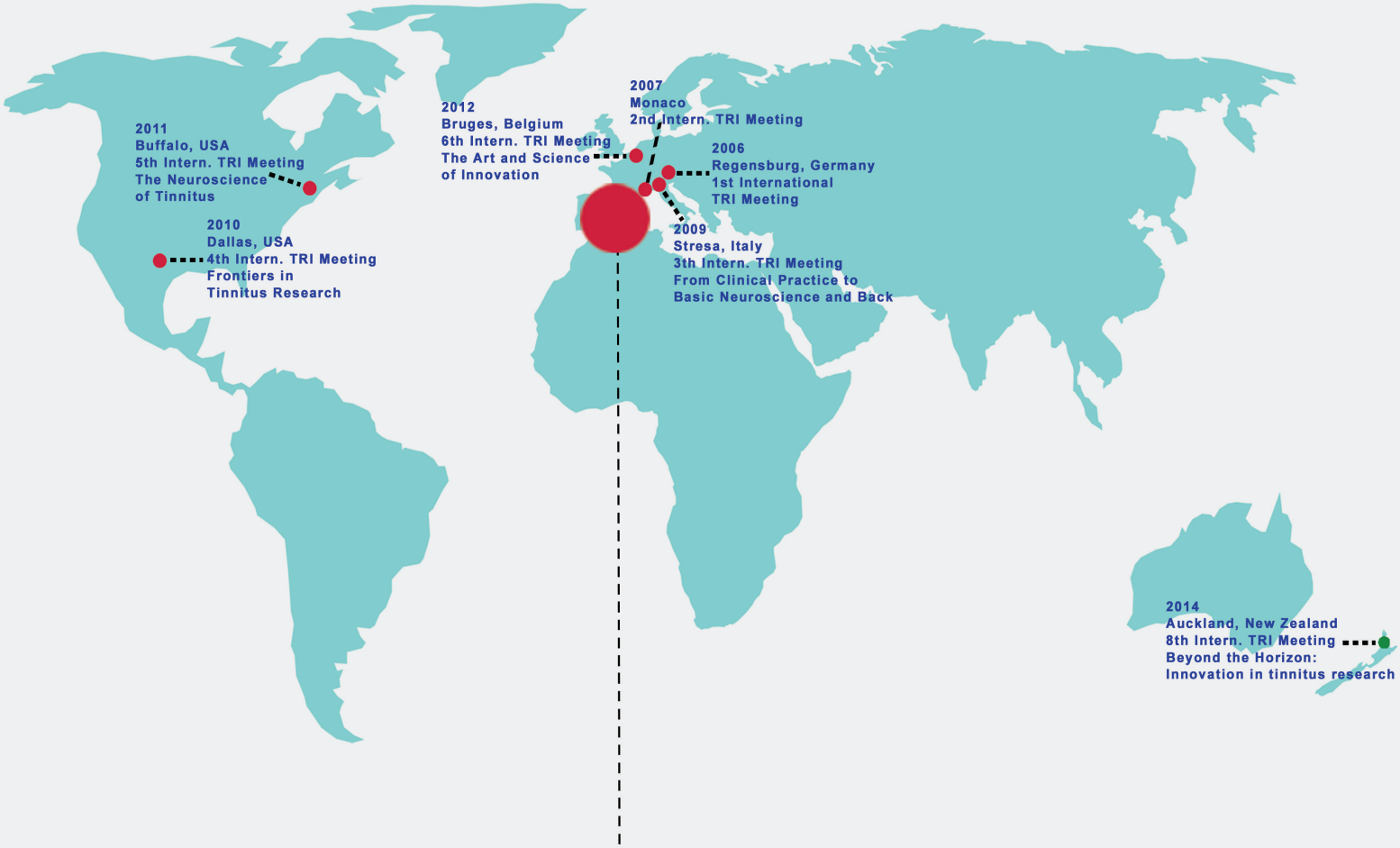

7th International TRI Tinnitus Conference

Tinnitus: A Treatable Disease

May 15 - May 18, 2013
Valencia, Spain

Program and Abstract Book

Organized by
Tinnitus Research Initiative Foundation and
Hospital Clínico Universitario, University of Valencia

Program and Abstracts

TRI 2013

Seventh International Conference on Tinnitus

Tinnitus: A Treatable Disease

Organized by the
Tinnitus Research Initiative Foundation
&
Hospital Clínico Universitario,
University of Valencia, Spain

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The organizers want to thank the people who have helped organizing this conference, especially Susanne Staudinger and Sylvia Dorner-Mitschke in Regensburg

Welcome to TRI2013

On behalf of the Tinnitus Research Initiative we are very pleased to welcome you to the “7th International Tinnitus Research Initiative Meeting”, which will be held May 15-18, 2013, at the SH Valencia Palace Hotel in Valencia, Spain.

The TRI Meeting will be the largest international tinnitus meeting in 2013.

Valencia is not only the city of the paella, but also a city that never sleeps, with an extensive cultural lineup such as the Ciudad de las Artes y las Ciencias (City of Arts and Sciences) and the Museo Príncipe Felipe (Prince Philip Museum). Thanks to the excellent climate and the attractive cityscape, Valencia invites to enjoying the cafe terraces, parks and gardens, strolling complacently by the seaside and through the city, combining both urban life and outings to the surrounding nature areas.

"Tinnitus: a treatable disease" has been chosen as the motto of the 7th TRI meeting in order to highlight treatment options for tinnitus. There will be a special focus on widely available treatments, but also on innovative treatments that are currently under development. A further focus will be laid on the diagnosis of tinnitus subtypes, which can be specifically treated. Similar like in previous years, the TRI meeting will also be the premiere venue for discussion of the latest developments in the neuroscience of tinnitus.

We cordially welcome you to Valencia in May 2013,

José Miguel Láinez, J Marco, Constantino Morera, MI Pitarch, Isabel Diges
Dirk De Ridder, Ana Belén Elgoyhen, Berthold Langguth

Valencia, May 2013

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09:40-10:15				**Keynote Speaker** *Sound Therapy: The Basic Neuroscientist's Perspective* **Arnaud Norena** France		**Invited Speaker** *Pulsatile Tinnitus* **Dirk De Ridder** New Zealand	
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15:45-17:15		**Session 5** **Research Methodology and Infrastructure** Chairs **D Hall** **M Landgrebe**	**Session 6** **Round Table: Tinnitus Management** Chairs **R Figueiredo** **C Morera**	*CBT based tinnitus treatment: A stepped care approach* **R Cima** The Netherlands *Treatment of Tinnitus with Cochlear Implant* **R Tyler** USA			
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21:00	*Welcome Cocktail*						

DETAILED SCIENTIFIC PROGRAM

	Wednesday, May 15
05:30- 08:00 p.m.	**Opening registration desk**
08:00 - 09:00 p.m.	**Openings Speaker** *To dream is to cure tinnitus* ***Dirk De Ridder*** *New Zealand*
09:00 p.m. - …	*Welcome Cocktail*

	Thursday, May 16	
09:00 - 10:15 a.m.	*Tinnitus Management: A Multidisciplinary Approach: Essentials in Diagnosis and Therapy* **T Kleinjung (ENT)** **G Searchfield (Audiologist)** **JM Láinez (Neurologist)** **P Kreuzer (Psychiatrist)** **R Cima (Psychotherapist)** **D De Ridder (Neurosurgeon)** **B Langguth (moderation)**	
----------Coffee Break (30 min)---------Coffee Break (30 min)----------Coffee Break (30 min)----------		
10:45 a.m. - 12:45 p.m.	**Session 1: Sound Therapy** **Chairs: R Tyler, I Diges** 1 **Adamchic I:** *Reducing tinnitus-related auditory binding in a pitch processing network by acoustic CR neuromodulation* 2 **Förster U**: *Patients with asymmetric hearing loss/single-sided deafness benefit from CI regarding health-related quality of life, tinnitus, and psychological comorbidity* 3 **Reimer Å:** *Change of tinnitus severity over time and trial with listening to notched music* 4 **Silchenko A:** *Impact of acoustic coordinated reset neuromodulation on effective connectivity in a neural network of phantom sound* 5 **Shekhawat GS:** *double blind, sham-controlled, randomized clinical trial of transcranial direct current stimulation (tDCS) and hearing aids for tinnitus management*	**Session 2: Animal Models of Tinnitus** **Chairs: J Turner, M Knipper** 1 **Gold J:** *Towards a better model of tinnitus: Gap detection behaviour in adult ferrets* 2 **Knipper M:** *Molecular basis of tinnitus* 3 **Berger J:** *Neuronal gap detection in the inferior colliculus in a guinea pig model of noise-induced tinnitus* 4 **Coomber B:** *Changes in nitric oxide synthase distribution in a guinea pig model* 5 **Miyakawa A:** *Strain differences in hearing loss-induced GAD65 reduction and a putative tinnitus behaviour in mice*
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03:45 - 05:15 p.m.	**Session 5: Research Methodology and Infrastructure** **Chairs: D Hall, M Landgrebe** 1 **Cima R:** *Clinical trial methodology for CBT based interventions* 2 **Hall D:** *Tinnitus Research Infrastructure* 3 **Landgrebe M:** *The TRI Tinnitus Database* 4 **Langguth B:** *The european COST-program*	**Session 6: Round Table - Tinnitus Management** **Chairs: R Figueiredo, C Morera** 1 **Diges I:** *The neurovegetative dystonia as a cause of pulsatile tinnitus: an interesting response to osteopathic manipulation* 2 **Azevedo A:** *Pharmacological treatment of tinnitus*
05:15 – 06:30 p.m.	**Poster Session I (guided tours)** 1 **Pathophysiology –** guided by **A Møller** 2 **Tinnitus Assessment –** guided by **M Landgrebe** 3 **Clinical Management –** guided by **R Figueiredo** 4 **Others –** guided by **T Sanchez**	

Friday, May 17

09:00 - 09:40 a.m.	**Keynote Speaker** *Sound Therapy: Masking or Curing: The Clinical Perspective* **Grant Searchfield,** *New Zealand*	
09:40 - 10:15 a.m.	**Keynote Speaker** *Sound Therapy: The Basic Neuroscientist's Perspective* **Arnaud Norena,** *France*	
----------Coffee Break (30 min)---------Coffee Break (30 min)----------Coffee Break (30 min)----------		
10:45 a.m. - 12:45 p.m.	**Session 7: Neurostimulation** **Chairs: D De Ridder, T Kleinjung** 1 **Cheung SW:** *Striatal neuromodulation effects on tinnitus* 2 **De Ridder D:** *The cingulate cortex as target for tinnitus treatment* 3 **Landgrebe M:** *rTMS for the treatment of tinnitus: A randomized controlled multicentric study* 4 **Zhang J:** *Auditory cortex stimulation to suppress tinnitus: Mechanisms and parameters* 5 **Joos K:** *Head-to-head comparison of transcranial random noise stimulation, transcranial AC stimulation and transcranial DC stimulation for tinnitus*	**Session 8: Tinnitus Pathophysiology: The Auditory Pathways** **Chairs: A Norena, R Salvi** 1 **Galazyuk A:** *Sound-triggered suppression of background activity in auditory neurons: Implications for residual inhibition of tinnitus* 2 **Zheng Y:** *Cell proliferation in the rat cochlear nucleus following noise exposure* 3 **Schulze H:** *Noise trauma induced development of subjective tinnitus: Predispositon and prevention* 4 **Bao S:** *Roles of homeostatic and sensory map plasticity in hearing loss-induced tinnitus*
12:45 - 01:45 p.m.----------LUNCH----------LUNCH----------LUNCH----------		
01:45 - 03:15 p.m.	**Session 9: Epidemiology and Prevention** **Chair: D Hall** 1 **Hall D**: *Non-otologic risk factors of significant tinnitus: 10-year trends from a nested case-control study in the UK* 2 **Sanchez T:** *Tinnitus among teenagers: Simple facts leading to chronicity. What can we do?* 3 **Rabau S:** *Noise-induced symptoms in a young population* 4 **Wallhaeusser-Franke E:** *Progression of tinnitus-related distress in patients with chronic tinnitus in a 6 year period*	**Session 10: Posttraumatic Tinnitus** **Chairs: J Zhang, S Hébert** 1 **Kleinjung T:** *Trauma associated tinnitus: The clinical perspective* 2 **Kreuzer P:** *Posttraumatic tinnitus: TRI database analysis* 3 **Woodard JL:** *A neuropsychological profile of blast-induced tinnitus* 4 **Zhang J:** *Blast-induced tinnitus and its related traumatic brain injury* 5 **Cacace A***: Investigating the brain "connectome" of blast-induced tinnitus: Some initial observations of a resting-state functional magnetic resonance imaging (RS-fMRI) connectivity analysis*
----------Coffee Break (30 min)---------Coffee Break (30 min)----------Coffee Break (30 min)----------		
03:45 - 04:30 p.m.	*CBT based tinnitus treatment: A stepped care approach* **Rilana Cima,** *The Netherlands*	
04:30 - 05:15 p.m.	*Treatment of Tinnitus with Cochlear Implant* **Richard Tyler,** *USA*	
05:15 – 06:30 p.m.	**Poster Session II (guided tours)** 5 **Sound Treatment –** guided by **G Searchfield** 6 **Neuroimaging –** guided by **A Cacace** 7 **CBT/TRT –** guided by **P Jastreboff** 8 **Neurostimulation –** guided by **T Kleinjung** 9 **Others –** guided by **C Coelho**	
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Saturday, May 18		
09:00 - 09:40 a.m.	**Keynote Speaker** *Tinnitus: Brain Connectivity and its Dynamics: Relevance for Treatment* **Winfried Schlee,** *Germany*	
09:40 - 10:15 a.m.	**Invited Speaker** *Pulsatile Tinnitus* **Dirk De Ridder,** *New Zealand*	
----------Coffee Break (30 min)---------Coffee Break (30 min)----------Coffee Break (30 min)----------		
10:45 - 12:45 p.m.	**Session 11: Neuroimaging of Tinnitus** **Chairs: A Cacace, S Vanneste** 1 **Davies J:** *Auditory network connectivity in tinnitus patients: A resting-state fMRI replication study* 2 **Kong W:** *Evaluation of resting state brain functional activity in patients with tinnitus by functional magnetic resonance imaging* 3 **Melcher J:** *Functional connectivity between primary auditory cortex, cognitive control and default mode networks in tinnitus and hearing loss* 4 **Schecklmann M:** *Functional near-infrared spectroscopy in tinnitus* 5 **Vanneste S:** *Towards an objectivation of tinnitus. Machine learning approach of resting state electrical brain activity can detect the presence of tinnitus*	**Session 12: Tinnitus Pathophysiology: Interaction between Auditory and Non-Auditory Pathways** **Chairs: AB Elgoyhen, A Møller** 1 **Mazurek B:** *Stress changes the protein expression in auditory pathway* 2 **Salvi R:** *Neural alterations in outside the classical auditory pathway after treatment with tinnitus inducers: Noise and salicylate* 3 **Shore S:** *Altered stimulus-timing dependent multisensory plasticity in dorsal cochlear nucleus following noise exposure and tinnitus induction* 4 **Elgoyhen AB:** *Tinnitus as side effect: a drug-target network analysis*
12:45 - 01:45 p.m.----------LUNCH----------LUNCH----------LUNCH----------		
01:45 - 02:30 p.m.	**Keynote Speaker** *Tinnitus and Stress* **Sylvie Hébert,** *Canada*	
02:30 - 03:15 p.m.	**Closing Remarks** *Tinnitus: A Treatable Disease*	

