is related to gamma band activity in the auditory cortex left parahippocampus, as well as alpha in the left insula, low beta right dorsal anterior cingulate cortex.

A significant correlation is found between the subjective loudness and lagged phased synchronization (=functional connectivity) between the left parahippocampus and the left auditory cortex for the theta frequency band, as well as for the percentage of time there is theta-gamma nesting in the left parahippocampus and auditory cortex.

The effective connectivity depends on the hearing loss. The more hearing loss a patient has the more information is transferred from the parahippocampal area to the auditory cortex

### Discussion and conclusion

The parahippocampus and auditory cortex communicate using the theta band as a carrier wave on which gamma band activity is nested. The gamma band correlates with the tinnitus loudness. In hearing loss the missing information seems to be pulled from hippocampal memory.

## MODULATING ALPHA AND BETA OSCILLATIONS WITHIN POSTERIOR CINGULATE CORTEX THROUGH REAL-TIME SOURCE LOCALIZED NEUROFEEDBACK AND ITS EFFECT ON TINNITUS RELATED DISTRESS

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Up to 25% of the people affected by tinnitus report interference with their lives as tinnitus causes a considerable amount of distress. It is known that distress can play an important role in the development of tinnitus leading to psychological complications such as annoyance, concentration problems, depression, anxiety, irritability, sleep disturbances, and intense worrying. Previous research already indicated that decreased alpha power is associated with actively engaging in processing a stimulus and that the posterior cingulate cortex forms a core region of the default network. Highly distressed tinnitus patients are actively engaged to their tinnitus as such it seems reasonable that a decreased alpha power is obtained within the posterior cingulate cortex. The beta-band oscillations on the other hand have been associated to maintenance of the current cognitive state. That is, beta oscillations are related to endogenous modulation of early auditory responses and may be enhanced if the status quo is given priority over a new signal. As this phantom sound is constantly present and could be interpreted as status quo that has priority over a new signal, certainly in patient that are really distressed by their tinnitus. This fits with the findings that highly distressed tinnitus patients have increased beta-band oscillations within the posterior cingulate cortex. Consequently, it can be hypothesized that real-time source localized neurofeedback to voluntarily up-regulate alpha activity and down-regulate beta activity within the posterior cingulate cortex can modulate tinnitus related distress. This approach goes beyond conventional imaging studies that only correlate ongoing activity with changes in tinnitus, as neurofeedback allows us to directly manipulate ongoing brain activity and thereby to establish a causal link between ongoing activity and tinnitus perception. The posterior cingulate cortex is a particular well-suited target for neurofeedback because its activity can be modulated by top-down control mechanisms, such as attention and imagery. Here we show in a large group of 50 tinnitus patients, in a placebo-controlled way, that up-regulating alpha and down-regulating beta oscillations targeting the posterior cingulate cortex through real-time source localized neurofeedback has a clear effect on the tinnitus related distress but not on the loudness. These results are supported by power changes and changes in phase coherence.

## CHANGE IN SPONTANEOUS CORTICAL ACTIVITY DURING TINNITUS REMEDIATION

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### Introduction

Tinnitus remediation programs vary in their effectiveness to provide long-term relief for tinnitus sufferers. Understanding the link between subjective benefit and the neurophysiological changes which occur throughout remediation may provide a better understanding of the physiological mechanisms underpinning tinnitus relief and may be important for developing individualised therapies. However, currently this is limited by a paucity of sensitive and objective tests. Recent advances in imaging techniques have shown some promise in identifying and quantifying tinnitus-related neural activity and its relationship with subjective indicators of the impact of the tinnitus on the individual (Hoke, Feldmann et al. 1989; Weisz, Moratti et al. 2005). In this study, we aim to evaluate the neurophysiological changes evident in tinnitus and non-tinnitus sufferers and to evaluate the changes in spontaneous brain activity during a tinnitus treatment program.

### Aims / Objectives

The aims of the present study are:

1. Identify changes in the spontaneous activity of the brain in patients with clinically significant tinnitus using Magnetoencephalography (MEG).
2. Measure changes in spontaneous brain activity prior, during and post tinnitus remediation program.
3. Identify if any association exists between the subjective (TRQ) and objective (MEG) measures of tinnitus.

### Method

The tinnitus group (N=12) underwent extended audiometric evaluation and completed a battery of questionnaires ruling out clinical depression and anxiety as a probable cause of, or association with tinnitus. A five minute spontaneous MEG recording was acquired while they were in a state of relaxed wakefulness. The tinnitus participants were provided with Neuromonics treatment program, while at the same time had their MEG data recorded prior to, during and post treatment program. As a comparison, spontaneous MEG recordings of control group (N=10) with clinically normal hearing and no complaint of tinnitus were also acquired. The MEG data were analysed using Brain Electrical Source Analysis (BESA) software.

**Results and Conclusion**

Our results showed that the spontaneous alpha (8-13Hz) temporal-parietal brain activities in the tinnitus group were smaller when compared to that of the control group. Incremental changes of alpha were seen as the treatment progressed. In addition, an inverse association between the TRQ score and alpha power measured from the cortex were found. We will discuss the potential implications of using MEG as a tool to objectively measure tinnitus.

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## TONOTOPIC MAP CHANGES DURING TINNITUS REMEDIATION

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### Background

Tinnitus has been associated with the abnormal organisation of the tonotopic map in the auditory cortex (Eggermont, 2006). However, it is currently not clear whether successful tinnitus remediation which shows improved subjective outcomes, can affect the reorganisation of the tonotopic map towards a non-disrupted state. Therefore the aims of the present study were: (i) to compare tonotopic maps acquired from magnetoencephalography (MEG) recordings in individuals with significant tinnitus with non-tinnitus participants to determine whether disruptions could be measured; (ii) to identify whether changes in the tonotopic map and evoked responses occurred during and after a tinnitus remediation program; and (iii) to identify whether these changes occurred in parallel with subjective changes of tinnitus impact.

### Method

Twelve tinnitus participants were recruited and completed audiometric evaluation, subjective measurement of tinnitus using the tinnitus reaction questionnaire (TRQ), measurement of psychoacoustic characteristics of tinnitus, and evaluation of depression and anxiety before during and after tinnitus remediation. Ten normal hearing non-tinnitus participants were recruited for comparison. Sound stimuli of 500Hz, 1kHz, 2kHz, 4kHz and 8kHz tones were presented to each ear individually and cortical activity was measured using MEG. All tinnitus participants completed a Neuromonics rehabilitation program over 25 weeks and MEG was measured at 5 or 10 week intervals. MEG data were analysed using Brain Electrical Source Analysis (BESA).

### Results & conclusions

MEG results indicated that the tinnitus subjects' source locations were more anterior compared to that of the control group (for all presented frequencies). After undergoing remediation, the tinnitus subjects' source strengths increased (for normal hearing frequencies) while source locations moved towards a more posterior location (towards that of non-tinnitus participants). These results suggests that tinnitus remediation using Neuromonics affects source strength and tonotopic map of the tinnitus participants.

*Reference*

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## CHANGES IN RESTING-STATE FMRI ACTIVITY DURING SALICYLATE-INDUCED TINNITUS AND SOUND STIMULATION

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### Aims / Objectives

The neural mechanisms that give rise to the phantom sound of tinnitus are poorly understood, but recent studies suggest that low frequency neural oscillatory activity contributes to tinnitus generation. To explore this issue, we measured the amplitude of low-frequency fluctuations (ALFF) in resting-state functional magnetic resonance imaging (fMRI) during salicylate-induced tinnitus and during sound stimulation.

### Methods

Rats were scanned with a 7.0 T MRI system; 15 were treated with 300 mg/kg of salicylate to induce tinnitus and the remaining 15 were injected with saline as controls. Baseline fMRI scans were collected with music stimulation (85 dB SPL Leq) and without music (control). Afterwards, the measurements were repeated 2 h after salicylate or saline treatment. Statistical parametric mapping was used to determine which regions of the brain showed significant changes in ALFF activity due to salicylate or music stimulation.

### Results

Salicylate induced significant bilateral increases of ALFF activity in several auditory region (auditory cortex, medial geniculate body, inferior colliculus, trapezoid body) as well as several non-auditory regions including the paraflocculus of the cerebellum, visual cortex, somatosensory cortex and amygdala. In contrast, salicylate significantly decreased ALFF activity in the hippocampus and striatum. Furthermore, salicylate treatment enhanced (hyperactivity) the ALFF neural responses to music stimuli in several brain regions, including the auditory cortex, inferior colliculus, medial geniculate body, trapezoid body and somatosensory cortex.

## Conclusions

Salicylate significantly increased ALFF oscillatory activity in several auditory and non-auditory regions previously implicated in salicylate and/or noise-induced tinnitus. Interestingly, several new regions of aberrant ALFF activity were observed in visual and somatosensory cortex, sensory areas known to interconnect with the auditory cortex. Music stimulation tended to potentiate the salicylate-induced hyperactivity in the ALFF responses in many auditory areas, consistent with previous electrophysiological reports of sound evoked hyperactivity in the central auditory pathway. These results suggest that the perception of tinnitus may be due in part to large increases in low-frequency neural oscillations within the central auditory pathway along with aberrant neural oscillations in the amygdala, paraflocculus and visual and somatosensory cortices. Resting-state ALFF fMRI might therefore prove useful in identifying the aberrant neural networks in humans who suffer from severe, debilitating tinnitus.

## AUDITORY-LIMBIC NETWORK IN TINNITUS REVEALED BY RESTING-STATE FUNCTIONAL CONNECTIVITY MRI

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Tinnitus is characterized by the perception of sound in the absence of an external source. Despite the prevalence of this disorder, its pathophysiology remains poorly understood. A large body of evidence has revealed plasticity-related changes in the auditory system of patients with tinnitus, including modifications in one or more sites along the auditory pathway, both peripheral and central. Although lesion-induced plasticity of auditory structures may be a necessary precondition, it does not seem sufficient to cause chronic tinnitus. Given this constraint, and the growing body of evidence implicating limbic involvement in tinnitus, we propose that limbic dysfunction may play a critical role in causing, as well as perpetuating, the tinnitus percept.

For our current study, we chose to elucidate this dysfunction by using magnetic resonance imaging to measure functional connectivity (fcMRI). Since the tinnitus percept is most noticeable at rest, i.e. in the absence of tasks or distractors, we chose to analyze connectivity from resting-state fcMRI data, that is, data acquired when subjects were not performing any tasks. Specifically, we used Independent Component Analysis (ICA), a data-driven, non-a-priori statistical technique, to identify roughly 25 functionally connected resting-state networks (RSNs). Auditory, visual, "default-mode," and other neurophysiologically plausible networks were consistently detected in all subjects, along with non-neurophysiological networks, having to do with, e.g., respiration and heart rate, which were removed from further analysis. Of particular interest was a network that appeared in ICAs of tinnitus patients, but not of controls matched for age and hearing loss. This network demonstrated a unique inverse relationship between medial Heschl's gyrus (mHG) and the Nucleus Accumbens (NAc), suggesting a direct or indirect connection between the two regions. Apart from revealing a novel auditory-limbic network, these results are consistent with previous reports of NAc involvement in tinnitus [1], and suggest a far-reaching tinnitus network incorporating non-auditory regions [2]. The present study offers the additional advantage of superior spatial resolution afforded by fcMRI while elucidating this network more precisely.

Overall, our data suggest a much larger role for the limbic system in tinnitus pathophysiology than previously thought, thus opening new avenues for potential treatments of the disorder. Furthermore, additional study of limbic connectivity may shed light on the system's involvement in multiple sensory pathways, which could provide a robust multidisciplinary approach for the study of tinnitus as well as certain forms of chronic pain.

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## INFLUENCE OF TINNITUS ON AUDITORY SPECTRAL AND TEMPORAL RESOLUTION, AND SPEECH PERCEPTION ABILITY IN TINNITUS PATIENTS

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### Aims

The aims of this study were to investigate 1) the influence of tinnitus upon the auditory spectral and temporal resolution and 2) the effect of tinnitus on speech perception ability in noise.

### Methods

To exclude the effect of decreased hearing threshold, unilateral idiopathic tinnitus patients with symmetric hearing thresholds were enrolled in this study. Subjects were 19 patients who have symmetric hearing loss > 20dB HL and a binaural difference < 10 dB at 0.25, 0.5, 1, 2, 3, 4, and 8 kHz, or who have normal hearing thresholds and a binaural difference < 10 dB at 0.25, 0.5, 1, 2, 3, 4, and 8 kHz, and threshold discrepancies < 15 dB at 9, 11.2, 12.5, 14, 16, 18 and 20 kHz. Seventeen normal hearing subjects without tinnitus were enrolled as a control group. Four different psychoacoustic measurements were performed: 1) spectral-ripple discrimination, 2) temporal modulation detection, 3) Schroeder-phase discrimination, and 4) word recognition in noise.

### Results

There were no significant differences in spectral-ripple thresholds, temporal modulation detection thresholds, and Schroeder-phase discrimination scores between affected sides and non-affected sides of unilateral tinnitus patients. For the word in noise test, affected sides showed significantly worse performance compared to non-affected sides ($p < 0.05$).

### Conclusion

We could not find any evidence that the tinnitus-affected ears show worse spectral and temporal processing compared to non-tinnitus ears in unilateral tinnitus patients. The spectral ripple discrimination data suggests that the tinnitus-affected ears may not have broader auditory filters compared to non-affected ears with the same hearing thresholds. However, the difference in

speech perception ability in noise suggests that tinnitus might have a masking effect when subjects try to understand target speech. These results imply that the occurrence of tinnitus does not depend upon the degree of cochlear damage, but upon the change of central auditory pathway by deafferentation.

**Acknowledgement**

The psychoacoustic test materials were provided by the Rubinstein Lab at Virginia Merrill Bloedel Hearing Research Center.

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## EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON AUDITORY RESIDUAL INHIBITION OF TINNITUS

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### Aims / Objectives

Transcranial direct current stimulation (tDCS) is a painless, safe and non-invasive neuromodulation technique1, where electrodes (anode or cathode) are positioned over the target area of the head, to facilitate or suppress cortical activity. Feldman (1971)2 observed brief tinnitus suppression following cessation of the masker and this phenomenon of tinnitus suppression for a brief period following the offset of an appropriate masking stimulus was later known as Residual Inhibition (RI). RI usually lasts for less than a minute. The effect of anodal tDCS of the left temporoparietal area on auditory residual inhibition of tinnitus was investigated in this sham controlled study.

### Methods

Ten participants (mean age 59.18 years, ranging from 45 years to 76 years) with chronic tinnitus (suffering from tinnitus for more than 2 years) were recruited to undertake four sessions of tDCS combined with 1 minute of broadband noise stimulation (presented at minimum masking level [MML] + 10 dB), either: before, during, immediately after tDCS or in a sham controlled session. Volunteers were excluded if they had any contraindications for undergoing tDCS (as screened by a neurologist). One participant declined continuing in the trial half way through the testing (after two sessions) due to worsening of tinnitus symptoms. Participants rated their tinnitus loudness on a rating scale twice before the testing (immediately after arrival in sound treated room and 10 minutes after the arrival) and once after the completion of testing. Participants were required to continuously select their tinnitus MML by using a dial and custom software. The testing within each session took approximately 60 minutes (5 minutes of initial monitoring of MML with no stimulation, followed by MML monitoring during 20 minutes of anodal tDCS of LTA, followed by 30 minutes of MML monitoring post tDCS).

### Results

Although 7 out of 9 participants reported tinnitus suppression with anodal tDCS of the LTA, changes in MML were seen primarily when auditory stimuli was presented immediately after tDCS (2 out of 9 participants only).

## Conclusion

This pilot study was an attempt to explore the implications of neuromodulation (tDCS) on auditory residual inhibition to find ways to increase auditory residual inhibition and investigate its underlying mechanisms. Preliminary evidence suggests that tDCS of the LTA may enhance auditory RI when acoustic stimulation follows immediately after tDCS. However, further investigation is needed using modified methodology (short testing time, screening participants for RI and a larger sample size) to confirm these findings.

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## CHANGES OF TINNITUS IN SUDDEN SENSORINEURAL HEARING LOSS: RELATIONSHIP BETWEEN TINNITUS PITCH AND AUDIOMETRIC SHAPE

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### Objectives

Different mechanisms, such as lateral inhibition and homeostatic plasticity, are proposed to be involved in tinnitus generation. The aims of this study were to evaluate the changes of the acute and 1-month follow-up tinnitus pitch in patients with idiopathic sudden sensorineural hearing loss (SSNHL) and to explore the mechanisms of tinnitus generation.

### Design

Thirty-six patients with SSNHL with new-onset tinnitus who underwent audiological tests, including pure-tone audiometry and pitch-matching and loudness-balance tests, at both initial and follow-up examinations were included. The relationship between the tinnitus pitch and the maximum hearing loss or the edge frequency was evaluated.

### Results

The initial mean tinnitus pitch (2.9 kHz), which was close to the initial edge frequency (2.7 kHz), increased to a significantly higher frequency (4.6 kHz) at 1-month follow-up, which was close to the frequency of maximum hearing loss (5.6 kHz). There were no significant differences in the frequency of maximum hearing loss, the edge frequency, and the loudness of tinnitus between initial and follow-up examinations. The tinnitus pitch had a more significant correlation with the edge frequency ($r=0.46$, $p=0.005$) than the frequency of maximum hearing loss ($r=0.33$, $p=0.047$) at initial examination; however, at 1-month follow-up, the tinnitus pitch showed a significant correlation only with the frequency of maximum hearing loss ($r=0.52$, $p=0.001$), not with the edge frequency.

### Conclusion

Our findings suggest that there may be diverse mechanisms by which tinnitus can occur in patients with SSNHL. The change in the tinnitus pitch from the edge frequency at initial examination towards the frequency of maximum hearing loss at follow-up suggests that tinnitus is generated mostly by reduced lateral inhibition at acute hearing loss and that a homeostatic mechanism plays a major role in tinnitus generation at the chronic stage.

## EXAMINING THE ROLES OF CONTEXTUAL STIMULI AND PERSONALITY TRAITS UNDER THE ADAPTATION LEVEL THEORY MODEL OF TINNITUS

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### Objective

This study assessed the validity of a novel psychoacoustic ALT model of tinnitus proposed by Searchfield et al. (2012) [1], based on Helson's (1964) adaptation level theory (ALT) [2]. Tinnitus is conceptualized as a sensory stimulus with an existing internal adaptation level (AL), which acts as a reference point for all tinnitus-related judgments. This AL is susceptible to change from attention, background (context) and residual (personality, memory/prediction, physiological arousal and emotion) influences. The effects of each component can theoretically be quantified and modeled mathematically, making the model significant for empirical tinnitus research. The ideal level of intervention sound for tinnitus remains debatable. Personality traits act as predictors for tinnitus distress and perception: it is possible these traits can influence tinnitus-sound interactions. Two components of the model were investigated: background noise (context) and personality traits (single residual component), in an attempt to isolate their effects on tinnitus.

### Design

Loudness level matches, and rating scales for loudness and distress were measured before and after20 minutes of: quiet, Narrow Band Noise (NBN) at threshold level, 10 dB sensation level and 20 dB sensation level. Personality variables were assessed using the Multidimensional Personality Questionnaire Form NZ (MPQ-Form NZ). Study sample: Twenty participants with chronic tinnitus participated in the study.

### Results

Tinnitus distress interacted with contextual noise levels in a manner consistent with the ALT model; tinnitus loudness matches to sound did not change. The 20 dB sensation level noise led to the greatest reduction in tinnitus measures; however this was not statistically significant. The personality traits of social closeness, positive emotionality, stress reaction and negative emotionality were seen to influence contextual noise-tinnitus interactions. The emergence of 'adaptation-sensitive' and 'adaptation-insensitive' persons was observed. The ALT model's conceptualization of the tinnitus loudness paradox was supported.

## Conclusions

The first empirical study testing the ALT model of tinnitus is promising. Tinnitus loudness and distress might represent two separate underlying constructs with different adaptation levels. Also, underlying individual differences in adaptation sensitivity may be present.

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## CORTICAL PLASTICITY IN TINNITUS PATIENTS AFTER REPETITIVE EXPOSURE TO TAILOR-MADE NOTCHED MUSIC

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### Objectives

Chronic tinnitus is assumed to be a result of reduced inhibition of neurons corresponding to the tinnitus frequency. One possibility to reverse the effects of this maladaptation is to induce inhibition on neurons corresponding to the tinnitus frequency by auditory stimulation. This can be achieved by presenting music with reduced energy in the frequency bandwidths centered at the tinnitus frequency using a notch filter (tailor-made notched music). The aim of this study was to assess the impact of repetitive stimulation with tailor-made notched music on the neural and behavioral correlates of tinnitus perception. We expected to find plastic changes in the neural activity of auditory cortical regions. Furthermore, we wanted to investigate whether other brain regions are involved in the process of short-term plasticity.

### Methods

Ten subjects suffering from chronic tonal tinnitus listened to music passing through a notch-filter centered at the tinnitus frequency for three hours on each of three consecutive days. Neural activity evoked by either a tone at the tinnitus frequency (tinnitus tone) or by a control tone of 500 Hz was measured by magnetoencephalography (MEG) before and immediately after music exposure. Tinnitus loudness was measured via visual analog scales. A distributed source model was used to investigate the neural activity in auditory as well as in frontal cortical regions in the N1m time window.

### Results

After music exposure, neural activity evoked by the tinnitus tone in the temporal lobe decreased significantly, whereas neural activity evoked by the control tone remained unaffected. Additionally, tinnitus loudness was rated significantly lower after music exposure. There was a significant correlation between the reduction of neural activity in the temporal lobe evoked by the tinnitus tone and the tinnitus loudness ratings. Furthermore, there was a significant increase of neural activity evoked by the control tone in the frontal lobe after music exposure, which could not be observed in the neural activity evoked by the tinnitus tone.

## Conclusion

Tailor-made notched music evokes neural plasticity in temporal as well as in frontal cortical areas of tinnitus patients. Additionally, there is a clear connection between the reduction of tinnitus loudness and the neural reorganization in the temporal cortex. These effects were found after a short period of music exposure, indicating a fast neural reorganization and behavioral adaptation.

## ABNORMAL BRAIN ACTIVITY AND CROSS-FREQUENCY COUPLING IN THE TINNITUS NETWORK

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### Background and aims

Neuroimaging studies have identified networks of brain areas and oscillations associated with tinnitus perception. Nevertheless, it is still unclear how oscillations in the different frequency bands within various nodes of the tinnitus network interact. Cross-frequency coupling (CFC) of the amplitude of high-frequency activity to the phase of slower oscillations has been described both in humans and in animals, but has never been investigated in subjective tinnitus. Here we used EEG recordings to test the hypothesis that in human tinnitus patients aside from the known alterations of oscillatory activity, there is also an altered periodicity of amplitude variations of higher frequency (gamma) oscillations with certain phases of lower (delta/theta/alpha) frequency oscillations.

### Methods

Hierarchical phase-amplitude coupling for a tinnitus related network of localized EEG brain sources was calculated in tinnitus patients and in the group of tinnitus free controls. For this, we used the comodulation analysis and the modulation index between the time course of the power in a number of gamma frequency sub-bands and phases of a set of intrinsic mode functions of lower frequency oscillations (provided by empirical mode decomposition).

### Results

In tinnitus patients as compared to tinnitus free controls, aside from the previously described changes of oscillatory activity, there were also changes of CFC within nodes of the tinnitus network and between these nodes. Reduction of tinnitus severity after acoustic coordinated reset therapy led to a partial normalization of cross-frequency interaction in various nodes of the tinnitus network and between these nodes.

## Conclusions

In our study we found clear evidence of increased delta/theta-gamma and decreased alpha-gamma coupling in tinnitus patients. Tinnitus intensity was also associated with a more pronounced cross-frequency interaction between cognitive, sensory areas and anterior cingulate cortex region. The tinnitus specific pattern of CFC was at least partially reverted by a 12 weeks acoustic CR treatment. CFC can coordinate tinnitus-relevant activity in the tinnitus network providing a mechanism for effective communication between nodes of this network in processing of the different aspects of tinnitus.

## SURFACE BASED MORPHOMETRY ANALYSIS OF NEUROPLASTICITY INDUCED CHANGES IN THE BRAIN OF PATIENTS WITH TINNITUS

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### Objectives

Different neuroimaging techniques (MRI, PET, EEG, MEG) have been used to identify brain structures involved in tinnitus pathophysiology. Multiple studies detected neuronal correlates of tinnitus in auditory (temporal) and non-auditory (frontal, parietal, limbic, subcallosal) brain regions suggesting the existence of a wide-spread neural network responsible for tinnitus awareness. Most of these studies applied a functional approach and measured tinnitus related activity changes in involved brain regions and networks. Only a few studies concentrated on structural changes analyzing volume differences of gray and white matter by comparing subjects with and without tinnitus (voxel-based morphometry). The studies published so far demonstrated some inconsistency in the extent of volume changes and the localization of involved structures. To reconcile these contradictory results the aim of this project is a systematic re-analysis of neuroanatomical traits (cortical thickness, cortical area, cortical volume) by means of an innovative observer-idependent surface-based morphometry approach (FreeSurfer). Unlike the traditional voxel-based morphometry (VBM) approach, FreeSurfer allows the separate computation of independent neuroanatomical traits, namely surface area and cortical thickness

### Methods

FreeSurfer is a set of software tools for the study of cortical and subcortical anatomy. In the cortical surface stream, the tools construct models of the boundary between white matter and cortical gray matter as well as the pial surface. Once these surfaces are known, an array of anatomical measures becomes possible, including: cortical thickness, surface area, curvature, and surface normal at each point on the cortex. 333 structural MRI datasets of patients) with tinnitus which were already analyzed by means of VBM1 were included in the study. Additional MRI data of 100 subjects without tinnitus allowed a global analysis of structural neuroplastic changes as a function of chronic tinnitus perception in terms of a group comparison. Accurate phenotypical characterization of tinnitus subjects allowed an identification of tinnitus subgroups (e.g. low vs. high tinnitus related distress; impaired vs. normal hearing, etc.).

## Results

A negative correlation between tinnitus distress and temporal grey matter (proposed core networks) could be replicated methodwise and corrected for multiple comparisons. Further correlations of tinnitus distress in salience or self-perception networks including ACC, insula, parietal and (pre)cuneus were observed. Group comparisons of two subsets matched for age and gender and age, gender and hearing function respectively (normal vs. impaired hearing) were performed. These analyses revealed differences in bilateral parietal areas (corrected), ACC, PCC, parahippocampal, (pre)cuneus temporal (incl. insula) and in frontal areas.

## Conclusions

Re-analysis of the large dataset by means surface based morphometry (FreeSurfer) showed consistent effects in comparison to a previous analysis with VBM1. However, the FreeSurfer method seems to be more sensitive and generates a wider array of results. The findings fit into a framework as proposed by De Ridder et al.2 and contribute solid anatomical evidence. The interpretation of volume and thickness changes related to distress and group affiliation must be discussed. Furthermore, an analysis and comparison of the parameters (volume, thickness, area and gyrification) and their interplay is of large interest.

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## ELECTROPHYSIOLOGICAL EFFECTS OF ATTENTION IN NORMAL HEARING AND IN TINNITUS

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### Objective

We recently reported that modulation of the amplitude of the 40-Hz auditory steady-state response (ASSR, localizing tonotopically to primary auditory cortex) and N1 response (localizing to nontonotopic secondary auditory regions) by attention is impaired in individuals with tinnitus compared to control subjects, when the responses are evoked by 5 kHz 40-Hz AM sound in the tinnitus frequency region (TFR) of the tinnitus group.1 One explanation of this finding is that persistent aberrant network activity occurring in the TFR of tinnitus subjects may drive neural activity in this region as well as in A2, making the ASSR and N1 resistant to modulation by the auditory attention system.

### Methods

We assessed this hypothesis by determining whether modulation of ASSR and N1 responses by attention is impaired in tinnitus when the carrier frequency used to evoke these responses is 500 Hz, which is well below the TFR where tinnitus-related neural activity is expected to occur. The task was identical to the auditory detection task used previously, except for the change in the carrier frequency of the 40-Hz AM sound. We also extended the analysis to include P1, P2, and N2 transient responses and the auditory sustained response in the tinnitus and control groups tested here at 500 Hz, and in the tinnitus and control groups tested previously at 5 kHz.

### Results

ASSR responses were modulated significantly by attention at 500 Hz (ASSR larger on active attended compared to passive unattended blocks) in control subjects as well as in subjects with tinnitus. Modulation of N1 by attention was also observed at 500 Hz in control subjects; however modulation of N1 by attention at 500 Hz was not significant in the tinnitus group. Modulation of N2 and the auditory sustained response by the attentional requirement was significant in the tinnitus and control groups tested at 500 Hz, and in these groups tested earlier at 5 kHz.

## Conclusion

Tinnitus-related neural activity in primary auditory cortex may be responsible for the failure of task attention to modulate the 5 kHz 40-Hz ASSR in individuals with tinnitus. This activity could also explain the failure of N1 modulation in tinnitus subjects at 500 Hz, if it drives activity in A2 which is not tonotopically organized. Modulation of long latency responses (N2 and the sustained response) requires a different interpretation. These responses have a topography different from N1 and may reflect neural activity in nonauditory regions that support task requirements not related to attention.

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## PARAHIPPOCAMPAL-AUDITORY CORTEX COMMUNICATION IN TINNITUS

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### Introduction

The parahippocampal area and auditory cortex are important hubs in tinnitus, as demonstrated by EEG, MEG, fMRI and PET. Furthermore, the functional connectivity between these areas is the only robust finding in resting state fMRI studies in tinnitus.

### Methods and materials

To further explore this critical connection we performed EEGs in 129 tinnitus patients We analyzed the neural correlates of hearing loss and subjective tinnitus loudness (NRS) on a whole brain analysis as well as the functional and effective connectivity between the auditory cortex and parahippocampal area.

### Results

Hearing loss is related to bilateral parahippocampal theta activity and right-sided alpha parahippocampal activity. Tinnitus loudness is related to gamma band activity in the auditory cortex left parahippocampus, as well as alpha in the left insula, low beta right dorsal anterior cingulate cortex.

A significant correlation is found between the subjective loudness and lagged phased synchronization (=functional connectivity) between the left parahippocampus and the left auditory cortex for the theta frequency band, as well as for the percentage of time there is theta-gamma nesting in the left parahippocampus and auditory cortex.

The effective connectivity depends on the hearing loss. The more hearing loss a patient has the more information is transferred from the parahippocampal area to the auditory cortex

### Discussion and conclusion

The parahippocampus and auditory cortex communicate using the theta band as a carrier wave on which gamma band activity is nested. The gamma band correlates with the tinnitus loudness. In hearing loss the missing information seems to be pulled from hippocampal memory.

## MODULATING ALPHA AND BETA OSCILLATIONS WITHIN POSTERIOR CINGULATE CORTEX THROUGH REAL-TIME SOURCE LOCALIZED NEUROFEEDBACK AND ITS EFFECT ON TINNITUS RELATED DISTRESS

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Up to 25% of the people affected by tinnitus report interference with their lives as tinnitus causes a considerable amount of distress. It is known that distress can play an important role in the development of tinnitus leading to psychological complications such as annoyance, concentration problems, depression, anxiety, irritability, sleep disturbances, and intense worrying. Previous research already indicated that decreased alpha power is associated with actively engaging in processing a stimulus and that the posterior cingulate cortex forms a core region of the default network. Highly distressed tinnitus patients are actively engaged to their tinnitus as such it seems reasonable that a decreased alpha power is obtained within the posterior cingulate cortex. The beta-band oscillations on the other hand have been associated to maintenance of the current cognitive state. That is, beta oscillations are related to endogenous modulation of early auditory responses and may be enhanced if the status quo is given priority over a new signal. As this phantom sound is constantly present and could be interpreted as status quo that has priority over a new signal, certainly in patient that are really distressed by their tinnitus. This fits with the findings that highly distressed tinnitus patients have increased beta-band oscillations within the posterior cingulate cortex. Consequently, it can be hypothesized that real-time source localized neurofeedback to voluntarily up-regulate alpha activity and down-regulate beta activity within the posterior cingulate cortex can modulate tinnitus related distress. This approach goes beyond conventional imaging studies that only correlate ongoing activity with changes in tinnitus, as neurofeedback allows us to directly manipulate ongoing brain activity and thereby to establish a causal link between ongoing activity and tinnitus perception. The posterior cingulate cortex is a particular well-suited target for neurofeedback because its activity can be modulated by top-down control mechanisms, such as attention and imagery. Here we show in a large group of 50 tinnitus patients, in a placebo-controlled way, that up-regulating alpha and down-regulating beta oscillations targeting the posterior cingulate cortex through real-time source localized neurofeedback has a clear effect on the tinnitus related distress but not on the loudness. These results are supported by power changes and changes in phase coherence.

## CHANGE IN SPONTANEOUS CORTICAL ACTIVITY DURING TINNITUS REMEDIATION

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### Introduction

Tinnitus remediation programs vary in their effectiveness to provide long-term relief for tinnitus sufferers. Understanding the link between subjective benefit and the neurophysiological changes which occur throughout remediation may provide a better understanding of the physiological mechanisms underpinning tinnitus relief and may be important for developing individualised therapies. However, currently this is limited by a paucity of sensitive and objective tests. Recent advances in imaging techniques have shown some promise in identifying and quantifying tinnitus-related neural activity and its relationship with subjective indicators of the impact of the tinnitus on the individual (Hoke, Feldmann et al. 1989; Weisz, Moratti et al. 2005). In this study, we aim to evaluate the neurophysiological changes evident in tinnitus and non-tinnitus sufferers and to evaluate the changes in spontaneous brain activity during a tinnitus treatment program.

### Aims / Objectives

The aims of the present study are:

4. Identify changes in the spontaneous activity of the brain in patients with clinically significant tinnitus using Magnetoencephalography (MEG).
5. Measure changes in spontaneous brain activity prior, during and post tinnitus remediation program.
6. Identify if any association exists between the subjective (TRQ) and objective (MEG) measures of tinnitus.

### Method

The tinnitus group (N=12) underwent extended audiometric evaluation and completed a battery of questionnaires ruling out clinical depression and anxiety as a probable cause of, or association with tinnitus. A five minute spontaneous MEG recording was acquired while they were in a state of relaxed wakefulness. The tinnitus participants were provided with Neuromonics treatment program, while at the same time had their MEG data recorded prior to, during and post treatment program. As a comparison, spontaneous MEG recordings of control group (N=10) with clinically normal hearing and no complaint of tinnitus were also acquired. The MEG data were analysed using Brain Electrical Source Analysis (BESA) software.

## Results and Conclusion

Our results showed that the spontaneous alpha (8-13Hz) temporal-parietal brain activities in the tinnitus group were smaller when compared to that of the control group. Incremental changes of alpha were seen as the treatment progressed. In addition, an inverse association between the TRQ score and alpha power measured from the cortex were found. We will discuss the potential implications of using MEG as a tool to objectively measure tinnitus.

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## TONOTOPIC MAP CHANGES DURING TINNITUS REMEDIATION

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### Background

Tinnitus has been associated with the abnormal organisation of the tonotopic map in the auditory cortex (Eggermont, 2006). However, it is currently not clear whether successful tinnitus remediation which shows improved subjective outcomes, can affect the reorganisation of the tonotopic map towards a non-disrupted state. Therefore the aims of the present study were: (i) to compare tonotopic maps acquired from magnetoencephalography (MEG) recordings in individuals with significant tinnitus with non-tinnitus participants to determine whether disruptions could be measured; (ii) to identify whether changes in the tonotopic map and evoked responses occurred during and after a tinnitus remediation program; and (iii) to identify whether these changes occurred in parallel with subjective changes of tinnitus impact.

### Method

Twelve tinnitus participants were recruited and completed audiometric evaluation, subjective measurement of tinnitus using the tinnitus reaction questionnaire (TRQ), measurement of psychoacoustic characteristics of tinnitus, and evaluation of depression and anxiety before during and after tinnitus remediation. Ten normal hearing non-tinnitus participants were recruited for comparison. Sound stimuli of 500Hz, 1kHz, 2kHz, 4kHz and 8kHz tones were presented to each ear individually and cortical activity was measured using MEG. All tinnitus participants completed a Neuromonics rehabilitation program over 25 weeks and MEG was measured at 5 or 10 week intervals. MEG data were analysed using Brain Electrical Source Analysis (BESA).

### Results & conclusions

MEG results indicated that the tinnitus subjects' source locations were more anterior compared to that of the control group (for all presented frequencies). After undergoing remediation, the tinnitus subjects' source strengths increased (for normal hearing frequencies) while source locations moved towards a more posterior location (towards that of non-tinnitus participants). These results suggests that tinnitus remediation using Neuromonics affects source strength and tonotopic map of the tinnitus participants.

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## CHANGES IN RESTING-STATE FMRI ACTIVITY DURING SALICYLATE-INDUCED TINNITUS AND SOUND STIMULATION

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### Aims / Objectives

The neural mechanisms that give rise to the phantom sound of tinnitus are poorly understood, but recent studies suggest that low frequency neural oscillatory activity contributes to tinnitus generation. To explore this issue, we measured the amplitude of low-frequency fluctuations (ALFF) in resting-state functional magnetic resonance imaging (fMRI) during salicylate-induced tinnitus and during sound stimulation.

### Methods

Rats were scanned with a 7.0 T MRI system; 15 were treated with 300 mg/kg of salicylate to induce tinnitus and the remaining 15 were injected with saline as controls. Baseline fMRI scans were collected with music stimulation (85 dB SPL Leq) and without music (control). Afterwards, the measurements were repeated 2 h after salicylate or saline treatment. Statistical parametric mapping was used to determine which regions of the brain showed significant changes in ALFF activity due to salicylate or music stimulation.

### Results

Salicylate induced significant bilateral increases of ALFF activity in several auditory region (auditory cortex, medial geniculate body, inferior colliculus, trapezoid body) as well as several non-auditory regions including the paraflocculus of the cerebellum, visual cortex, somatosensory cortex and amygdala. In contrast, salicylate significantly decreased ALFF activity in the hippocampus and striatum. Furthermore, salicylate treatment enhanced (hyperactivity) the ALFF neural responses to music stimuli in several brain regions, including the auditory cortex, inferior colliculus, medial geniculate body, trapezoid body and somatosensory cortex.

## Conclusions

Salicylate significantly increased ALFF oscillatory activity in several auditory and non-auditory regions previously implicated in salicylate and/or noise-induced tinnitus. Interestingly, several new regions of aberrant ALFF activity were observed in visual and somatosensory cortex, sensory areas known to interconnect with the auditory cortex. Music stimulation tended to potentiate the salicylate-induced hyperactivity in the ALFF responses in many auditory areas, consistent with previous electrophysiological reports of sound evoked hyperactivity in the central auditory pathway. These results suggest that the perception of tinnitus may be due in part to large increases in low-frequency neural oscillations within the central auditory pathway along with aberrant neural oscillations in the amygdala, paraflocculus and visual and somatosensory cortices. Resting-state ALFF fMRI might therefore prove useful in identifying the aberrant neural networks in humans who suffer from severe, debilitating tinnitus.

## AUDITORY-LIMBIC NETWORK IN TINNITUS REVEALED BY RESTING-STATE FUNCTIONAL CONNECTIVITY MRI

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Tinnitus is characterized by the perception of sound in the absence of an external source. Despite the prevalence of this disorder, its pathophysiology remains poorly understood. A large body of evidence has revealed plasticity-related changes in the auditory system of patients with tinnitus, including modifications in one or more sites along the auditory pathway, both peripheral and central. Although lesion-induced plasticity of auditory structures may be a necessary precondition, it does not seem sufficient to cause chronic tinnitus. Given this constraint, and the growing body of evidence implicating limbic involvement in tinnitus, we propose that limbic dysfunction may play a critical role in causing, as well as perpetuating, the tinnitus percept.

For our current study, we chose to elucidate this dysfunction by using magnetic resonance imaging to measure functional connectivity (fcMRI). Since the tinnitus percept is most noticeable at rest, i.e. in the absence of tasks or distractors, we chose to analyze connectivity from resting-state fcMRI data, that is, data acquired when subjects were not performing any tasks. Specifically, we used Independent Component Analysis (ICA), a data-driven, non-a-priori statistical technique, to identify roughly 25 functionally connected resting-state networks (RSNs). Auditory, visual, "default-mode," and other neurophysiologically plausible networks were consistently detected in all subjects, along with non-neurophysiological networks, having to do with, e.g., respiration and heart rate, which were removed from further analysis. Of particular interest was a network that appeared in ICAs of tinnitus patients, but not of controls matched for age and hearing loss. This network demonstrated a unique inverse relationship between medial Heschl's gyrus (mHG) and the Nucleus Accumbens (NAc), suggesting a direct or indirect connection between the two regions. Apart from revealing a novel auditory-limbic network, these results are consistent with previous reports of NAc involvement in tinnitus [1], and suggest a far-reaching tinnitus network incorporating non-auditory regions [2]. The present study offers the additional advantage of superior spatial resolution afforded by fcMRI while elucidating this network more precisely.

Overall, our data suggest a much larger role for the limbic system in tinnitus pathophysiology than previously thought, thus opening new avenues for potential treatments of the disorder.

Furthermore, additional study of limbic connectivity may shed light on the system's involvement in multiple sensory pathways, which could provide a robust multidisciplinary approach for the study of tinnitus as well as certain forms of chronic pain.


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## TINNITUS AND DYSFUNCTIONAL INTERACTIONS BETWEEN DISTRIBUTED RESTING STATE NETWORKS

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It is known that peripheral lesions in the cochlea or the auditory nerve produce dysfunctional input to central auditory structures and induce changes in the auditory system. Associated to plastic changes in central auditory structures, extra-auditory regions have been implicated in the tinnitus pathophysiology. Recently, it has been proposed that the unified percept of tinnitus could be considered as an emergent property of multiple overlapping dynamic brain networks, each encoding a specific tinnitus characteristic. Indeed, more and more researches suggest that the brain cortex is organized into parallel, segregated systems of brain networks that are specialized for processing distinct forms of information. Regarding tinnitus, preliminary evidence using EEG, MEG and PET indicates that specific clinical characteristics are correlated to specific brain area activations. These evidences provide a first insight about the role of network interaction for the emergence of clinical tinnitus characteristics.

The aim of our study was to investigate the neuronal activation patterns associated with specific clinical tinnitus characteristics using fMRI. We hypothesize that tinnitus clinical characteristics could be associated with specific resting-state activity and connectivity patterns and that this could be tested by looking at the spontaneous brain activity of 136 tinnitus patients. All tinnitus subjects

benefited from an in depth clinical evaluation. We combine an individual independent component analysis (ICA) with an automated component selection method to select 10 components of interest to be used in a second level analysis. We performed an analysis to identify the correlation between different tinnitus characteristics (distress, duration, intensity, type, lateralization…) and the functional connectivity pattern of these 10 different resting-state networks (RSN). We will discuss our results and relate these to previous findings using different neuroimaging techniques and tinnitus pathophysiological models.

## INFUSION OF $GABA_B$ RECEPTOR AGONISTS INTO THE COCHLEAR NUCLEUS ON TINNITUS DEVELOPMENT FOLLOWING ACOUSTIC TRAUMA IN RATS

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### Background

Chronic tinnitus is experienced by about 10% of the population and produces many detrimental effects on the quality of life. There are very limited drug treatment options, mainly due to a lack of understanding of the underlying mechanisms. It has been suggested that tinnitus is generated by neuronal hyperactivity in multiple areas of the brain, including the dorsal cochlear nucleus, inferior colliculus and primary auditory cortex. Furthermore, bilateral lesions of the dorsal cochlear nucleus before the acoustic-trauma, but not afterwards, prevented the development of tinnitus in rats. Recently, we have demonstrated that L-baclofen, which activates inhibitory neurotransmission through GABAB receptors, dose-dependently reduced noise trauma-induced tinnitus in rats. In the present study, we further investigated the possibility of preventing the development of tinnitus by infusing the GABAB receptor agonists, L-baclofen or CGP7930, into the cochlear nucleus prior to acoustic trauma.

### Materials and Methods

Male Wistar rats were divided into 8 groups (n = 8 - 19 per group): Sham-saline, Sham-DMSO, Sham-Baclofen, Sham-CGP7930, Acoustic trauma-saline, Acoustic trauma-DMSO, Acoustic trauma-Baclofen and Acoustic trauma-CGP-7930. The acoustic trauma consisted of a 16 kHz, 115 dB pure tone delivered unilaterally for 1 h under anaesthesia. Saline, DMSO, L-baclofen (2 mM at 0.5 µl/h) or CGP7930 (100 µM at 0.5 µl/h) was administered into bilateral cochlear nuclei through cannulae connected to Osmotic minipumps for 7 days starting at 24h before the acoustic trauma. The behavioural signs of tinnitus in each rat were measured by a conditioned lick suppression paradigm at about 1 month after the acoustic trauma. Following the tinnitus testing, the animals were perfused transcardially with 10% neutral buffered formalin and the brains were removed, sectioned and stained with Cresyl Violet to confirm the cannula placement.

### Results

The preliminary results suggested that neither the L-balofen nor the CGP7930 infused into the cochlear nucleus prevented the development of tinnitus induced by acoustic trauma. The results will be finalized with the confirmation of the cannula placement.

## Conclusion

Directly activating the GABAB receptors in the cochlear nucleus may not be sufficient to prevent the development of tinnitus induced by acoustic trauma.

## STRESS-ASSOCIATED CHANGES OF MITOCHONDRIAL PROTEINS IN AUDITORY CORTEX

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### Aims

Chronic form of tinnitus has been proposed to reflect called plastic changes in the auditory structures. Emotional and psycho-social stress was shown to induce functional changes in the auditory system of experimental animals consistent with hypersensitivity in the inner ear (increased amplitudes of DPOAEs) and in the auditory brainstem (changes in ABR). However, little is known about the mechanisms, in which emotional and psycho-social stress affects the auditory system. To find out if stress affects mitochondrial integrity or mitochondrial protein-mediated plasticity, we have monitored the levels of mitochondrial proteins Bcl-2, Bax and Bcl-xL in the auditory cortex following experimental stress.

### Methods

Two strains of rats (four weeks old, female, 100 – 120 g weight) were used – Wistar Hannover and Lewis. Wistar Hannover is an outbread strain derived from Wistar used as a general, all-purpose outbred model for use in biomedical research and known as developing relatively low level of anxiety under stressful conditions. Lewis rats are an inbread strain characterized in neuro-psychological research as developing relatively high level of anxiety under stressful conditions. The rats were exposed to 24-h psycho-social stress. After functional tests of auditory pathways, auditory cortices were dissected from sacrificed animals, and the proteins were purified and analyzed using Western blot followed by chemiluminescence and densitometry. The results were statistically analyzed with Sigma Stat.

### Results

Auditory cortices of Wistar rats contained significantly more Bax immediately after finishing the stress period, as compared to non-stressed animals ($P<0.01$, one-way ANOVA). The Bax levels returned to baseline six hours later. Bcl-2 and Bcl-xL remained unchanged. In contrast, auditory cortices of Levis rats contained significantly more Bcl-xL following stress, as compared to the controls ($P<0.01$, one-way ANOVA).

## Conclusions

Psycho-social stress can modulate Bax and Bcl-xL levels in the auditory cortex of had increased amount of Bax after finishing stress whereas the anxiety-prone Lewis rats had increased amount of Bcl-xL in the auditory cortex after finishing stress. Besides playing an important role in mitochondrial integrity and cell survival, Bax and Bcl-xL have the ability to regulate synaptic plasticity and thus, can contribute to and reflect the plastic changes in auditory central system following psycho-social stress.

## EVIDENCE FOR NEUROGENESIS IN THE COCHLEAR NUCLEUS FOLLOWING ACOUSTIC TRAUMA IN RATS

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### Background

Tinnitus induced by acoustic trauma results in electrophysiological changes in the cochlear nucleus (CN) which appear to cause neuronal hyperactivity. In neurogenic areas of the brain, for example, the dentate gyrus, such electrophysiological changes have been shown to alter neurogenesis. The present study investigated the effects of acoustic trauma that has been proven to cause tinnitus, on cell proliferation and neurogenesis in the CN of rats.

### Materials and Methods

Rats received either sham or unilateral acoustic trauma (16 kHz at 115 dB for 1 h) under anaesthesia. Auditory brainstem responses (ABRs) were measured to determine the effects of the acoustic trauma on hearing. Animals were injected with the cellular proliferation marker, BrdU, at 72 hs following the acoustic trauma, and then 2 hs or 24 hs later, were sacrificed by transcardial perfusion with 4% paraformaldehyde and the brains were removed, sectioned and stained for BrdU using immunohistochemistry. Double labelling immunofluorescence immunohistochemistry was performed for BrdU and Ki-67, a marker for cells in the S phase of the cell cycle, CD11b, a marker for microglial cells, and doublecortin (DCX), a marker for immature neurons.

### Results

Acoustic trauma resulted in a significant elevation of the ABR thresholds, indicative of hearing loss. Acoutic trauma also resulted in an increase in BrdU
labeling in the CN, which significantly co-labeled with an antibody for Ki-67, suggested was due to the generation of new cells rather than DNA repair. There was no significant co-labeling for CD11b, suggesting that the new cells were not microglial cells. However, there was significant co-labeling for DCX, suggesting that many of the new cells were immature neurons.

### Conclusion

The present study suggests that the cell proliferation that occurs in the CN following acoustic trauma represents neurogenesis.

## SOUND-TRIGGERED SUPPRESSION OF NEURONAL FIRING IN THE AUDITORY CORTEX: IMPLICATION TO THE RESIDUAL INHIBITION OF TINNITUS

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### Aims / Objectives

Tinnitus can be suppressed briefly following the offset of an external sound. This phenomenon, termed "residual inhibition," has been known for almost four decades, although its underlying cellular mechanism remains unknown. In our previous work we have shown that the majority of neurons in the inferior colliculus (IC) exhibit long lasting suppression of spontaneous activity following the offset of an external sound. The time course of suppression corresponded to the time course of residual inhibition in tinnitus patients. Tinnitus patients often report an increased effect of tinnitus-matched pure tones on the duration of their residual inhibition. Our data show pure tones induce longer suppression than wideband noise. If the suppression is an underlying mechanism, the auditory cortex (AC) neurons should also exhibit suppression because residual inhibition of tinnitus is a perceptual phenomenon. To test this hypothesis, we studied sound evoked suppression in auditory cortex neurons of awake mice. Animals with behavioral signs of tinnitus and control unexposed mice were used.

### Methods

Experiments were conducted on adult CBA/CaJ mice. For tinnitus induction mice were exposed to a narrowband noise centered at 12.5 kHz presented at 116 dB SPL unilaterally for 1 hour under general anesthesia (Ketamine/Xylazine). Tinnitus was then assessed utilizing gap-induced prepulse inhibition of the acoustic startle reflex. Extracellular recordings were performed in auditory cortex contra- and/or ipsilateral to the exposed ear in awake restrained animals. Pure tones at neurons' characteristic frequency and/or wideband noise stimuli 30 sec duration were delivered in the free-field.

### Results

We found that auditory cortex neurons in control mice exhibited sound-triggered suppression of their spontaneous firing. Similar to the IC, the duration of this suppression after sound offset in AC neurons roughly corresponded to the stimulus duration (about 30 s). AC neurons also showed longer suppression to tones at their characteristic frequency than to wideband noise stimuli.

Unlike the IC, in addition to the suppression after stimulus offset, the majority of AC neurons also showed suppression during stimulus presentation.

### Conclusions

Similar to the IC, AC neurons exhibit long lasting suppression of their spontaneous firing following sound offsets. The time course of this suppression corresponds to the time course of residual inhibition in tinnitus patients. These data further suggest that suppression may be a neural correlate of the residual inhibition of tinnitus in humans.

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## EFFECTS OF PARAFLOCCULUS REMOVAL ON HYPERACTIVITY AFTER ACOUSTIC TRAUMA

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Acoustic trauma not only causes hearing loss but also results in a variety of plastic changes in central auditory pathways, such as increased spontaneous activity. This so-called hyperactivity may be involved in the generation of tinnitus, a phantom auditory sensation. Though many animal studies have consistently shown hyperactivity in auditory centres after hearing loss, tinnitus does not always develop. It has therefore been suggested that there may be involvement of non-auditory structures performing a regulatory role bringing the increased activity in the auditory system to conscious perception. Recent evidence points to the paraflocculus of the cerebellum as having such a role. The paraflocculus receives direct input from the cochlea and is anatomically connected to central auditory structures. Therefore, we investigated the effects of paraflocculus removal on hyperactivity in guinea pig inferior colliculus 2 weeks after acoustic trauma (continuous 10 kHz tone at 124 dB SPL for 2 hours). Spontaneous activity was recorded from 477 neurons (4 animals) with paraflocculus and from 559 neurons (5 animals) with paraflocculus aspirated. Results showed a significant increase in hyperactivity ($p = 0.02$) with paraflocculus removed. These results suggest that paraflocculus exerts an inhibitory effect on hyperactivity in inferior colliculus at 2 weeks after acoustic trauma. The results are surprising in view of observations in another animal model that paraflocculus removal results in reduction of tinnitus measured behaviourally. However, these latter studies were performed at much later time-points after acoustic trauma. Studies are underway to investigate the effects of paraflocculus removal on hyperactivity at later time-points.

## HYPERACTIVITY IN THE INFERIOR COLLICULUS AFTER NOISE TRAUMA AND ITS MODULATION BY EXTRA-COCHLEAR ELECTRIC STIMULATION

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Many studies have shown an increase of spontaneous firing in the auditory centers after noise trauma. It has been suggested that this central hyperactivity may underlie the perception of tinnitus. Recent studies showed that central hyperactivity depends on cochlear activity: reducing the spontaneous firing in the cochlear nerve abolishes neural hyperactivity in the inferior colliculus (at least within the first few weeks after noise trauma). Extra-cochlear stimulation of the cochlea has been shown to modulate the firing in the cochlear nerve: while positive direct current (DC) reduced neural activity in the cochlear nerve, negative DC has the opposite effect. Interestingly, some human studies showed that positive DC applied at the promontory or round window could reliably suppress tinnitus. The goal of the present study was to investigate whether extra-cochlear DC current applied at the round window was able to modulate neural (hyper)activity in the inferior colliculus. Our results show that, for neurons with a characteristic frequency higher than around 10 kHz, positive DC suppresses neural activity in inferior colliculus while negative DC enhances it. For neurons with lower characteristics frequencies, effects of electrical stimulation were either absent or reversed. Our results suggest that extra-cochlear electric stimulation may reduce the tinnitus percept by reducing central (hyper)activity,. This approach may lead to important future developments providing that the electrical stimulation used in clinic is innocuous for biological tissues.