Poster Sessions

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P2	**Modulatory Effects of Spectral Energy Contrasts on Lateral Inhibition in the Human Auditory Cortex** Stein A, Engell A, Okamoto H, Wollbrink A, Pantev C
P3	**The Enigma of the Tinnitus-free Dream-state. Data from 100 Questionnaires and its Implications for the Pathophysiology of Tinnitus** Joos K, Vanneste S, De Ridder D
P4	**Sound-trauma-related Changes of Activity in Circuits of the Auditory Cortex** Jeschke M, Happel MFK, Tziridis K, Schulze H, Ohl FW
P5	**Microglia in the Rat Cochlear Nuclei: A Player in Tinnitus-related Circuit Reorganization?** Venturino A, Barbaro S, Oda A, Boselli C, Ferraro D, Pizzala R, Perin P
P6	**A Novel Method for Reliable Repeated Measurements of Auditory Brainstem Response in Rats Treated with Deep Brain Stimulation** Smit JV, Janssen MLF, Jahanshahi A, Temel Y, Stokroos RJ
P7	**Modulation of auditory cortical responses by attention inside and outside of the tinnitus frequency region** Paul B, Roberts L
2 Tinnitus Assessment	
P8	**Headache in Tinnitus: Findings of a Questionnaire Survey** Schecklmann M, Hund V, Landgrebe M, Langguth B
P9	**Hyperacusis in Tinnitus: A TRI Database Analysis** Schecklmann M, Langguth B, Kreuzer PM, Landgrebe M, TRI Database study group
P10	**The Tinnitus/Epilepsy Connection: Establishing Linkage through an On-Line Survey** AT Cacace, Y Ye
P11	**Evaluation of the Acoustic Coordinated Reset® Neuromodulation Device for Tinnitus: Study Protocol for a Double-Blind Randomised Controlled Trial** Hoare DJ, Pierzycki R, Thomas H, Schaette R, McAlpine D, Hall DA
P12	**Comparison of Recent Tinnitus Treatments Effect Sizes** Davis PB, Moruf S
P13	**UK Validation of the Tinnitus Functional Index (TFI): Discriminant and Convergent Validity** Fackrell K, Hoare DJ, Barry JG, Hall DA
P14	**Tinnitus and Psychological Distress: Evaluating the Effectiveness of Treatment** Zaytseva O
3 Clinical Management	
P15	**Speech-In-Noise Test with Amplitude Modulated Noise in Normal Hearing Subjects with and without Tinnitus** Rabau S, Gilles A, Mertens G, Van de Heyning P
P16	**How much additional information is provided by the high-frequency audiogram in tinnitus patients with normal standard audiogram?** Vielsmeier V, Lehner A, Fiedler I, Strutz J, Steffens T, Kreuzer P, Schecklmann M, Landgrebe M, Langguth B, Kleinjung T
P17	**Affected speech perception in tinnitus patients** Veronika Vielsmeier, Thomas Steffens, Isabella Fiedler, Jürgen Strutz, Peter Kreuzer, Martin Schecklmann, Berthold Langguth
P18	**Comparing a Software Tool for Self-Administered Tinnitus Pitch Matching with a Standardized Audiometric Procedure** Wunderlich R, Waasem L, Teismann H, Pantev C
P19	**Efficacy of Tailored Psychotropic treatment in Tinnitus Patients with Psychiatric Disorders in Co-Morbidity: A Follow-Up Study** Salviati M, Terlizzi S, Melcore C, Panico R, Romano G, Valeriani G, Macrì F, Mazzei F, Altissimi G, Cianfrone G

P20	**Tianeptine: A Possible Action in Neuronal Plasticity in Tinnitus Patients: A Preliminary 16-Week Prospective open-lable Trial** Coelho C
P21	**Multisensory Congruence Treatment for Tinnitus** Joos K, Raymond van EE, Estrella Mena, Marijn Van Dongen, Wouter Serdijn, Vanneste S, De Ridder D
P22	**A University Based Tinnitus Management Program: Structure and Experience** Stocking C, Stecker N
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P24	**Tensor Tympany Syndrome (TTTS): One Case** Heitzmann T, Valdivieso A
P25	**Long-Term Outcomes of Tinnitus after Treatment of Sudden Sensorineural Hearing Loss Accompanied by Tinnitus** Kim YH, Park KT, Seok J, Yi YJ, Kang S
P26	**Clinical Study on Patient's disability in the Case of Unilateral Sudden Sensorineural Hearing Loss and Tinnitus** Lee DH
P27	**Petrosquamosal Sinus in the Temporal Bone as a Cause of Pulsatile Tinnitus: A Radiological Detection** Liu ZH, Wang ZC, Gong SS, Xian JF, Wang GP, Jiang H, Zhao PF, Lv H
P28	**Sigmoid Sinus Diverticulum and Pulsatile Tinnitus: Analysis of CT Scans from 15 Cases** Liu ZH, Wang ZC, Gong SS, Xian JF, Wang GP, Jiang H, Zhao PF, Lv H
P29	**Hyperacusis and other Inner Ear Disorders are Improving after Irradiation with Photobiostimulating Lasers** Prósper J, Hack E, Martin T

Friday, May 17, 5:15 – 6:30 p.m

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P31	**Intracochlear Electrical Stimulation to Suppress Tinnitus – Towards a Tinnitus Implant** Arts.R, George.E, Stokroos R
P32	**Sound Therapy of Tinnitus Based on the Equalization of the Hearing Loss Curve: A Multicenter Study** Diges I, CoboP, Harguindey A
P33	**Graphical User Interface for the Sound Therapy of Tinnitus** Diges I, Rodríguez A, Cobo P, Harguindey A
P34	**Neuromonics Tinnitus Treatment – Experience at a National University Hospital, Singapore** Perumal B, Yusuf ABR, Lim LHY
P35	**Perceptual Attention Training in Tinnitus Treatment** Wise KJ, Kobayashi K, Spiegel DP, Magnusson J, Searchfield GD
P36	**Follow-Up of CR-Neuromodulation Therapy with Tinnitus Characterization Using a Numeric Scale for the Tinnitus Spectrum** Tóth T, Adamchic I, Tass PA
P37	**Playing and listening to tailor-made notched music: the effectiveness of multimodal and unimodal musictraining in tinnitus therapy** Pape J, Paraskevopoulos E, Bruchmann M, Wollbrink A, Pantev C
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P39	**Neuroimaging in Patients with Chronic Tinnitus Underwent Acupuncture Treatment** Laureano MR, Onishi ET, Moreira HC, Andrade AN, Garcia MV, Garrido GEJ, Batista IR, Reis MA, Jackowski AP
P40	**Short-Term Plasticity of the Auditory Cortex in Tinnitus Patients** Engell A, Stein A, Pantev *C*

P41	**Structural Changes in Relation to Tinnitus Distress: A VBM Study** Golm D, Barke A, Schmidt-Samoa C, Dechent P, Kroener-Herwig B
P42	**Pathological Oscillations in Hyperacusis Brain even without Sound Stimuli: A Hyperresponsiveness Network with Paradoxically Inactive Auditory Cortex** Song JJ, De Ridder D, N Weisz, W Schlee, Van de Heyning P, Vanneste S
	7 CBT / TRT
P43	**Mindfulness- and Body-Psychotherapy-Based Group-Treatment of Chronic Tinnitus: A Randomized Controlled Pilot Study** Kreuzer PM, Goetz M, Holl M, Schecklmann M, Landgrebe M, Staudinger S, Langguth B
P44	**Clinically-Significant Tinnitus Symptoms: The Role of Top-Down Cognitive Processes** Toostani IG, Zana Y
P45	**Effects of Counseling, Amplification and Sound Stimulation in Tinnitus Management** Skellgaard PH, Kristensen AM, Caporali S
P46	**Tinnitus and Hypersensitivity to Sound, Integral Therapy of Tinnitus Associated with Auditory Rehabilitation (Knaster Method) and Hearing Systems** Moreno Vidal C, Almenara Rodriguez Y, Hernando Leal M, Martine*z Mintegui D*, Ibeas Franco L, Antón Canales A, Jimeno Brabo C, Atares Ures A, Gonzalo Dominguez C, Bardal Prieto M, Mora Diaz L, Sanz Cuesta L, Starczewska Navarro P Martin Padrón Y, Perez Duarte U, Cisneros Moral S, Martinez Usano A, Lepe Rojas P, García Cabrera V
P47	**Correlation Type of Masker Noise of the Minimum Masking Level and tinnitus Questionnaire in Chronic Tinnitus Patients** Rabau S, Cox T, Waelkens B, Janssens de Varebeke S, Wouters K, Van de Heyning P
	8 Neurostimulation
P48	**Effectiveness of Repetitive Transcranial Magnetic Stimulation to Different Characteristics of Chronic Tinnitus** Lin CD, Wang CY, Chung HK, Tsaib CH, Tsai MH
P49	**P300 in the Assessment of chronic Tinnitus Patients Following Repetitive Transcranial Magnetic Stimulation** Chung H, Wang CY, Chung HK, Tsaib CH, Tsai MH
P50	**tVNS for the Treatment of Tinnitus** Kreuzer PM, Landgrebe M, Husser O, Resch M, Schecklmann M, Geisreiter F, Poeppl TB, Prasser SJ, Hajak G, Langguth B
P51	**Structural Brain Changes after 10 Sessions of Left Temporal Low-Frequency rTMS in Patients with Chronic Tinnitus** Lehner A, Schecklmann M, Kreuzer PM, Poeppl TB, Landgrebe M, Langguth B
P52	**Repeated Courses of rTMS Treatment in Patients with Chronic Tinnitus** Lehner A,
P53	**Efficacy and Safety of Transcutaneous Vagus Nerve Stimulation in Tinnitus: A Case Control Study** Lehtimäki J, Ylikoski M, Bergholm M, Pirvola U, Aarnisalo A, Mäkitie A, Ylikoski J
P54	**Comparison of rTMS outcomes between Ipsilateral and Contralateral Auditory Cortex Application in Unilateral Tinnitus** Song MH, Kim BG, Moon IS
	9 Others
P55	**Misophonia from Aristotle to Levitin** Bauman N
P56	**A Novel Mechanism for the Cochlear Amplifier** Hampton P
P57	**Otosociology: The Cause of Tinnitus is Outside the Ear in the Social Environment** Lora Diaz JJ, López-González MA, Abrante A, Esteban F
P58	**Tinnitus: Not only Treatable but Also Curable Disease** Vergara R
P59	**Tinnitus among teenagers: Exposure to potential risky leisure habits** Sanchez T, Moraes F, Casseb J, Cota J, Kii M, Freire K
P60	**The effect of prevention campaigns on youngsters** Gilles A, Rabau S, Van de Heyning P

Abstracts

WEDNESDAY
MAY 15, 2013

08:00 - 09:00 p.m.
OPENINGS SPEAKER

TO DREAM IS TO CURE TINNITUS

Dirk De Ridder
Department of Surgical Sciences, Section of Neurosurgery, Dunedin School of Medicine, University of Otago, New Zealand.
Dirk.deridder@otago.ac.nz

THURSDAY
MAY 16, 2013

9:00 - 10:15 a.m.
PLENARY TALKS

TINNITUS MANAGEMENT - A MULTIDISCIPLINARY APPROACH: ESSENTIAL IN DIAGNOSIS AND THERAPY

T Kleinjung (ENT), G Searchfield (Audiologist), JM Láinez (Neurologist), P Kreuzer (Psychiatrist), R Cima (Psychotherapist), D De Ridder (Neurosurgeon), B Langguth (moderation)

In this plenary session the relevance of a multidisciplinary approach to tinnitus patients will be illustrated by short presentation from tinnitus experts from different disciplines. In these short presentations they will highlight essential aspects of diagnosis and treatment from the perspective of their discipline. The session aims to reflect the motto of the meeting by highlighting what can currently be offered for the treatment of tinnitus.

10:45 a.m. - 12:45 p.m.
SESSION 1: Sound Therapy
Chairs: R Tyler, I Diges

REDUCING TINNITUS-RELATED AUDITORY BINDING IN A PITCH PROCESSING NETWORK BY ACOUSITIC CR NEUROMODULATION

I Adamchic[1], C Hauptmann[1] and P A Tass[1, 2]
[1] *Institute of Neuroscience and Medicine–Neuromodulation, Research Center Jülich, Jülich, Germany.*
[2] *Department of Neuromodulation, University of Cologne, Cologne, Germany.*

Background and aims: Acoustic coordinated reset (CR) neuromodulation causes a significant reduction of tinnitus severity[1] that is paralleled by a reversal of pathological oscillatory activity and is often accompanied with a significant tinnitus pitch change[2]. Here we study if the changes of tinnitus pitch change correlate with changes of tinnitus severity as assessed using visual analog scale (VAS). We also study whether the changes of the pattern of brain synchrony in tinnitus patients, induced by 12 weeks of CR therapy, depend on the amount of tinnitus pitch change.

Methods: Clinical data and spontaneous EEG from 59 tinnitus patients were analyzed. We applied standardized low-resolution brain electromagnetic tomography (sLORETA) to EEG recordings from two groups of patients with a sustained CR-induced relief of tinnitus symptoms with and without tinnitus pitch change.

Results: Changes of VAS scores significantly correlated with the modulus, i.e. the absolute value, of the tinnitus pitch change. Moreover, a significantly stronger decrease in gamma power was found in patients with pronounced tinnitus pitch change in the right parietal cortex (Brodmann area, BA 40), right frontal cortex (BA 9, 46), left temporal cortex (BA 22, 42), and left frontal cortex (BA 4, 6), combined with a significantly stronger increase of alpha (10–12 Hz) activity in the right and left anterior cingulate cortex (ACC; BA 32, 24). In patients with pronounced pitch change a significantly lower functional connectivity in the gamma band between the right dorsolateral prefrontal cortex (BA 46) and the right ACC (BA 32) was found after 12 weeks of CR therapy.

Conclusions: Our results indicate a substantial reduction of tinnitus-related auditory binding in a pitch processing network.

1. *Tass PA, Adamchic I, Freund HJ, von Stackelberg T, Hauptmann C (2012). Counteracting tinnitus by acoustic coordinated reset neuromodulation. Restor Neurol Neurosci. 30(2): 137-159.*
2. *Adamchic I, Hauptmann C, Tass PA (2012). Changes of oscillatory activity in pitch processing network and related tinnitus relief induced by acoustic CR neuromodulation. Front Syst Neurosci. 6, 18.*

PATIENTS WITH ASYMMETRIC HEARING LOSS/ SINGLE-SIDED DEAFNESS BENEFIT FROM CI REGARDING HEALTH-RELATED QUALITY OF LIFE, TINNITUS, AND PSYCHOLOGICAL COMORBIDITY

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Objectives: Recent studies have demonstrated significant improvement of speech perception in patients with asymmetric hearing loss (AHL) and single-sided deafness (SSD) following CI. The purpose of this study was to evaluate if the AHL/SSD patients benefit from CI regarding health-related quality of life, tinnitus and psychological comorbidity.

Study design: Thirty-one adult patients implanted with a CI for at least 6 months were included in this prospective study. We evaluated the quality of life, tinnitus impairment, perceived stress, depressive and anxiety symptoms and coping strategies using six validated questionnaires: the Nijmegen Cochlear Implant Questionnaire (NCIQ), the Tinnitus-Questionnaire (TQ), the Perceived Stress Questionnaire (PSQ), and finally the General Depressions Scale (ADSL) and the General Anxiety Disorder- 7-questionnaire (GAD-7). In addition, speech perception tests for the implanted ear and in the binaural condition in quiet and noise (Freiburger monosyllables, HSM and OLSA sentences) were evaluated.

Results: CI in AHL/SSD resulted in a statistically significant improvement of HRQoL. There was a significant decrease of tinnitus-related distress in the AHL group. Furthermore, the number of patients with severe perceived stress, anxiety and depressive symptoms was reduced after CI. CI resulted in a significant improvement in all speech perception tests in quiet and noise. In addition, following CI, SSD patients benefited from the head-shadow-effect.

Conclusions: Cochlear implantation positively influences the quality of life, induces habituation of tinnitus and lowers the stress perception and psychological comorbidity in AHL/SSD patients.

CHANGE OF TINNITUS SEVERITY OVER TIME AND TRIAL WITH LISTENING TO NOTCHED MUSIC

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Objectives: The aims of the present studies were to examine whether perceived tinnitus severity changes over time, and which factors contribute to change. A second objective was to select patients for treatment with notched music.

Material and Methods: A tinnitus severity questionnaire was completed by 480 patients visiting an ENT-outpatient department between the years 2000 and 2008.The same questionnaire was in 2010 sent to 455 of the patients and 267 responded. The change of severity and relation to age, gender, hearing loss and etiologic diagnosis was examined. A second inquiry to the responders 267 responders got 158 answers. Relation of tinnitus severity to indicators of depression and anxiety (HADS) was studied and character of tinnitus was described. Notched music treatment has been offered patients with pure tonal tinnitus (1).

Results: Tinnitus severity had decreased for the majority of patients on follow-up assessment. In noise induced hearing loss tinnitus improved less than in unspecified sensorineural hearing loss. Pure tonal character of tinnitus is uncommon. Pitch of tinnitus is often difficult to assess. Preliminary treatment results with notched music are in a few patients promising

Conclusion: Most patients experienced less severity of tinnitus with time, but exceptions were many. Severity of tinnitus in noise induced hearing was more frequently unchanged. Tonal tinnitus suitable for treatment by listening to notched music was not frequent, but the method is practiced in a few cases.

Reference:

(1)Music-induced cortical plasticity and lateral inhibition in the human auditory cortex as foundations for tonal tinnitus treatment. Pantev C ,Okamoto H and Teismann H. Frontiers in Systemic Neuroscience. 2012; 6: 50

IMPACT OF ACOUSTIC COORDINATED RESET NEUROMODULATION ON EFFECTIVE CONNECTIVITY IN A NEURAL NETWORK OF PHANTOM SOUND

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Background: Chronic subjective tinnitus is an auditory phantom sensation, which evolves as a consequence of damage to the peripheral auditory system and causes characteristic changes of brain activity in the central auditory system. A mechanism, underlying the perception of a phantom sound, is likely to include the imbalance in communication between auditory and non-auditory brain areas. Recently, it was shown that acoustic coordinated reset (CR) neuromodulation significantly counteracts both tinnitus symptoms and tinnitus related alterations in EEG power spectra1. The objective of the present study was to analyze whether CR neuromodulation caused an alteration of the effective connectivity in a tinnitus related network of localized EEG brain sources.

Methods: EEG recordings were performed at baseline and after 12 weeks of CR therapy in 28 patients with bilateral chronic tinnitus and in a control group of healthy subjects. To increase the signal-to-noise ratio, we focused on a subgroup of good responders, which is characterized by a substantial reduction in TQ scores ($\Delta TQ \geq 12$) after 12 weeks. To determine which connections matter, we performed a BESA source reconstruction in the following predefined regions of interest: temporal and frontal areas, parietal cortex, and anterior and posterior cingulate cortex. To that network we applied a data-

driven approach, combining empirical mode decomposition and partial directed coherence analysis2, in patients with bilateral tinnitus before and after 12 weeks of CR therapy as well as in healthy controls. Dynamic causal modeling (DCM) was used to infer about the types of interactions, which were altered by CR neuromodulation. We also studied nonlinear interactions between different frequency bands by means of higher-order spectral analysis.

Results: Prior to CR therapy and compared to the healthy controls, the good responders showed a significantly increased connectivity between the left primary auditory cortex and the posterior cingulate cortex in the gamma and delta bands together with a significantly decreased effective connectivity between the right primary auditory cortex and the dorsolateral prefrontal cortex in the alpha band. After 12 weeks of CR therapy most of the pathological interactions were gone, so that the connectivity patterns of good responders and healthy controls became statistically indistinguishable. Our DCM results show that CR therapy specifically counteracted the imbalance of excitation and inhibition. CR therapy significantly weakened the excitatory connection between posterior cingulate cortex and primary auditory cortex and significantly strengthened inhibitory connections between auditory cortices and the dorsolateral prefrontal cortex.

1 Tass P.A., et al. Rest. Neurol. Neurosci. v.30, 1-23, (2012)
2 Silchenko A.N., et al. J. Neurosci. Meth., v.191, 32-44, (2010).

DOUBLE BLIND, SHAM-CONTROLLED, RANDOMIZED CLINICAL TRIAL OF TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) AND HEARING AIDS FOR TINNITUS MANAGEMENT

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Background/Aims: Perception of sound in the absence of an external auditory source is called tinnitus. Tinnitus negatively impacts the quality of life of sufferers. The aim of this study was to investigate the role of multi-session anodal tDCS of the Left Temporoparietal Area (LTA) in combination with hearing aid use, for tinnitus management.

Methods: Forty participants with a mean age of 54 years, suffering from chronic tinnitus (minimum 2 years) completed a seven month long clinical trial. Participants were randomized in to two groups: control and experimental group with 20 participants in each group. This was a double blind study with multisession (five consecutive sessions with 24 hour wash out period) anodal tDCS (2mA intensity and 20 minutes duration) of LTA, followed by hearing aid fitting and use for six months. The impact of tDCS and hearing aid fitting on tinnitus was measured with questionnaires (THQ, TFI, HADS, TSNS, HHI, CGI, and VAS) and Minimum Masking Levels before, immediately after the stimulation, 3rd and 6th months after hearing aid use.

Results: Hearing aid use lead to a significant improvement in overall Tinnitus Functional Index (TFI, primary outcome measure) scores across both the groups. The effect of tDCS was less clear, although some preliminary evidence suggests that tDCS may have reduced the time to maximum hearing aid benefit, further research is needed to confirm this.

Conclusion: Hearing aids (without tinnitus counselling), resulted in significant improvement in tinnitus after 3 months of use. These hearing aid benefits were independent of use of tDCS. Further investigations of tDCS or other neuromodulators may prove that priming the auditory system for hearing aid use may be clinically beneficial.

10:45 a.m. - 12:45 p.m.
SESSION 2:
Animal Models of Tinnitus
Chairs: J Turner, M Knipper

TOWARDS A NEW ANIMAL MODEL OF TINNITUS: GAP DETECTION BEHAVIOUR IN ADULT FERRETS

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Background/Aims: The current lack of consensus regarding the neurobiological basis of tinnitus indicates a need for novel animal models to be developed to understand the changes in cortical processing following partial hearing loss and to correlate those changes with behavioural data identifying the presence of the phantom percept. The ferret (Mustela putorius furo) may represent a suitable candidate for tinnitus research: ferrets perform effectively in audio-guided behaviour, and are able to hear over a range of frequencies akin to those perceived by humans. Additionally, its large skull and well-defined auditory cortical fields make this species very appropriate for investigating cortical changes. Therefore, we sought to examine behavioural outcomes in a gap detection task following partial peripheral deafferentation in the cochlea of the ferret, in an attempt to develop a behavioural assay for tinnitus.

Methods: Two naive adult female ferrets were positively conditioned to perform a gap detection task using a two-alternative forced-choice paradigm. Animals were trained to discriminate an uninterrupted sound (0-30 kHz bandwidth, digitally flattened, 77 dB SPL, 2080 ms) from the same sound in which gaps are embedded (four interleaved gaps, varying between 3-270 ms in duration). After consistent behaviour was obtained, animals underwent unilateral mechanical lesion of the high frequency domain of the spiral ganglion in the cochlea, as previously described1. Following recovery, animals were retested on the same behavioural protocol, while the extent and frequency content of hearing loss were assessed via auditory brainstem response (ABR) measurements.

Results: Psychometric functions were based on two different parameters: (i) the adjusted proportion of correct responses to take into account the false alarm rate and (ii) the sensitivity index (d') based on signal

detection theory. By calculating hit and false alarm rates from animal responses over >1000 trials, psychometric functions were derived according to a corrected performance measure2, (pHit – pFA)/(1 – pFA), allowing detection thresholds and slopes to be calculated. After operant training, ferrets showed a stable performance with near-perfect discrimination of longer gaps (>50 ms) and threshold of 7.0 ms (defined as performance = 0.48, equivalent to pHit=50% and pFA=3.5%). Animals were biased toward no-gap responses for gaps < 20 ms, whereas bias was towards gap-type response for longer gaps. During no-gap stimuli, animals initiated correct (hit) responses earlier, whereas during gap-containing stimulus presentation, animals responded earlier when the response was incorrect, suggesting that on false alarm trials, interrupted stimuli were perceived as continuous. Notably, performance thresholds were elevated (11.2 ms) following lesion induction, with asymptote gap values remaining unchanged. Response times before and after the lesion were similar. However, in the post-lesion condition, response bias was uniformly weighted towards no-gap responses.

Conclusions: Partial unilateral lesion of the spiral ganglion impairs the gap-detection sensitivity to broadband auditory stimuli of awake, behaving ferrets. This is being extended to investigate behavioural performance in response to narrow-band stimuli, alongside potential changes in ABRs following peripheral lesions.

1. *Snyder RL, Sinex DG, McGee JD, Walsh EW. Hear Res, 2000; 147:200-220.*
2. *Kelly JB, Rooney BJ, Phillips DP. Behav Neurosci, 1996; 110:542-550.*

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

MOLECULAR BASIS OF TINNITUS

Rüttiger L., Singer W., Zuccotti A., Panford-Walsh R., Matsumoto M., Zimmermann U., Jaumann M., Franz C., Geisler H.-S., Köpschall I., Rohbock K., Xiong H., Varakina K., Lee S.C., Verpoorten S., Schimmang T.[2], Knipper M.

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Tinnitus is a non-curable stress-related brain disorder, that is mostly noise-induced and whose origin is unknown. We have addressed the molecular and physiological basis of this disease using a combined approach that included behaviorally tested tinnitus (Rüttiger et al., Knipper, Hear Res 2003), hearing measurements (including DPOAEs, ABRs and ABR wave analysis) and markers that trace network activity (Arc/Arg3.1). Data analysed the first time equally hearing impaired animals that were behaviorally distinguished in hearing impaired animals with and without tinnitus. We compared animals between the periphery of the cochlea and the auditory cortex, including the hippocampus and amygdala. We also included an analysis of altered responsiveness after stress priming. We unraveled a tinnitus and hyperacusis specific trait that may explain some of the existing controversies about the molecular basis of both symptoms.

Acknowledgements. This work was supported by the Marie Curie Research Training Network CavNET MRTN-CT-2006-035367, the Deutsche Forschungsgemeinschaft DFG-Kni-316-4-1 and Hahn Stiftung (Index AG).

NEURONAL GAP DETECTION IN THE INFERIOR COLLICULUS IN A GUINEA PIG MODEL OF NOISE-INDUCED TINNITUS

Berger J, Coomber B, Shackleton T, Wallace M & Palmer A

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Animal models of tinnitus allow correlations between changes in neural activity in the auditory system and objective behavioural measures of tinnitus. We have developed a variation on the widely-used gap detection method in which we measure prepulse inhibition (PPI) of the pinna reflex in guinea pigs (GPs) [1]. Impaired gap detection following noise exposure – and subsequent PPI deficits – is thought to be caused by tinnitus 'filling in' the gap, thus reducing its salience. An alternative explanation is that PPI deficits are indicative of impaired auditory processing, rather than tinnitus obscuring the gap in the background noise. In this scenario, temporal information processing is impaired i.e., gap recognition. In the present study, we attempted to address this issue by examining gap detection in inferior colliculus (IC) neurones.

GPs were subjected to unilateral noise trauma and tested behaviourally for the presence of tinnitus over an 8-week period (n = 5). Hearing status was assessed using auditory brainstem responses. Animals were then anaesthetised and single-unit extracellular recordings were made from the right and left IC. For each single-unit, a frequency-response area was first measured. Neuronal gap detection thresholds were then measured in response to pure tone and broadband noise (BBN) stimuli, and to narrow band noise (NBN) stimuli (4-6, 8-10, 12-14 and 16-18 kHz) that evoked neuronal firing. This threshold was defined as the minimum gap duration where a significant response could be detected to the onset of the post-gap noise. These NBN conditions match the behavioural stimuli used to detect tinnitus and were selected with the aim of correlating neural gap detection ability to an animal's behavioural performance. Neural gap detection data from noise-exposed GPs were compared to a control group (n = 2).

Using strict criteria (0% PPI and hearing threshold recovery to ≤20 dB SPL of pre-exposure levels), the presence of tinnitus was objectively measured in GPs at 7-8 weeks post-noise exposure; two GPs exhibited tinnitus, while three GPs were assigned to the 'no tinnitus' group. In general, neural gap detection thresholds were increased in noise-exposed GPs compared with control animals. In controls, the mean (± SEM) gap detection threshold across all animals was 12.8 ± 2.6 ms for BBN, 10.9 ± 2.3 ms for tones, and 12.0 ± 3.3 ms for NBN (selected as the closest to the characteristic frequency of a particular neurone). In noise-exposed GPs,

the mean gap detection threshold was 18.3 ms ± 2.7 for BBN, 19.5 ± 2.9 ms for tones, and 19.6 ± 3.6 ms for NBN. No differences were seen between 'tinnitus' and no tinnitus' groups when noise-exposed GPs were sub-divided based on behavioural data.

These preliminary data suggest that neural gap detection is altered by noise exposure. It is unclear whether tinnitus affects this, owing to a small sample size and relatively large margins of error. The mean neural gap detection threshold in noise-exposed GPs is, however, considerably shorter than the size of the gap used in the behavioural task (50 ms), so this may not be a factor in PPI measurement.

[1]Berger JI, Coomber B, Shackleton TM, Palmer AR, Wallace MN. (2013) A novel behavioural approach to detecting tinnitus in the guinea pig. J Neurosci Methods 213: 188-195

CHANGES IN NITRIC OXIDE SYNTHASE DISTRIBUTION IN A GUINEA PIG MODEL OF TINNITUS

Coomber B, Kowalkowski V, Berger J, Palmer A, & Wallace M
MRC Institute of Hearing Research, Nottingham, UK

Animal models of tinnitus, often induced by acoustic trauma, allow correlations between changes in neural activity in the auditory system and objective behavioural measures of tinnitus. To identify animals with tinnitus, we have developed a variation on the widely-used gap detection method in which we measure prepulse inhibition (PPI) of the pinna reflex in guinea pigs (GPs) [1]. We have used nitric oxide (NO) as an indicator of neural activity. NO is a gaseous signalling molecule capable of acting through a variety of protein targets: low levels of NO are generally associated with physiological activity, while high levels are often associated with inflammatory pathology. NO in the central nervous system is produced by neuronal NO synthase (nNOS); in pathological conditions, excess NO is produced by inducible NOS (iNOS), an alternative isoform of the enzyme. In the present study, we aimed to ascertain whether changes in NOS activity in the cochlear nucleus (CN) correlated with behavioural evidence of tinnitus.