## REFLEX MODIFICATION AUDIOMETRY AS A TOOL TO ASSESS HEARING IN MICE

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### Aims / Objectives

Traditional methods for measuring animal hearing performance can be invasive and time consuming. A behavioral test that does not require formal operant training would be useful to quickly measure an animal's hearing. In our previous work we have demonstrated that continuous narrowband noise suppresses startle responses in mice, to startle stimuli, embedded in that noise. Furthermore, this suppression was sound level- and frequency-depended. The frequency-dependent suppression curve approximated the known behavioral audiogram. The goal of this study was to develop a reliable method for assessment of hearing performance in normal animals and possible hearing deficits in the animals exposed to loud sounds.

### Methods

Initial acoustic startle performance was assessed for each CBA/CaJ mouse by producing a statle input/output function. To effectively alter a startle with background noise, the startle value was set to 75% of the maximum startle response. Narrowband noise ranging in center frequency from 4 to 31.5 kHz (in one third octave steps) was presented at 0 to 80 dB SPL. For acoustic trauma induction, a group of mice were exposed to a narrowband noise centered at 12.5 kHz presented at 116 dB SPL unilaterally for 2 hour under general anesthesia (Ketamine/Xylazine).

### Results

Prior to sound exposure, all mice showed thresholds similar to that of an audiogram for CBA/CaJ mice. Although there was some variance between mice, the greatest degree of startle masking was achieved by 12.5 and 16 kHz background noise. The startle reflex was masked the least by 4 kHz and 31.5 kHz background noise. Following sound exposure the input/ouput curve was altered, showing higher thresholds at 12.5 to 16kHz, reflecting damage at the frequency range of the exposure. Masking thresholds at this range increased significantly compared to the pre-exposured thresholds.

## Conclusions

Reflex modification audiometry could be a useful tool for fast assessing animals' audiometry.

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## UNILATERAL HEARING LOSS IN THE FERRET: A NEW DIRECTION FOR TINNITUS RESEARCH

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### Background / Aims

The current lack of consensus regarding the neurobiological basis of tinnitus necessitates the development of novel animal models of the disease, to not only understand cortical processing changes that develop following partial hearing loss (a key comorbidity associated with tinnitus in human patients), but also to correlate those changes with behavioural and electrophysiological data that objectively identify the presence of a phantom percept. The ferret (Mustela putorius furo) may represent a suitable candidate for tinnitus research: ferrets perform effectively in audio-guided behaviours, while its large skull and well-defined auditory cortical fields make this animal very appropriate for investigating cortical changes. Therefore, within the same cohort of ferrets (N = 7), we sought to examine changes in behavioural performance on a gap detection task, as well as changes in brainstem and cortical neurophysiology following a unilateral lesion made selectively in the high frequency domain of the spiral ganglion.

### Methods

In a two-alternative categorisation task, animals were trained under positive operant conditioning to discriminate an uninterrupted sound (bandwidth 0-30 kHz or 0.5-octave bandpassed, centred at 1kHz, 4kHz, or 16kHz; digitally flattened; 77dB SPL; 2080 ms) from the same sound in which gaps are embedded (four interleaved gaps, varying between 3-270 ms in duration). After consistent performance was obtained, animals underwent unilateral mechanical lesion of the high frequency domain of the spiral ganglion. Following recovery, animals were retested on the same behavioural protocol. Auditory brainstem responses (ABRs) were recorded in response to monaurally presented broadband clicks and narrowband noise bursts, and acute bilateral electrophysiological recordings were performed in the primary auditory cortices of a subset of animals (N = 3) to establish tonotopy and cortical multi-unit response properties.

### Results

Prior to lesion, stable performance in gap detection behaviour was obtained for all animals, with group performance on broadband and narrow band-passed stimuli resembling that previously described in the ferret. Following lesion, behavioural performance measurements

were heterogeneous, with a subset of animals displaying signs of tinnitus-like behaviour. Upon investigation of ABR modulations in the mid-to-chronic phase post-lesion, deviations of ABR latency and waveform amplitude were found to be associated with a behaviourally-defined tinnitus-like percept, as distinct from those animals with hearing loss in the absence of a phantom percept. On the basis of these data, cortical multi-unit neurophysiology indicated tinnitus-correlated changes - including modified tonotopy, elevated spontaneous firing rates, and temporal coding changes - consistent with our behavioural and ABR-defined criteria.



## Conclusions

Partial unilateral lesion of the spiral ganglion impairs the gap-detection sensitivity of awake, behaving ferrets, possibly through the development of a phantom tinnitus-like percept; the observations of lesion-related changes to brainstem and cortical auditory processing suggest possible substrates for intervention and behavioural rescue, which we will seek to explore with optogenetic silencing of the auditory cortex.

*This study was supported by Action on Hearing Loss and the Wellcome Trust.*

## EFFECTS OF STRESS-INDUCED SLEEP DISTURBANCE ON TINNITUS PERCEPTION AND BRAIN OREXIN EXPRESSION IN RATS FOLLOWING ACOUSTIC TRAUMA

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### Background

Tinnitus treatment is complicated not only by a poor understanding of its mechanisms, but also by the variations in individuals' reactions to its perception. Tinnitus severity has been associated with high levels of anxiety, depression and sleep disturbance. Moreover, the sleep measurements in tinnitus patients with disturbed sleep are very similar to those that occur in insomnia. Studies have suggested that insomnia may, in fact, be a risk factor/predictor for tinnitus-related distress and the two conditions may share common neurobiological mechanisms. Since orexin plays an important role in sleep-wake regulation and inappropriate activation of the orexin system has been attributed to the pathophysiology of insomnia, it might also be a promoter for tinnitus perception. The present study investigated the effects of stress on sleeping patterns and the susceptibility to acoustic trauma-induced tinnitus in rats.

### Materials and Methods

Thirty male Wistar rats were divided into three groups: control (n = 6), acoustic trauma only (n = 12) and acoustic trauma with stress (n = 12). The animals received either sham or unilateral acoustic trauma (16 kHz at 110 dB for 1 h) under anaesthesia. Twenty-four hours after acoustic trauma, stress was induced by placing the animal in a cage previously occupied by another male rat for 5.5 h during which the animal's sleeping behaviour was recorded. Tinnitus assessment was carried out 2 weeks post-exposure using a conditioned lick suppression paradigm. At the conclusion of the experiment, the animals were sacrificed by transcardial perfusion with 4% paraformaldehyde and the brains were removed, sectioned and stained for orexin-A using immunohistochemistry.

### Results

Stress resulted in a significant reduction in the number of sleep periods in acoustic trauma exposed animals. However, there was no difference in the number of rats exhibiting behavioural signs of tinnitus between stress and non-stress groups and there was also no difference in the total number of orexinergic neurons in hypothalamus.

### Conclusion

In the present study, stress-induced sleep disturbance did not result in long-term changes in orexin system and did not change the perception of tinnitus in rats.

## PAIRED ASSOCIATIVE STIMULATION OF THE HUMAN AUDITORY CORTEX AND ITS EFFECTS ON THE AUDITORY STEADY STATE RESPONSE

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### Aims

Paired associative stimulation (PAS) has often been shown to induce changes in neuroplasticity of the motorcortex. Pairing an acoustic stimulus with a TMS pulse over the auditory cortex has the potential to change the amplitude of late acoustic evoked potentials, which has firstly been proven in a recent pilot study. The aim of the present study was to investigate if PAS of the auditory cortex is capable to change auditory steady state responses (ASSR).

### Methods

20 healthy objects have been presented two different PAS protocols, both with 200 acoustic stimuli (4 kHz), a frequency of 0.1 Hz, and an interstimulus interval (ISI) of 45ms between tone onset and the TMS pulse. With respect to the conditions, the acoustic stimuli differed in their length (PAS (23ms) vs. PAS (400ms)). Auditory steady state responses with 40 Hz amplitude modulated tones (800ms) were measured before and after the intervention using the paired tone (4 kHz) and a control tone (1 kHz).

### Results

After the PAS (400ms) protocol increased power of the ASSR was found in the left and right fronto-temporal electrodes, but none after the PAS (23ms) protocol. There was no difference in changes concerning the tone paired during the PAS intervention (4 kHz) and the control tone (1 kHz).

### Conclusion

Earlier findings about the effects of PAS on the auditory cortex could be partially repeated, but specific effects with respect to the tone frequency were not observed. The increase of 40Hz ASSR power affirms the model of ASSRs as superposition of middle latency acoustic evoked potentials - in this case the Pa which has a latency of 25ms. According to the model of spike-timing dependent plasticity potentials which are cortically processed before the TMS pulse are facilitated. Additionally, attention is a potential factor impacting the results of PAS on the auditory cortex.

*1. Stefan K, Kunesch E. Brain, 2000; 123:572-584*

*2. Schecklmann M, Volberg G. PLoS One, 2011; 6:e27088*

## PAIRED ASSOCIATIVE STIMULATION OF THE HUMAN AUDITORY CORTEX AND ITS EFFECTS ON LATE AUDITORY EVOKED POTENTIALS

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### Aims / Objectives

Paired associative stimulation (PAS), a form of noninvasive cortical stimulation that consists of the application of transcranial magnetic stimulation being paired with peripheral somatosensory input, has been shown to be capable of inducing neuroplastic effects in the human motor cortex. In one recently conducted experiment, these findings were shown to be applicable to the human auditory cortex as well. One question arising from this pilot study was if the length of the paired stimulus is essential for the induction of PAS-like effects. Thus, the aim of this study is to investigate the effects of two different PAS conditions (short and long PAS tone) on late auditory evoked potentials (LAEPs).

### Methods

Two different protocols of PAS were compared in two different sessions carried out one week apart in randomized order. Both consisted of an acoustic stimulus (4kHz) being paired with TMS with an interstimulus interval of 45ms, i.e., tone onset was followed by the TMS pulse. The protocols differed with respect to the duration of the acoustic stimulus, which was defined to be 400ms (PAS(400ms)) or 23ms (PAS(23ms)). A total of 20 healthy subjects were presented with 200 paired stimuli (tone + TMS pulse) at a frequency of 0.1 Hz. Prior to, as well as after the intervention AEPs were measured using an amplitude modulated tone of 4 kHz (comparable to the PAS tone) as well as a control tone of 1 kHz (both 800ms).

### Results

A reduction in the amplitude of the P1-N1-P2 complex was observed only after PAS(400ms), with no effects for the PAS(23ms) condition. This effect was found for the 4kHz and the 1kHz control tone.

## Conclusion

These observations reinforce earlier findings that PAS can be employed to induce neuroplastic changes in the auditory cortex. Furthermore, they seem to suggest an influence of attention on the effects of PAS as the long tone is perceived more consciously. A specific effect depending on the frequency of the paired acoustic stimulus could not be confirmed.

*1 Stefan K, Kunesch E. Brain, 2000; 123:572-578*

*2 Schecklmann M, Volberg G. PLoS ONE, 2011; 6:e27088*

## BUILDING A NEURAL-PSYCHOLOGICAL-IMMUNE- ENDOCRINAL MODEL OF TINNITUS (T-NPIE)

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A sound that is percept in the brain in absence of actual external acoustic stimulus is known as tinnitus. It has long been observed that patients vary in how disturbing tinnitus is to their daily lives. Individual differ in their reactions to stressful situations by the autonomic nervous system (measured by alpha amylase), adrenal cortical secretions (measured by cortisol), and circadian cycles (measured by melatonin) contributes to such individual differences in the experience of tinnitus. Concerns for the experience of the person (e.g., with tinnitus) with the empirical and systematic examination of the physiological (endocrine and neural) processes underlying such experience is not fully understood yet. This, due to tinnitus complex nature, those with tinnitus can experience a disabling sense of haplessness, depression, anxiety, stress, sleep difficulties, and in some cases suicide. Studies that examine the complex nature of tinnitus should pay special attention to identifying the emotional and psychological disturbances associated with tinnitus to better the application of treatment and management options.

### Objective

The aim of this preliminary study is to build a model of the experience of tinnitus with a focus on the influences of physiological changes in the endocrine and immune systems. By assessing how disruption of specific endocrine secretions and a weakening of the immune system contribute to the manifestation and experience (i.e., how disturbing tinnitus is to the patient) of tinnitus symptoms.

**Methods:** two male participants with tinnitus and five male controls without tinnitus ages 21 to 35 years were exposed to an induced stress task and saliva sampling for cortisol, alpha-amylase, melatonin and Neopterin were obtained. The tinnitus intake history questionnaire (TIHQ) and the tinnitus severity index were administrated, followed by audiologic test measures.

### Preliminary results

Two participants with tinnitus, and 7 controls were exposed to an induced stress task (counting backward) and cortisol, alpha-amylase, melatonin and neopterin sampling, were obtained at

four different point of times (baseline, 5min posttest, 30min posttest, 60min posttest). Mean values were compared and used as a suggestive evidence of a potential difference of cortisol and alpha-amylase responses at 5min posttest and at baseline, and a possible difference at 5 and 60min posttest for melatonin responses. In addition, this preliminary data suggested a possible difference at baseline for neopterin in the tinnitus group when compared with healthy controls.

### Conclusion

To date, there is no cure for tinnitus, although different causes of tinnitus have been proposed, none of them are exclusive. The aim of this preliminary study was to document whether hypothalamic nuclei that control autonomic neural activity and those that control adrenal hormones contribute to chronic tinnitus perception, and aid in the building of a new T-NPIE model of tinnitus that demonstrates the role of stress disturbances in adrenal regulation and ANS control in chronic tinnitus. Results of this preliminary research study demonstrated the feasibility of this project to the discovery of new forms of tinnitus networks not limited to the brain, but that involve the autonomic, immune, and endocrinal systems.

## GAP DETECTION THRESHOLDS IN TINNITUS SUBJECTS: DOES TINNITUS FILL IN THE SILENT GAPS?

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### Objectives

Evaluation of tinnitus in humans greatly relies on subjective measures such as questionnaires, visual rating scales and self-reports. Recently, it was hypothesized that tinnitus would perceptually fill in gaps in ongoing stimuli. Based on this, the gap detection paradigm was proposed as an objective measure to model tinnitus in animals. The main purpose of this study was to evaluate the applicability of this approach in tinnitus patients. Hence, we first hypothesized that gap detection would be impaired in tinnitus patients, and second, that gap detection would be more impaired at frequencies close to the tinnitus frequency of the patient.

### Methods

Twenty-two adults with bilateral tinnitus and twenty age- and hearing loss-matched subjects without tinnitus participated in the study. To determine the characteristics of the tinnitus, subjects matched an externally provided sound to their perceived tinnitus pitch and loudness. To determine the minimum detectable gap, an adaptive psychoacoustic test was performed three times by each subject. In this gap detection test, four different stimuli, with varying frequencies and bandwidth, were presented at three different intensity levels, determined with respect to hearing thresholds measured with the test stimuli.

### Results

Similar to previous reports of gap detection, increasing sensation level yielded better gap detection performance for all stimuli in both groups. Interestingly, the tinnitus group did not display gap detection impairment in any of the four frequency stimulus bands compared to the matched control group. Moreover, visual inspection of the data revealed no relation between perceived tinnitus pitch and stimulus frequency band.

## Conclusion

These findings show that tinnitus in humans has no effect on the ability to detect gaps in auditory stimuli. Thus, the testing procedure in its present form is not suitable for clinical detection or diagnosis of tinnitus. Moreover, gap detection paradigms, as applied in animals, may not be able to detect tinnitus in humans.

## TINNITUS CLINICAL SYMPTOMS GENERATION AND MAINTENANCE

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*[2] Universidade Federal do ABC, Cognitive and Complex Systems Unit, São Paulo, Brazil*

*[3] FGSco research and development department, Tehran, Iran*



Our knowledge about Tinnitus has vigorously improved in current decay, but main mechanisms of changing perceiving neutral phantom sound into tinnitus distress have not yet been understood. Non-causal association of Tinnitus clinical symptoms with neutral phantom sound specifications can be elucidated by learning operation. Our suggesting for explaining negative symptoms related to tinnitus is based on top-down cognitive processes together with classical conditioning learning procedure when emotionally neutral conditioned stimulus (CS) is presented in association with an aversive unconditioned stimulus (US), and the conditioned response is the learned response to the previously neutral stimulus. Current models condition, or at least emphasize, the role of external events congruently paired with the causal physical event that originated the phantom perception(1).

To better understanding this phenomenon in tinnitus initiation and reinforcement, we proposed a new Neurofunctional model for tinnitus in early stages and its development. Our detailed model included ascending auditory pathways, the thalamus (reticular, medial geniculate and dorsal nuclei), the limbic system, brain stem, basal ganglia, striatum, and the auditory and prefrontal cortices. We projected the mediating pathways of tinnitus distress incorporate with the convergence of the CS and US pathways in the medial geniculate nucleus(MGN) and lateral nucleus of the amygdala (LA) from thalamic and cortical processing regions in the sensory systems that process the CS (auditory system) and US (emotional mechanism). The MGN projects into auditory cortices and LA. It also receives inhibitory input from thalamic reticular nucleus (TRN). The LA then connects with the central nucleus of amygdala (CE) directly and by the way of other amygdala regions. Outputs of the CE then control the expression of fear responses and related autonomic nervous system (e.g., blood pressure and heart rate) and endocrine (pituitary adrenal hormones) responses.
Functionally, we assume continuous or intermittent abnormal signal at the peripheral auditory system or midbrain auditory pathways. Depending on cognitive-emotional initiated value and the availability of attentional resources lead to conscious awareness perceiving of the neutral Tinnitus which can cognitively interpret as suspicious and contingents with emotional appraisal (US) such as feel of fear. The negative reaction (e.g. fear) is the learned response to neutral Tinnitus. Fear

individually can trigger the feel of fear in a positive feedback loop, therefore continuing perceiving Tinnitus contingent with feel of fear reinforces the negative reaction. Furthermore Tinnitus negative reaction is being weakened by the both fearing in the absence of perceiving tinnitus, and perceive Tinnitus without triggering the feel of fear. Development of neuroplasticity in MGN (2), LA and auditory primary cortex are exhibited dynamic molecular neuron modification in brain which can cause reciprocal psychiatric comorbidities such as anxiety, stress, phobias and/or depression symptoms. We present empirical evidence from studies using neuroimaging, electrophysiology, brain lesion and behavioral techniques to support the model. This model represents an advance in our understanding of clinically-significant tinnitus symptoms and might eventually help to improve current treatments.


1. *Jastreboff PJ, Gray WC, Gold SL. Neurophysiological approach to tinnitus patients. The American journal of otology. 1996;17(2):236-40.*
2. *Weinberger NM. The medial geniculate, not the amygdala, as the root of auditory fear conditioning. Hear Res. 2011;274(1-2):61-74.*

## INFUSION OF GABAB RECEPTOR AGONISTS INTO THE COCHLEAR NUCLEUS ON TINNITUS DEVELOPMENT FOLLOWING ACOUSTIC TRAUMA IN RATS

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### Background

Chronic tinnitus is experienced by about 10% of the population and produces many detrimental effects on the quality of life. There are very limited drug treatment options, mainly due to a lack of understanding of the underlying mechanisms. It has been suggested that tinnitus is generated by neuronal hyperactivity in multiple areas of the brain, including the dorsal cochlear nucleus, inferior colliculus and primary auditory cortex. Furthermore, bilateral lesions of the dorsal cochlear nucleus before the acoustic-trauma, but not afterwards, prevented the development of tinnitus in rats. Recently, we have demonstrated that L-baclofen, which activates inhibitory neurotransmission through GABAB receptors, dose-dependently reduced noise trauma-induced tinnitus in rats. In the present study, we further investigated the possibility of preventing the development of tinnitus by infusing the GABAB receptor agonists, L-baclofen or CGP7930, into the cochlear nucleus prior to acoustic trauma.

### Materials and Methods

Male Wistar rats were divided into 8 groups (n = 8 - 19 per group): Sham-saline, Sham-DMSO, Sham-Baclofen, Sham-CGP7930, Acoustic trauma-saline, Acoustic trauma-DMSO, Acoustic trauma-Baclofen and Acoustic trauma-CGP-7930. The acoustic trauma consisted of a 16 kHz, 115 dB pure tone delivered unilaterally for 1 h under anaesthesia. Saline, DMSO, L-baclofen (2 mM at 0.5 µl/h) or CGP7930 (100 µM at 0.5 µl/h) was administered into bilateral cochlear nuclei through cannulae connected to Osmotic minipumps for 7 days starting at 24h before the acoustic trauma. The behavioural signs of tinnitus in each rat were measured by a conditioned lick suppression paradigm at about 1 month after the acoustic trauma. Following the tinnitus testing, the animals were perfused transcardially with 10% neutral buffered formalin and the brains were removed, sectioned and stained with Cresyl Violet to confirm the cannula placement.

## Results

The preliminary results suggested that neither the L-balofen nor the CGP7930 infused into the cochlear nucleus prevented the development of tinnitus induced by acoustic trauma. The results will be finalized with the confirmation of the cannula placement.

## Conclusion

Directly activating the GABAB receptors in the cochlear nucleus may not be sufficient to prevent the development of tinnitus induced by acoustic trauma.

## STRESS-ASSOCIATED CHANGES OF MITOCHONDRIAL PROTEINS IN AUDITORY CORTEX

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### Aims

Chronic form of tinnitus has been proposed to reflect called plastic changes in the auditory structures. Emotional and psycho-social stress was shown to induce functional changes in the auditory system of experimental animals consistent with hypersensitivity in the inner ear (increased amplitudes of DPOAEs) and in the auditory brainstem (changes in ABR). However, little is known about the mechanisms, in which emotional and psycho-social stress affects the auditory system. To find out if stress affects mitochondrial integrity or mitochondrial protein-mediated plasticity, we have monitored the levels of mitochondrial proteins Bcl-2, Bax and Bcl-xL in the auditory cortex following experimental stress.

### Methods

Two strains of rats (four weeks old, female, 100 – 120 g weight) were used – Wistar Hannover and Lewis. Wistar Hannover is an outbread strain derived from Wistar used as a general, all-purpose outbred model for use in biomedical research and known as developing relatively low level of anxiety under stressful conditions. Lewis rats are an inbread strain characterized in neuro-psychological research as developing relatively high level of anxiety under stressful conditions. The rats were exposed to 24-h psycho-social stress. After functional tests of auditory pathways, auditory cortices were dissected from sacrificed animals, and the proteins were purified and analyzed using Western blot followed by chemiluminescence and densitometry. The results were statistically analyzed with Sigma Stat.

### Results

Auditory cortices of Wistar rats contained significantly more Bax immediately after finishing the stress period, as compared to non-stressed animals ($P<0.01$, one-way ANOVA). The Bax levels returned to baseline six hours later. Bcl-2 and Bcl-xL remained unchanged. In contrast, auditory cortices of Levis rats contained significantly more Bcl-xL following stress, as compared to the controls ($P<0.01$, one-way ANOVA).

## Conclusions

Psycho-social stress can modulate Bax and Bcl-xL levels in the auditory cortex of had increased amount of Bax after finishing stress whereas the anxiety-prone Lewis rats had increased amount of Bcl-xL in the auditory cortex after finishing stress. Besides playing an important role in mitochondrial integrity and cell survival, Bax and Bcl-xL have the ability to regulate synaptic plasticity and thus, can contribute to and reflect the plastic changes in auditory central system following psycho-social stress.

## EVIDENCE FOR NEUROGENESIS IN THE COCHLEAR NUCLEUS FOLLOWING ACOUSTIC TRAUMA IN RATS

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### Background

Tinnitus induced by acoustic trauma results in electrophysiological changes in the cochlear nucleus (CN) which appear to cause neuronal hyperactivity. In neurogenic areas of the brain, for example, the dentate gyrus, such electrophysiological changes have been shown to alter neurogenesis. The present study investigated the effects of acoustic trauma that has been proven to cause tinnitus, on cell proliferation and neurogenesis in the CN of rats.

### Materials and Methods

Rats received either sham or unilateral acoustic trauma (16 kHz at 115 dB for 1 h) under anaesthesia. Auditory brainstem responses (ABRs) were measured to determine the effects of the acoustic trauma on hearing. Animals were injected with the cellular proliferation marker, BrdU, at 72 hs following the acoustic trauma, and then 2 hs or 24 hs later, were sacrificed by transcardial perfusion with 4% paraformaldehyde and the brains were removed, sectioned and stained for BrdU using immunohistochemistry. Double labelling immunofluorescence immunohistochemistry was performed for BrdU and Ki-67, a marker for cells in the S phase of the cell cycle, CD11b, a marker for microglial cells, and doublecortin (DCX), a marker for immature neurons.

### Results

Acoustic trauma resulted in a significant elevation of the ABR thresholds, indicative of hearing loss. Acoutic trauma also resulted in an increase in BrdU labeling in the CN, which significantly co-labeled with an antibody for Ki-67, suggested was due to the generation of new cells rather than DNA repair. There was no significant co-labeling for CD11b, suggesting that the new cells were not microglial cells. However, there was significant co-labeling for DCX, suggesting that many of the new cells were immature neurons.

### Conclusion

The present study suggests that the cell proliferation that occurs in the CN following acoustic trauma represents neurogenesis.

## SOUND-TRIGGERED SUPPRESSION OF NEURONAL FIRING IN THE AUDITORY CORTEX: IMPLICATION TO THE RESIDUAL INHIBITION OF TINNITUS

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*2 Kent State University, Biomedical Science Program, Kent, Ohio, USA*



### Aims / Objectives

Tinnitus can be suppressed briefly following the offset of an external sound. This phenomenon, termed "residual inhibition," has been known for almost four decades, although its underlying cellular mechanism remains unknown. In our previous work we have shown that the majority of neurons in the inferior colliculus (IC) exhibit long lasting suppression of spontaneous activity following the offset of an external sound. The time course of suppression corresponded to the time course of residual inhibition in tinnitus patients. Tinnitus patients often report an increased effect of tinnitus-matched pure tones on the duration of their residual inhibition. Our data show pure tones induce longer suppression than wideband noise. If the suppression is an underlying mechanism, the auditory cortex (AC) neurons should also exhibit suppression because residual inhibition of tinnitus is a perceptual phenomenon. To test this hypothesis, we studied sound evoked suppression in auditory cortex neurons of awake mice. Animals with behavioral signs of tinnitus and control unexposed mice were used.

### Methods

Experiments were conducted on adult CBA/CaJ mice. For tinnitus induction mice were exposed to a narrowband noise centered at 12.5 kHz presented at 116 dB SPL unilaterally for 1 hour under general anesthesia (Ketamine/Xylazine). Tinnitus was then assessed utilizing gap-induced prepulse inhibition of the acoustic startle reflex. Extracellular recordings were performed in auditory cortex contra- and/or ipsilateral to the exposed ear in awake restrained animals. Pure tones at neurons' characteristic frequency and/or wideband noise stimuli 30 sec duration were delivered in the free-field.

### Results

We found that auditory cortex neurons in control mice exhibited sound-triggered suppression of their spontaneous firing. Similar to the IC, the duration of this suppression after sound offset in AC neurons roughly corresponded to the stimulus duration (about 30 s). AC neurons also showed longer suppression to tones at their characteristic frequency than to wideband noise stimuli.

Unlike the IC, in addition to the suppression after stimulus offset, the majority of AC neurons also showed suppression during stimulus presentation.

### Conclusions

Similar to the IC, AC neurons exhibit long lasting suppression of their spontaneous firing following sound offsets. The time course of this suppression corresponds to the time course of residual inhibition in tinnitus patients. These data further suggest that suppression may be a neural correlate of the residual inhibition of tinnitus in humans.