GPs were anaesthetised and subjected to unilateral noise trauma. Hearing status was assessed using auditory brainstem responses immediately before and after noise exposure, and then prior to histological processing at a series of time-points post-noise trauma. At the 8-week time-point, GPs were also assessed for behavioural evidence of tinnitus using the gap detection method, before sacrifice. Brains of the unilaterally noise-exposed GPs were examined histologically for asymmetrical changes in NOS expression in the CN and compared with a control group of GPs. Brain sections were stained with nicotinamide adenine dinucleotide phosphate diaphorase (NAPDH-d), which represents the activity of NOS in aldehyde-fixed tissue, and cell counts were performed. NADPH-d activity is shown by all isoforms of NOS; thus to confirm that any change in NOS expression was due to nNOS, we also performed immunohistochemical staining with a primary antibody specific for nNOS.

Unilateral (left ear) noise exposure resulted in more NOS-positive cells in the left ventral CN (VCN) in some, but not all, GPs at 24h (n = 5), 72h (n = 5), 7 days (n = 3), and 3 weeks (n = 4) after acoustic trauma. Using rigorous criteria for objective behavioural tinnitus measurement – eliminating GPs with substantial asymmetric hearing loss – we found a significant left-right asymmetry in NOS staining at the 8-week time-point in the VCN of 'tinnitus' GPs (n = 5), compared with control animals (n = 5). The distribution of nNOS immunohistochemistry was the same as NADPH-d staining, and hence the changes were due to nNOS.

Our data show a marked, sustained change in the numbers of NOS-containing neurones in the VCN of GPs with tinnitus. It is unlikely that GPs without a left-right NOS asymmetry at the short-term time-points would have developed tinnitus. In GPs that do exhibit a short-term left-right asymmetry, elevated NOS activity could be sustained and an animal subsequently develop tinnitus. Based on these results, NO plays a role in post-acoustic trauma pathology in the VCN.

[1] Berger JI, Coomber B, Shackleton TM, Palmer AR, Wallace MN. (2013) A novel behavioural approach to detecting tinnitus in the guinea pig. J Neurosci Methods 213: 188-195

STRAIN DIFFERENCES IN HEARING LOSS-INDUCED GAD65 REDUCTION AND A PUTATIVE TINNITUS BEHAVIOR IN MICE

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Aims/Objectives: Some strains of mice are more susceptible to developing tinnitus behavior following noise-induced hearing loss (NIHL), while others are resistant. The cause of such strain differences is not entirely clear. Tinnitus is associated with increased activity in the central auditory pathway, which may be caused by NIHL-induced reduction of glutamate decarboxylase (GAD) expression [1]. Here, we examine the hypothesis that strain differences in tinnitus susceptibility is correlated with the degree of NIHL-induced GAD65 reduction.

Methods: Two strains of mice, C57BL/6 (n= 8) and FVB (n =11), underwent unilateral NIHL (8kHz, 112dB, 2 hours). Ten days after NIHL, putative tinnitus behavior was measured using a gap detection task [2]. GAD65 mRNA levels were measured bilaterally in noise-exposed and intact auditory cortex using reverse transcription polymerase chain reaction (RT-PCR). The relationship between genotype, tinnitus behavior, and cortical GAD65 level was examined. Following the identification of tinnitus-resistant strain of mice, we artificially knocked-down GAD65 in the auditory cortex using post-transcriptional mRNA silencer (GAD65 shRNA lentiviral particles) to examine whether cortical reduction of GAD65 was sufficient to induce tinnitus behavior.

Results: C57BL/6 showed significant tinnitus behavior, measured by gap detection impairment, following NIHL. This behavioral change was accompanied by a 40% reduction of GAD65 mRNA in the auditory cortex contralateral to the lesioned ear. FVB mice showed neither gap detection impairment nor cortical GAD65 reduction following the same NIHL protocol. Cortical GAD65 in auditory cortex was knocked down in tinnitus-resistant FVB. FVB developed a significant impairment in gap detection following GAD65 knockdown. No such change was observed in FVB mice treated with control shRNA lentiviral particles under same surgical protocol.

Conclusion: Strain differences in tinnitus behavior are correlated with GAD65 reduction in auditory cortex following NIHL. Cortical GAD65 knockdown is sufficient to induce gap detection impairment in a tinnitus-resistant strain. Taken together, these results suggest a link between cortical GAD65 reduction and a NIHL-induced putative tinnitus behavior. Genetic differences are an important, yet under-considered factor in tinnitus research. Our results suggest a biological pathway that might influence individual differences in tinnitus susceptibility in humans.

[1]Yang S, Weiner BD, Zhang LS, Cho S-J, Bao S. PNAS, 2011;108(36): 14974-14979.

[2]Turner JG, Brozoski TJ, Bauer CA, Parrish JL, Myers K, Hughes LF, Caspary DM. Behav Neurosci, 2006; 120(1): 188-95.

01:45 - 03:15 p.m.

SESSION 3: Pharmacological Treatment Chairs: J Marco, P Smith

EFFECTS OF FUROSEMIDE ON CENTRAL HYPERACTIVITY AND TINNITUS IN A GUINEA PIG MODEL

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Hearing loss causes increased spontaneous activity (hyperactivity) in the central auditory pathways and this phenomenon has been suggested as a neural substrate for tinnitus. Using a guinea pig model, we have shown that acoustic trauma results in hearing loss, the development of hyperactivity in neurons in the inferior colliculus (IC), and tinnitus. Importantly, in previous studies we have demonstrated that for some time after cochlear trauma (up to 6 weeks), central hyperactivity is still dependent on peripheral afferent drive and only later becomes centralized and independent of afferent input (1). This suggests there might be a "therapeutic window" for early-onset tinnitus, using treatments that reduce afferent firing. This observation also suggests a physiological explanation for the partial success with tinnitus treatment using furosemide (2), a drug that is known to reduce the spontaneous firing of the auditory afferent nerve fibres.

Objectives: We investigated in our guinea pig model the efficacy of furosemide in reducing hyperactivity and tinnitus at early time-points after acoustic trauma.

Methods: For acoustic trauma adult guinea pigs were exposed unilaterally to a 10 kHz, 124 dB SPL continuous tone for 2 hours under general anaesthesia and allowed to recover. To assess hyperactivity, spontaneous firing rates and characteristic frequency of IC neurons were obtained using extracellular single neuron recordings. Tinnitus was assessed using gap prepulse inhibition of acoustic startle (GPIAS). Furosemide was administered intraperitoneally (i.p. 80 mg/kg). To verify the effect of furosemide on spontaneous firing of the auditory afferent nerve fibres measurements of the spectrum of the neural noise (SNN) were made using round window recording.

Results: At time-points between 2 and 4 weeks after acoustic trauma, furosemide caused a 40 to 60% decrease in SNN and simultaneously significantly reduced the mean spontaneous firing rate in the IC (8.1±1.1 before furosemide vs 2.0±0.5 spikes/sec after furosemide; $p<0.001$). GPIAS experiments confirmed the presence of tinnitus in some animals. Preliminary data from these latter experiments (n=5) also suggest a reduction of tinnitus in these animals after an injection with furosemide, i.e. an increase in gap detection was observed.

Conclusion: Our results confirm previous observations that i.p. furosemide reduces spontaneous firing of auditory afferents, most likely by a reduction in endocochlear potential. In addition, furosemide reduced hyperactivity in the IC, most likely as a result of the decreased spontaneous firing of the auditory nerve fibres, in line with our previous work (1). Most importantly, our results suggest that furosemide can suppress the behavioural signs of tinnitus in our animal model. Our data strengthens the argument that hyperactivity is involved in the generation of tinnitus and supports the notion that there may be a therapeutic window for some time after acoustic trauma.

1. Mulders WHAM, Robertson D. Neuroscience, 2011; 192:753-760.

2. Risey JA, Guth PS, Amedee RG. Int Tinnitus J, 1995; 1:99-103.

AUT3, A KV3.1 POSITIVE MODULATOR, SUPPRESSES CHRONIC NOISE-INDUCED TINNITUS IN A RAT MODEL

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Kv3.1 channels are voltage-gated potassium channels that enable fast repolarization of the neuronal action potential, and are essential for the high frequency, high fidelity firing of neurons in the auditory brainstem and midbrain. Altered activity of these neurons has been implicated in the generation of tinnitus induced by noise exposure. Furthermore, loss of Kv3 channel function has been observed shortly after noise exposure, which may contribute to the maladaptive plasticity leading to the emergence of tinnitus. In the current study, 20 Long Evans rats (and 10 sham controls) were exposed to a unilateral 116 dB, 16 kHz octave-band noise for one hour in order to induce temporary hearing loss and chronic

tinnitus. Thirty days after the noise exposure, a subset of approximately half of the noise-exposed rats demonstrated deficits in auditory gap processing, consistent with the presence of tinnitus. All 30 rats were administered 30 and 60 mg/kg of AUT3 (a Kv3.1 positive modulator) and vehicle in a counterbalanced order, with 48-hours washout between treatments. Both the 30 and 60 mg/kg doses of AUT3 abolished evidence of tinnitus, while the drug had no effect on the behavior of control animals or noise-exposed animals without tinnitus. These results suggest that AUT3 has potential in the treatment of chronic tinnitus associated with noise-induced hearing loss.

EFFECT OF EARLY TREATMENT WITH L-BACLOFEN ON THE DEVELOPMENT OF TINNITUS INDUCED BY ACOUSTIC TRAUMA IN RATS

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Background: Chronic tinnitus is a debilitating condition affecting approximately 10% of the population and there are very limited drug treatment options, mainly due to a lack of understanding of the underlying mechanisms. The prevailing view is that tinnitus is generated by neuronal hyperactivity in the brain. Therefore, drugs that reduce hyperactivity are sometimes prescribed. 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 initiating a short period of L-baclofen treatment soon after noise trauma.

Materials and Methods: Thirty-two male Wistar rats were divided into 4 groups (n = 8 per group): Sham-Vehicle, Sham-Baclofen, Acoustic trauma-Vehicle and Acoustic trauma-Baclofen. The acoustic trauma consisted of a 16 kHz, 115 dB pure tone delivered unilaterally for 1 h under anaesthesia. Vehicle or L-baclofen (5 mg/kg, s.c.) was administered at 30 min after the acoustic trauma and then once a day for 5 days. The behavioural signs of tinnitus in each rat were measured by a conditioned lick suppression paradigm at various time points after acoustic trauma.

Results: When tested at 1 month after the acoustic trauma and the drug treatment, there was a significant downward shift of the frequency discrimination curve in acoustic trauma-exposed animals compared to sham controls in response to various acoustic stimuli, which is a behavioural indication of tinnitus. The drug treatment elevated the curve of the Acoustic trauma-Baclofen group compared to the Acoustic trauma-Vehicle group; however, the difference between these two groups was not statistically significant. Similar results were observed at 3 months after the acoustic trauma.

Conclusion: Early treatment with L-baclofen following acoustic trauma may provide partial prevention of the development of tinnitus in rats.

SAFETY AND PRACTICAL ASPECTS OF INTRATYMPANIC INJECTIONS FOR TINNITUS THERAPY – RESULTS AND INSIGHTS FROM THE CLINICAL DEVELOPMENT OF AM-101

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5 Private ENT practice, Tarnowskie Góry, Poland;
6 Auris Medical AG, Basel, Switzerland

Objectives: Since the 1940s, various attempts have been made to treat peripheral tinnitus by way of intratympanic (i.t.) injection. However, in spite of its compelling advantages, namely the highly targeted drug delivery with minimal systemic exposure, this administration route did not find widespread use so far – primarily due to the lack of specific and effective medication. In recent years the i.t. approach saw renewed interest thanks to a better understanding of local pharmacokinetics and the development of new drug treatments for inner ear disorders such as tinnitus. While usually considered a safe and straightforward procedure by otolaryngologists, there has been a dearth of comprehensive safety data on i.t. injections. As part of the clinical development of AM-101, a small molecule NMDA receptor antagonist for i.t. treatment of acute inner ear tinnitus, procedure related safety outcomes could be systematically collected and analysed.

Methods: Safety outcome data from 2 completed double blind randomised placebo controlled clinical trials with AM-101 were compiled, comprising 272 tinnitus patients who received more than 700 i.t. injections in total. Approximately 0.25 mL of the study drug was administered either in a single dose or 3 doses over 3 consecutive days through a paracentesis in the posterior-inferior quadrant of the tympanic membrane or – following otoendoscopy – in the anterior-superior to anterior-inferior region. For local anaesthesia, xylocaine was applied; for the injection either spinal needles or bent microsuction cannulas were used. Safety was evaluated by the frequency of clinically relevant changes in hearing thresholds and by the type and incidence of adverse events. Outcomes were compared with data from published studies identified through a Pubmed literature search.

Results: Overall, i.t. injections were well tolerated by participants in the AM-101 studies. Adverse events occurred in low numbers only and were mostly of transient nature and mild to moderate severity. They included changes in tinnitus perception and hearing while the eardrum was still open and, rarely, transient caloric vertigo, ear or injection site pain or middle ear

inflammation. Procedure related study withdrawals occurred very infrequently. While incidences of adverse events were shown to be higher in other studies, they appear to be influenced by local intolerances to the drug or drug formulation under evaluation.

Conclusion: When carried out with due care and following some "best practices", an i.t. injection is indeed a safe and well tolerated procedure. Proper patient information prior to the procedure is important for its good acceptance.

NANOQUINONE Q10 AS A PROMISING TREATMENT FOR TINNITUS IN A SUBGROUP OF PATIENTS

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Aims: In our previous pilot study with small sample (20 patients), we have demonstrated that nanoquinone (Coenzyme Q10 in nanodispersion) diminishes tinnitus-induced distress in a group of patients, as per tinnitus questionnaire (TQ) score (1). An interesting finding about the responder group was their low endogenous Q10 serum concentration. Here, we present the results of a double blind, placebo-controlled randomized study performed with tinnitus patients selected based on a low endogenous values of CoQ10 in serum.

Methods: This investigation was a prospective, double blind, placebo controlled randomized study. Between the year 2008 and 2012, CoQ10 concentration was screened in serum of 229 patients with chronic tinnitus. Fifty-eight patients had the serum CoQ10 concentration below normal values of 0.6 µg/ml (lipid-corrected CoQ10 below 0.194 µmol/mol) and were included in the study after signing written consent. Of those 58 patients, five (four from nanoquinone and one from placebo group) dropped out for various reasons. The verum group (20 persons) has received CoQ10 in a liquid form of nanoquinone @ 100 mg/40 drops three times a day (Sanomit®, MSE Pharmaceutika GmbH, Bad Homburg, Germany). The control group (23 persons) has received placebo (40 drops three times a day). The concentration of CoQ10 in serum was controlled at day zero and at four and 12 weeks after the onset of study. Tinnitus-induced distress was measured at the same time points.

Results: Four and 12 weeks after the onset of study, the concentration of CoQ10 has increased in serum of all patients receiving nanoquinone. In this group, a statistically significant decrease of tinnitus-induced distress restricted to male patients was observed. In detail, 4 weeks after the onset of treatment, the male nanoquinone group had mean TQ score of 21.000 (vs. mean TQ 37.267 in placebo group) and following 12 weeks of treatment mean TQ score of 18.364 (vs. mean TQ 39.421 in placebo group). Analysis of variance and Tukey's studentized range test confirmed the significance of differences between the male study groups (p less than 0.05). Significant differences between nanoquinone and placebo groups of men were seen within all TQ subscales.

Conclusion: Of 229 patients with chronic tinnitus, 25% had abnormally low CoQ10 concentration in serum. Supplementation of this group with nanoquinone resulted in significantly improved tinnitus-distress in male patients. Our results suggest possible role of reversible mitochondrial insufficiency as a tinnitus cause in a subgroup of patients.

(1)Khan M, Gross J, Haupt H, Jainz A, Niklowitz P, Scherer H, Schmidt FP, Klapp BF, Reisshauer A, Mazurek B., Otolaryngol Head Neck Surg.2007:72-7.

01:45 - 03:15 p.m.
SESSION 4:
CBT / TRT
Chairs: L Roberts, G Searchfield

MINDFULNESS-BASED TINNITUS STRESS REDUCTION PILOT STUDY: A SYMPTOM PERCEPTION SHIFT PROGRAM

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Abstract: Estimates suggest that 50-million people in the United States experience tinnitus. For 16-million Americans, tinnitus is a chronic condition that severely impacts quality of life; common clinical symptoms include significant sleep disorder, depression, and anxiety. The exact physiological causes of tinnitus are often unknown, making it difficult to treat; interventions often meet with only variable success. This pilot study aims to investigate whether Mindfulness Based Tinnitus Stress Reduction (MBTSR), may be a beneficial treatment for chronic tinnitus.

Methods: Eight tinnitus patients who had previously received Tinnitus Counseling at the UCSF Audiology Clinic participated in the MBTSR program. Using a pre-post intervention design, mean differences were calculated. Benefits were measured by a reduction in clinical symptoms, if present, and a tinnitus symptom perception shift. Tinnitus symptom activity and discomfort as well as psychological outcomes were assessed by self-report questionnaires. Both quantitative and participant comments were gathered.

Results: Results indicate that Effect Sizes, if supported by a larger study, may be clinically significant and demonstrate a substantial decrease for items measuring perceived handicap of tinnitus (VAS d=.99; THI d=.69), an increase in HRQoL in the area of social functioning (d=.70) (SF-36), as well as a substantial increase in the mindfulness quality of non-judging (d=1.29) (FFMQ). Moderate levels of change in mindfulness were suggested by an increase in observing (d=.46), reactivity to inner experience (d=.52), and describe (d=.57) items as measured by the FFMQ. A moderate decrease was also suggested in Depression (d=.52), Anxiety (d=.41), and Somatization (d=.58) (SCL-90-R), tinnitus awareness

(d=.64), and overall mental health indexes (d=.62) (SF-36). Change scores across all measures moved in hypothesized directions.

Conclusions: This pilot study provides preliminary evidence that an eight-week MBTSR program may be an effective intervention for treating chronic tinnitus and co-morbid symptoms. These promising findings warrant further investigation with a randomized controlled trial.

COGNITIVE-BEHAVIORAL SELF-HELP INTERVENTIONS IN TINNITUS: A META-ANALYSIS

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Objectives: Cognitive-behavioural therapy delivered in a face-to-face setting is probably the most promising method for the treatment of tinnitus distress. In the last decade cognitive-behavioural techniques have also been applied as self-help interventions via bibliotherapy or the Internet. So far, no meta-analysis exists on the efficacy of these recently developed interventions. Thus, the present study is a review and meta-analysis on the efficacy of cognitive-behavioural self-help interventions for tinnitus.

Methods: Randomized controlled trials were identified by searching in databases (ISI Web of Knowledge, PubMed, Cochrane library, PSYNDEX) and by manual search. Ten studies with 1188 participants in total were included in the meta-analysis. Participants were 49.2 years old and had tinnitus for 5.2 years.

Results: Self-help interventions significantly reduced tinnitus distress (d = 0.48) and depressiveness (d = 0.25) compared to a passive control (e.g., information only, discussion forums) at post-assessment. There was no difference to the active controls (group treatment). The presence of therapists and the methodological quality of the studies did not influence the results. Sensitivity analysis revealed that there might be a publication bias regarding the comparison to the active control.

Conclusion: However, the results suggest that cognitive-behavioural self-help interventions are an effective treatment for tinnitus distress. Since few studies were identified, this conclusion must be supported by future meta-analyses.

ROLE OF AUDITORY ATTENTION IN THE GENERATION AND MAINTENANCE OF TINNITUS: EVIDENCE AND A MODEL

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Several lines of evidence point to an involvement of the auditory attention system in tinnitus, among them the following: (1) Brain regions that show increased metabolic activity when sounds are processed in attention by normal hearing subjects are also active in individuals with tinnitus compared to individuals without tinnitus. (2) Performance on cognitive tasks requiring attentional resources is impaired in tinnitus sufferers compared to normal hearing controls. (3) In unilateral cases of tinnitus distractor cues presented to one ear fail to call attention to that ear if tinnitus is present in the other ear. (4) Event-related potentials known to be sensitive to attention are not modulated by attention in individuals with tinnitus compared to control subjects, when the responses are evoked by sounds in the tinnitus frequency region. (5) Phantom sounds experienced by normal hearing subjects in a silent environment are suppressed when auditory attention is diverted by engagement in nonauditory tasks. (6) Similarly, tinnitus suffers anecdotally report that their awareness of tinnitus diminishes when they are engaged in cognitively demanding tasks that draw attention away from auditory cues. In this presentation we first review the evidence for the above findings and then describe a neuropsychological model to account for them. The model is based on the assumption that one role of the auditory cortex in normal hearing is to predict sensory state. In tinnitus prediction failure occurs, because the representation on which prediction is based is dominated by aberrant neural activity forged by neuroplastic mechanisms in frequency regions of primary auditory cortex deafferented by hearing loss. The disparity between predicted and obtained afferent inputs activates sustained auditory attention which may contribute to the centralization of neural changes underlying tinnitus. Implications of the model for tinnitus research and treatment are considered. (Supported by NSERC of Canada and the Tinnitus Research Initiative)

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TREATMENT OF DECREASED SOUND TOLERANCE WITH TRT: THEORY AND CLINICAL IMPLEMENTATION

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Definitions: Decreased Sound Tolerance (DST) occurs when a subject exhibits negative reactions (e.g., discomfort, annoyance, pain) as a result of exposure to every-day sounds that would not evoke such aversive reactions in the average listener. It can be the sole problem, or co-exist with other complaints, e.g., tinnitus. DST can result from hyperacusis, misophonia, or a combination of both of these conditions.

In pure hyperacusis, the intensity of the negative reaction is determined solely by the physical characteristics of the offending sound, e.g., its spectrum and intensity; the context in which the sound occurs, and its subjective meaning are not important. In pure misophonia reactions to sound are NOT simply related to physical parameters of a sound, but depend on previous association with a bothersome sound and the context in which the sound occurs. Misophonia can include a variety of negative emotions, e.g., dislike, annoyance, hate, discomfort, fear. In practice hyperacusis and misophonia frequently occur together. Behavioral as well as neurophysiological mechanism-based definitions of hyperacusis and misophonia will be presented and discussed.

Diagnosis: Pure tone Loudness Discomfort Levels are insufficient for the diagnosis and characterization of DST. Therefore, taking a detailed patient's history of offending sounds and the context in which they occur, is essential for correct diagnosis. Differentiating whether a patient's DST is due to hyperacusis and/or misophonia is critical for implementing the appropriate treatment. While patients' reactions to sounds may be the same, but treatments are distinctively different and effective treatment for hyperacusis is not helpful for misophonia, and vice versa.

Treatment: Tinnitus Retraining Therapy (TRT) has been used for treatment of hyperacusis since 1990 and for misophonia since 2001. The counseling and sound therapy need to be modified as comparing with TRT used for tinnitus only treatment as well as protocols for optimal use of ear-level instrumentation. While treatment of hyperacusis with desensitization approach is relatively straightforward, treatment for tinnitus or misophonia is more complex. For misophonia specific 4 protocols are utilized. The proper diagnosis and treatment of hyperacusis and/or misophonia frequently result in complete resolution of DST in affected patients.

Conclusion: Tinnitus Retraining Therapy is an effective treatment option for both hyperacusis and/or misophonia.

TREATMENT OF TINNITUS AND DECREASED SOUND TOLERANCE WITH TRT IN CHILDREN

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Objective. The presence of clinically significant tinnitus and decreased sound tolerance (DST) in children have been recognized for many years, but both tinnitus and DST are still under appreciated as problems which need to be evaluated and treated. Results presented in literature during last years confirmed that these problems are common in pediatric population, both, with normal hearing and hearing loss.

Children rarely complain of tinnitus spontaneously and their unexplained reactions and suffering are often treated without recognition of tinnitus at all. Severe cases of DST, frequently debilitating, influencing significantly children' lives are easier to identify by care givers, but commonly stay untreated or worsen with time as a consequence of the use of overprotection and / or avoidance strategies.

Tinnitus Retraining Therapy (TRT) has been shown to be an effective treatment option for tinnitus and DST in adults. Since 1990 we are helping patients of all ages including children as young as 4 ½ years old and teenagers. Our patients' population includes children with autism spectrum as well.

Methods. This presentation describes a retrospective analysis of TRT implementation and treatment outcome in children seen in Tinnitus and DST Clinic providing care for all ages.

Results. Taking tinnitus and DST history in children, particularly of young age, is challenging; for professionals, there is a problem in asking specific questions (there is no questionnaire for children), using appropriate to age language; children cannot always properly describe their complaints and they are influenced by caring, protective parents.

Audiological evaluation is not always possible and for youngest children frequently limited to the behavioral audiometry. For the most effective treatment there is a need to assess hearing difficulties, severity of the problem, the degree of distress and impact of problems on child's and family life.

The treatment of children by TRT requires modifications of counseling, including simplification of language, use of easy to understand illustrations, story telling and good explanation of the protocol to parents. The choice of proper sound therapy is crucial. Contrary to common belief, most children do not have problems with accepting ear-level instruments if suggested for them. Choice of background sounds and proper music is important in the speed of recovery. Recognizing the presence of misophonia (decreased tolerance to specific sounds) and applying specific treatment protocols is very important. Good understanding and thoughtful, flexible implementation of the treatment by care givers in case of autistic children with DST is crucial.

There is a trend to achieve faster improvement in tinnitus and hyperacusis in children as compared with adults, with similar time needed to observe positive changes in misophonia.

Conclusion. Proper diagnosis and properly adjusted TRT protocols for tinnitus and DST result in the positive outcome in pediatric patients.

03:45 - 05:15 p.m.

SESSION 5: Research Methology and Infrastructure Chairs: D Hall, M Landgrebe

CLINICAL TRIAL METHODOLOGY FOR CBT BASED INTERVENTIONS

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Current treatment approaches in tinnitus management are diverse, consist of combinations of different treatment elements, and tinnitus diagnostics and outcome assessments differ widely, not only across investigations, but as well across treatment approaches, and clinical settings. The lack of a standard diagnostic algorithm, and therefore heterogeneous outcomes of the existing studies lead to challenges in interpretability and comparability. Moreover, the low methodological quality of studies reveal relatively low levels of evidence for the benefits of any of the investigated approaches. An overall CBT based approach is recommended, since evidence for this approach seems most promising. (Cima, Anderson, Schmidt, & Henry, 2013)

Presently a research protocol is proposed for CBT-based clinical trials. Since most tinnitus treatment protocols in literature are multidisciplinary by nature and usually consist of several therapeutic approaches and counselling, including sound-based therapy, cognitive and behavioural coping techniques, relaxation therapy, stress management, daily life counselling and extensive audiological counselling, a stepped care approach is recommended. Furthermore, little is known about the processes of change as a result of treatment. Important mediators, explaining why a particular tinnitus treatment is beneficial or not, and moderators, providing information about what is beneficial for whom, for the largest part still remain to be discovered.

The methodology
A two group, 2-stepped, single-centre randomized controlled trial was carried out with adult tinnitus patients, with 3 follow-up assessments up to 12 months after randomization. A total of 492 tinnitus patients were included, after which they were allocated to either to Usual Care (UC) or Specialized Care (SC). A basic repeated measures design, with group (UC, SC) as a between subjects factor time (Baseline, follow up 1, follow up 2 and follow up 3) as the within-subject factor was used in an intention to treat analysis. Mixed regression analyses were performed with general health, tinnitus distress and tinnitus annoyance in daily life as dependent variables. (Cima, et al., 2012)

Moderation and Mediation analyses
Furthermore, mild and severe tinnitus sufferers, as measured with the Tinnitus Questionnaire at baseline, appeared to benefit equally from getting SC treatment, instead of UC treatment. These findings support our main hypothesis that a CBT based stepped care approach with elements from TRT, is effective in tinnitus management, both for milder forms of tinnitus suffering as well as for more severe tinnitus incapacitation.

Post-hoc analyses of the data from the RCT revealed that patients in the specialised treatment group were significantly less disturbed by their tinnitus, as a result of decreased tinnitus-related fear. These findings corroborate the notion that CBT has an attenuating effect on fear and fear related behaviours, thereby decreasing tinnitus complaints.(Cima, van Breukelen, et al., 2013)

Experimental data
Following the notion that fear and fear related behaviours are of importance in chronic tinnitus suffering, in an experimental study it was hypothesized that responsiveness to tinnitus is determined by the perceived harmfulness of the tinnitus, leading to, as a result of fearful reactions, depletion of cognitive resources. To test this hypothesis the influence of perceived threat value of neutral tones on responsiveness was studied in a selective attention paradigm. It was hypothesised that performance on a primary decision task is negatively influenced by increased perceived threat of distracting neutral tones.

Cima, R. F. F., Anderson, G. J., Schmidt, C. J., & Henry, J. (2013). Cognitive-behavioral therapy for Tinnitus: A review of literature. Journal of the American Acadamy of Audiology, In press.

Cima, R. F. F., Maes, I. H., Joore, M. A., Scheyen, D. J. W. M., El Refaie, A., Baguley, D. M., et al. (2012). Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. The Lancet, 379(9830), 1951-1959.

Cima, R. F. F., van Breukelen, G. J. P., Maes, I. H., Joore, M. A., Anteunis, L. J. C., & Vlaeyen, J. W. S. (2013). Tinnitus-related fear mediates the effects of a CBT-based specialised tinnitus treatment (Submitted).

THE NATIONAL INSTITUTE FOR HEALTH RESEARCH (NIHR) RESEARCH INNOVATION PATHWAY

Deborah A Hall
NIHR Nottingham Hearing Biomedical Research Unit

In the UK, NIHR commissions and funds NHS, social care and public health research that is essential for delivering its responsibilities in public, health and personal social services. NIHR's role is to develop the research evidence to support decision making by professionals, policy makers and patients, make this evidence available, and encourage its uptake and use in clinical practice. Its annual NIHR budget is about £900M (>€1,000M).

NIHR's objective is to improve the quality, relevance, and focus of research in the NHS and social care by distributing funds in a transparent way after open competition and peer review.

Methods: All major UK government-funded programmes and initiatives fit into a 'research innovation pathway' ('invention-evaluation-adoption-diffusion'). The pathway starts with the creation of an innovation (e.g. basic laboratory research) and ends with its use in a patient care setting. NIHR promotes research that improves diagnosis and evaluates existing and novel interventions.

This presentation will briefly outline a number of NIHR-supported initiatives and describe why they are relevant for tinnitus researchers, clinicians and patients.