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## EFFECTS OF PARAFLOCCULUS REMOVAL ON HYPERACTIVITY AFTER ACOUSTIC TRAUMA

**Vogler, D.P.**[1]; Robertson, D.[1]; Mulders, WHAM.[1]

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Acoustic trauma not only causes hearing loss but also results in a variety of plastic changes in central auditory pathways, such as increased spontaneous activity. This so-called hyperactivity may be involved in the generation of tinnitus, a phantom auditory sensation. Though many animal studies have consistently shown hyperactivity in auditory centres after hearing loss, tinnitus does not always develop. It has therefore been suggested that there may be involvement of non-auditory structures performing a regulatory role bringing the increased activity in the auditory system to conscious perception. Recent evidence points to the paraflocculus of the cerebellum as having such a role. The paraflocculus receives direct input from the cochlea and is anatomically connected to central auditory structures. Therefore, we investigated the effects of paraflocculus removal on hyperactivity in guinea pig inferior colliculus 2 weeks after acoustic trauma (continuous 10 kHz tone at 124 dB SPL for 2 hours). Spontaneous activity was recorded from 477 neurons (4 animals) with paraflocculus and from 559 neurons (5 animals) with paraflocculus aspirated. Results showed a significant increase in hyperactivity ($p = 0.02$) with paraflocculus removed. These results suggest that paraflocculus exerts an inhibitory effect on hyperactivity in inferior colliculus at 2 weeks after acoustic trauma. The results are surprising in view of observations in another animal model that paraflocculus removal results in reduction of tinnitus measured behaviourally. However, these latter studies were performed at much later time-points after acoustic trauma. Studies are underway to investigate the effects of paraflocculus removal on hyperactivity at later time-points.

## HYPERACTIVITY IN THE INFERIOR COLLICULUS AFTER NOISE TRAUMA AND ITS MODULATION BY EXTRA-COCHLEAR ELECTRIC STIMULATION

**Norena, A.**[1]; Mulders, H.[2]; Robertson, D.[2]

*1 National Center of Scientific Research, Aix-Marseille University,*
*2 University of Western Australia*

Many studies have shown an increase of spontaneous firing in the auditory centers after noise trauma. It has been suggested that this central hyperactivity may underlie the perception of tinnitus. Recent studies showed that central hyperactivity depends on cochlear activity: reducing the spontaneous firing in the cochlear nerve abolishes neural hyperactivity in the inferior colliculus (at least within the first few weeks after noise trauma). Extra-cochlear stimulation of the cochlea has been shown to modulate the firing in the cochlear nerve: while positive direct current (DC) reduced neural activity in the cochlear nerve, negative DC has the opposite effect. Interestingly, some human studies showed that positive DC applied at the promontory or round window could reliably suppress tinnitus. The goal of the present study was to investigate whether extra-cochlear DC current applied at the round window was able to modulate neural (hyper)activity in the inferior colliculus. Our results show that, for neurons with a characteristic frequency higher than around 10 kHz, positive DC suppresses neural activity in inferior colliculus while negative DC enhances it. For neurons with lower characteristics frequencies, effects of electrical stimulation were either absent or reversed. Our results suggest that extra-cochlear electric stimulation may reduce the tinnitus percept by reducing central (hyper)activity,. This approach may lead to important future developments providing that the electrical stimulation used in clinic is innocuous for biological tissues.

## MULTIDISCIPLINARY ASSOCIATION FOR PSYCHEDELIC STUDIES

Doblin, R.

A review of the regulatory routes of approval for Schedule 1 drugs especially MDMA, marijuana, psilocybin, LSD, Ibogaine, Ayahuasca. Discussion will include national rules and international treaty obligations. A summary of MAPS' research portfolio which includes: multisite studies for MDMA-assisted psychotherapy for PTSD, US-based studies on MDMA therapy for Autistic adults with social anxiety, and MDMA-assisted psychotherapy for people with life threatening illness who are dealing with anxiety related to end of life issues. MAPS' studies on psilocybin, LSD, Ibogaine and Ayahuasca will be outlined. Also included will be a risk/benefit analysis based on over 4,000 papers on Medline with topics on MDMA or ecstasy, along with a discussion of remaining methodological issues to be addressed prior to phase 3 studies.

## MDMA-ASSISTED PSYCHOTHERAPY FOR TINNITUS AND PTSD

Emerson, A.

This presentation will summarize the MAPS clinical research studies of psychotherapy assisted with 3,4-methylenedioxymethamphetamine (MDMA) for the treatment of severe chronic, treatment-resistant PTSD. Pilot studies indicate large effect sizes that may necessitate a paradigm shift in treatment of refractory cases of PTSD.

Data from 2 completed MAPS-sponsored Phase 2 clinical trials and Preliminary data from one ongoing trial in veterans and first responders will be summarized. Case reports of changes in Tinnitus symptoms during treatment of PTSD will be presented.

## NEURAL PLASTICITY AND ATTENTION IN NORMAL HEARING AND IN TINNITUS

Roberts, L.E.

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Most if not all models of tinnitus generation propose that neural plasticity contributes to the neural changes that underlie tinnitus. Sensory training therapies for tinnitus are similarly based on the assumption that, notwithstanding neural changes related to tinnitus, auditory training can alter the response properties of neurons in auditory pathways. In this talk I will summarize what we have learned about the rules that describe how neural plasticity is expressed in the normal hearing human brain, and how these rules appear to be modified in individuals experiencing tinnitus. The findings support the view that stimulus-driven forms of neural plasticity contribute strongly to auditory remodeling in normal hearing individuals throughout the lifespan. While these forms are likely at work in tinnitus as well, the outcome of auditory remodeling is modified by the presence of tinnitus-related neural activity. Tinnitus-related modifications include a relaxation of constraints on auditory representations in primary auditory cortex, impaired temporal plasticity in subcortical pathways, and reduced modulation by attention of brain responses evoked by sounds in the tinnitus frequency region. Implications of these findings for models of tinnitus and for sound therapies will be discussed. (Supported by NSERC of Canada and the Tinnitus Research Initiative)

## Poster Session 3 / Toru

*Numbers refer to poster board allocation*

INFLUENCE OF TINNITUS ON AUDITORY SPECTRAL AND TEMPORAL RESOLUTION, AND SPEECH PERCEPTION ABILITY IN TINNITUS PATIENTS
Shim, HJ.; Kang, HW.; An, YH.; Won, JH.
03

EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON AUDITORY RESIDUAL INHIBITION OF TINNITUS
Shekhawat, G.S.; Searchfield, G.D.; Stinear, C.M.
09

CHANGES OF TINNITUS IN SUDDEN SENSORINEURAL HEARING LOSS: RELATIONSHIP BETWEEN TINNITUS PITCH AND AUDIOMETRIC SHAPE
Jong-Ik Lee, Tae Su Kim, Hye Ran Hong, Byung Soo Shim, Hwan Seo Lee, Joong Ho Ahn, Jong Woo Chung, Tae Hyun Yoon, Hong Ju Park
15

EXAMINING THE ROLES OF CONTEXTUAL STIMULI AND PERSONALITY TRAITS UNDER THE ADAPTATION LEVEL THEORY MODEL OF TINNITUS
Aruldasan, M.; Kobayashi, K.; Searchfield, G.D.
21

CORTICAL PLASTICITY IN TINNITUS PATIENTS AFTER REPETITIVE EXPOSURE TO TAILOR-MADE NOTCHED MUSIC
Engell, A.; Stein, A.; Pantev, C.
27

ABNORMAL BRAIN ACTIVITY AND CROSS-FREQUENCY COUPLING IN THE TINNITUS NETWORK
**Adamchic, I.**; Langguth, B.; Hauptmann, C.; Tass P.A.
33

SURFACE BASED MORPHOMETRY ANALYSIS OF NEUROPLASTICITY INDUCED CHANGES IN THE BRAIN OF PATIENTS WITH TINNITUS

Kleinjung, T.; Neff, P.; Langguth, B.; Meyer, M.; Schecklmann, M.

39

ELECTROPHYSIOLOGICAL EFFECTS OF ATTENTION IN NORMAL HEARING AND IN TINNITUS

Paul, B.; Bruce, I.; Bosynak, D.J.; Thompson, D.C.; Roberts, L.E.

45

PARAHIPPOCAMPAL-AUDITORY CORTEX COMMUNICATION IN TINNITUS

**De Ridder, D.**; Congedo, M.; Vanneste, S.

53

MODULATING ALPHA AND BETA OSCILLATIONS WITHIN POSTERIOR CINGULATE CORTEX THROUGH REAL-TIME SOURCE LOCALIZED NEUROFEEDBACK AND ITS EFFECT ON TINNITUS RELATED DISTRESS

Joos, K.1; De Ridder, D.2; Vanneste, S.3

59

CHANGE IN SPONTANEOUS CORTICAL ACTIVITY DURING TINNITUS REMEDIATION

Mathur, A.; Ibrahim, R.; McMahon, C. M.

65

TONOTOPIC MAP CHANGES DURING TINNITUS REMEDIATION

**Ibrahim, R.K**.; McMahon, C.M.; Mathur, A.

71

CHANGES IN RESTING-STATE FMRI ACTIVITY DURING SALICYLATE-INDUCED TINNITUS AND SOUND STIMULATION

Chen, Y.-C.; Wang, J.; Jiao, Y.; Zang, F.-C.; Yang, M.; Tong, J.-X.; **Salvi, R**.; Teng, G.-J

77

AUDITORY-LIMBIC NETWORK IN TINNITUS REVEALED BY RESTING-STATE FUNCTIONAL CONNECTIVITY MRI

Turesky, T.; Leaver, A.M.; Seydell-Greenwald, A.S.; Rauschecker, J.P.

81

TINNITUS AND DYSFUNCTIONAL INTERACTIONS BETWEEN DISTRIBUTED RESTING STATE NETWORKS

Maudoux, A.; Vanneste, S.; De Ridder, D.; Vanhecke, W.; Van de Heyning, P.; Cabay, J.-E.; Demertzi, A.; Laureys, S.; Soddu, A.; Lefebvre, Ph.; Gomez F.

97

## Poster Session 4 / Wha

*Numbers refer to poster board allocation*



REFLEX MODIFICATION AUDIOMETRY AS A TOOL TO ASSESS HEARING IN MICE

Longenecker, R.J.; Alghamdi, F. ;Galazyuk, A.V.

04

UNILATERAL HEARING LOSS IN THE FERRET: A NEW DIRECTION FOR TINNITUS RESEARCH

**Gold, J.R**.; Nodal, F.R.; King, A.J.; Bajo, V.M.

10

EFFECTS OF STRESS-INDUCED SLEEP DISTURBANCE ON TINNITUS PERCEPTION AND BRAIN OREXIN EXPRESSION IN RATS FOLLOWING ACOUSTIC TRAUMA

**Chien,Y.T**.; Stiles, L.; Milne, M.; Darlington, C.L.; Smith, P.F.; Zheng, Y.

16

PAIRED ASSOCIATIVE STIMULATION OF THE HUMAN AUDITORY CORTEX AND ITS EFFECTS ON THE AUDITORY STEADY STATE RESPONSE

Engel, S.; Markewitz, R.; Schecklmann, M.; Langguth, B.

22

PAIRED ASSOCIATIVE STIMULATION OF THE HUMAN AUDITORY CORTEX AND ITS EFFECTS ON LATE AUDITORY EVOKED POTENTIALS

**Markewitz, R.D.H**.; Engel, S.; Schecklmann, M.; Langguth, B.

28

BUILDING A NEURAL-PSYCHOLOGICAL-IMMUNE- ENDOCRINAL MODEL OF TINNITUS (T-NPIE)

Alsalman, O.; Tucker, D; Michel, G.

34

**Moseley, G.L.**

Lorimer's work into the role of the brain and mind in chronic pain has clear relevance for our understanding and treatment of tinnitus. Many of the problems that face pain researchers and clinicians seem to be mirrored in the tinnitus world. In many chronic pain states, the pain is effectively an illusion because it is alerting the sufferer to a problem that does not in fact exist - that problem being tissue in need of protection. This situation is terrifically difficult to understand if one thinks about pain as an entity that exists in the tissues themselves. An important part of Lorimer's research has been to take on the substantial challenge of helping people in pain to reconceptualise what pain actually is and how it works. The approach, colloquially called 'Explain Pain' is now endorsed in clinical guidelines around the world. Other work targets findings of functional changes in the brain's representation of sensory input and those techniques too, are now supported by clinical trial evidence. In this lecture, Lorimer will give an overview of this work and speculate, from the perspective of a tinnitus outsider, on how the two fields might learn from each other to more quickly progress both.

## ATTENTION AND SUBJECTIVE TINNITUS: FROM A CLINICAL POINT OF VIEW

Londero, A.

*Hôpital Européen G. Pompidou, Paris, France*

In a challenging world, auditory attention is an essential property of mammalian brains. Rather than processing all of the auditory information which is mostly relegated in the background of the auditory scene, we selectively shift our attention to various relevant auditory events, either events of interest or events that capture our attention spontaneously.

Even if tinnitus is usually defined as a "phantom sound", it is indeed an auditory form. In impaired tinnitus patients, it is mainly perceived as a distressing component of the auditory scene foreground that captures attention. On the contrary non bothered patients deal with their tinnitus as if it were a meaningless background signal. Real life patients' statements highlight the importance of attention processes in the clinical context of invalidating tinnitus. However, to date and from a clinical point of view, very little medical "attention" has been paid to these attention-related issues within the tinnitus field.

One plausible reason for this discrepancy is the difficulty to give a clear-cut definition of what attention actually is. For example, auditory attention not only depends on the psycho-acoustic properties of auditory events that make specific sounds more salient and more prone to pop-out in the auditory scene, but also on high level cognitive functions including short and long-term memory or emotional connotation of sounds. Moreover, in a quite puzzling auto-referential way, attention is closely linked to the notions of object and motion. Top-down intentional attention literally creates the auditory objects. Indeed objects that do not exist for the brain before our attention has been focused toward them with subsequent gaze and body orientating reactions. But in reverse way bottom-up attention detects specific unexpected or threatening objects in order to allow us proper reaction.

A pragmatic way to understand attention is to consider it as a "biased" way to analyze and filter our sensations, that systematically favors either unpredicted events (i.e. deviant from brain expectations) via a bottom-up filtering that mainly relies on basic properties of sensory input or interesting events via a top-down modulation based on memory and emotions. Neural correlates involved in these complex attentional processes are still a matter of debate.

The clinical usefulness of such a paradigm of analysis of tinnitus intrusiveness is still an open question. However virtual reality techniques that allow a standardized and reproducible immersion in controlled environments could represent an interesting novel tool to better understand the implication of attention processes in impaired tinnitus patients.

## AN ENT DOCTOR'S JOURNEY TO THE BRAIN: THE AUDITORY AND NON-AUDITORY BRAIN AREAS INVOLVED IN TINNITUS AND TINNITUS-RELATED DISTRESS

Song, J.J.

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Tinnitus is a phantom sound perception without an identifiable sound source. It is characterized by sensory components such as perceived loudness and pitch, the laterality (uni- or bilateral), the tinnitus type (pure tone or noise-like) and associated emotional components, such as distress and mood changes. Functional imaging studies using positron emission tomography (PET), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and quantitative electroencephalography (qEEG) have demonstrated the involvement of not only the auditory brain areas such as the primary- and secondary auditory cortices but also several non-auditory brain areas such as the anterior- and posterior cingulate cortices, dorsolateral prefrontal cortex, insula, supplementary motor area, orbitofrontal cortex (including the inferior frontal gyrus), parahippocampus, and the precuneus, in different aspects of tinnitus. Also, many researchers have explained these auditory and non-auditory brain areas as constituents of separable subnetworks, each reflecting a specific aspect of the tinnitus percept and tinnitus-related distress.

In this talk, I would like to first summarize cortical areas that have been found to be involved in tinnitus perception and tinnitus-related distress, then combine those areas to form alleged subnetworks. During the talk, also, I would like to introduce my short research experience and results found primarily by qEEG-based source localization and functional connectivity studies.

## PRISM (PICTORIAL REPRESENTATION OF ILLNESS AND SELF MEASURE) AS A NEW ASSESSMENT TOOL FOR SUFFERING IN TINNITUS PATIENTS

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### Objectives

Chronic subjective tinnitus is a frequent condition that affects the quality of life of millions of sufferers worldwide. The lack of objective measures of tinnitus necessitates the use of self-report questionnaires for evaluating tinnitus severity and annoyance. The analyses of these questionnaires allow medical staff to select adequate treatment modalities and monitor treatment effects. However, the wide range of different questionnaires hampers an international and comparable standard in tinnitus assessment. Furthermore, most of these questionnaires have shortcomings in terms of responsiveness to treatment related changes, insufficient translation and validation in different languages and time-consuming aspects. PRISM (Pictorial Representation of Illness and Self Measure) is a method to assess suffering and quality of life. So far, PRISM was validated as a marker of burden in different psychological and physical conditions like PTSD, rheumatoid arthritis, chronic urticaria and orofacial pain. The aim of this study is to validate PRISM as a marker of impairment in tinnitus patients in a prospective observational study. The results of PRISM assessment were compared to different standard questionnaires used in tinnitus evaluation.

### Methods

Participating subjects were asked to fulfill an online-base survey including the following questionnaires: THI (Tinnitus Handicap Inventory), TQ (Tinnitus Questionnaire) TBF-12 (German short version of THI), WHOQOL-BREF (WHO Quality of Life-Questionnaire), BDI (Beck Depression Inventory). At the time of consultation in the clinic the subjects were asked to perform an audio-visual task on PRISM using an IPad. Patients were shown a white panel on the whole display (14.7x19.6cm) of the Ipad (representing their life) with a yellow circle (diameter 4.9cm) at the bottom right-hand corner representing his or her "self" at this time. Afterwards they were asked to move another smaller red circle (3.5cm) representing their tinnitus in relation to their self at this moment. The answers on the two dimensional PRISM were divided into 4 groups. Comparisons to the questionnaire scores were correlated using t-test or ANOVA (SPSS).

## Results

A total of 130 subjects were included in the analysis (48 women, 82 men) since 2012. The answers on the two dimensional PRISM were divided into 4 groups reflecting different grades of tinnitus severity : In group 1 the red tinnitus-circle was completely placed in the yellow self-circle (most severe); in group 2 the red tinnitus-circle was overlapping the yellow self-circle and was not part of group 1; in group 3 the red tinnitus-circle was placed under a virtual diagonal line from the left bottom to the right upper corner and was not part of group 1 or 2; in group 4 the red tinnitus-circle was placed in the triangle above the virtual diagonal line from the left bottom to the right upper corner (least severe). The different PRISM groups demonstrated a statistically significant correlation with the corresponding grading in the traditional tinnitus questionnaires (e.g. THI, TQ).

## Conclusion

PRISM is a new visual method to assess suffering in patients with tinnitus in a short time. We could show a significant correlation between the traditionally used tinnitus-questionnaires and PRISM.

## PROPORTION AND DIVERSIFICATION OF UNDERLYING CAUSES OF 242 UNILATERAL VENOUS PULSATILE TINNITUS CASES IN DUAL-PHASE CONTRAST-ENHANCED CT

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### Objectives

To evaluate the proportion and diversification of underlying venous PT causes.

### Materials and Methods

The dual-phase contrast-enhanced CT (DP-CECT) images of 242 patients with unilateral venous PT were retrospectively reviewed. The underlying causes of venous PT reported in previous literatures were evaluated. Furthermore, the number of underlying causes of venous PT in each patient was counted.

### Results

(1) Of all patients, only 58 patients (24.0%) were diagnosed with only one underlying cause, while 170 patients (70.2%) were with more than one cause. (2)The most common underlying cause of venous PT was dehiscent sigmoid plate (86.4%), followed by lateral sinus stenosis (55.8%), high jugular bulb (47.1%), sigmoid sinus diverticulum (34.3%), jugular bulb diverticulum (13.6%), dehiscent jugular bulb (13.6%), large emissary vein (4.1%), sinus thrombosis (1.2%), petrosquamosal sinus (0.8%).

### Conclusion

Dehiscent sigmoid plate is common in venous PT. The causes of venous PT could be diversified in most PT patients.

Keywords: Pulsatile tinnitus, computed tomography

## THE DURAL SINUS WALL DEHISCENCE PRESENTING WITH PULSATILE TINNITUS: EVALUATION WITH CT VENOGRAPHY

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### Objectives

To assess the detailed CT findings about dura sinus wall dehiscence in patients presenting with pulsatile tinnitus (PT) on CT venography (CTV)

### Methods

Following approval of the institutional review board, 131 hospitalized patients with PT from 2008 to 2013, who underwent thorough clinical and laboratory tests including CT arteriography and venography and digital subtraction angiography, were retrospectively evaluated. Finally, 30 patients were included. All these patiens were found with dural sinus wall dehiscence on the symptomatic side and their noise was totally eliminated after covering the dehiscence with tempralis facia. The signs were invesgated as follows: the location,extent and amount of the dehiscence, the presence of one or more arachnoid granulations beneath the transverse sinus, the presence of transverse sinus stenosis, the presence of high jugular bulb and the presence of venous outflow dominance.

### Results

Forty two dehiscence were detected in these 30 patients, with the area range from 2*2 to 5*8 mm(average 3*5 mm). The single dehiscence was found in 24 of 30 patients (80%). The bony wall above the common crus was involved in 29 of 42 dehiscence (69%). The anterolateral wall was involved in 35 of 42 patients (83%). For other imaging findings, the large arachnoid granulation beneath the transverse sinus was demonstrated in 25 patients (83%) on the symptomatic side while in 26 (87%) on the contralateral side; the ipsilateral high jugular bulb was revealed in 28 patients (93%); the symptomatic side was consistent with the dominant side in 23 of 25 patients (92%) with unilateral dominant venous system. The transverse sinus stenosis was found in 25 (83%) patient on the symptomatic side while 28 (93%) on the contralateral side.

### Conclusion

The dural sinus dehiscence presenting with PT, which seems to be a direct cause of PT, mostly

manifests as single bony defect with the lateral wall of dural sinus at a relatively high level involved. The hemodynamic abnormalities caused by diversified factors, including bilateral transverse sinus stenosis, ipsilateral high jugular bulb, ipsilateral outflow dominance bilateral arachnoid granulation(s) beneath the transverse sinus, may be the root cause of dural sinus wall dehiscence presenting with PT.

I am in reading MD of Radiology in Beijing Tongren hospital which was the No 1 at the diagnosis and treatment of otolaryngology in China. My main direction is about pulsatile tinnitus. In last four years, I have made diagnosis for more than one thousand patients with pulsatile tinnitus with various causes. Besides, I have submitted five papers in Chinese until now and I have written three papers in English, one of which has been accepted by Acta Radiologica.

## DEEP BRAIN STIMULATION OF THE INFERIOR COLLICULUS FOR TREATING TINNITUS

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One possible tinnitus treatment option is to utilize deep brain stimulation on non-lemniscal or secondary auditory nuclei to directly modulate and create plastic changes in lemniscal auditory nuclei with aberrant neural activity related to tinnitus. A potential strategy is to stimulate the dorsal cortex of the inferior colliculus (ICD) to modulate neural activity in the central region (ICC), a nucleus in the auditory midbrain shown to have hyperactivity and increased neural synchrony in tinnitus patients and/or animals. ICD can also modulate other lemniscal regions involved with tinnitus through ascending and descending pathways. We have a unique opportunity to stimulate the ICD directly in tinnitus patients in an upcoming clinical trial with a new auditory midbrain implant (AMI). The AMI will be implanted in the inferior colliculus in patients for hearing restoration, but many of these patients also have tinnitus. Prior to this clinical trial, we sought to identify effective stimulation locations in ICD and a stimulation strategy that could alter ICC activity relevant for tinnitus suppression in an animal model.

Multi-site electrodes arrays were positioned across the ICC and ICD of ketamine-anesthetized guinea pigs. Spike activity in ICC was recorded in response to broadband noise stimulation before and after repeated electrical stimulation of the ICD to identify residual changes in neural activity. Electrical stimulation was paired with broadband noise stimulation at different inter-stimulus intervals and alone to compare residual effects. Histological steps were taken to produce 3-D reconstructions of the midbrain and to identify the location of electrode sites across the IC.

Our results reveal that every ICD stimulation location induces a complex pattern of modulation of neural activity in ICC, with significantly more inhibition than facilitation. Additionally, modulation is significantly dependent on the electrical stimulation paradigm used. Electrical stimulation paired with broadband noise with a long inter-stimulus delay (18 ms) resulted in more inhibition than either electrical stimulation paired with broadband noise with a short inter-stimulus delay (8 ms) or electrical stimulation alone.

Based on our findings, we can stimulate any ICD location to modulate ICC activity. The stronger

residual inhibition that occurs when pairing the electric and acoustic stimulation with a longer delay (i.e., 18 ms versus 8 ms) may be from weakened synaptic connections, perhaps due to spike timing dependent plasticity. With the correct timing, the paired stimulation could inhibit hyperactivity and disrupt neural synchrony with long-lasting effects, which may induce plasticity in the ICC that leads to suppression of the tinnitus percept. The results from this study are encouraging for deep brain stimulation as a treatment for tinnitus. Future studies will need to investigate how ICD stimulation alters activation patterns in other auditory nuclei linked to tinnitus, such as in the auditory cortex, and in tinnitus animal models. We will initially test ICD stimulation paired with ICC stimulation (since acoustic stimulation is not possible) in deaf patients with tinnitus who will be implanted with the AMI.

## IMPACT OF SPECTRAL NOTCH WIDTH ON THE CLINICAL EFFECTIVENESS OF THE TAILOR-MADE NOTCHED MUSIC TRAINING

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Tinnitus, the ringing in the ears that is unrelated to any external source, causes a significant loss in quality of life, involving sleep disturbance and depression for 1 to 3 % of the general population. In the first place tinnitus may be triggered by damage to the inner ear cells, but the neural generators of noise-induced tinnitus are located in central regions of the brain. A loss of lateral inhibition, tonotopical reorganization and a gain-increase in response to the sensory deprivation result in hypersensitivity and hyperactivity in the auditory cortex. Negative emotional appraisal and attention might support the development of a tinnitus network. Within the training with tailor-made notched music (TMNMT) patients listen to music from which the frequency spectrum of the tinnitus has been removed. This evokes strong lateral inhibition of the neurons involved in the tinnitus percept from neurons tuned to other frequencies. A reduction of tinnitus loudness was achieved with TMNMT is previous studies. The effect of lateral inhibition can be enhanced with a smaller bandwidth of the notch. We assume that the training will be more effective with a notch width of a ½ octave or even a ¼ octave compared to one whole octave. Participants can choose their favorite music for the training that includes three month of two hours daily listening. Our outcome variables were standardized tinnitus questionnaires, visual analog scales and Magnetoencephalography (MEG). We found a reduction of tinnitus distress in all groups. Participants in the ½ octave group show the strongest improvement. We also found a positive correlation of tinnitus loudness reduction and reduction of the evoked auditory response in the MEG.

## COMPARISON OF POSITIONING THE CATHODE IN TDCS

**Rabau, S.**[1,2]; Mariën, P.[1]; Van de Heyning, P.[1,2]

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### Objectives

In the case of tDCS, current is applied to the brain by means of 2 electrodes: the anode on the dysfunctional site and the cathode on a 'silent' part of the body. Nowadays, mostly bifrontal tDCS is applied in tinnitus patients: the anode and cathode placed on respectively the right and left dorsolateral prefrontal cortex (DLPC). Our hypothesis is that the placement of the cathode on the shoulder minimises the risk that the current just flows through the skin to the other electrode and not reaches the grey matter. As a consequence of the shoulder placement the actual current could stimulate a deeper and wider brain area and lateralises more to the contralateral DLPC. The objective of the present study was to compare the outcome of the placement of the cathode on the left DLPC with the placement on the shoulder.

### Methods

Patients considered for the trial were chronic non-pulsatile tinnitus patients with complaints longer than 6 months and a Tinnitus Functional Index (TFI) score that exceeded 25. Patients were randomised by minimisation in order to create two equal groups based on the parameters age, TFI score, aetiology, gender and degree of hearing loss. In the first group 'bifrontal' the electrodes were placed on the left and right DLPC, while in the second group 'shoulder' the cathode was placed on the shoulder. Each patient received 2 sessions tDCS every week and in total 8 sessions. Evaluations took place at the first visit on the ENT-consultation, at the start of therapy, after 8 sessions of tDCS and at last the follow-up visit took place after 84 days of the start of the therapy. Subjective outcome measurements such as TFI , Visual Analog Scales of loudness (VAS) and percentage of consciousness of tinnitus were taken with every patient. To reveal the preference of one placement, statistical analysis was performed on the data.

### Results

The results will be presented at the congress.

### Acknowledgements

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## OBJECTIVE MEASUREMENTS OF TINNITUS DISTRESS

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### Objectives

Tinnitus is intrinsic uncomfortable sound for patients with tinnitus, so it is distress for tinnitus patients. In the present study, we exposed subjects to uncomfortable sound and analyzed stress responses objectively and quantitatively.

### Methods

Subjects

The subjects were thirteen adults without tinnitus (healthy subjects) and six tinnitus patients.

Determination of the simulated tinnitus sound: To determine pitch and loudness of tinnitus of each patient, standard pitch- and loudness-match tests were conducted. We defined the same pitch and 10 dB SPL louder sound as the simulated intrinsic uncomfortable sound (Tinnitus +10). In other words, it is the simulated tinnitus sound.

Sound exposure

Each tinnitus patient was exposed to the own simulated tinnitus sound and a band noise centered at 500 Hz with loudness of the uncomfortable level + 10 dB HL (500 Hz UCL +10). Healthy subjects were exposed to two kinds of band noises centered at 500 and 4 kHz with loudness of the uncomfortable level + 10 dB HL (500 Hz UCL+10, 4 kHz UCL+10), although they are extrinsic uncomfortable sound but not intrinsic sound. In addition to those uncomfortable sounds, tinnitus patients and healthy subjects were exposed to a band noise centered at 500 Hz with loudness of the comfortable level (500 Hz MCL). A subject lay down on a reclining bed for four minutes without any sound, were exposed to one of the sounds mentioned above for two minutes, and lay down for seven minutes. Therefore, it took thirteen minutes to analyze stress responses to one sound.

### Measurement parameters

The following five parameters were measured sequentially and simultaneously. 1. Hematoencepalography with near infrared, 2. Electroencephalography, 3. Heart rate variability, 4. Fingertip temperature, 5. Skin conductance.

### Results

The fingertip temperature significantly decreased when tinnitus patients were exposed to Tinnitus +10 but not to 500 Hz +10 and 500 Hz MCL. On the other hand, the temperature significantly decreased when healthy subjects were exposed to 500 Hz +10 but not to 4 kHz +10 and 500 Hz MCL. Other parameters did not show significant change.

### Conclusion

Tinnitus patients must have the specific stress response to their tinnitus sound, and we could detect the response objectively.

## DEEP BRAIN STIMULATION OF THE INFERIOR COLLICULUS FOR TREATING TINNITUS

Offutt, S.J.; Konop, A.R.; Lim, H.H.

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One possible tinnitus treatment option is to utilize deep brain stimulation on non-lemniscal or secondary auditory nuclei to directly modulate and create plastic changes in lemniscal auditory nuclei with aberrant neural activity related to tinnitus. A potential strategy is to stimulate the dorsal cortex of the inferior colliculus (ICD) to modulate neural activity in the central region (ICC), a nucleus in the auditory midbrain shown to have hyperactivity and increased neural synchrony in tinnitus patients and/or animals. ICD can also modulate other lemniscal regions involved with tinnitus through ascending and descending pathways. We have a unique opportunity to stimulate the ICD directly in tinnitus patients in an upcoming clinical trial with a new auditory midbrain implant (AMI). The AMI will be implanted in the inferior colliculus in patients for hearing restoration, but many of these patients also have tinnitus. Prior to this clinical trial, we sought to identify effective stimulation locations in ICD and a stimulation strategy that could alter ICC activity relevant for tinnitus suppression in an animal model.

Multi-site electrodes arrays were positioned across the ICC and ICD of ketamine-anesthetized guinea pigs. Spike activity in ICC was recorded in response to broadband noise stimulation before and after repeated electrical stimulation of the ICD to identify residual changes in neural activity. Electrical stimulation was paired with broadband noise stimulation at different inter-stimulus intervals and alone to compare residual effects. Histological steps were taken to produce 3-D reconstructions of the midbrain and to identify the location of electrode sites across the IC.

Our results reveal that every ICD stimulation location induces a complex pattern of modulation of neural activity in ICC, with significantly more inhibition than facilitation. Additionally, modulation is significantly dependent on the electrical stimulation paradigm used. Electrical stimulation paired with broadband noise with a long inter-stimulus delay (18 ms) resulted in more inhibition than either electrical stimulation paired with broadband noise with a short inter-stimulus delay (8 ms) or electrical stimulation alone.

Based on our findings, we can stimulate any ICD location to modulate ICC activity. The stronger

residual inhibition that occurs when pairing the electric and acoustic stimulation with a longer delay (i.e., 18 ms versus 8 ms) may be from weakened synaptic connections, perhaps due to spike timing dependent plasticity. With the correct timing, the paired stimulation could inhibit hyperactivity and disrupt neural synchrony with long-lasting effects, which may induce plasticity in the ICC that leads to suppression of the tinnitus percept. The results from this study are encouraging for deep brain stimulation as a treatment for tinnitus. Future studies will need to investigate how ICD stimulation alters activation patterns in other auditory nuclei linked to tinnitus, such as in the auditory cortex, and in tinnitus animal models. We will initially test ICD stimulation paired with ICC stimulation (since acoustic stimulation is not possible) in deaf patients with tinnitus who will be implanted with the AMI.

## Evaluation of a Self-administered Tinnitus Measurement System

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### Introduction

The basic step in most tinnitus management programs is to quantify the characteristics, including pitch and loudness, of the perceived tinnitus. The success of some contemporary tinnitus management approaches, such as tinnitus notched therapy, relies on the accuracy of the tinnitus pitch matched. Our research team developed a self-administered tinnitus measurement system which is capable to measure tinnitus frequency in one hertz resolution via a tablet.

### Aim

To investigate the application feasibility and accuracy of the self-administered tinnitus measurement system.

### Methods

Forty patients with subjective tinnitus were recruited in an audiology clinic in a hospital setting. The subjects completed the conventional procedures or the automated tinnitus measurement in a randomized order. Subjects were asked to rate on an 11-point visual analog scale on the similarity of the measured tinnitus and the one perceived. Tinnitus pitch and loudness obtained with both methods were compared. Test-retest reliability of the self-administered tinnitus measurement was investigated both within-session and between sessions which were one week apart.

### Results

There was significant difference in the tinnitus pitch and loudness matched with the two methods. Self-matched tinnitus pitch and loudness were reported to be more similar to the perceived one. Good test-retest reliability with the self-administered tinnitus measurement method was observed both within- and between-session. More variability was observed in between-session measures.

### Conclusion

It is feasible to perform tinnitus pitch and loudness measurement with the self-administered system.

## THE ROLE OF INDIVIDUAL PAIN TOLERANCE AND PAIN TRESHOLD IN BEARING TINNITUS

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Tinnitus is a chronic and disturbing symptom that affects millions of people worldwide.

In this study, the differences (and similarities) between short term and long term tinnitus and pain is evaluated. Pain threshold and pain tolerance of patients with tinnitus were measured three times and the average was recorded.

Forty-five patients attending the Audiology department of Hacettepe University (HU) Hospital were evaluated. Patients consisted of 19 female and 26 male, with an age range between 24 to 79 years, and duration of tinnitus of at least 3 months prior to testing. The results were compared to a control group of healthy (non- tinnitus sufferers) individuals, 20 females and 25 males, with an age range between 21 and 48 years.

Pain threshold and pain tolerance measurements of the patients and control group have been recorded in the Department of Physical Therapy and Rehabilitation of HU. These measurements were taken using electrical stimulation. For pain threshold and tolerance measurement Dimeq Med Module 5 (Bosch) instrument was used.

Measurements were made at room temperature of 22 degrees Celsius, in a sitting position, 90 degrees flexion of the elbow and forearm pronation and Supination, while recorded between the neutral positions. Measurements of the radial side of the forearm, proximal to the right passive electrode, the active electrode was placed at the distal end of the Radius. The patients were asked to respond when they feel pain sensation. Pain threshold and pain tolerance measurements were repeated for three times. The average of these three values obtained and recorded in milliamp's. The results from the patients group and the control group were statistically compared using the Mann-Whitney U test and Student's T-Test.

### Results

There was no statistically significant difference in pain threshold between the study and control groups, the same goes for the pain tolerance results.

### Conclusion

It was possible to endure short-term pain and tinnitus. However, it was not possible to endure the pain and tinnitus when the duration is increased.

Tolerance to tinnitus was associated with cortical familiarization (habituation) or brain plastisite and cortical printmaking (suppression). Research and studies in this direction are expected to give positive results.

Key words: Pain, Threshold, Tinnitus, Tinnitus Suferer

## MODERN THERAPEUTIC APPROACH TO THE DISEASE OF TINNITUS

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### Introduction

The hypothesis of the involvement of the limbic system and the autonomic nervous system in the pathology of tinnitus is due to PJ Jastreboff neurophysiological model that establishes the tinnitus and the subsequent therapeutic strategy: Tinnitus Retraining Therapy (TRT). The purpose of the following study was to evaluate the results of the TRT at a distance of about 5 years since its introduction as a treatment protocol of tinnitus in our clinic.

### Subjects and Methods

Intheperiodbetween1January2008andDecember31,2010wereprogressivelyrecruited53subjects, including 30malesand 23females, sufferingfromtinnitusand/orhyperacusis. The selected patients were monitored for a period of 18 months at monthly intervals for the first three months and thereafter at intervals of three months. All subjects underwent testing emory and audiological evaluation, including tonal and vocal audiometry and brainstem auditory evoked potentialsDizionario - Visualizza dizionario dettagliato. Patients further selected from this second level of assessment were sent to therapy (TRT) following the methods described by Jastreboff.

### Results

Therapeutic success was found after 18 months, the established duration of treatment in 38 patients (82.6%). In other cases, regarded as failure, there was persistence of symptoms in 5 (10.8%) and abandonment of treatment by 3 subjects (6.6%).Ascolta
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### Conclusions

The overall results of our experience shows a good efficacy of TRT in the study population (82.6%) in line with the literature (Sheldrake et al., 1999) that cannot be attributed to a placebo effect given the long duration of therapy.

## LONG-TERM EFFECTS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION TO THE AUDITORY CORTEX IN CHRONIC UNILATERAL TINNITUS: IPSILATERAL VS. CONTRALATERAL

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### Background

Repetitive transcranial magnetic stimulation (rTMS) applied over the temporoparietal cortex has been reported to be effective in the treatment of tinnitus. We investigated the long-term effects of 1-Hz rTMS delivered to the temporoparietal area and compared contralateral and ipsilateral application to the symptomatic ear in patients with unilateral tinnitus.

### Material and methods

A total of 61 patients with asymmetric hearing loss and non-pulsatile chronic tinnitus localized to the poorer ear who were refractory to medical treatment were enrolled in this study. Patients were randomly assigned to one of two treatment groups: 1-Hz stimulation applied to the temporoparietal junction either ipsilaterally (n = 30) or contralaterally (n = 31) to the symptomatic ear. The patients were given 600 pulses per session daily forfive days. Changes in the tinnitus handicap inventory (THI) scores and self-rating visual analog scores (VAS) for loudness, awareness, and annoyance were analyzed before and after treatment for 6 months. Improved patients were defined as those with decreases in their THI scores by more than 10 points and 20%.

### Results

There were no major complications or worsening of hearing threshold. When analyzing the THI scores and VAS pre-rTMS and 6 months after rTMS, significant decreases in THI scores and VAS were observed in patients overall ($p<0.001$). For the comparison of long-term outcomes between the ipsilateral and contralateral stimulation groups, there were no differences in the degree of decrease in THI scores or VAS between the two groups ($p>0.05$). In addition, there was no significant difference in the rate of patients who improved between the ipsilateral (14/30) and contralateral (16/31) stimulation groups ($p=0.800$). In terms of the speed of improvement, the ipsilateral group showed a more rapid improvement than the contralateral group.

### Conclusion

Daily application of 1-Hz rTMS to the auditory cortex is a safe treatment modality for tinnitus and has long-term beneficial effects. The laterality of stimulation is not the decisive factor in relieving symptoms.

## COMPARISON OF POSITIONING THE CATHODE IN TDCS

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### Objectives

In the case of tDCS, current is applied to the brain by means of 2 electrodes: the anode on the dysfunctional site and the cathode on a 'silent' part of the body. Nowadays, mostly bifrontal tDCS is applied in tinnitus patients: the anode and cathode placed on respectively the right and left dorsolateral prefrontal cortex (DLPC). Our hypothesis is that the placement of the cathode on the shoulder minimises the risk that the current just flows through the skin to the other electrode and not reaches the grey matter. As a consequence of the shoulder placement the actual current could stimulate a deeper and wider brain area and lateralises more to the contralateral DLPC. The objective of the present study was to compare the outcome of the placement of the cathode on the left DLPC with the placement on the shoulder.

### Methods

Patients considered for the trial were chronic non-pulsatile tinnitus patients with complaints longer than 6 months and a Tinnitus Functional Index (TFI) score that exceeded 25. Patients were randomised by minimisation in order to create two equal groups based on the parameters age, TFI score, aetiology, gender and degree of hearing loss. In the first group 'bifrontal' the electrodes were placed on the left and right DLPC, while in the second group 'shoulder' the cathode was placed on the shoulder. Each patient received 2 sessions tDCS every week and in total 8 sessions. Evaluations took place at the first visit on the ENT-consultation, at the start of therapy, after 8 sessions of tDCS and at last the follow-up visit took place after 84 days of the start of the therapy. Subjective outcome measurements such as TFI , Visual Analog Scales of loudness (VAS) and percentage of consciousness of tinnitus were taken with every patient. To reveal the preference of one placement, statistical analysis was performed on the data.

### Results

The results will be presented at the congress.

### Acknowledgements

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## ENDLYMPHATIC HYDROPS IN PATIENTS WITH TINNITUS AS MAJOR COMPLAIN

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### Objectives

Tinnitus is one of the symptoms of Meniere's disease. The relationship between a clinical presentation of subjective tinnitus or ear fullness and endolymphatic hydrops (EH) has not yet been explored.

### Methods

We studied 15 patients with symptoms of tinnitus as their major complaint, with or without hearing loss, who were evaluated using magnetic resonance imaging (MRI). The mean age of the subjects was 59 years (range 35–79 years). Nine were women and six were men. Patients were divided into two groups based on whether they had fluctuating or stable tinnitus. These groups were subdivided in the presence or absence of accompanying sensation of ear fullness. MRI was performed 4 h after intravenous gadolinium administration[1]. The grade of EH was diagnosed based on previous MRI studies which were obtained by same protocol. A radiologist who was blinded to the patients' clinical data evaluated the grade of EH. The data for age, sex, the degree of EH in the cochlea and the vestibule, subjective complaints and disease duration were encoded and analyzed using SPSS (SPSS ver. 19.0, SPSS, IBM, Armonk, New York, USA). The $\chi^2$ test and Mann–Whitney U test were used to analyze the data, and $P<0.05$ was considered significant.

### Results

Overall, 30 ears were evaluated. EH in the cochlea was present in 14 of 25 symptomatic ears (56 %) in patients with tinnitus as the major complaint. Significant hydrops was present in 7 of 14 ears and mild hydrops was present in the other ears. Of the five asymptomatic contralateral ears, one showed mild EH. There was a significant relationship between fluctuating tinnitus and the presence of EH in the cochlea of the affected inner ear ($p<0.01$; $\chi^2$ test). Patients with fluctuating tinnitus had EH more frequently than patients with stable tinnitus. Furthermore, the presence

of ear fullness also correlated with the presence of EH in the cochlea. However, there was no significant relationship between EH in the cochlea and age, sex, duration of tinnitus, hearing level or the configuration of the audiogram.

### Conclusion

Our study revealed that patients who had tinnitus as their major symptom often had EH. Using MRI to identify this covert early EH in patients who have tinnitus as their major symptom may broaden the treatment options for tinnitus.

1. *Tagaya, M., et al., 3 Tesla magnetic resonance imaging obtained 4 hours after intravenous gadolinium injection in patients with sudden deafness. Acta Otolaryngol, 2010. 130(6): p. 665-9.*

## CHANGE IN TINNITUS AFTER TREATMENT OF VESTIBULAR SCHWANNOMA: MICROSURGERY VS. GAMMA KNIFE RADIOSURGERY

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### Purpose

Tinnitus is a very common symptom of vestibular schwannoma, present in 45 to 80% of patients. We evaluated changes in tinnitus after translabyrinthine microsurgery(TLM) or gamma knife radiosurgery(GKS).

### Materials and Methods

Among 78 patients with vestibular schwannoma who underwent TLM or GKS at Severance Hospital from 2009-2012, 46 patients with pre- or postoperative tinnitus who agreed to participate were enrolled. Pure tone audiometry, tinnitus handicap inventory, visual analogue scale scores for loudness, awareness, and annoyance were measured before and after treatment. Changes of tinnitus handicap inventory and visual analogue scale scores were analysed and compared according to treatment modality, tumour volume, and preoperative residual hearing.

### Results

In the TLM group (n=27), vestibulocochlear nerves were definitely cut. There was a higher rate of tinnitus improvement in TLM group(52%) than GKS group(16%, p=0.016). The GKS group had a significantly higher rate of tinnitus worsening(74%) than TLM group(11%, p<0.001). Mean scores of tinnitus handicap inventory(THI) and visual analogue scale(VAS) scores significantly decreased in the TLM group in contrast to significant increases in the GKS group. Tumor volume and preoperative hearing did not affect the changes in tinnitus handicap inventory or visual analogue scales.

### Conclusion

Gamma knife radiosurgery can save vestibulocochlear nerve continuity but may damage the cochlea, cochlear nerve and can cause worsening tinnitus. In cases where hearing preservation is not intended, microsurgery with vestibulocochlear neurectomy during tumor removal can sometimes relieve or prevent tinnitus.

## OSTEOPOROSIS AND TINNITUS

**Kahveci, O.K.; Demirdal S.U**.

Osteoporosis is a painless weakening of the bones that constitutes an enormous socioeconomic crisis, with a harmful impact on morbidity and mortality. Metabolic changes and possible degeneration of cochlear capsule may cause hearing loss and otolaryngological symptoms such as tinnitus in osteoporotic patients. The aim of this study was to evaluate the possible link between tinnitus and osteoporosis. One hundred osteoporosis patients, 50 osteopenic patients and 25 healthy controls were evaluated prospectively. Bone mineral density (BMD) of patients was measured by dual-energy x-ray absorptiometry (DEXA). Otorhinolaryngologic examinations were performed in all patients together with an otologic symptoms survey, pure tone audiometry, speech discrimination test, and distortion product otoacoustic emission (DPOE). Forty-two patients in osteoporosis group, 9 patients in osteopenic group and 3 healthy controls had the complaint of tinnitus. Statistically, the incidence of tinnitus was found remarkably higher in osteoporosis patients than other groups ($p<0.01$). Mean pure tone audiometry findings of the patients and controls were significantly different in all frequencies ($p<0.01$). DPOE results of osteoporotic patients in 1kHz and 6kHz were significantly lower than controls and osteopenic patients ($p<0.05$). There was no difference in mean BMD scores of patients with tinnitus and without tinnitus. The data shows that osteoporosis may be associated with tinnitus. Cochlear degeneration and hearing loss may play role in this tinnitus complaint.

Keywords: Osteoporosis, tinnitus, hearing

## INTRATYMPANIC STEROID TREATMENT FOR TINNITUS PATIENTS WITH ACUTE LOW FREQUENCY SENSORINEURAL HEARING LOSS WITHOUT VERTIGO: PROSPECTIVE CONTROLLED STUDY

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### Objective

To compare the effectiveness of treatment for acute low frequency sensorineural hearing loss (LFHL) with tinnitus and without vertigo between intratympanic dexamethasone injections (ITDI) and oral diuretics

### Methods

A total 35 tinnitus patients with LFHL that had developed within previous 2 weeks were enrolled and then were randomly assigned into two groups: 1) treated with ITDI four times on each of 4 consecutive days (19 patients) and 2) treated with diuretics orally for 2 weeks (16 patients). The group assignments and the process of treatments were performed double-blindly. After 8 weeks, we analyzed treatment outcomes of LFHL using subjective symptom score and audiometric change.

### Results

The cure rate of ITDI group (42.1%) was significantly higher than that of diuretics group (25.0%). For subjective symptom score, there were no statistically significant differences of improvement rate in both groups (ITDI 63.2%, diuretics 56.3%). In pure tone audiometry, the improvement rate of ITDI group (73.7%) was significantly higher than that of diuretics group (62.5%). There was a significant correlation between the cure rate and duration of symptoms.

### Conclusion

ITDI is more effective treatment modality than oral diuretics for LFHL within 2 weeks of development. Duration of symptom affects the cure rate of acute LFHL with tinnitus and without vertigo.

## PRESCRIPTION AND NON-PRESCRIPTION DRUG USE AMONGST TINNITUS SUFFERERS

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### Aims and objectives

The aim of this study was to identify the frequency and nature of substance use amongst tinnitus patients in New Zealand, and to identify any substances which may have a direct effect on tinnitus loudness and merit further research.

### Methods

An anonymous questionnaire-based survey to evaluate the use of pharmaceutical medicines, complementary medicines and other drugs (including alcohol) amongst tinnitus sufferers was mailed to participants. A scoping review looking at the current information regarding substances for the treatment of tinnitus was also performed.

### Results

The study had a response rate of 36.5%, 119 participants reported treating their tinnitus with substances: 66 participants reported using complementary medicines for tinnitus, followed by 47 who used other drugs and 21 who used pharmaceuticals. The main reported benefit was improved sleep, followed by improved relaxation. Alcohol was the most commonly used drug, while vitamins/minerals and herbal remedies were the most commonly used complementary medicines. The main classes of pharmaceuticals identified as being beneficial by participants were SSRIs, anxiolytics, other hypnotics and TCAs. The anti-platelet drug clopdirogrel was identified by 2 patients has having a direct, negative effect on tinnitus loudness.

### Conclusion

This study has provided an insight into the nature of substance use amongst tinnitus patients. It has also allowed some substances to be identified which may merit further research (eg tinnitus onset with clopidogrel) and will hopefully provide more information into possible treatment strategies for the management of tinnitus.

## PRISM (PICTORIAL REPRESENTATION OF ILLNESS AND SELF MEASURE) AS A NEW ASSESSMENT TOOL FOR SUFFERING IN TINNITUS PATIENTS

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### Objectives

Chronic subjective tinnitus is a frequent condition that affects the quality of life of millions of sufferers worldwide. The lack of objective measures of tinnitus necessitates the use of self-report questionnaires for evaluating tinnitus severity and annoyance. The analyses of these questionnaires allow medical staff to select adequate treatment modalities and monitor treatment effects. However, the wide range of different questionnaires hampers an international and comparable standard in tinnitus assessment. Furthermore, most of these questionnaires have shortcomings in terms of responsiveness to treatment related changes, insufficient translation and validation in different languages and time-consuming aspects. PRISM (Pictorial Representation of Illness and Self Measure) is a method to assess suffering and quality of life. So far, PRISM was validated as a marker of burden in different psychological and physical conditions like PTSD, rheumatoid arthritis, chronic urticaria and orofacial pain. The aim of this study is to validate PRISM as a marker of impairment in tinnitus patients in a prospective observational study. The results of PRISM assessment were compared to different standard questionnaires used in tinnitus evaluation.

### Methods

Participating subjects were asked to fulfill an online-base survey including the following questionnaires: THI (Tinnitus Handicap Inventory), TQ (Tinnitus Questionnaire) TBF-12 (German short version of THI), WHOQOL-BREF (WHO Quality of Life-Questionnaire), BDI (Beck Depression Inventory). At the time of consultation in the clinic the subjects were asked to perform an audio-visual task on PRISM using an IPad. Patients were shown a white panel on the whole display (14.7x19.6cm) of the Ipad (representing their life) with a yellow circle (diameter 4.9cm) at the bottom right-hand corner representing his or her "self" at this time. Afterwards they were asked to move another smaller red circle (3.5cm) representing their tinnitus in relation to their self at this moment. The answers on the two dimensional PRISM were divided into 4 groups. Comparisons to the questionnaire scores were correlated using t-test or ANOVA (SPSS).

## Results

A total of 130 subjects were included in the analysis (48 women, 82 men) since 2012. The answers on the two dimensional PRISM were divided into 4 groups reflecting different grades of tinnitus severity : In group 1 the red tinnitus-circle was completely placed in the yellow self-circle (most severe); in group 2 the red tinnitus-circle was overlapping the yellow self-circle and was not part of group 1; in group 3 the red tinnitus-circle was placed under a virtual diagonal line from the left bottom to the right upper corner and was not part of group 1 or 2; in group 4 the red tinnitus-circle was placed in the triangle above the virtual diagonal line from the left bottom to the right upper corner (least severe). The different PRISM groups demonstrated a statistically significant correlation with the corresponding grading in the traditional tinnitus questionnaires (e.g. THI, TQ).

## Conclusion

PRISM is a new visual method to assess suffering in patients with tinnitus in a short time. We could show a significant correlation between the traditionally used tinnitus-questionnaires and PRISM.

## IMPACT OF SPECTRAL NOTCH WIDTH ON THE CLINICAL EFFECTIVENESS OF THE TAILOR-MADE NOTCHED MUSIC TRAINING

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Tinnitus, the ringing in the ears that is unrelated to any external source, causes a significant loss in quality of life, involving sleep disturbance and depression for 1 to 3 % of the general population. In the first place tinnitus may be triggered by damage to the inner ear cells, but the neural generators of noise-induced tinnitus are located in central regions of the brain. A loss of lateral inhibition, tonotopical reorganization and a gain-increase in response to the sensory deprivation result in hypersensitivity and hyperactivity in the auditory cortex. Negative emotional appraisal and attention might support the development of a tinnitus network. Within the training with tailor-made notched music (TMNMT) patients listen to music from which the frequency spectrum of the tinnitus has been removed. This evokes strong lateral inhibition of the neurons involved in the tinnitus percept from neurons tuned to other frequencies. A reduction of tinnitus loudness was achieved with TMNMT is previous studies. The effect of lateral inhibition can be enhanced with a smaller bandwidth of the notch. We assume that the training will be more effective with a notch width of a ½ octave or even a ¼ octave compared to one whole octave. Participants can choose their favorite music for the training that includes three month of two hours daily listening. Our outcome variables were standardized tinnitus questionnaires, visual analog scales and Magnetoencephalography (MEG). We found a reduction of tinnitus distress in all groups. Participants in the ½ octave group show the strongest improvement. We also found a positive correlation of tinnitus loudness reduction and reduction of the evoked auditory response in the MEG.