- James Lind Alliance brings patients and clinicians together to identify and prioritise treatment uncertainties to define the agenda for relevant clinical research. Tinnitus is one of about 10 completed partnerships.
- UK Database of Uncertainties about the Effects of Treatments publishes treatment uncertainties and research recommendations so that researchers and research funders can take account of where their efforts and resources are needed. Currently 27 uncertainties and 13 research recommendations on tinnitus.
- Research Design Service supports researchers to develop and design high quality research proposals for submission to NIHR and other national, peer-reviewed funding competitions for applied health or social care research.
- NIHR Office for Clinical Research Infrastructure helps public, charity and industry research funders work in partnership with NIHR infrastructure.
- INVOLVE is a national advisory group that supports greater public involvement in NHS, public health and social care research.
- UK Clinical Trials Gateway provides easy to understand information about clinical research trials running in the UK. Two tinnitus trials currently registered.
- UK Cochrane Centre supports the preparation, maintenance and accessibility of systematic reviews of the effects of healthcare interventions produced by 22 Cochrane Review Groups. The Cochrane ENT Disorders Group has so far supported 27 systematic reviews related to tinnitus.
- Centre for Reviews and Dissemination is an international centre engaged exclusively in evidence synthesis in the health field. The Centre manages a number of databases: PROSPERO, Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA).
- Nottingham Hearing Biomedical Research Unit has established a research programme dedicated to tinnitus. Our overall aim is to create reliable knowledge that can underpin evidence-based clinical practice.

Concluding remarks: NIHR support for hearing research includes substantial infrastructure support for two of the major centres of excellence in the UK (Nottingham and London). While the overall spend on tinnitus research is a fraction of the total budget, the targeted nature of the research strategy and the broad infrastructure support helps to ensure that tinnitus research outcomes have impact.

THE TRI TINNITUS DATABASE

Landgrebe M
Social Foundation Bamberg, Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, Bamberg, Germany

Tinnitus represents a heterogeneous condition, which causes significant morbidity in many patients. Up to now, there are different treatment options available from which some patients benefit while they fail in others suggesting that there are different forms of tinnitus, which differ in their pathophysiology and their response to specific treatments. A challenge for tinnitus treatment is therefore the identification of the most promising therapy for the individual patient based on clinical criteria. However most available clinical treatment studies have only enrolled relative small patient samples, making it difficult to identify predictors of treatment response for specific approaches. Furthermore, inter-study comparability is limited due to the use of varying methods of tinnitus measures and different outcome parameters. Taking these limitations of current clinical tinnitus research into account, the TRI database is an international research initiative aiming at collecting data from clinical studies in tinnitus in a standardized manner and following high methodological standards based on an international consensus. This international, multicentric approach enables collection of clinical data from tinnitus patients in a reasonable time. Starting in 2008, the database has rapidly grown. At present, the database contains data from 2758 patients treated in 9 centers in 6 countries. In general, every clinical researcher is invited to contribute to this unique project under the precondition that the defined standards of patient assessment and outcome measurement are followed. With the growing of this high quality dataset, the primary objectives of this research project can be achieved, namely subtypisation of tinnitus and identification of treatment predictors, which will be important steps forward to the ultimate goal in finding a cure for tinnitus!

THE EUROPEAN COST-PROGRAM

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

The European COST proggram is supporting european-wide research networking. The program and the application for a COST Action on tinnitus, which has been submitted, will be presented. The proposed 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 Action aims at substantially speeding up the clinical investigation of new treatments and their translation into marketable products.

03:45 - 05:15 p.m.

SESSION 6: Round Table – Tinnitus Management

Chairs: R Figueiredo, C Morera

THE NEUROVEGETATIVE DISTONIA AS A CAUSE OF PULSATILE TINNITUS: AN INTERESTING RESPONSE TO OSTEOPATHIC MANIPULATION

Juan Luis,Yubero[1,2], Isabel,Diges[1,3], Alejandro, Harguindey1,3)

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[2)] *Osteopathy Juan Yubero Clinic, Madrid (Spain)*
[3)] *Tinnitus and Hyperacusis Unit. ENT Antolí Candela Clinic. Madrid (Spain)*

Objectives: The neurovegetative distonia (NVD) includes several psychological and physical symptoms and syndromes, but its precise meaning continues unclear. We aim at reporting a tinnitus patient whose possible cause is NVD, focusing on the origin of this disorder and the key tissues like the vagus nerve, the respiratory diaphragm or some autonomic plexus, providing patients and professionals with a wider range of perspectives and solutions to avoid tinnitus. Osteopathic clinical and manual tests will be exposed, so that physicians could introduce them in their routine.

Methods: This case refers to a 43 years old male patient with unilateral pulsatile tinnitus in left ear (LE) that had a sudden beginning in the context of a period of anxiety. Patient also presents an old bilateral, neuro-sensorial and symmetric hearing loss caused by an acoustic trauma. The hearing loss had a sudden increase in LE two months before the beginning of the tinnitus. Patient refers mild bilateral hyperacusis and doesn´t present dizziness. Tinnitus is described as buzzing, fluctuating and pulsatile (not synchronized with the heartbeat). He also describes a beat sensation inside the head sometimes focused in one or both ears. Tinnitus increases in head flexion and decreases in head extension and in muscle contraction of the neck (vertex, occipital, left zygomatic and left parietal). From an osteopathic point of view is important to say that patient has previous background of hiatal hernia with past surgery about this problem.

After audiological and otological clinical assessments, patient underwent a classic exploration, which consists of taking arterial pressure, carotid beat, thoracic auscultation, abdominal palpation and exploration of cranial nerves V and VII to XII. Then, a complete osteopathic exploration reveals precise locations of important dysfunctions, with increasing tissue tension or poor mobility. Main findings are in the respiratory diaphragm, the solar plexus, the V cranial nerve, the cervical fascia and the C7-T1 vertebra joint. Main techniques used are inhibitory/desensitizing for soft tissues, high velocity low amplitude (HVLA) and muscle energy for joint dysfunction. Some peak moments with intense tissue´s response are accompanied with gestalt techniques like empty chair o body awareness. Because of the findings in anamnesis and exploration, NVD is suggested as possible diagnostic for this patient.

Results: After the first session, patient referred twelve days of almost full silence of tinnitus, with temporary return during physical effort and fatigue. After a severe gastroenteritis, tinnitus reappeared and more sessions were performed. After the fourth one, treatment has result in absolute silence of tinnitus till the day of this writing, four months after the first session.

Conclusion: Evidence found on tissue´s dysfunction has guided us to structured disorder that can have an origin on the Autonomic Nervous System (ANS). ANS could become dysfunctional over the influence of incomplete emotional processes. It´s essential closing these processes not only for decreasing patient´s anxiety but for enhance the tissue´s response to the treatment whatever it can be. The combined work of manual and psychotherapy is a key point to help patients to get their inner silence.

PHARMACOLOGICAL TREATMENT OF TINNITUS

Andréia Azevedo
OTOSUL, Clinical and Research Center, Volta Redonda, Brazil

Tinnitus is a symptom caused by various medical conditions that can be permanent or temporary. In the latter case, tinnitus may be considered a sequel. Tinnitus is primarily a symptom of medical liability and requires an investigation of possible causes. It usually occurs due to an imbalance between the excitatory and inhibitory neurotransmitters' effects, which can happens in any of the several stations of auditory and para-auditory system. The greatest challenge to the physician is to exactly establish the affected point and also the neurotransmitters involved. Many studies with several drugs have been performed and the general perception is that one drug does not make all patients with tinnitus feel better, but can always bring some benefit for some patients.

Several drugs have been tested and re-tested in different countries, with different climate and financial conditions and probably different tinnitus aetiologies. Additionally, the effects of many of them have been accessed by different models. Most of the results were not replicated and many of them have been condemned to the sentence: "there was no difference between the drug and placebo", which means that even the positive results were not considered sufficient. Tinnitus pharmacological treatment should be re-evaluated and every positive result must be investigated, so that the drug may be helpful to the specifically correlated tinnitus subtype.

05:15 - 06:30 p.m.
POSTER SESSION I

Pathophysiology
guided by
A Møller

P1. MOTOR CORTEX EXCITABILITY AS BIOMARKER FOR NEUROPLASTICITY IN TINNITUS

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Background: Chronic tinnitus is a brain network disorder with involvement of auditory and non-auditory areas. Repetitive transcranial magnetic stimulation (rTMS) over the temporal cortex has been investigated for the treatment of tinnitus. Several small studies suggest that motor cortex excitability is altered in people with tinnitus.

Methods: We analysed retrospectively data from 231 patients with chronic tinnitus and 120 healthy controls by pooling data from different studies. Variables of interest were resting motor threshold (RMT), short-interval intra-cortical inhibition (SICI), intra-cortical facilitation (ICF), and cortical silent period (CSP). 118 patients were tested twice - before and after ten rTMS treatment sessions over the left temporal cortex.

Results: In tinnitus patients SICI and ICF were increased and CSP was shortened as compared to healthy controls. There was no group difference in RMT. Treatment related amelioration of tinnitus symptoms were correlated with normalisations in SICI.

Conclusions: These findings confirm earlier studies of abnormal motor cortex excitability in tinnitus patients. Moreover our longitudinal data suggest that altered SICI may reflect a state parameter, whereas CSP and ICF may rather mirror a trait-like predisposing factor of tinnitus.

P2. MODULATORY EFFECTS OF SPECTRAL ENERGY CONTRASTS ON LATERAL INHIBITION IN THE HUMAN AUDITORY CORTEX

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Introduction: Noise-induced chronic tinnitus seems to be caused by reduced lateral inhibition (LI) in the auditory system resulting in a reorganization of the auditory cortex. Listening to music with a notch filter centered at the tinnitus frequency (tailor-made notched music training, TMNMT) resulted in a reduction of the neural activity evoked by the tinnitus frequency. These findings were argued in terms of LI, assuming that the characteristic frequencies (CF) corresponding to the edge frequency bands (EFB) around the notch are most activated and therefore evoke the greatest LI of neurons corresponding to the center-frequency of the notch. These LI effects depend on the bandwidth of the notch with a narrower notch-bandwidth resulting in a greater LI of neurons corresponding to the center-frequency of the notch. These findings indicate the important role of the EFB.

Objectives: The aim of this study was to investigate the role of the EFB on LI. We tested for a relationship between the activation of neurons corresponding to specific EFB and the LI of neurons corresponding to the center frequency of the notch. This was operationalized in an MEG study by means of a masking paradigm measuring the influence of notched white noise (NWN) with different spectral energy contrasts on a test tone.

Methods: 16 subjects with a normal hearing level participated in this study. Stimuli consisted of five different masker stimuli (MS), which were presented in a randomized order, and a test tone (TS) which was presented between two MS. The MS were white noise with a digital notch centered at 1kHz (NWN). The spectral energy of four MS was manipulated by amplifying respectively attenuating the energy in frequency bandwidths of 3/8 or 7/8 octave on each side of the notch. The TS was a 1kHz pure tone directly followed by a fully amplitude modulated tone with a modulation frequency of 40Hz and a carrier frequency of 1kHz. Equivalent current dipoles were fitted to the N1m respectively the auditory steady state response (ASSR). N1m and ASSR evoked by the TS were analyzed by means of source analysis.

Results: The greatest LI effect was induced in the 3/8 octave amplified condition, whereas the least LI was induced in the 7/8 octave attenuated condition, which was shown by the normalized mean N1m amplitude evoked by the pure tone (3/8 octave amplified < 7/8 octave amplified < NWN < 3/8 octave attenuated < 7/8 octave attenuated). Mean amplitudes of the ASSR evoked by the amplitude modulated tone revealed no significant differences between conditions.

Conclusions: These results highlight the modulatory effects of the energy in the EFB on LI in secondary auditory cortical structures, known to be a major generator of the N1m. Since noise-induced tinnitus perception seems to result in a lack of LI on tinnitus CF, these new insights could be used as a tool for further improvement of tinnitus treatments like the TMNMT.

P3. THE ENIGMA OF THE TINNITUS-FREE DREAM-STATE

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Background: Studies in patients with amputated limbs demonstrate that most of the patients have an intact body image during dreaming, as before amputation, and that phantom sensations fade away during their dreams. It has been hypothesized that during dreaming, a state of decreased consciousness, the embodied and functionally intact body scheme predominates as incoming sensory information is abolished. Similarly, we tried to objectify if tinnitus patients were aware of their phantom sound during the dream state.

Methods: Seventy-eight tinnitus patients with a mean age of 48.78 years (Sd = 12.87) and a mean tinnitus duration of 5.74 years (Sd = 6.96) filled in a questionnaire asking about the awareness of their tinnitus during dreaming.

Results: The questionnaire revealed that 97% of the tinnitus patients perceived no tinnitus during their dreams, while 3% did experienced the phantom sound while dreaming. Two patients denied having dreams at all.

Conclusion: Our study demonstrated that most of the tinnitus patients were not aware of their tinnitus during their dreams, analogous to what is observed for phantom limb perceptions. The unawareness of tinnitus in dreams can theoretically be explained by the Bayesian brain model. During our dreams we create an image of our environment in the absence of sensory input. In normal circumstances incoming information continuously updates our understanding of the environment by the violation of prior expectations. The mismatch between bottom-up sensory information and top-down predictions will not be recorded and the missing auditory input will not be filled in, resulting in the absence of tinnitus in the dream state.

P4. SOUND-TRAUMA-RELATED CHANGES OF ACTIVITY IN CIRCUITS OF THE AUDITORY CORTEX

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Aims/objectives: One of the major risk factors for developing hearing deficits or loss is exposure to intense sounds, which can ultimately lead to chronic tinnitus. Although some kind of peripheral damage is considered to be the initial driving force of many pathophysiological phenomena along the auditory pathway, it is becoming increasingly clear that sound trauma likely leads to temporally structured reorganizations of brain activity. Recent evidence supports the view that chronic tinnitus is related to neuronal plastic changes in auditory cortex due to the partial effective deafferentiation of distinct frequency channels. At the neuronal circuit level, it is however not clear which potentially different roles the different subcircuits in auditory cortex play in the induction, maintenance and recovery from trauma-induced hearing deficits. In this study we use newly developed electrophysiological techniques to study the dynamics of thalamocortically and intracortically relayed activity after acoustic trauma.

Methods: We used a recently developed new technique for dissociating thalamocortical from intracortical contributions to the stimulus-induced neuronal activity in the auditory cortex [1]. The method is based on evaluating the residual current source density (CSD) from laminar CSD recordings in auditory cortex. After induction of hearing loss in Mongolian gerbils (Meriones unguiculatus) by presenting a 2 kHz pure tone at 115 dB SPL for 75 min we characterized the immediate and long-term (4-6 weeks) changes of CSD-derived frequency-response-functions at specific locations within the tonotopic gradient of field AI of the auditory cortex.

Results: At the trauma frequency, sound trauma led to an increase in cortical activation thresholds up to 60 dB. Interestingly, the increase in threshold was not limited to a narrow region surrounding the trauma frequency but extended several octaves towards higher frequencies. This result cannot be explained by the experimentally well-controlled spectrum of the trauma stimulus. A laminar CSD analysis revealed that acoustic trauma led to qualitative changes of the laminar activation patterns characterized by a stronger recruitment of synaptic inputs in infragranular layers and altered supragranular inputs. Moreover, analysis of the residual CSD revealed in addition a different pattern of recruitment of thalamocortical and intracortical contributions. We currently investigate the long-term dynamics of both effects.

Conclusion: Our findings suggest that sound-trauma-induced plastic changes in auditory cortical circuits are long-lasting and not limited to the tonotopic region that corresponds to the spectrum of the trauma stimulus. The newly developed residual CSD analysis revealed a disturbance in the balance of thalamocortical and intracortical circuits as the underlying mechanism of the observed trauma-induced cortical activity changes.