## PROPORTION AND DIVERSIFICATION OF UNDERLYING CAUSES OF 242 UNILATERAL VENOUS PULSATILE TINNITUS CASES IN DUAL-PHASE CONTRAST-ENHANCED CT

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### Objectives

To evaluate the proportion and diversification of underlying venous PT causes.

### Materials and Methods

The dual-phase contrast-enhanced CT (DP-CECT) images of 242 patients with unilateral venous PT were retrospectively reviewed. The underlying causes of venous PT reported in previous literatures were evaluated. Furthermore, the number of underlying causes of venous PT in each patient was counted.

### Results

(1) Of all patients, only 58 patients (24.0%) were diagnosed with only one underlying cause, while 170 patients (70.2%) were with more than one cause. (2)The most common underlying cause of venous PT was dehiscent sigmoid plate (86.4%), followed by lateral sinus stenosis (55.8%), high jugular bulb (47.1%), sigmoid sinus diverticulum (34.3%), jugular bulb diverticulum (13.6%), dehiscent jugular bulb (13.6%), large emissary vein (4.1%), sinus thrombosis (1.2%), petrosquamosal sinus (0.8%).

### Conclusion

Dehiscent sigmoid plate is common in venous PT. The causes of venous PT could be diversified in most PT patients.

Keywords: Pulsatile tinnitus, computed tomography

## THE DURAL SINUS WALL DEHISCENCE PRESENTING WITH PULSATILE TINNITUS: EVALUATION WITH CT VENOGRAPHY

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### Objectives

To assess the detailed CT findings about dura sinus wall dehiscence in patients presenting with pulsatile tinnitus (PT) on CT venography (CTV)

### Methods

Following approval of the institutional review board, 131 hospitalized patients with PT from 2008 to 2013, who underwent thorough clinical and laboratory tests including CT arteriography and venography and digital subtraction angiography, were retrospectively evaluated. Finally, 30 patients were included. All these patiens were found with dural sinus wall dehiscence on the symptomatic side and their noise was totally eliminated after covering the dehiscence with tempralis facia. The signs were invesgated as follows: the location,extent and amount of the dehiscence, the presence of one or more arachnoid granulations beneath the transverse sinus, the presence of transverse sinus stenosis, the presence of high jugular bulb and the presence of venous outflow dominance.

### Results

Forty two dehiscence were detected in these 30 patients, with the area range from 2*2 to 5*8 mm(average 3*5 mm). The single dehiscence was found in 24 of 30 patients (80%). The bony wall above the common crus was involved in 29 of 42 dehiscence (69%). The anterolateral wall was involved in 35 of 42 patients (83%). For other imaging findings, the large arachnoid granulation beneath the transverse sinus was demonstrated in 25 patients (83%) on the symptomatic side while in 26 (87%) on the contralateral side; the ipsilateral high jugular bulb was revealed in 28 patients (93%); the symptomatic side was consistent with the dominant side in 23 of 25 patients (92%) with unilateral dominant venous system. The transverse sinus stenosis was found in 25 (83%) patient on the symptomatic side while 28 (93%) on the contralateral side.

## Conclusion

The dural sinus dehiscence presenting with PT, which seems to be a direct cause of PT, mostly manifests as single bony defect with the lateral wall of dural sinus at a relatively high level involved. The hemodynamic abnormalities caused by diversified factors, including bilateral transverse sinus stenosis, ipsilateral high jugular bulb, ipsilateral outflow dominance bilateral arachnoid granulation(s) beneath the transverse sinus, may be the root cause of dural sinus wall dehiscence presenting with PT.

I am in reading MD of Radiology in Beijing Tongren hospital which was the No 1 at the diagnosis and treatment of otolaryngology in China. My main direction is about pulsatile tinnitus. In last four years, I have made diagnosis for more than one thousand patients with pulsatile tinnitus with various causes. Besides, I have submitted five papers in Chinese until now and I have written three papers in English, one of which has been accepted by Acta Radiologica.

## SUSTAINED BENEFIT OF MINDFULNESS BASED TINNITUS STRESS REDUCTION (MBTSR) IN ADULTS WITH CHRONIC TINNITUS

**Gans, J.J.**; Cole, M.A.

This 12-month follow-up aims to evaluate the long-term effects of an 8-week Mindfulness Based Tinnitus Stress Reduction (MBTSR) course on tinnitus handicap in adults with chronic tinnitus. Seven individuals with chronic tinnitus who had participated in an 8-week Mindfulness Based Tinnitus Stress Reduction (MBTSR) pilot study were assessed in a subsequent 12-month follow-up. After 12 months, continued reduction in tinnitus handicap was observed across all subjects. Mean THI scores immediately at post MBTSR intervention were 41.7. Mean THI scores at 12-months post MBTSR intervention were 22.8. Effect sizes are clinically significant and demonstrate a substantial decrease for items measuring perceived tinnitus handicap (d=1.25) at 12-months post-intervention. In adults with chronic tinnitus, benefits in perceived tinnitus handicap from the mindfulness skills taught in an 8-week MBTSR program can be sustained showing continued improvement for 12-months.

## CONSENSUS ON HEARING-AID CANDIDATURE AND FITTING FOR MILD HEARING LOSS, WITH AND WITHOUT TINNITUS: DELPHI REVIEW

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### Objectives

Hearing aids are often a first-line of audiological intervention for many people with tinnitus. Nevertheless there is a lack of high quality evidence to support their benefit for tinnitus and wide variability in clinical practice1. The aim of this study was to identify clinical consensus on the criteria for hearing aid candidature and clinical practice in fitting devices for mild hearing loss with and without tinnitus in the UK.

### Methods

We chose to use the Delphi technique, a systematic methodology that seeks consensus amongst experts through consultation using a series of iterative questionnaires2. A three-round Delphi survey explored this clinical consensus among a panel of experts comprising 29 UK hearing health professionals. We measured panel agreement on 115 statements covering: (i) General factors affecting decision to fit hearing aids, (ii) Protocol driven factors affecting decision to fit hearing aids, (iii) General practice, and (iv) Clinical observations. Consensus was defined as ≥70% agreement.

### Results

Consensus was reached for 58 out of 115 statements. The main areas of consensus were: factors important to consider when fitting hearing aids; device technology/features offered and routine; and important clinical assessment to verify hearing aid fit. For patients with mild hearing loss, greatest importance was given by clinicians to patient-centred criteria for fitting hearing aids: hearing difficulties; motivation to wear hearing aids, and impact of hearing loss on quality of life. More objective measures had a lower priority for fitting decisions: degree of hearing loss; shape of the audiogram. The main areas where consensus was not reached were: the use of questionnaires to predict and verify benefit for both hearing and tinnitus; audiometric criteria for fitting hearing aids; and the safety of using loud sounds when verifying hearing aid fitting for patients with tinnitus.

## Conclusions

The study identified areas of consensus and lack of consensus in the clinical practice of fitting hearing aids and differences in practice between patients with and without tinnitus. Statements for which consensus was reached in this review should be considered as inclusion/exclusion criteria in clinical trials evaluating the benefits of hearing aids for tinnitus. Statements for which consensus was not reached should guide selection of baseline and outcome measurements so that some of the individual variability in hearing aid outcomes might be better explained.


## Acknowledgements

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## FREQUENCIES CHARACTERESTICS OF TINNITUS AND ITS IMPACT ON DIFFERENT SOUND-RELATED TREATMENT METHODS

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### Objectives

To observe the frequencies characterestics of tinnitus and different impact on different treatments which use certain sound by analysis information from clinical patients suffered from tinnitus.

Methods: The 337 tinnitus patients in average age 41.15+14.33 with 368 ears were examined by audiometric threshold test, tinnitus matching test, residual inhibition(RI) test, and then divided into different groups according to characteristic frequencies(CF), hearing loss frequencies region ,shape of audiogram.All of the 209 ears with hearing loss are all sensorineural hearing loss and the pathogeny about patients with middle-ear inflammation history and metabolism syndrome were analysis either. Then 121 patients accepted the detailed RI tests , which were operated by both pure-tone sound(PT) and narrow band noise(NBN),in 10dB louder, smaller and just at the mixmal-masking-level(MML) at 125Hz, 250Hz,500Hz ,1000Hz,2000 Hz,3000Hz,4000 Hz,6000Hz,8000Hz pitches respectively. Besides,we give 161 patients who were not so good to the inhibition test a new method in the way of tinnitus relievator,which can give patients a narrow band or white noise sound ,or the hearing aid with a Zen sound (the sound aims to reduce emotion problems and give some kind of inhibition to tinnitus )for 85 patients who were hearing lost at high frequencies.Then we get some follow up data.

### Results

The patients with normal hearing threshold and light hearing loss get morepositive ratio(73.1% and 77.8%)than the severe hearing loss group(58.4%).The 10dB louder suppressive sound get better inhibition results: the positive ratio at low frequencies group is 54.2% while at MML 39.6% and 10dB lower 20.8%; at middle frequencies group is 62.5% while at MML 50.0% and 10dB lower 37.5%; at high frequencies group is 26.3% while at MML 26.3% and 10dB lower 11.3%.And for each CF group,the effect is better when the inhibition sound is at the same pitch,details in the article. The higher CF group gets better effect(2000Hz-81.5%,3000Hz 87.5%,4000Hz78.8%, 6000Hz 74.3%,and 8000Hz 80.5%) than the lower CF(125Hz 73.9%,250Hz61.1%,and500Hz76.0%). In the 14 middle ear disease history patients all of which the disease were cured and ear

membranes were contact,and only 2 of them CF are in low frequency region and others are in high.The 41 metabolism syndrome patients get the similar audiometric and inhibition pattern as the patients without the histories. And the discending audiometric curve and flat curve groups get better results at each CF groups.The tinnitus-relievator show positive effect in 73% of patients. The ZEN sound hearing aid give a better life quality in 81% patients.

**Conclusion**

The residual inhibition and sound therapy should choose the type-frequency, and the loudness according to different characteristic frequencies which is more individually effective. And different sound and method can be combounded for a better effect both in relieve tinnitus and level-up of life quality.

Key words: tinnitus,residual inhibition,frequency,history

## SPACE: THE 3RD DIMENSION OF TINNITUS

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### Aims and objectives

Tinnitus is usually characterised psychoacoustically by its loudness and intensity. An often overlooked or oversimplified aspect of tinnitus is its percieved location in space. We will present a review of work undertaken in the last 5 years to characterise and manage tinnitus using "3-Dimensional" sounds. The review has two primary aims, 1) to ascertain the ability to obtain, and the reliability of, a 3D location match in auditory space relative to perceived tinnitus location and 2) to compare the effectiveness of 3D maskers with bilateral maskers.

### Methods

The 3D tinnitus assessment and 3D masker used audio tracks manipulated by an average Head Related Transfer Function (HRTF). A spatial match was achieved by playing the individual their tinnitus pitch-matched tone at different horizontal and vertical positions rendered by the software, masking was achieved using the same technique but the tonal stimulus was replaced by broadband "rain" noise. Three separate studies will be presented: 1) A proof of concept study investigating tinnitus localisation and masking using sound played over headphones at the same perceived location (N=19). 2) An evaluation of test-retest reliability (1 week between tests) of the 3D assessment technique (N=50). 3) A cross-over trial of short-term tinnitus masking (using tracks stored on iPods played via Direct Audio Input to binaural ReSound Azure hearing aids (N=14)) at a perceived location at the centre of the head versus one overlapping with the tinnitus in space (3D). Each arm of the trial was 2 weeks in duration.

### Results – Study 1

The 3D location was reported as a good location match to tinnitus for the majority of participants. More participants preferred the 3D masker to conventional maskers (left, right, centre). Minimum Masking Levels (MML) were lower for the 3D masker in the majority of participants, but the MML was not statistically different between groups. Study 2. Tinnitus 3D measures were consistent with participants' global tinnitus localization (left, right, centre) but the tester enabled more accurate descriptions of localization (e.g. left front, above the eyes). Test-retest reliability (horizontal r=0.63, vertical r=0.48) was similar to tinnitus pitch (r=0.62) and loudness

(r=0.39) measures. Study 3. There was a strong preference for the 3D masking stimulus, with a significantly greater reduction in Tinnitus Handicap Inventory scores ($p < 0.01$) following 3D masking. The change in MML was greater (marginal difference, $p = 0.08$) after 2 weeks' use of the 3D masker than change with the conventional masker.

### Conclusions

This early evidence supports the use of a technique employing HRTF altered sounds in the assessment and management of tinnitus. Use of 3D sounds enabled an accurate assessment of the participants' perceived tinnitus location and appears to be a superior masking stimulus to conventional masking. The method has ramifications for studies attempting to replicate tinnitus psychoacoustic characteristics for EEG and MRI measures; and may prove to be an important consideration for future sound therapies.

## TOTAL OR SIGNIFICANT REMISSION OF TINNITUS – WHAT CAN WE LEARN FROM PATIENTS WHO HAVE REACHED THIS STAGE?

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### Introduction

In the past 20 years, the number of scientific papers published per year about tinnitus has changed from 150 references (Pubmed, 1994) to 641 (Pubmed, 2012), meaning an increase of more than 400%. This reflects a greater worldwide interest in understanding this phenomenon and reaching improvement and eventually the cure. However, the gold standard way of researching treatment attempts through clinical trials is expensive and time consuming.

### Objective

In order to accelerate the search for the cure, we aimed to interview patients who have already reached total/significant remission of tinnitus – such as an on/off mechanism - to verify a possible subgroup suitable to have better prognosis for treatment.

### Methods

This study was performed in two centers (São Paulo/Brazil and Milan/Italy). We included patients who have had tinnitus of any etiology for at least 1 month and reached one of two stages: 1. Total remission (TR,100%), defined as complete absence of tinnitus in 10 out of 10 regular days; 2. Significant partial remission (SPR, 80-90%): complete absence of tinnitus in 8 or 9 out of 10 regular days, associated to possible short recurrences (1-2 days) related to a well-known factor (stress, noise exposure, intake of food/drink/drug, infections etc). We excluded patients with pulsatile tinnitus and those who reached a comfortable level of habituation or masking, but still perceive it, somehow, very often. A specific protocol was created to interview the selected patients, considering the regional differences of attending patients.

### Results

In the first 6 months of research, 20 patients were selected (55% males; 45% females). Their mean age was 47.95 years (26 to 89y), and the mean time of existence of tinnitus was 7.6 months (1 to 18mo) in Brazil and 5.3 years (2 to 15y) in Italy. Before treatment, the mean handicap was 6.72 (through VAS in 11 cases) and 43.22 (through THI in 9 cases). Hearing thresholds were

symmetrically normal in 60% of cases (n=12). Considering that all patients have been minimally counseled, the main methods that allowed the stage of TR were medication and specific diets in Brazil, and manual therapy and hearing devices in Italy. The stage of SPR was reached by medication and sound stimulation. The mean time that patients reached the levels of TR or SPR was 7.18 years ago.

### Conclusions

Initial results show that total or significant partial remission of tinnitus (considering and on-off behavior) may be achievable for a stable period of time. The normal audiometry seemed to be a relevant factor for good prognosis in both centers, as well as the short time of tinnitus before treatment in Brazilian center. Further inclusion of patients from different places might help to accelerate the search for the cure.

## THE SHORT-TERM EFFECTS OF EXTENDED BANDWIDTH COMBINATION INSTRUMENTS ON TINNITUS PERCEPTION

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### Aims and objectives

A common treatment for tinnitus is the use of sound; sound therapy. Sound therapy is commonly undertaken using ear-level devices, which have an maximum high frequency limit of 6-8 kHz, which is often below tinnitus pitch. Although some researchers believe that the frequency of sound relative to tinnitus pitch is not important, others believe that the most effective therapeutic sound will incorporate the tinnitus pitch range. The devices used in this study (Austar Lenx 16 Receiver-In-The-Ear combination hearing devices) had a masking output up to 16 kHz. This study was undertaken to explore the effects on tinnitus perception (loudness and annoyance), noise perception and masking function of extended high frequency masking noise.

### Methods

Sixteen participants had psychoacoustic (e.g. audiometry, pitch, loudness) and psychometric (e.g. Tinnitus Functional Index) assessments. Masking functions were determined by first finding threshold and minimum masking level (MML) for 4 different bandwidths of bilateral therapeutic sound (broadband noise, high pass, low pass and filtered relative to hearing loss), and then having participants rate tinnitus loudness and annoyance, masking noise loudness and annoyance, and mixing point on 11-point rating scales as the level was increased from threshold to MML. Both the rating at MML and the slope (change in rating as a function of masking intensity) were calculated and analysed.

### Results

There was no significant difference between the noise loudness, noise annoyance or mixing point ratings for the bandwidths. However, there was a statistically significant difference for tinnitus annoyance: at MML, the broadband noise bandwidth resulted in significantly lower tinnitus annoyance than the high pass, low pass or filtered conditions. In addition, at MML the high pass and filter bandwidths yielded less tinnitus annoyance than the low pass condition.

### Conclusions

Results indicate a broader bandwidth yielded a greater effect of masking on tinnitus perception.

## AN ADAPTATION INDEX FOR INDIVIDUALISED SELECTION OF SOUND THERAPY LEVEL

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### Aim and objectives

The appropriate level for tinnitus sound therapy is a controversial topic; levels from near threshold to mixing to total masking are used clinically. There is a need for a better empirical understanding of how to select sound therapy for an individual. A model of tinnitus audibility based on Helson's Adaptation Level Theory (ALT) has been hypothesized (1) to explain the relationship between tinnitus audibility, personality, memory and attention. This theory attempts to describe how tinnitus audibility or might change with context. In this study we use ALT to model the sound level for sound therapy, and describe an optimum level the "Comfortable Point" (CP). This CP was designed by using assessments of tinnitus annoyance and noise annoyance to find an adaptation level in annoyance at which the patient can comfortably accommodate both the tinnitus and sound therapy.

### Method

This was a secondary analysis of data obtained by Warr (2). 27 participants with tinnitus of a constant and bothersome nature were recruited from our Hearing and Tinnitus Clinic. The sound level of broadband noise from an audiometer was increased in 2dB steps between hearing threshold and minimum masking level. At each step, tinnitus annoyance, noise annoyance and tinnitus + noise annoyance were rated on 11 or 21 point scales to create masking intensity functions. The point at which tinnitus and sound mixed (both audible but blending) was recording as the mixing point (MP). The ratings were then fitted to a linear regression to calculate the adaptation level to tinnitus annoyance. The CP was calculated:

$CP = (N5/T0p)1/q$

where N5 was sound level at medium noise annoyance, T0 was a converted sound level of tinnitus annoyance in silence, p and q were weighting factors representing the focus on stimulus (tinnitus) and background stimulus (therapeutic sound - broadband noise).

## Results

The CP was able to be accurately calculated for 16 of 27 participants. For 8 participants tinnitus annoyance increased with increase in sound level and 3 participants had atypical masking functions. Four of the successful participants showed that the CP was a close match to the MP. For 12 participants the CP was predicted to be lower than the MP, with less tinnitus and lower annoyance to the therapeutic sound.

## Conclusion

The CP is suggested as a new index of appropriate sound level for tinnitus therapy, and enables the empirical evaluation between tinnitus magnitude and background noise level. Although this first attempt to mathematically model sound therapy level could not accommodate all masking functions, it is an important step towards being able to identify a starting point for selection of sound therapy level based on individual psychoacoustic characteristics.


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## EFFECTIVE CLINIC PRACTICE AND STAGED MANAGEMENT OF THE TINNITUS: 14 YEARS OF THE UNIVERSITY OF AUCKLAND HEARING AND TINNITUS CLINIC

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### Aims and objectives

The University of Auckland Hearing and Tinnitus clinic was established in 2001 with a strong commitment to alleviating tinnitus and rapid translation of research into clinical practice. With an increase in awareness amongst the broader public and the professionals, the number of clients seeking help for the management of tinnitus has increased and new treatments have developed. Tinnitus perception can be a variable and an individual experience; our clients may be curious, bothered or distraught. To cater to the varying needs of the clients the clinic has developed a staged approach to cater for the individual needs of the tinnitus population.

### Methods

A review of the clinical protocols of the Hearing and Tinnitus Clinic is presented. More management clients are divided into three main categories i) hearing loss and tinnitus not bothersome ii) annoying tinnitus but coping alright and iii) tinnitus and unable to cope.

### Results

Clinical methods have been developed keeping in mind optimal use of resources, time constraints and tinnitus clinic effectiveness. Evidence based practice guidelines which involve a combination of counseling and sound therapy are being continually refined. Recently a new therapy structure "Tinnitus Adaptation Level Therapy" has been introduced which integrates computer based tinnitus assessment, a specific form of adaptation counseling (the AREA model) and sound therapy selection based on audiometric, psychometric and psychoacoustic tinnitus assessment.

### Conclusions

Constant research has shaped our guidelines resulting in both an effective and efficient tinnitus clinic.

## HEARING AIDS WITH FRACTAL TONE AND PORTABLE MUSIC PLAYER IN TINNITUS RETRAINING THERAPY

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### Method

Treatment outcomes of 51 tinnitus patients who visited the outpatient clinic for tinnitus at the Department of Otolaryngology – Head and Neck Surgery, Tohoku University Hospital since 2012 were reviewed retrospectively. After the initial assessment using THI and VAS at our facility, the therapeutic strategy was determined based on the THI score, hearing condition, and informed consent for the actual therapy. Of the 51 patients, 15 severe cases with hearing loss underwent TRT using a fractal tone with amplification. Also, TRT was conducted for 8 cases without remarkable hearing loss using white noise with a portable music player substituted for commercial SG. Another 28 cases were treated with educational counseling only (this group included mild cases with tinnitus and severe cases providing no agreement to TRT recommended by the doctor). This study compared the therapeutic effectiveness recorded for these three different treatment groups.

### Results

In a group using the HA with a fractal tone, 80% (12/15) of patients subjectively reported relief of tinnitus. In this group, the average THI score before the treatment was 66.1. However, that at three months after the treatment was improved significantly to 32.1 ($p<0.01$). Average VAS was improved significantly from 71.4 (before treatment) to 41.4 (3 months after treatment) ($p<0.01$). However, in a group using a portable music player, only 50.0% (4/8) of the patients subjectively reported relief of tinnitus. The average THI score improved only slightly, from 39.3 before treatment to 35.3 after treatment. In a group with educational counseling, only 32.1% (9/28) of patients improved subjectively. No significant difference was found between THI scores before treatment (48.3) and after treatment (38.9).

## Conclusion

Because THI scores before the treatment differed greatly among the three groups, these data are not necessarily comparable among groups. Nevertheless, the results suggest the effectiveness of the TRT with HA with a fractal tone.

Abbreviations: HA, Hearing aid; SG, Sound generators; TRT, Tinnitus retraining therapy; THI, Tinnutis handicap inventory; VAS, Visual analog scale

## THE EFFECTS OF INFORMATIONAL VERSUS ENERGETIC MASKING ON TINNITUS MINIMUM MASKING LEVELS

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### Aims

Recent tinnitus research suggests an important role for attention in tinnitus perception, particularly within the context of Auditory Scene Analysis and the relative salience of exogenous and endogenous auditory objects. Similar proposals have been made for mechanisms underlying informational masking, which appears to affect cognitive processing and the ability to focus attention selectively on target auditory streams. Based on these theories suggesting influence of attentional mechanisms on both tinnitus and informational masking, the primary aim of this study was to determine if informational masking would result in lower tinnitus minimum masking levels (MML) than energetic masking.

### Methods

Stimuli known to produce informational masking (one-, four- and seven-talker speech) and energetic masking (one-, four- and seven-talker reversed speech and speech-modulated noise, derived from and energetically equivalent to the one-, four- and seven-talker speech stimuli) were randomly presented to 22 participants with constant tinnitus. Tinnitus MMLs for each stimulus was measured and participants were asked to subjectively rate the stimulus.

### Results

A comparison between speech and reversed speech revealed no difference in tinnitus MMLs in a mild-to-moderate tinnitus severity group, but a lower tinnitus MML for the four-talker speech stimulus was found in a severe tinnitus group. A comparison of the speech and speech-modulated noise stimuli revealed lower tinnitus MMLs for speech in the severe tinnitus group and the opposite effect for the mild-to- moderate tinnitus group. No difference between the reversed-speech and speech-modulated- noise masking stimuli was observed for either tinnitus severity group. The one-talker masking stimuli across all three masking types resulted in higher tinnitus MMLs than the four- and seven-talker masking stimuli for both tinnitus severity groups. Stimuli preference ratings revealed that, on the whole, the most preferred stimuli resulted in the lowest tinnitus MMLs for the severe tinnitus group; however the results were less clear for the mild-to-moderate tinnitus group.

## Conclusion

Overall, the results suggested that informational masking resulted in lower tinnitus MMLs in individuals with severe tinnitus than the equivalent energetic masking stimuli. These results were interpreted as indicating that in cases of severe tinnitus perception informational masking disrupts the attentional or cognitive resources allocated to tinnitus, resulting in lower tinnitus MMLs. For the mild-to-moderate tinnitus group, the results suggested that acoustically similar, but subjectively different, masking stimuli affected tinnitus MMLs in different, as yet to be determined, ways. The study suggests that individuals experiencing severe tinnitus may constitute a special clinical sub-group. The primary finding of the study, that informational masking resulted in lower tinnitus MMLs in participants with severe tinnitus, could potentially provide insight into the underlying mechanisms of both tinnitus and informational masking.

## TINNITUS ADAPTATION LEVEL THERAPY AND THE AREA MODEL OF TINNITUS COUNSELLING

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### Aims and objectives

Tinnitus has been linked to auditory, neurological, cognitive, emotional and attentional processes; neurology, pharmacology, ophthalmology, psychology, otology and audiology fields have all sought treat tinnitus. Despite this the primary means of managing tinnitus is through counselling. However tinnitus clinicians are often insufficiently trained in psychotherapeutic approaches, or believe that tinnitus counselling is too time consuming and impractical to use in most clinical settings. There is a need to provide practical counselling tools which can be utilised within the clinical setting on their own or as an adjunct to other therapies (such as sound therapy). Our aim was to create a counselling tool, based on adaptation level theory and the AREA (Attend, React, Explain, Adapt) model of affective adaptation as proposed by Wilson et al. (1), whereby it is postulated that we adapt to events which we can understand.

### Methods

A counselling framework has been developed and tested in the clinic, this study is a presentation of the counselling concepts and preliminary results. The counselling material is picture-based and implemented as an easy to understand and patient friendly flip chart presentation.. The flip chart incorporates imagery which is both entertaining and informative. The method makes use of guided imagery and relaxation therapy, and patients are encouraged to identify their tinnitus with a neutral or safe object. They are then encouraged to place their tinnitus object in a peaceful environment. Practice is provided and an object is chosen in the session after which patients are provided with homework hand outs to continue this practice at home.

### Results

Preliminary results and observations have been very positive with patients indicating that they find this tool very useful. Tinnitus sufferers have particularly reported the benefit of this counselling method as it provides them with practical tools to assist with adapting to their tinnitus.

## Conclusions

There is a need for easily implemented tinnitus counselling tools. The AREA model appears to provide an effective framwork for tinnitus therapy.

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## INGENUITY OF TRT WITH NATURAL ENVIRONMENT SOUNDS, OPTICAL ILLUSIONS AND PARABLES

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In Tinnitus Retraining Therapy (TRT), we realized that we essentially hear with the brain, and that plasticity of brain causes enormously harmful influences of tinnitus pain due to vicious circle, while producing excellent abilities. At our hospital, patients are therefore treated under condition that plasticity of brain effectively exhibits the effects.

The followings are the ingenuity to enhance the effect of TRT.

**1. Sound Therapy**

Lower frequency in use of noise of Sound Generator (SG) could be seen than before, because the frequency of suggestion to patients for murmur of the river and sound of forest, which has similar frequency spectrum to a hearing aid and broadband noise, has increased. Sound volume of natural environment sounds is a partial cover as well as SG.

According to the data of previous investigations, it was shown that a sound of wave was not suitable for natural environment sounds, and that a sound of birds and insects had the tendency to encourage hyperacusis of patients with auditory disorder. And also, SG exhibited better portability than MP3 player.

It is thought that even with the sound therapy during daytime, brain plasticity does not have the proper efficacy for improving vicious circle of tinnitus, in case the patients feel tinnitus pain at the time of night awakening and their bedtime. Using natural environment sounds during nighttime is, therefore, considerably valuable including the relaxation effects.

And also, frequency of applying a hearing aid has increased for patients with auditory disorder regardless of the degrees even with slight disorder. Thus, more cases such as a hearing aid during daytime and BGM of natural environment sounds during nighttime should be suggested can be seen. However, commercially available CDs of natural environment sounds need to be selected, because some of them are unsuitable for sound therapy.

**2. Directive counseling**

As a first step, necessity to avoid nighttime tranquility and the importance of sleep should be explained and instructed to practice.

The second step begins with explanation of philosophy of TRT using slide presentation by clinical psychologists.

As the third step, mainly medical doctors and speech therapists conduct the additional explanation of the essence of tinnitus treatment. Regarding that the brain controls tinnitus intensity, it would promote better understandings of the patients by using the examples of optical illusion and parables. For example, we present an illusion produced by lateral inhibition of visual sense to patients instead of showing lateral inhibition of auditory systems, which is considered a trigger for increase of tinnitus intensity. And also, the patients can experience that the misleading intensity cannot be overcome even consciously due to an illusion of Edward H Adelson.

**3. Et Cetera**

Clinically, leading patients to have positive feeling about the treatment is also of great importance. Medical cooperation with the department of psychosomatic medicine and the department of psychiatry should be conducted according to the cases.

And also, a dose of strong tranquilizer needs to be considered depending on the cases, because it inhibits the plasticity of brain.

## EVALUATION OF TINNITUS USING HIGH FREQUENCY AUDIOMETRY, LOUDNESS -PITCH MATCH, TINNITUS HANDICAP INVENTORY AND IT'S SUPPRESSION USING HEARING AIDS

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Tinnitus is the perception of a sound by an individual without an external stimulus, often occurring in conjunction with hearing impairment. Individuals with complaint of tinnitus but with and without hearing difficulty, using high-frequency audiometry has a threshold difference in both groups at high frequencies. Greater tinnitus intensity, when loudness matching done, in hearing impaired group denoted a worse hearing [1]. The perceived pitch of tinnitus is very often associated with audiometric losses at the corresponding frequencies. The Tinnitus Handicap Inventory (THI) questionnaire may be used as a measure for quantifying the impact of tinnitus on daily living [2]. Use of a hearing aid for hearing-impaired people providing improved perception of external sounds, can be beneficial against tinnitus [1].

### Aim

To evaluate the tinnitus using high frequency audiometry thresholds, loudness- pitch match and effect on quality of life using tinnitus handicap inventory among both normal hearing and hearing impaired group with tinnitus and also to understand the use of hearing aids in suppression of tinnitus in individuals with hearing impairment.

### Methodology

The subjects participated in the age group of 45 and 65 years, all with complaint of bilateral tinnitus. The subjects were divided into two groups, one with Normal hearing with tinnitus and other group complaint of tinnitus but with moderate to severe sensory neural hearing loss

High-frequency audiometry done using circum-aural headphones. Subjective pitch matching and Subjective loudness matching was done using supra aural ear phones for frequency 250-8,000 Hz.. The subjects were asked to self-assess the effect of tinnitus on their quality of life by answering questionnaire in Tinnitus handicap inventory. Subjects with hearing impairment and tinnitus were given a week trial with suitable Hearing aid to see for any suppression in perception of tinnitus.

## Results

The hearing impaired group subjects exhibited higher hearing thresholds at all frequencies in High frequency Audiometry. Statistically significance difference was found at frequencies 10 kHz, 12 kHz, 14 kHz, 16 kHz between both normal and hearing impaired group. Statistically significance differences were found for loudness and pitch matching in both groups. The tinnitus handicap inventory results indicated mild handicap for normal hearing group and moderate handicap for hearing impaired group. With regard to hearing aid benefits, among those hearing impaired group , 35% reported tinnitus suppression with varying degrees. This result shows no noticeable suppression effect with use of hearing aid.

## Conclusion

Individuals with tinnitus and hearing impairment have higher high-frequency thresholds, with complete hearing loss at some frequencies, as compared to those without hearing loss. The pitch of the tinnitus is higher among individuals without hearing loss, whereas hearing impaired perceives loud tinnitus than normals with tinnitus. Individuals with hearing loss have a poorer quality of life than individuals without hearing loss. Hearing aid is not a treatment option of patients who suffering from tinnitus.

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## THE EFFECTIVENESS OF TURKISH STANDARDIZED VISUAL COUNSELING MATERIAL ABOUT TINNITUS

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### Objective

Tinnitus is defined as perception of sound in the absence of a corresponding external stimulus has lead to decrement in quality of life people who have tinnitus (PWT). Therefore, several treatments all of which have counseling step could be applied for this debilitating symptom. It is necessary to consult the PWT about all aspects of tinnitus in order to cope with it more effectively regardless of which kind of treatments applied. The counseling included both information and coping strategies related to tinnitus has to been provided by suitable, understandable and standardized materials. The aim of this study is to develop a Turkish standardized visual counseling material about tinnitus and to assess its effectives in terms of satisfaction of PWT.

### Methods

After given ethical permission, forty people diagnosed with subjective tinnitus included the study. All participants were conducted initial interview to evaluate their conditions (especially tinnitus severity with visual analog scale) before the counseling, audiological assessments (Audiological evaluation, DPOAE, ABR and tinnitus mapping) and completed the Tinnitus Handicap Inventory (THI) to determine tinnitus severity. Turkish standardized visual counseling material was developed according to basically neurophysiological model of tinnitus and information gained in the American Tinnitus Association websites. Its comprehensibleness and suitability were assessed with a pilot study which included an expert person and four PWT and then it was revised according to results of pilot study. The participants were dived and randomly assigned two groups; first one was given counseling with Turkish standardized visual counseling material and second was given counseling only verbally with same content. After counseling, the follow-up interview and THI were applied to evaluate their conditions and satisfaction levels.

### Results

The collected data will be in analysis phase. It will be expected that there will be differences between people given counseling with Turkish standardized visual counseling material and people given only verbally counseling in terms of the tinnitus severity and satisfaction level.

## Conclusion

The counseling step including information and coping strategies about tinnitus will be mandatory in the all treatments offered for tinnitus because it will provide high satisfaction level and increase positive thought related to handling to that problem. The usage of standardized visual material will facilitate to achieve these due to the fact that given the information by visual, standard and suitable way could improve the comprehensibleness of information.

## CLINICAL VALIDATION OF A NOVEL COMBINATION HEARING AID AND TINNITUS THERAPY DEVICE

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### Objective

Hearing aids are well known to ameliorate both hearing and tinnitus problems. Some hearing aids have built-in noise/sound generators that are intended to provide added benefit to patients with tinnitus. However, it has not been proven that "combination instruments" are more effective for tinnitus management than hearing aids alone. The purpose of this study was to acquire data addressing this question.

### Methods

Thirty individuals meeting study requirements (bothersome tinnitus, hearing aid candidate, no use of hearing aids for the previous 12 months) were enrolled. All participants completed the Tinnitus Functional Index (TFI) and were fitted with the combination instruments adjusted to optimize hearing ability. Participants were randomized to either the experimental group (N=15) which had the noise stimulus turned on and adjusted to achieve the greatest degree of relief from tinnitus, or the control group (N=15) which did not have the noise stimulus on. All participants returned 1-2 weeks after fitting to check the proper fitting and adjustment of the instruments, and to receive counseling based on Progressive Tinnitus Management. Three months after fitting, the participants returned and completed the TFI twice; once to indicate their responses with respect to when they were using hearing aids, and again when not using hearing aids.

### Results

Data were analyzed for the experimental and control groups separately. For each group, mean TFI scores were calculated for three conditions: baseline, 3-months with hearing aids, and 3-months without hearing aids. Repeated measures ANOVA was used to compare between groups between conditions. For the experimental group, the mean baseline TFI score was 56.1. At 3 months, the mean score was 16.8 (with hearing aids) and 45.3 (without hearing aids). The mean reductions of 41.5 points (with hearing aids) and 10.8 points (without hearing aids) were both significant ($p<.0001$ and $p=.034$, respectively). For the control group, the mean baseline TFI score was 60.5. At 3 months, the mean score was 27.6 (with hearing aids) and 44.3 (without hearing aids).

The mean reductions of 32.9 points (with hearing aids) and 16.2 points (without hearing aids) were both significant ($p<.0001$ and $p=.002$, respectively). Comparing groups, there were no significant differences in mean TFI scores between groups (all p's>.05) at baseline, 3 months with hearing aids, and 3 months without hearing aids.

### Conclusion

Both groups of subjects revealed significant improvement based on reductions in mean TFI scores, indicating that hearing aids alone or hearing aids plus sound generators both provided significant benefit for alleviating the effects of tinnitus. Differences between the two groups at 3 months were not statistically significant. However, it should be noted that the experimental group showed a mean reduction in the TFI that was 8.6 points greater than the control group. This difference approached significance ($p=.09$), suggesting that a larger group of subjects may have resulted in a significant difference between groups. It thus may be concluded that use of hearing aids plus a sound generator appears to provide greater benefit than hearing aids alone, although a larger study is needed to confirm this finding.

## COUNSELING FOR TINNITUS PATIENTS

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Patients with subjective tinnitus tend to think that tinnitus indicates that something is wrong. Counseling has been advocated as initial treatment for such patients.

### Objective

To illustrate key learning points from patients managed by tinnitus counseling.

### Methods

All patients who were counseled were referrals from ear, nose and throat specialists and all had the relevant hearing and other diagnostic tests performed. Four cases were selected from patients seen in the Tinnitus Counselling Clinic at Changi General Hospital in Singapore.

### Results

Case 1. A 75 year old female had bilateral moderately severe sensorineural hearing loss and unbearable bilateral roaring tinnitus. She appeared 'very deaf' and a hearing aid trial was conducted after brief counseling. The patient subsequently bought the hearing aid. After one month, she was very satisfied with her 'new-found' hearing and learnt to ignore her tinnitus.

Case 2. A 66 year old tinnitus-distressed male had normal hearing in both ears. After counseling, he gradually accepted his tinnitus as part of his life. A few months after the counseling, he complained of unilateral ear blockage and loud tinnitus. He was quickly scheduled for full audiological assessment. He was unaware he suffered a mild hearing loss in the discomfort ear and was treated with medications for sudden hearing loss.
After two weeks, he had no more ear discomfort and no audiological abnormality. He felt happy his tinnitus remains the same.

Case 3. A 37 year old male patient had sudden unilateral hearing loss and tinnitus. He is occasionally depressed but refused psychological referral and is not keen to use hearing aid. As such, constant encouragement and reinforcement on various self- help strategies were given whenever he requested help with his tinnitus.

Case 4. A 50 year old female tinnitus patient attended initial counseling. A year later, she returned feeling stressed. In her new quiet working environment, everyone spoke softly. Her tinnitus became louder and masked the speech sounds. There was no change in her audiogram which revealed a borderline 25 dB hearing level. A hearing aid with Zen program trial was conducted. The trial was very positive with one hearing aid. She is able to hear well. The Zen program provides her with soothing sounds to reduce her attention to the tinnitus whenever it is needed.

**Conclusion**

Managing tinnitus patients with counseling can be challenging. The above cases demonstrate the importance of the following:

1. Hearing aids can be useful in managing tinnitus when combined with counseling. Tinnitus patients with hearing loss may be unaware that tinnitus may not be the real issue.
2. Tinnitus may be a life-long condition. It is important for tinnitus patients to recognize other ear-related conditions and seek immediate help when sudden ear discomforts or any hearing loss occurs; even when tinnitus is not bothersome.
3. Patients need time to accept their tinnitus. Providing constant empathy, encouragement and support to patients is helpful.
4. Whenever tinnitus becomes bothersome, counseled patients should be taught alternative coping strategies to empower them to manage their condition effectively.

## TINNITUS THERAPY BASED ON THE TINNATURA MODEL

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### Aims / Objective

Tinnitus Retraining Therapy is still a young and developing procedure and regarding the literature, the information introduced about it up till now, is not sufficient to describe it thoroughly. The purpose of this study is to form an effective, short-term, specially customized for the individual and on-line controllable tinnitus therapy model for the therapy of Tinnitus using the TINNATURA model.

### Methods

After being granted necessary permissions from the ethical committee, a total number of twenty people diagnosed with subjective tinnitus, were included the study. After carrying out the complete audiological, immitansmetric and objective evaluations, the patients were asked to fill out the Tinnitus Handicap Inventory in order to assess the severity of the tinnitus. According to the results of the THI, only the patients assessed with grade 2 and over, were included to the study. The evaluations: Specific Tinnitus Measurements (Pitch, Loudness, Minimal Masking Level – MML and Residual Inhibition – RI) and Specific Sound Tolerance Measurements (Loudness Discomfort Level – LDL and Uncomfortable Loudness Level – UCL) were carried out respectively. For all the individuals taking part in the study, the "Tinnitus Initial Interview Forms" were filled and they were monitored using the Follow-Up Forms. In line with the results of the evaluations, a specially customized TINNATURA programme was prepared for each individual after informing her/him regarding the application. The monitoring process for all the individuals was planned to record the follow-ups on the 3rd – 4th weeks and 2nd, 3rd and 6th months. In addition, patients were requested to call should any questions or concerns arise.

### Results

With the use of the TINNATURA model, it is determined that within the 80 % of the patients, the severity of tinnitus drops significantly at the end of the first month and at the end of the third month, the effectiveness is observed to increase over 80 %. Consequently, a therapy programme that has no side effects, causes no harm to the individual, is driven to increase the life quality, decreases

the perception of tinnitus and overcomes the discomfort resulting from tinnitus, is successfully achieved. Even though some negative aspects of the Comprehensive Approach TINNATURA model had been observed during the first stages, together with the active participation and training of the individuals, positive results were obtained.

## Conclusion

Success rate of known Tinnitus Therapy techniques is rather high, however the time reserved for the individual patient is redundantly too much, and among the commercially available tinnitus sound generators in the market today, many of them need significant improvements. With the use of the new technique and supporting it with new generation sound generators and systems, the therapy is expected to be expanded to a wider audience. In this technique, the time reserved for the individual patient will decrease significantly and together with using today's communication technologies, the patients' behaviours and their daily improvements can be monitored almost simultaneously by online remote connection. This system and related new devices, will be available in the market starting from 4rd quarter of the year 2014.

## AMPLIFICATION WITH HEARING AIDS FOR PEOPLE WITH TINNITUS AND COEXISTING HEARING LOSS: COCHRANE REVIEW

**Hoare, D.**[1]; Edmondson-Jones, M.[1]; Sereda, M.[1]; Akeroyd, M.[2]; Hall, D.[1]

[1] *NIHR Nottingham Hearing Biomedical Research Unit, University of Nottingham, UK*

[2] *MRC Institute of Hearing Research, Glasgow, UK*

### Background

In the current absence of a cure for tinnitus, clinical management typically focuses on reducing the effects of co-morbid symptoms such as distress or hearing loss. Hearing loss is commonly co-morbid with tinnitus and so logic implies that amplification of external sounds by hearing aids will reduce perception of the tinnitus sound and the distress associated with it. The objective of the review was to assess the effects of hearing aids specifically in terms of tinnitus benefit, compared to other medical devices, other forms of standard or complimentary therapy or combinations of therapies, no intervention, or a placebo intervention.

### Methods

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. Randomised controlled trials and non-randomised controlled trials recruiting adults with subjective tinnitus were selected, where the intervention involves amplification with hearing aids and this is compared to interventions involving other medical devices, other forms of standard or complementary therapy or combinations of therapies, no intervention, or placebo interventions. Three authors independently screened all selected abstracts. Two authors independently extracted data and assessed those potentially suitable studies for risk of bias. For studies meeting the inclusion criteria, we used standardised mean differences (SMD) to compare effects.

### Results

One randomised controlled trial (91 participants) was included. The trial was judged to have low risk of bias for method of randomisation and outcome reporting, and an unclear risk of bias for other criteria. No non-randomised controlled trials meeting our criteria were identified. The included study measured change in tinnitus severity using a tinnitus questionnaire measure, and change in tinnitus loudness on a visual analogue scale. Other secondary measures of interest, namely change in psychoacoustic characteristics of tinnitus, change in self-reported anxiety,

depression, quality of life, and change in neurophysiological measures were not investigated in this study. The included study compared hearing aid use to sound generator use and found no significant difference in change of severity or loudness. No negative or adverse events were reported.

### Conclusions

The current evidence base for hearing aid prescription for tinnitus is of limited quality due to a lack of randomised and non-randomised controlled trials. To be useful, future studies of these designs will need to make adequate use of blinding and observe a level of consistency in their use of outcome measures. Whilst hearing aids are sometimes prescribed as part of tinnitus management, there is currently no evidence to support or refute their use as a more routine intervention for tinnitus, certainly in the absence of co-morbid hearing difficulties.

## SOUND THERAPY ON PATIENTS WITH TINNITUS ACCOMPANYING ONE-SIDED SENSORINEURAL HEARING LOSS – COMPARISON BETWEEN HEARING AIDS AND NOISE GENERATORS

Oishi, N.[1]; Shinden, S.[1, 2]; Inagaki, Y.[1]; Suzuki, D.[2]; Wakabayashi, S.[1]; Kanzaki, S.[1]; Watabe, T.[1]; Yamada, H.[1]; Kojima, T.[1]; Okazaki, H.[2]; Ogawa, K.[1]

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[2] *Department of Otolaryngology, Saiseikai Utsunomiya Hospital, Tochigi, Japan*

### Aims / Objectives

To compare the effects of sound therapy on patients with tinnitus accompanying one-sided sensorineural hearing loss between by hearing aids (HAs) and by noise generators (NGs)

### Methods

The subjects are patients with chronic tinnitus who have one-sided sensorineural hearing loss. The hearing levels are worse than 30 dBHL in average in an affected ear and better than 30 dBHL in average in an unaffected ear. Thirty-three patients were treated by NGs at Keio University Hospital from 2002 and 2008 (NG group), and 22 patients were treated by HAs at Saiseikai Utsunomiya Hospital or Keio University Hospital from 2007 and 2012 (HA group). All the patients had suffered from tinnitus for more than 3 months. Of the 33 patients in the NG group, the mean pure tone average was 57.0 dBHL in affected ears and 64 % of the patients were diagnosed with sudden sensorineural hearing loss. Of the 22 patients in the HA group, the mean pure tone average was 56.5 dBHL in affected ears and 64 % of the patients were diagnosed with sudden sensorineural hearing loss.

The effects of treatment were assessed with THI and VASs for tinnitus loudness and tinnitus annoyance at 6 months after the start of treatment.

### Results

In the NG group, the mean THI score significantly improved from 61.5 to 49.8, and the mean VAS for tinnitus annoyance significantly improved from 87.8 to 76.2, whereas the mean VAS for tinnitus did not change. On the other hand, in the HA group, the mean THI score improved from 56.6 to 19.0; the mean VAS for tinnitus loudness improved from 64.0 to 32.9; and the mean VAS for tinnitus annoyance improved from 67.8 to 27.6. These changes in the HA group were

all significant, and the improvement was much more obvious compared to the improvement in the NG group. Moreover, about 40 % of the patients in the HA group reported complete or nearly complete disappearance of tinnitus, whereas no patients in the NG group reported disappearance of tinnitus.

### Conclusion

The results of this study indicated that sound therapy by HAs can be a very effective method to treat tinnitus in patients with one-sided sensorineural hearing loss. As a TRT protocol by Jastreboff recommends, an active compensation for hearing impairment can be more effective in treating tinnitus than just enriching background sound in patients with hearing loss.

## DEVELOPMENT OF A PLACEBO CONTROL FOR ACOUSTIC COORDINATED RESET NEUROMODULATION

**Adamchic, I.**[1]; Toth, T.[1]; Hauptmann, C.[1]; Walger, M.[2]; Langguth, B.[3,4]; Klingmann, I.[5]; von Wedel, H.[2]; Tass, P.A.[1,7]

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### Background and aims

Acoustic coordinated reset (CR) neuromodulation is a novel, noninvasive tinnitus therapy1. To conduct high-quality randomized, placebo-controlled clinical studies using acoustic CR neuromodulation, it is necessary to have a convincing acoustic placebo treatment at hand. Acoustic CR neuromodulation consists of a randomized sequence of four phase resetting tones that cause a desynchronization of pathological rhythms (i.e., a decrease of the power in the certain frequency bands) and a reduction of tinnitus sensation. Accordingly, an optimal acoustic placebo stimulation is required to psychophysically mimic the acoustic sensation of CR neuromodulation without having a therapeutic effect on the tinnitus sensation and without inducing a desynchronization of cortical activity. The aim of this study was to test the hypothesis that our newly developed acoustic placebo stimulation: (i) causes no reduction of tinnitus sensation after switching the placebo stimulation off and (ii) causes no lasting modulation of cortical activity.

### Methods

The hypothesis was studied in a single-blind cross over design in 18 patients with chronic tonal tinnitus by administering three different stimulation protocols: acoustic CR neuromodulation, an noisy CR-like stimulation (noisy refers to the pseudorandom selection of the frequencies of the stimulation tones) and a low frequency range (LFR) stimulation. We measured visual analogue scale and spontaneous EEG activity before, during and after each type of stimulation.

## Results

The three stimulation techniques - acoustic CR neuromodulation, the noisy CR-like stimulation and the LFR stimulation - differed with respect to their effect on the tinnitus loudness, annoyance and the oscillatory brain activity. Furthermore, acoustic CR neuromodulation caused the longest significant reduction of delta and increase of alpha oscillatory activity. The noisy CR-like stimulation and the LFR stimulation showed changes in the oscillatory activity that differed both in strength and in time course from the changes caused by acoustic CR neuromodulation.

## Conclusions

These findings suggest that acoustic CR neuromodulation induces changes in tinnitus intensity and oscillatory brain activity that are distinct from those associated with the noisy CR-like stimulation and the LFR stimulation. We conclude that it is possible to create an acoustic placebo stimulation with the clinical and neurophysiological effects significantly different from acoustic CR neuromodulation.

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## CONSENSUS ON HEARING-AID CANDIDATURE AND FITTING FOR MILD HEARING LOSS, WITH AND WITHOUT TINNITUS: DELPHI REVIEW

Sereda, M.[1]; Hoare, D.J.[1]; **Nicholson, R.[2]**; Smith, S.[1]; **Hall, D.A.[1]**

*[1] NIHR Nottingham Hearing Biomedical Research Unit, Nottingham, UK*

*[2] Nottingham Audiology Services, Nottingham, UK*

### Objectives

Hearing aids are often a first-line of audiological intervention for many people with tinnitus. Nevertheless there is a lack of high quality evidence to support their benefit for tinnitus and wide variability in clinical practice1. The aim of this study was to identify clinical consensus on the criteria for hearing aid candidature and clinical practice in fitting devices for mild hearing loss with and without tinnitus in the UK.

### Methods

We chose to use the Delphi technique, a systematic methodology that seeks consensus amongst experts through consultation using a series of iterative questionnaires2. A three-round Delphi survey explored this clinical consensus among a panel of experts comprising 29 UK hearing health professionals. We measured panel agreement on 115 statements covering: (i) General factors affecting decision to fit hearing aids, (ii) Protocol driven factors affecting decision to fit hearing aids, (iii) General practice, and (iv) Clinical observations. Consensus was defined as ≥70% agreement.

### Results

Consensus was reached for 58 out of 115 statements. The main areas of consensus were: factors important to consider when fitting hearing aids; device technology/features offered and routine; and important clinical assessment to verify hearing aid fit. For patients with mild hearing loss, greatest importance was given by clinicians to patient-centred criteria for fitting hearing aids: hearing difficulties; motivation to wear hearing aids, and impact of hearing loss on quality of life. More objective measures had a lower priority for fitting decisions: degree of hearing loss; shape of the audiogram. The main areas where consensus was not reached were: the use of questionnaires to predict and verify benefit for both hearing and tinnitus; audiometric criteria for fitting hearing aids; and the safety of using loud sounds when verifying hearing aid fitting for patients with tinnitus.

## Conclusions

The study identified areas of consensus and lack of consensus in the clinical practice of fitting hearing aids and differences in practice between patients with and without tinnitus. Statements for which consensus was reached in this review should be considered as inclusion/exclusion criteria in clinical trials evaluating the benefits of hearing aids for tinnitus. Statements for which consensus was not reached should guide selection of baseline and outcome measurements so that some of the individual variability in hearing aid outcomes might be better explained.


## Acknowledgements

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.Part-funded by the British Society of Audiology Applied Research Grant.


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2. *Lindstone H.A. & Turoff M (eds.) The Delphi Method: Techniques and Applications. Reading, MA: 1975. Addison-Wesley Publishing Company.*

## FREQUENCIES CHARACTERESTICS OF TINNITUS AND ITS IMPACT ON DIFFERENT SOUND-RELATED TREATMENT METHODS

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[2] *Hearing and Deafness Center, the State University of New York at Buffalo*

### Objectives

To observe the frequencies characterestics of tinnitus and different impact on different treatments which use certain sound by analysis information from clinical patients suffered from tinnitus.

Methods: The 337 tinnitus patients in average age 41.15+14.33 with 368 ears were examined by audiometric threshold test, tinnitus matching test, residual inhibition(RI) test, and then divided into different groups according to characteristic frequencies(CF), hearing loss frequencies region ,shape of audiogram.All of the 209 ears with hearing loss are all sensorineural hearing loss and the pathogeny about patients with middle-ear inflammation history and metabolism syndrome were analysis either. Then 121 patients accepted the detailed RI tests , which were operated by both pure-tone sound(PT) and narrow band noise(NBN),in 10dB louder, smaller and just at the mixmal-masking-level(MML) at 125Hz, 250Hz,500Hz ,1000Hz,2000 Hz,3000Hz,4000 Hz,6000Hz,8000Hz pitches respectively. Besides,we give 161 patients who were not so good to the inhibition test a new method in the way of tinnitus relievator,which can give patients a narrow band or white noise sound ,or the hearing aid with a Zen sound (the sound aims to reduce emotion problems and give some kind of inhibition to tinnitus )for 85 patients who were hearing lost at high frequencies.Then we get some follow up data.