[1]Happel MF, Jeschke M, Ohl FW. J Neurosci, 2010; 30:11114-11127.

P5. MICROGLIA IN THE RAT COCHLEAR NUCLEI: A PLAYER IN TINNITUS-RELATED CIRCUIT REORGANIZATION?

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BACKGROUND- Salicylate and cochlear damage (by noise, drugs or surgery) are the most studied tinnitus inducers in animal models. However, salicylate-induced tinnitus is reversible, whereas cochlear damage-induced tinnitus is not, suggesting some key plastic phenomena differ between the two. Although tinnitus origins are still elusive, hyperactivation of cochlear nuclei (especially DCN) is consistently observed in its early stages, presumably as a result of signals from an unbalanced/damaged periphery; upon chronicization, cochlear nuclei inputs trigger plasticity at higher CNS structures, which eventually become independent from them.

Microglia, the resident macrophage of nervous tissue, has been found to contribute to synaptic plasticity in healthy brains, and to modify its localization and activation state in response to inflammation and tissue damage, regulating the excitability of surrounding neural circuits in several pathological states. In chronic pain, microglial-dependent maladaptive plastic remodeling of the first central station follows peripheral damage. In cochlear nuclei, cochlear destruction rapidly activates and recruits microglia (1). Salicylate is a tinnitus inducer, but also an anti-inflammatory drug which counteracts microglia activation. In this work we started testing the possible role of microglia activation in cochlear nuclei as a trigger for permanent circuital changes.

METHODS- Wistar rats (age: 25 days) either received three salycilate injections (300 mg/kg, i.p, daily), and were sacrificed 2h, 24h and 48h from last treatment (n=18 plus 6 saline-injected controls) or underwent unilateral surgical cochlear destruction (under ether-diazepam anesthesia) by removing cochlear turns with fine forceps, and were sacrificed 15, 30 and 45 days after surgery. After sacrificing, rat heads were placed in carbogen-bubbled Krebs' solution, brains were extracted and placed in 4% PFA. Care was taken not to exceed 6 min between sacrifice and fixation, because times longer than 10 min have been reported to induce tissue damage and microglial activation. After fixation and paraffin inclusion, brains were sliced at 3-10 micron and immunohistochemistry for Iba-1 was performed using DAB staining. The number of microglial cell processes and cochlear nuclei areas were measured using imageJ, by experimenters not aware of the nature (treated or control) of the samples observed.

RESULTS AND CONCLUSIONS- In control conditions, microglial density in cochlear nuclei was 430±262 processes/mm2. After salicylate treatment, density was not significantly different from control (483±236 processes/mm2); no differences were noted between 2h, 24h and 48h samples. Microglial morphology also appeared similar in control and salicylate samples. After cochlear destruction, on the other hand, microglia displayed clear morphological activation signs (thicker processes, larger soma) in the ipsilateral cochlear nuclei, whereas no activated microglia was observed in contralateral nuclei or control animals. We suggest that the anti-inflammatory action of salicylate, by blocking microglial activation, counteracts plastic remodeling of CN neurons, thus keeping tinnitus dependent on peripheral input.

1. Fuentes-Santamaria V, Alvarado JC, Juiz JM J Comp Neurol 2012;520:2974-90.

P7. MODULATION OF AUDITORY CORTICAL RESPONSES BY ATTENTION INSIDE AND OUTSIDE OF THE TINNITUS FREQUENCY REGION

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We recently reported that modulation of the amplitude of the 40-Hz auditory state response (ASSR, localizing to primary auditory cortex) and N1 response (localizing to secondary auditory cortex) 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 forged by neuroplastic mechanisms in the TFR of auditory cortex (this activity underlying the tinnitus percept) may have been resistant to modulation by the auditory attention system in tinnitus sufferers. Alternatively, modulation failure may relate to some feature of the auditory attention system itself in tinnitus. We assessed these hypotheses by determining whether attentional modulation of ASSR and N1 responses is impaired in tinnitus when the 40-Hz AM 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. Normal attentional modulation at 500 Hz in tinnitus and control groups but not at 5 kHz in tinnitus would be consistent with tinnitus-related neural activity as the source of the modulation deficit. Alternatively, modulation failure at 500 Hz in the tinnitus group but not in controls would suggest a more general effect of tinnitus on the auditory attention system. Results will be reported at the Valencia TRI meeting. (Supported by NSERC of Canada)

1. Roberts LE, Bosnyak DJ, Thompson DC. Front Syst Neurosci, 2012; doi: 10.3389/fnsys.2012.00040).

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P8. HEADACHE IN TINNITUS: FINDINGS OF A QUESTIONNAIRE SURVEY

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Background: Treatment of chronic tinnitus is still a challenge and treatment effects are characterized by high inter-individual variability. This might be related to limited knowledge about the pathophysiology of this condition. Identifying putative sub-types (e.g., somatosensory tinnitus) might help to discover individual efficient therapies. A lot of patients with tinnitus report headache. However, it is not clear if this is only a coincidence by chance as incidence of headache is high in the general population. Here we aimed to conduct a questionnaire survey to find out if headache and tinnitus are inter-dependent conditions.

Methods: Patients of the Center Regensburg (Germany) of Tinnitus Research Initiative database who declared that they are suffering from headache were invited via letter to fill in a headache questionnaire and specific questions with respect to the interdependence of tinnitus and headache. Tinnitus distress was measures with the tinnitus questionnaire total score.

Results: 39.0% (n=489) out of 1254 patients of the database had headache. 10.6% (n=193) of these patients could be included in the analysis as they completely filled in the questions. 44.6% (n=86) suffered from migraine, 13.0% (n=25) from tension-type headache, 5.7% (n=11) from a combination of both headache types, and 4.1% (n=8) from cluster headache. Headache in 32.6% (n=63) could not be classified. Several variables indicate an association of both conditions independent from the headache type: coincidence of tinnitus and headache laterality, positive correlation of the number of days with headache and tinnitus distress, high tinnitus distress for patients with onset of the tinnitus before headache or at the same time and for patients with reciprocal acute and chronic interference of both conditions.

Bilateral and left-sided headache were associated with distress, vertigo, temporomandibular joint (TMJ) complaints, neck pain, and current psychiatric treatment in contrast to patients with right-sided and no headache. Bilateral headache was associated with hyperacusis. Headache laterality was not associated with other characteristics such as hearing level, tinnitus duration, modulation by somatic manoeuvres, maskability by sounds, and onset related events.

With respect to headache type, each type of headache resulted in higher distress (peaking for cluster headache) and in higher prevalence for vertigo, TMJ complaints, and neck pain. Patients with migraine could rather modulate their tinnitus by somatic manoeuvres, had higher hyperacusis scores, and were more often in current psychiatric treatment. Headache type was not associated with other characteristics such as hearing level, tinnitus duration, maskability by sounds, and onset related events.

Conclusions: With respect to population based prevalence headache seem to be under-represented in chronic tinnitus. In contrast, the prevalence of migraine and cluster headache is increased, and the prevalence of tension-type headache is decreased. One main finding is that the interdependence of headache and tinnitus lead to higher tinnitus distress, especially for bilateral, left-sided, and cluster headache. Furthermore, patients with tinnitus and migraine might represent one distinct sub-type in chronic tinnitus probably mediated by dysfunctional trigeminal nerve activity.

P9. HYPERACUSIS IN TINNITUS: A TRI DATABASAE ANALYSIS

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Background: Hyperacusis is a common medical condition in chronic tinnitus. However, not every patient with tinnitus has hyperacusis and vice versa. Thus, patients with hyperacusis might display a putative sub-group in tinnitus. Here we aimed to analyze chronic tinnitus patients with and without hyperacusis with respect to clinical and demographic characteristics.

Methods: We analyzed 1713 patients enclosed in the Tinnitus Research Initiative database with respect to demographic variables (age, gender), audiology characteristics (laterality, hearing level, etc.), questionnaires (tinnitus questionnaire, quality of life, etc.), and tinnitus rating scales (loudness, annoyance, etc.).

Hyperacusis was defined by two questions: “Do sounds cause you pain or physical discomfort? (Answers: Yes, No, I don’t know)” and “Do you have a problem tolerating sounds because they often seem much too loud? That is, do you often find too loud or hurtful sounds which other people around you find quite comfortable? (Answers: never, rarely, sometimes, usually, always)”.

Results: Both questions were highly correlated and showed comparable results. Hyperacusis was associated with younger age, pulsatile tinnitus, modulation by somatic maneuvers, noise, stress, sleep, and somatic complaints, higher number of treatments, current psychiatric treatment, and higher scores in tinnitus, depression, and quality of life questionnaires, and in numeric rating scales. Patients with hyperacusis rated the pitch and loudness of their tinnitus higher and the

hearing inferior which was in contrast to audiology measures.

Conclusions: Our preliminary analysis indicates that hyperacusis in tinnitus is related to higher distress. Additionally, clinical characteristics (e.g., younger age) might argue for the existence of a putative sub-type. Divergences between subjective and objective measures might be the expression of a hypersensitive sensory processing in these patients.

P10. INVESTIGATING THE BRAIN "CONNECTOME" OF BLAST-INDUCED TINNITUS: SOME INITIAL OBSERVATIONS OF A RESTING-STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING (RS-FMRI) CONNECTIVITY ANALYSIS

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Aims/Objectives: To investigate whole brain connectivity under the effects of tinnitus following blast over pressures using resting state functional magnetic resonance imaging (RS-fMRI) connectivity analysis. Research has shown that single or multiple exposures to blasts can produce complex and heterogeneous changes in the brain. Consequently, it is not surprising that the entity of blast-induced tinnitus and associated neural activity in the central nervous system is poorly understood. Therefore, to improve this state-of-affairs, methodological strategies capable of global functional analysis are needed. RS-fMRI represents one of several contemporary neuroimaging-based paradigms which can assess the spontaneous activities of both whole-brain and particular regions-of-interest (ROI), and can lead to the development of testable hypotheses to advance the knowledge base in this area.

Methods: We applied RS-fMRI connectivity analysis to 13 adults with blast-induced tinnitus and compared results to 7 normal controls without tinnitus. RS-fMRI data were collected on a Siemens Verio 3T scanner using an Gradient Echo EPI sequence with following scanning protocol: TR/TE = 2500/30 ms, 3.3 x 3.3 x 3.3 mm3 isotropic voxels, and 43 axial slices to cover the whole brain. For preprocessing, all functional images were first co-registered and normalized to Montreal Neurological Institute (MNI) space, 6 movement parameters generated during co-registration were regressed out, then data were detrended to remove baseline drifting, low-pass filtered (0.01~0.08 Hz), and spatially smoothed using a Gaussian filter with 6 mm full width at half maximum. To calculate the correlation matrix, 90 brain regions from the Automated Anatomical Labeling (AAL) atlas, also in MNI space, were used as a ROI to extract the corresponding signal time courses, and then the autocorrelation coefficient between every pair of the ROIs were calculated to create the correlation matrix for each subject.

Results: While the patterns of correlation coefficients in the connectivity matrix were similar between the two groups, the overall connectivity level was notably higher in the blast vs. the normal control group. Interestingly, connectivity between the thalamus and occipital lobe, inferior frontal lobe and cuneus and between cuneus and occipital lobe was significantly higher in the blast group. While the inter-subject deviation of the correlation coefficients was similar for both groups, in the area of occipital lobe, cuneus, and fusiform areas, very low inter-subject variation was observed. These results suggest elevated whole-brain connectivity for the blast-induced tinnitus group, while certain brain regions were more affected than others.

Conclusion: The generalized increase in connectivity may be consistent with neurophysiologic studies of tinnitus, where increases in neural hyperactivity, neural synchrony across brain areas, and other factors could have an influence on these results. Keep in mind however, that the blast wave becomes a compression wave in the brain, inducing various structural and neurobiochemical effects on the whole-brain scale. Therefore, blast-induced differences in connectivity analysis may be a unique entity, in large part because modality specific (auditory) effects may not necessarily be the only sensory modality or brain area/pathway affected under these circumstances. Lastly, we emphasize that a larger sample size is needed to validate and extend these results.

P11. EVALUATION OF THE ACOUSTIC COORDINATED RESET® NEUROMODULATION DEVICE FOR TINNITUS: STUDY PROTOCOL FOR A DOUBLE-BLIND RANDOMISED CONTROLLED TRIAL

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Current theories of tinnitus assume that the phantom sound is generated either through increased spontaneous activity of neurons in the auditory brain, or through pathological synchrony of the spontaneous neuronal discharge, or a combination of both factors. Tass et al [1] recently conducted a proof of concept study testing a number of acoustic stimulation strategies. Potentially therapeutic sound stimuli were derived according to a paradigm assumed to disrupt hyper-synchronous neuronal activity and promote plasticity that stabilises a state of asynchronous spontaneous activity. This would correspond to a permanent reduction of tinnitus. The proof of concept study, conducted in Germany, confirmed the safety of the acoustic stimulation for use in tinnitus and exploratory results indicated modulation of tinnitus-related pathological synchronous activity with potential therapeutic benefit. The most effective stimulation paradigm is now used clinically as the Acoustic Coordinated Reset (CR®) Neuromodulation sound therapy device.

To determine the efficacy of CR® Neuromodulation we devised a powered, two-centre randomised controlled trial (RCT) according to the reporting standards defined in the CONSORT statement. The RCT design also addresses

the recent call for an international standard within the tinnitus community [2]. The design uses a between-subjects comparison with minimised allocation of participants to treatment and placebo groups. A minimisation approach was selected to ensure that the two groups are balanced with respect to age, gender, hearing, and baseline tinnitus severity. The protocol ensures double blinding, with crossover of the placebo group to receive the proprietary intervention after 12 weeks. The primary endpoints are the 12 week pre- and post-treatment measures of efficacy, namely validated and sensitive questionnaire measures of tinnitus severity and handicap. The trial is also designed to capture changes in tinnitus quality (pitch, loudness, bandwidth), and changes in tinnitus-related pathological synchronous brain activity using electroencephalography. Here we present the protocol for this trial to highlight elements of design that we see as necessary to determine a confident estimate of the efficacy of CR® Neuromodulation for tinnitus.

1. *Tass PA, Adamchic I, Freund H-J, von Stackelberg T, Hauptmann C. Rest Neurol Neurosci 2012; 30:137-59.*
2. *Landgrebe M, Azevedo A, Baguley D, et al. J Psychosom Res. 2012; 73: 112-21.*

P12. COMPARISON OF RECENT TINNITUS TREATMENT'S EFFECT SIZES

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Aims/Objectives: A number of new tinnitus treatment studies have been reported, but the relative clinical significance of these findings often remains obscure. Many of the more rigorous medical journals have begun insisting that researchers publish the Effect Sizes (ES's) of their clinical outcomes, and so provide a meaningful evidenced-based index of how consistency effective the treatments actually are.

Methods: Cohen's d Effect Sizes (ES's) were calculated on recent tinnitus treatments that used the two most common indexes of tinnitus distress, the THI & TRQ. These are both highly validated psychometric questionnaire measures of symptoms that have been found to simultaneously display virtually identical changes over the same therapies. Many studies were excluded due to inadequate measures or reporting. The relative performance of each eligible treatment was tabled to compare outcomes at discrete time intervals. To maximize comparability, they also were stratified according to level of experimental rigor.

Results: A new multi-modal treatment incorporating CBT and TRT was found to be superior to a standard of care group (average effect vs. minor effect). Other CBT-alone studies were found to have progressively lower ES's, according to whether they were 1:1 clinical contact, group counseling or internet-based.