### Results

The patients with normal hearing threshold and light hearing loss get morepositive ratio(73.1% and 77.8%)than the severe hearing loss group(58.4%).The 10dB louder suppressive sound get better inhibition results: the positive ratio at low frequencies group is 54.2% while at MML 39.6% and 10dB lower 20.8%; at middle frequencies group is 62.5% while at MML 50.0% and 10dB lower 37.5%; at high frequencies group is 26.3% while at MML 26.3% and 10dB lower 11.3%.And for each CF group,the effect is better when the inhibition sound is at the same pitch,details in the article. The higher CF group gets better effect(2000Hz-81.5%,3000Hz 87.5%,4000Hz78.8%, 6000Hz 74.3%,and 8000Hz 80.5%) than the lower CF(125Hz 73.9%,250Hz61.1%,and500Hz76.0%).

In the 14 middle ear disease history patients all of which the disease were cured and ear membranes were contact,and only 2 of them CF are in low frequency region and others are in high.The 41 metabolism syndrome patients get the similar audiometric and inhibition pattern as the patients without the histories. And the discending audiometric curve and flat curve groups get better results at each CF groups.The tinnitus-relievator show positive effect in 73% of patients. The ZEN sound hearing aid give a better life quality in 81% patients.

**Conclusion**

The residual inhibition and sound therapy should choose the type-frequency, and the loudness according to different characteristic frequencies which is more individually effective. And different sound and method can be combounded for a better effect both in relieve tinnitus and level-up of life quality.

Key words: tinnitus,residual inhibition,frequency,history

## SPACE: THE 3RD DIMENSION OF TINNITUS

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*[2] Bionics Institute and University of Melbourne, Melbourne, Australia*

### Aims and objectives

Tinnitus is usually characterised psychoacoustically by its loudness and intensity. An often overlooked or oversimplified aspect of tinnitus is its percieved location in space. We will present a review of work undertaken in the last 5 years to characterise and manage tinnitus using "3-Dimensional" sounds. The review has two primary aims, 1) to ascertain the ability to obtain, and the reliability of, a 3D location match in auditory space relative to perceived tinnitus location and 2) to compare the effectiveness of 3D maskers with bilateral maskers.

### Methods

The 3D tinnitus assessment and 3D masker used audio tracks manipulated by an average Head Related Transfer Function (HRTF). A spatial match was achieved by playing the individual their tinnitus pitch-matched tone at different horizontal and vertical positions rendered by the software, masking was achieved using the same technique but the tonal stimulus was replaced by broadband "rain" noise. Three separate studies will be presented: 1) A proof of concept study investigating tinnitus localisation and masking using sound played over headphones at the same perceived location (N=19). 2) An evaluation of test-retest reliability (1 week between tests) of the 3D assessment technique (N=50). 3) A cross-over trial of short-term tinnitus masking (using tracks stored on iPods played via Direct Audio Input to binaural ReSound Azure hearing aids (N=14)) at a perceived location at the centre of the head versus one overlapping with the tinnitus in space (3D). Each arm of the trial was 2 weeks in duration.

### Results – Study 1

The 3D location was reported as a good location match to tinnitus for the majority of participants. More participants preferred the 3D masker to conventional maskers (left, right, centre). Minimum Masking Levels (MML) were lower for the 3D masker in the majority of participants, but the MML was not statistically different between groups. Study 2. Tinnitus 3D measures were consistent with participants' global tinnitus localization (left, right, centre) but the tester enabled more accurate descriptions of localization (e.g. left front, above the eyes). Test-retest

reliability (horizontal r=0.63, vertical r=0.48) was similar to tinnitus pitch (r=0.62) and loudness (r=0.39) measures. Study 3. There was a strong preference for the 3D masking stimulus, with a significantly greater reduction in Tinnitus Handicap Inventory scores ($p < 0.01$) following 3D masking. The change in MML was greater (marginal difference, $p = 0.08$) after 2 weeks' use of the 3D masker than change with the conventional masker.

### Conclusions

This early evidence supports the use of a technique employing HRTF altered sounds in the assessment and management of tinnitus. Use of 3D sounds enabled an accurate assessment of the participants' perceived tinnitus location and appears to be a superior masking stimulus to conventional masking. The method has ramifications for studies attempting to replicate tinnitus psychoacoustic characteristics for EEG and MRI measures; and may prove to be an important consideration for future sound therapies.

## TOTAL OR SIGNIFICANT REMISSION OF TINNITUS – WHAT CAN WE LEARN FROM PATIENTS WHO HAVE REACHED THIS STAGE?

Sanchez, T.G[1]; Del Bo, L.[2]

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[2] *Fondazione Ascolta e Vivi, Milan, Italy*

### Introduction

In the past 20 years, the number of scientific papers published per year about tinnitus has changed from 150 references (Pubmed, 1994) to 641 (Pubmed, 2012), meaning an increase of more than 400%. This reflects a greater worldwide interest in understanding this phenomenon and reaching improvement and eventually the cure. However, the gold standard way of researching treatment attempts through clinical trials is expensive and time consuming.

### Objective

In order to accelerate the search for the cure, we aimed to interview patients who have already reached total/significant remission of tinnitus – such as an on/off mechanism - to verify a possible subgroup suitable to have better prognosis for treatment.

### Methods

This study was performed in two centers (São Paulo/Brazil and Milan/Italy). We included patients who have had tinnitus of any etiology for at least 1 month and reached one of two stages: 1. Total remission (TR,100%), defined as complete absence of tinnitus in 10 out of 10 regular days; 2. Significant partial remission (SPR, 80-90%): complete absence of tinnitus in 8 or 9 out of 10 regular days, associated to possible short recurrences (1-2 days) related to a well-known factor (stress, noise exposure, intake of food/drink/drug, infections etc). We excluded patients with pulsatile tinnitus and those who reached a comfortable level of habituation or masking, but still perceive it, somehow, very often. A specific protocol was created to interview the selected patients, considering the regional differences of attending patients.

### Results

In the first 6 months of research, 20 patients were selected (55% males; 45% females). Their mean age was 47.95 years (26 to 89y), and the mean time of existence of tinnitus was 7.6 months (1 to 18mo) in Brazil and 5.3 years (2 to 15y) in Italy. Before treatment, the mean handicap was 6.72 (through VAS in 11 cases) and 43.22 (through THI in 9 cases). Hearing thresholds were

symmetrically normal in 60% of cases (n=12). Considering that all patients have been minimally counseled, the main methods that allowed the stage of TR were medication and specific diets in Brazil, and manual therapy and hearing devices in Italy. The stage of SPR was reached by medication and sound stimulation. The mean time that patients reached the levels of TR or SPR was 7.18 years ago.

### Conclusions

Initial results show that total or significant partial remission of tinnitus (considering and on-off behavior) may be achievable for a stable period of time. The normal audiometry seemed to be a relevant factor for good prognosis in both centers, as well as the short time of tinnitus before treatment in Brazilian center. Further inclusion of patients from different places might help to accelerate the search for the cure.

## TINNITUS: WHY NOT STOP IT BEFORE IT STARTS?

Martin, W.H.

What can we do until we find a cure? Tinnitus prevention

Tinnitus is a complex condition triggered by several factors the most common of which is exposure to loud sounds. Noise induced hearing loss and resulting tinnitus have been commonly associated and sound exposure is the most commonly reported factor related to the onset of tinnitus. The good news is that the vast majority of these cases can be prevented through simple strategies. Dangerous Decibels® is an evidence-based program with several interventions that have been demonstrated to change knowledge, attitudes and intended behaviors related to sound exposure and appropriate use of hearing protective strategies in elementary school student. The program has resources in use in all 50 U.S. States and 37 countries. A review of tinnitus reported in children and an overview of the Dangerous Decibels program will be presented.

## Poster Session 5 / Rima

*Numbers refer to poster board allocation*

OBJECTIVE MEASUREMENTS OF TINNITUS DISTRESS
Masuda, M.; Kohno, N.; Ogawa, K.
11

DEEP BRAIN STIMULATION OF THE INFERIOR COLLICULUS FOR TREATING TINNITUS
Offutt, S.J.; Konop, A.R.; Lim, H.H.
17

EVALUATION OF A SELF-ADMINISTERED TINNITUS MEASUREMENT SYSTEM
**Kam, A.C.S**.; Leung, E.K.S.; Sung, J.K.K.; Lee, T.; van Hasselt, C.A.
23

THE ROLE OF INDIVIDUAL PAIN TOLERANCE AND PAIN TRESHOLD IN BEARING TINNITUS
Aksoy, S. ;Yılmaz, T.; Keser, I.; Aslan, S.; Kırdı, N.
29

MODERN THERAPEUTIC APPROACH TO THE DISEASE OF TINNITUS
Calenti, C; Ciabattoni, A.
35

LONG-TERM EFFECTS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION TO THE AUDITORY CORTEX IN CHRONIC UNILATERAL TINNITUS: IPSILATERAL VS. CONTRALATERAL
**Moon, I.**; Kim, H.; Oh, H.; Sim, N.; Kim, D.
41

COMPARISON OF POSITIONING THE CATHODE IN TDCS
**Rabau, S**.; Mariën, P.; Van de Heyning, P.
47

ENDLYMPHATIC HYDROPS IN PATIENTS WITH TINNITUS AS MAJOR COMPLAIN
Yoshida, T.; Teranishi, M.; Kato, M.; Otake, H.; Kato, K.; Sone, M.; Naganawa, S.; Nakashima, T..
51

THE DURAL SINUS WALL DEHISCENCE PRESENTING WITH PULSATILE TINNITUS: EVALUATION WITH CT VENOGRAPHY

Zhao, P. Beijing China; Wang, Z.; Xian, J.; Yan, Y.; et al.

87

## Poster Session 6 / Ono

*Numbers refer to poster board allocation*

THE SHORT-TERM EFFECTS OF EXTENDED BANDWIDTH COMBINATION INSTRUMENTS ON TINNITUS PERCEPTION

Cummins, A.; Searchfield, G.D.

06

AN ADAPTATION INDEX FOR INDIVIDUALISED SELECTION OF SOUND THERAPY LEVEL

Kobayashi, K.; Searchfield, G.D.

12

EFFECTIVE CLINIC PRACTICE AND STAGED MANAGEMENT OF THE TINNITUS: 14 YEARS OF THE UNIVERSITY OF AUCKLAND HEARING AND TINNITUS CLINIC

**Kaur, M.; Hadfield, D.; Searchfield, G.D.**

18

HEARING AIDS WITH FRACTAL TONE AND PORTABLE MUSIC PLAYER IN TINNITUS RETRAINING THERAPY

Takanashi, Y.; Kawase, T.; Oda, K.; Miyazaki, H.; Yahata, I.; Katori, Y.

24

THE EFFECTS OF INFORMATIONAL VERSUS ENERGETIC MASKING ON TINNITUS MINIMUM MASKING LEVELS

Proudfoot, K.; Kobayashi, K.; Searchfield, G.

30

TINNITUS ADAPTATION LEVEL THERAPY AND THE AREA MODEL OF TINNITUS COUNSELLING

Hodgson, S.A.; Searchfield, G.D.

36

SOUND THERAPY ON PATIENTS WITH TINNITUS ACCOMPANYING ONE-SIDED SENSORINEURAL HEARING LOSS – COMPARISON BETWEEN HEARING AIDS AND NOISE GENERATORS

Oishi, N.; Shinden, S., Inagaki, Y.; Suzuki, D.; Wakabayashi, S.; Kanzaki, S.; Watabe, T.; Yamada, H.; Kojima, T.; Okazaki, H.; Ogawa, K.

79

DEVELOPMENT OF A PLACEBO CONTROL FOR ACOUSTIC COORDINATED RESET NEUROMODULATION

**Adamchic, I.**; Toth, T.; Hauptmann, C.; Walger, M.; Langguth, B.; Klingmann, I.; von Wedel, H.; Tass, P.A.

86

CONSENSUS ON HEARING-AID CANDIDATURE AND FITTING FOR MILD HEARING LOSS, WITH AND WITHOUT TINNITUS: DELPHI REVIEW

Sereda, M.; Hoare, D.J.; **Nicholson, R.**; Smith, S.; **Hall, D.A.**

91

FREQUENCIES CHARACTERESTICS OF TINNITUS AND ITS IMPACT ON DIFFERENT SOUND-RELATED TREATMENT METHODS

Kong, W.; Wang, Z. ; Xie, M.; Xie, W.; Cheng, H.; Salvi, R.J.

92

SPACE: THE 3RD DIMENSION OF TINNITUS

Searchfield, G.D.; Kobayashi, K., Irving, S.

93

TOTAL OR SIGNIFICANT REMISSION OF TINNITUS – WHAT CAN WE LEARN FROM PATIENTS WHO HAVE REACHED THIS STAGE?

Sanchez, T.G; Del Bo, L.

94

# Index of authors

over the horizon

# 8th International TRI Tinnitus Conference

10 - 13 March 2014
Auckland, New Zealand

## Pre Conference Workshop

# Programme

## Monday 10 March - Pre Conference Workshop

| | |
|---|---|
| 0830 – 0910 | Welcome & workshop objectives<br>Dr Grant Searchfield |
| 0910 – 0950 | Recent onset-tinnitus: The ENT perspective<br>Dr Alain Londero |
| 0950 – 1030 | Tinnitus: A warning symptom in non otological pathologies<br>Assoc Prof Amr El Refaie |
| 1030 – 1100 | Morning tea |
| 1100 – 1140 | Choosing patient pathways<br>Prof Dirk De Ridder |
| 1140 – 1220 | Mindfulness Based Tinnitus Stress Reduction (MBTSR) Workshop: Making mindfulness accessible to patients<br>Dr Jennifer Gans |
| 1220 – 1300 | How, when and what-ifs of transcranial direct current stimulation for tinnitus<br>Assoc Prof Cathy Stinear & Dr Giriraj Shekhawat |
| 1300 – 1400 | Lunch |
| 1400 – 1440 | Cognitive habituation tinnitus therapy<br>Dr Natan Bauman |
| 1440 – 1520 | Client centred sound therapy selection: Tinnitus assessment into practice<br>Dr Grant Searchfield |
| 1520 – 1550 | Afternoon tea |
| 1550 – 1630 | Assessment and management of acoustic shock / tonic tensor tympani syndrome (TTS) / hyperacusis<br>Myriam Westcott |
| 1630 – 1710 | Building a tinnitus practice from the ground up: How to bring tinnitus and sound tolerance care to places where it doesn't exist<br>Prof William Martin |
| 1710 – 1930 | Welcome Reception |

## RECENT ONSET-TINNITUS: THE ENT PERSPECTIVE

Londero, A.

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Chronic subjective tinnitus is a very common symptom affecting, with various degrees of intrusiveness, about 10% of the general population. Basic and clinical research efforts are, for the most part, actually aimed at treating chronic tinnitus patients. But, on another hand, it is a truism to state that, at an early stage of its evolution, every single chronic tinnitus has been an acute one. However, little is known on the grounds that explain why, in a minority of patients, appears a harmful evolution towards a chronic long-standing disabling tinnitus. Similarly, to-date, there is no consensus and no scientifically validated guidelines for the management of such a common clinical situation, especially in the ENT practice. Indeed, because subjective tinnitus is often perceived in one or both ears and because it is almost always associated with other cochleo-vestibular symptoms ENTs are most of the time the first health-care professionals to which the patients ask for assistance.

It has to be highlighted, here, that subjective tinnitus is not a diagnosis nor a disease, but rather a symptom of some other pathological condition. Then, according to a step-by-step procedure, the main goal of ENT management is to determine the aetiology and to provide a causally orientated treatment.

The first step is to make a differential diagnosis with less frequent conditions such as the perception of somato-sounds and auditory hallucinations which require specific management.
The second step is to determine the origin of subjective tinnitus. Even if there are numerous causes of tinnitus, in our experience this can almost always be done, or at least strongly suspected, by the simple means of a structured medical interview, a careful tympanic membrane evaluation, and a standard audiometry. Additional audiologic testing and radiologic imaging or other laboratory examinations are only aimed at proving or confirming clinical evidence.

That last step is to provide, if possible, a causally oriented treatment and to address specifically the tinnitus symptom itself, if necessary. Despite a weak evidence-based rationale, a wide variety of early-stage interventions can eventually be proposed including: drug therapies, intra-tympanic injections, hyperbaric oxygen therapy, sound therapies, psychological interventions, surgical procedures. Integrating these different therapeutic options into one single structured,

and patient-oriented, intervention program is the core of ENT expertise in initial subjective tinnitus management.

During the “How I do it” session of the TRI Meeting 2014, our purpose will be to highlight practical and archetypal cases of ENTs’ management for recent-onset subjective tinnitus.

Notes

## TINNITUS: A WARNING SYMPTOM IN NON-OTOLOGICAL PATHOLOGIES

El Refaie, A.

Tinnitus is a presenting symptom for a large array of otological and non-otological pathologies. Management of idiopathic tinnitus should not start before a full diagnostic evaluation of the patient to discover any treatable or sinister causes, which should be the first aim of management (though treating the causative pathology does not automatically lead to the disappearance of tinnitus) Audiologist is often the first clinician to encounter the tinnitus sufferer, and a good knowledge of the symptoms and signs of pathologies contributing to the sensation of tinnitus is essential for proper and timely referral to other medical specialists. This talk will concentrate on two of the non-otological pathologies that can present as tinnitus, namely Temporo-Mandibular Pain Dysfunction Syndrome and Multiple sclerosis (MS). The talk will include a brief discussion of the aetiologies, epidemiology and clinical presentations, as well as the onset and characteristics of tinnitus and other audio-vestibular symptoms in both conditions.

Notes

## CHOOSING PATIENT PATHWAYS

De Ridder, D.

Tinnitus is notoriously difficult to cure, even though many treatment options exist. From a clinical point of view a flowchart can be created to guide tinnitus treatment, based on a pathophysiological evidence based basis. This has been proposed by the TRI (http://www.tinnitusresearch.org/en/projects/flowchart).

But how to go about it practically, especially considering that there is not a lot of evidence available to guide tinnitus treatment ? As a health care provider one should always remember that the absence of proof is not proof of absence of treatment effect.

After asking some numeric rating scales for loudness and distress (0=not bothered at all, 10= suicidal) and what percentage of time the tinnitus is dominantly present, which gives an impression of the impact on daily living, an initial step is to get a history that can guide the therapy, aided by one or more questionnaires that evaluate the affective components of the tinnitus (distress, depression).

A first question is whether the tinnitus is pulsatile in nature or not, and if pulsatile whether it is heart beat synchronous or sounds more like hum which is respiratory synchronous. Is it uni-or bilateral, positional or can it be suppressed by pressing at specific points in the neck or head ? This suggests different possible causes, but most of the time imaging and audiometry will be required.

Also in non-pulsatile tinnitus associated symptoms can direct the health care provider to further targeted investigations: headaches, vertigo, hemifacial spasms, geniculate neuralgia, autophony, Tulio's phenomenon, masticatory pain, head and neck problems, sensory or motor changes in limbs or body, or tinnitus worsening on Valsalva manoeuvers are important symptoms suggesting specific treatable causes for tinnitus which can guide further investigations such as ABR, MRI, angiography etc.

However, most patients present without a treatable cause resulting in a more symptomatic approach. In general it is helpful to tell the patient that multiple treatment trials might be necessary and that each treatment only has 20 to 30% change of giving a clinically meaningful benefit, in

order to prevent desillusions with any form of treatment. Counseling with or without masking (TRT) can be helpful for some patients and can be combined with other treatment options.

If there is hearing loss it depends on the amount of hearing loss what can be offered. For example complete unilateral deafness in the tinnitus ear can be approached either by a trial with a BAHA or CI, whereas in hearing loss matching the tinnitus frequency hearing aids could be offered, with or without masking. If the tinnitus is not too loud, active audiological treatment can also be considered (neuromonics, coordinated reset etc).

If this is not beneficial, medication can be tried, but this only if the tinnitus is either very loud or perceived dominantly most of the day. A stepwise approach of 3 to 4 different drugs can be tried, all at low doses to prevent side effects that could potentially further worsen the patient's quality of life.
If neither audiological nor medication benefits the patient, neuromodulation is an option. This can consist of rTMS, tDCS, tACS, tRNS or neurofeedback. These techniques can either be used as a prognostic test for more invasive procedures or as a treatment attempt. They can be guided by functional imaging if nothing else works.

It should be kept in mind that how far one goes in offering treatment options depends on how much distress and how loud the tinnitus is perceived, and how much of the time the tinnitus is dominantly present. But all of this within a context of reasonable expectations of the patient, and accepting that some patient groups are more difficult to treat, such as musicians, people with OCD, people who are controle freaks, or people with suicidal tendencies, each for their own particular reasons.

The workshop will be practically oriented (how I do it?) and should demonstrate how a multidisciplinary approach can benefit both the patient and the health car provider.

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## MINDFULNESS BASED TINNITUS STRESS REDUCTION (MBTSR) WORKSHOP: MAKING MINDFULNESS ACCESSIBLE TO PATIENTS

Gans, J.

The Mindfulness Based Tinnitus Stress Reduction (MBTSR) Workshop will be part experiential and part instructional on implementation of a mindfulness program in a busy clinical practice. In order to understand and gain a sense of how practicing mindfulness in day-to-day life can affect one's relationship to a symptom such as tinnitus, it is important to experience mindfulness first hand. We will then explore brain science and what appears to be happening in the meditating brain and the overlap with what we believe is happening in the brain to generate the perception of the tinnitus signal. Making the MBTSR program accessible to patients will be explored through discussion and practice with the online course MindfulTinnitusRelief.com.

Notes

## HOW, WHEN AND WHAT IFS OF TRANSCRANIAL DIRECT CURRENT STIMULATION FOR TINNITUS

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Tinnitus is an auditory phantom sensation (ringing of the ears) experienced when no external sound is present 1. In the past decade attention has been drawn towards the use of non-invasive brain stimulation for tinnitus management. More recently, the effects of transcranial direct current stimulation (tDCS) have been explored in humans, in both healthy and neurological populations. Depending upon the polarity of the stimulation, tDCS can increase or decrease the excitability of the underlying cortex. Anodal stimulation increases excitability due to neuronal depolarisation and cathodal stimulation decreases excitability due to neuronal hyperpolarisation. It is postulated that the after-effects of tDCS could possibly be due to change in intracortical inhibition or facilitation which is controlled by synaptic activity 2. In this presentation we will be discussing the clinical factors associated with tDCS, its safety and application especially for people with tinnitus. Existing research will be critically discussed along with the possibilities of future research to understand and further develop this technique and its applicability for tinnitus.

*References*

1. *Eggermont JJ, Roberts LE. The neuroscience of tinnitus. Trends Neurosci. 2004;27:676-682.*
2. *Nitsche MA. Modulating parameters of excitability during and after transcranial direct current stimulation of the human motor cortex. J. Physiol. 2005;568:291-303.*

Notes

## COGNITIVE HABITUATION TINNITUS THERAPY

Bauman, N.

Cognitive Habituation Tinnitus Treatment, aka CHaTT, was developed by an audiologist, Dr. Natan Bauman. CHaTT is an outgrowth of working with hundreds of tinnitus and Sound Sensitivity Disorder patients, over ten years. It was officially introduced to the audiologists via seminars sponsored by the Tinnitus Practitioners Association (TPA) organization in 2009.

CHaTT is a treatment program which is based on the neurophysiological model described by Dr. Pawel Jastreboff. Which means its basic principle is habituation of the reaction. The difference is in its more comprehensive therapeutic approach which includes a heavy dose of CBT as part of counseling in addition to sound therapy.

CHaTT categorizes tinnitus patients into 6 categories based on their tinnitus reaction score. The categories are linked to the calculated reaction score and presence or absence of hearing loss. Additional 4 categories are for those who have SSD with tinnitus or without tinnitus and with or without hearing loss. Thus, all together, there are well defined 10 categories. Each category has its own step by step defined protocol which helps the clinician to engage patients in their treatment program. In addition, there are special protocols which deal with phonophobia, TTTS, acoustic shock and misophonia.

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## CLIENT CENTRED SOUND THERAPY SELECTION: TINNITUS ASSESSMENT INTO PRACTICE

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Tinnitus is a very individual experience. People with tinnitus perceive different sounds, in different locations in head or ears, with different reactions and different effects on daily activities. It appears that many clinicians have an a priori view of how tinnitus should be managed and this is applied uniformly, with limited contribution from the patient in decision making. It also appears that although clinicians often assess tinnitus this is seldom used to inform therapy selection. In this talk a person-centred approach to tinnitus will be introduced that makes use of an Adaptation Level framework for sound therapy. This framework considers the psychoacoustical and psychological characteristics of the individuals tinnitus that can be used to guide sound therapy selection, and how the patient can be actively involved as a partner in the therapy process.

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## ASSESSMENT AND MANAGEMENT OF ACOUSTIC SHOCK/TONIC TENSOR TYMPANI SYNDROME (TTTS)/HYPERACUSIS

Westcott, M.

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Hyperacusis is an abnormal intolerance of certain sounds, which most others tolerate well. It can develop in the belief that ears/hearing may be damaged by these sounds, or pre-existing tinnitus may be aggravated. The consensus is that about 40% of tinnitus patients have some degree of hyperacusis. Misophonia is a strongly aversive response to specific sounds, often made by other people. While hyperacusis and misophonia can occur concurrently, they are separate conditions.

Acoustic shock (AS) is an involuntary fright response to a sound perceived as traumatic (usually a sudden, unexpected, loud sound heard near the ear), resulting in a specific, consistent pattern of subjective neurophysiological symptoms. These can include; hyperacusis; tinnitus; aural pain/fullness; 'muffled' hearing; disequilibrium; and pain, numbness or a burning sensation around the ear. If symptoms persist, an AS becomes an acoustic shock disorder (ASD). The potential severity and persistence of ASD symptoms has significant clinical, occupational, military and medico-legal diagnostic/rehabilitation implications.

Tonic tensor tympani syndrome (TTTS) is an involuntary condition where the centrally mediated reflex threshold for tensor tympani muscle activity is lowered, resulting in a frequent spasm. This can trigger symptoms in and around the ear from tympanic membrane tension, alterations in middle ear ventilation and trigeminal nerve irritability.

TTTS has been proposed as the mechanism underlying many of the persistent symptoms of ASD. Symptoms consistent with TTTS are also frequently seen in tinnitus patients, particularly if they have developed hyperacusis. TTTS provides an explanation for aural pain and tinnitus aggravation triggered by intolerable sound exposure. If these patients are not given an explanation of their symptoms, the resultant anxiety and distress can play a role not only in tinnitus and hyperacusis escalation but also in limiting the degree of efficacy of therapeutic intervention.
Hyperacusis, misophonia, TTTS and AS evaluation, diagnosis and therapy will be discussed. Desensitisation can be achieved using a Tinnitus Retraining Therapy (TRT) approach, including demystification of any symptoms consistent with TTTS, with the addition of cognitive behavioural therapy (CBT) strategies to reframe maladaptive beliefs and manage auditory hypervigilance.

## BUILDING A TINNITUS PRACTICE FROM THE GROUND UP: HOW TO BRING TINNITUS AND SOUND TOLERANCE CARE TO PLACES WHERE IT DOESN'T EXIST

Martin, W. H.

In the US and Europe, the topics of tinnitus and sound tolerance conditions enjoy media attention, grant funding and general public awareness. What about the rest of the world? In many regions there the medical and patient communities know little or nothing about these conditions, their diagnosis, treatment and management. This presentation identifies issues and strategies that need consideration when introducing tinnitus and sound tolerance disorder care programs into new regions of the world. Topics and examples will include documenting needs, raising awareness, cultural barriers, political sensitivities, appropriating resources, building partnerships and funding. The concepts can apply to new and developing tinnitus care programs in any context.

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