None of the eligible pharmacological/homeopathic/ vitamin supplement studies reviewed were found to display Cohen's d ES's > 0.5 (minor effect) range. Outlined separately are the other studies (such as soundcure, notch-out music, electrical stimulation, and most vitamin/pharmacological treatments), as they did not use well-established and/or clinically meaningful long-term measures.

In the first randomized controlled study of hearing aids vs. noise generators in a TRT protocol, no significant differences were found, but their standard deviations were not published, so ES's couldn't be calculated.

A recent clinical review of various hearing aids, although not a randomized controlled study, published results showing ES's in the substantial range, with greatest results when the frequency of the patient's tinnitus pitch was low enough to be within the frequency response of their hearing aids.

One recent retrospective review of the Acoustic Desensitization Protocol (conducted in a highly abbreviated form), displayed markedly lower ES's than prior studies. Their noise generator group (non-randomized) displayed ES's that were much higher than any other studies of those devices to date. Another new independent study of ADP was published, displaying ES's in the substantial region, and of equivalent value to prior studies.

Conclusions: These ES calculations demonstrate that the treatments which simultaneously address the audiological, psychological and neurological components of tinnitus distress are the most consistently effective, and fastest to reduce distress. This was most apparent in structured 1:1 clinical rehabilitation programs. Overall, this innovative analysis did not uncover evidence of any new paradigm shifts in actual clinical significance, and found that the standard of evidence for most tinnitus treatments was still rather low.

P13. UK VALIDATION OF THE TINNITUS FUNCTIONAL INDEX (TFI): DISCRIMINANT AND CONVERGENT VALIDITY

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Background: The current standard questionnaire used in the UK for clinical assessment is the Tinnitus Handicap Inventory1. This was developed as a diagnostic tool to measure tinnitus severity. Even though it lacks sensitivity to treatment-related changes in tinnitus it is also often used as an outcome measures in both clinical practice and research. Other alternative tinnitus questionnaires are limited to be used either as a measure of severity OR as a measure of change, but not both. To address this, the Tinnitus Functional Index (TFI)[2] was developed to be used as both a diagnostic tool and to be a sensitive measure of treatment-related change, addressing eight separate subscales of tinnitus-related distress. We are currently validating this questionnaire for use in the UK.

Methods: In the first study, presented here, discriminant and convergent validity of the TFI was determined relative to 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). These questionnaires were administered to 109 consecutive tinnitus participants during initial screening for a multi-site clinical trial.

Results: The discriminant validity of the TFI total scores showed low correlations with BAI (r = .226) and moderate to low correlations with the BDI (r = .588). The WHOQOL-BREF subscale scores ranged from low (r = -.142) to moderate correlations (r = -.498) with the TFI total scores. High correlations were observed for the convergent validity between the TFI and THI (r = .790) and the TFI and THQ scores (r = .851). The correlations between the THI total, THQ total and the TFI subscales ranged between r =.227 and r = .798.

Conclusion: The TFI demonstrates low to moderate discriminant validity and high convergent validity. These results indicate that the TFI measures constructs that are independent of the BDI, BAI and WHOQOL-BREF and that are comparable to the THI and THQ dimensions of tinnitus severity.

1. Newman CW, Jacobson GP, Spitzer JB. Arch Otolaryngol Head Neck Surg, 1996; 122:143-148.

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

P14. TINNITUS AND PSYCHOLOGICAL DISTRESS: EVALUATING THE EFFECTIVENESS OF TREATMENT

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The objective of present retrospective study was to estimate the effectiveness of treatment of patients presenting with tinnitus into consideration their specific psychoemotional status.

Materials and Methods: The study included a total of 56 tinnitus patients with tinnitus diagnosed (25 women and 31 men) at the age from 18 to 42 years: 37 (66%) perceived tinnitus unilaterally, 19 (34%) bilaterally. Inclusion criteria: 1) tinnitus as main complaint and reason for consultation, 2) suffering from subjective, 3) chronic tinnitus, 4) no major comorbidity. The intensity of tinnitus was evaluated on Tinnitus Handicap Inventory (THI) and Mini-Tinnitus Questionnaire (Mini -TQ), the tonal auditory threshold and phonometry. 17 patients exhibiting moderate emotional lability (group 1) were treated with choline alfoscerate and vitamins of group B. Those characterized by enhanced emotional lability (21 patients) were given psychotherapy and treated with choline alfoscerate and vitamins of group B (group 2). Antidepressant drugs (selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs)) have been used to treat tinnitus in 18 patients with depressive symptoms (group 3).

Results: The follow-up testing has demonstrated that the best results were achieved in the patients receiving SSRIs and SNRIs drug despite minimal changes of the results of phonometry. In group 3 after the therapy questionnaire improved significantly ($p<0.05$): the severity of tinnitus was reduced more than by half in 72% of the patients and totally disappeared in 28% of the patients. In group 2 the severity of tinnitus was reduced more than by half in 62% of the patients and totally disappeared in 19% of the patients, whereas in group 1 the severity of tinnitus remained unchanged in 35% of the patients, despite significantly changes of the results of phonometry ($p<0.05$).

Conclusion: These results demonstrate that correction of the psychoemotional status significantly improves the quality of life in the patients with tinnitus.

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P15. SPEECH-IN-NOISE TEST WITH AMPLITUDE MODULATED NOISE IN NORMAL HEARING SUBJECTS WITH AND WITHOUT TINNITUS

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Background: The amplitude-modulated noise is a speech-weighted noise modulated with a square wave. Early research demonstrates that subjects with a normal hearing, have a better signal- to-noise ratio with noise modulated with frequencies between 10 Hz and 20 Hz in comparison to a speech weighted noise. Persons with hearing loss seem to have less benefit from the temporal gaps in the noise. This phenomenon is due to the reduced temporal resolution and the reduced audibility. Our hypothesis is that people with tinnitus have also less benefit from the temporal gaps than persons with no tinnitus.

Method and patients: The LIST, a Dutch sentence test, was taken within 27 patients without and with tinnitus. 3 different maskers were used as noise: speech weighted noise, amplitude modulated noise with a square wave of 10 Hz (AM-10) and 15 Hz (AM-15). The patients without and with tinnitus had a normal hearing, respectively mean PTA of 3,24 dBHL and 6, 98 dBHL. The mean age of the group of patients without tinnitus was 29 years old and for the group of patients with tinnitus the mean age was 40 years old.

Results: An independent t-test was performed. Patients with tinnitus had a significantly lower signal-to-noise ratio in comparison with patients without tinnitus. For LIST with speech weighted noise a difference of 2,05 dB was found ($p<0,001$; $t=3,859$), for AM-10 the difference was

3,86 dB (p=0,004; t=3,059), and for AM-15 the difference was 2,81 dB (p=0,015; t=2,548).

Conclusion: Patients with tinnitus had a significant lower speech comprehension in noise than patient with no tinnitus. The difference is the biggest with AM-10 as masker noise. We can conclude that patients with tinnitus have less benefit from the temporal gaps.

Acknowledgements: We thank the Stavros Niarchos Foundation and TOP-BOF mandate of the University of Antwerp for the financial support for tinnitus research.

P16. HOW MUCH ADDITIONAL INFORMATION IS PROVIDED BY THE HIGH-FREQUENCY AUDIOGRAM IN TINNITUS PATIENTS WITH NORMAL STANDARD AUDIOGRAM?

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Objective: The majority of tinnitus patients suffer from hearing loss. But a significant proportion of tinnitus patients show normal hearing thresholds in the pure tone audiogram. It has been argued that the pure tone audiogram is not sensitive for all forms of hearing impairment and the complementary performance of a high frequency audiogram has been proposed for the diagnostic set-up of tinnitus patients. Here we aimed to investigate, whether the results of the high frequency audiogram provide relevant additional information in tinnitus patients with normal standard audiogram. In detail we compared patients with normal and pathological high frequency audiogram with respect to their demographic and clinical characteristics.

Methods: From the database of the Tinnitus Clinic of the University Regensburg we identified 75 patients with normal hearing thresholds in the pure tone audiogram. We then contrasted patients with normal and pathological high-frequency audiogram and compared these two groups with respect to tinnitus severity, laterality, duration, tinnitus pitch, the presentation of selected somatic symptoms and triggers of tinnitus onset.

Results: Patients with pathological high-frequency audiogram were significantly older and had higher scores on the TQ and the THI in comparison to patients with normal high-frequency audiogram. Furthermore, there was an association of high frequency audiograms and the laterality of tinnitus: patients with left and bilateral tinnitus had more pronounced high frequency hearing loss in the left ear.

Conclusion: In summary, our data indicate, that in patients with normal hearing in the pure tone audiogram some additional information is provided by the high frequency audiogram. The association between tinnitus laterality and asymmetry of the high frequency audiogram suggests a potential causal role for the high frequency hearing loss in tinnitus etiopathogenesis.

P17. AFFECTED SPEECH PERCEPTION IN TINNITUS PATIENTS

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Objective: Tinnitus is frequently associated with hearing loss. However also tinnitus patients with normal pure tone audiogram frequently complain about difficulties with speech perception in background noise and for some of them this is their most disturbing symptom. Here we were interested whether the subjectively reported difficulties with speech perception can also be detected by an objective test.

Methods: We investigated 106 consecutive patients presenting at the Interdisciplinary Tinnitus Clinic at the University of Regensburg. In addition to a detailed audiological assessment including pure and high frequency audiogram speech perception was evaluated by a short subjective questionnaire and by the Göttinger speech audiogram. In addition to the comparison of subjective and objective measurements the relationship with demographic and clinical tinnitus characteristics was analysed.

Results: Subjective complaints of speech perception were reflected by worse results in the Göttinger speech audiogram. Speech perception difficulties were related to older age and to subjectively reported concentration difficulties.

Conclusion: Speech perception difficulties are frequent complaints among tinnitus patients and are not only related to hearing function, but also to age and concentration difficulties.

P18. COMPARING A SOFTWARE TOOL FOR SELF-ADMINISTERED TINNITUS PITCH MATCHING WITH A STANDARDIZED AUDIOMETRIC PROCEDURE

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Objectives: Tinnitus retraining therapy (TRT) is composed Objectives: Measurement of tinnitus characteristics such as pitch matching is often a requirement for research focusing on neurophysiological aspects of tinnitus or tinnitus management trainings. Therefore it is crucial to develop and compare procedures to perform reliable measurements of tinnitus pitch, e.g. the tinnitus frequency of tonal tinnitus. For this reason we have developed an application for self-administered tinnitus pitch matching that was compared with a standardized audiometric procedure.

Methods: Eighteen patients with chronic tonal tinnitus participated in two sessions of pitch matching tasks. In the audiometric procedure the investigator adjusted the frequency and loudness of pure tones led by the responses of the patient and performed a two-forced-choice test and an octave confusion test with the seven before matched pitches. In the self-administered procedure patients performed an automated recursive two-interval forced choice test on an iPod, also including loudness matching and an octave confusion test. In addition a likeness rating was administered after the second session. Test-retest reliability of both methods as well as the likeness ratings for obtained tinnitus-pitch matches were compared.

Results: Preliminary analyses indicate higher test-retest reliability for the self-administered test procedure than for the audiometric procedure. Also patients rated the self-administered procedure as more easy and comfortable in use.

Conclusion: The employment of self-administered tinnitus-pitch matching procedures on a mobile device is feasible and easier in use. Although testing with different procedures provides more information about the ability of patients to match their tinnitus pitch.

P19. EFFICACY OF TAILORED PSYCHOTROPIC TREATMENT IN TINNITUS PATIENTS WITH PSYCHIATRIC DISORDER IN CO-MORBIDITY: A FOLLOW-UP STUDY

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Background. Psychiatric comorbidity in subjects who seek help for tinnitus problems is frequent – it is reported to reach 60% by some research studies(1). Such comorbidity appears to be correlated with tinnitus gravity scores measured by the Tinnitus Handicap Inventory (THI)(2). All clinical trials conducted in order to test the efficacy of a single psychotropic drug on the reduction of tinnitus produced inconclusive and contradictory evidence(3).

The aim of this study is to evaluate the efficacy of tailored tinnitus treatment in reducing THI scores in a population of tinnitus patients with psychiatric comorbidity.

Materials and Methods: Patients with psychiatric co-morbidity at time T0 were detected among the population of patients who request help at our tinnitus centre (at Policlinico Umberto I in Rome) and their psychopathological profile was screened and described using the methodology individuated by our team(2): THI test, Global Scale Index (GSI) sub-scale of the Symptom Checklist-90-R (SCL-90-R), Stress-related Vulnerability Scale (VRS), subsequent psychiatric assessment and diagnostic coding as according to the DSMIV-TR criteria. At time T1, after a 6-month treatment consisting in an individually tailored psychotropic therapy, patients underwent a follow up with the same tests battery used at time T0.

The goal of treatment was to reach a score of <36 (cut off level according to our previous study) for the THI test at the follow up.

Results. Among the 169 patients enrolled in this 6-month study, 86 patients were detected (50.88% of the global sample) to be affected by psychiatric comorbidity; the average THI baseline score (= 55.62± 16.91) significantly correlates (Pearson R test ; $p<0.01$) with both psychopathology (GSI scores) and stress levels (VRS scores). At the follow up 70 patients, i.e. 81.39% of those with psychiatric comorbidity (39 F and 31 M; aged 58.10 on average) showed a THI <36 at completion of the study. Patients who did not obtain a follow up THI score lower than 36 showed the following results: 3 patients were substantially unchanged, 5 improved but did not obtain a score lower than 36, and 8 dropped out of the study. Differences between time T0 and T1 resulted significant (T test; $p<0.001$) for what concerns THI (Δ=-36.68), VRS (Δ=-7.33) and GSI (Δ=-0.39).

Conclusions. Tailored psychotropic treatment administered to tinnitus patients, in parallel with ENT diagnostic evaluation and treatments, produces significant improvements on both level of tinnitus distress and global quality of life of the subjects affected.

References

1) *Malakouti S, Mahmoudian M, Alifattahi N, Salehi M. Comorbidity of chronic tinnitus and mental disorders.Int Tinnitus J. 2011;16(2):118-22.*
2) *Salviati M, Macrì F, Terlizzi S, Melcore C, Provenzano A, Capparelli E,Altissimi G, Cianfrone G. The Tinnitus Handicap Inventory as a Screening Test for Psychiatric Comorbidity in Patients with Tinnitus. Psychosomatics. 2012 Dec 6.doi:pii: S0033-3182(12)00088-6. 10.1016/j.psym.2012.05.007. [Epub ahead of print]*
3) *Belli H, Belli S, Oktay MF, Ural C. Psychopathological dimensions of tinnitus and psychopharmacologic approaches in its treatment. Gen Hosp Psychiatry. 2012 May-Jun;34(3):282-9. doi: 10.1016/j.genhosppsych.2011.12.006. Epub 2012 Jan 27*

P20. TIANEPTINE: A POSSIBLE ACTION ON NEURONAL PLASTICITY IN TINNITUS PATIENTS: A PRELIMINARY 16-WEEK PROSPECTIVE OPEN-LABEL TRIAL
PRELIMINARY POSITIVE RESULTS OF TIANEPTINE TO TREAT TINNITUS IN AN OPEN TRIAL

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BACKGROUND: Tianeptine is a…. Therefore, it might influence tinnitus mechanisms mediated by these neurotransmitters.

OBJECTIVE: To determine if Tianeptine can reduce tinnitus and access whether a further controlled study is warranted

DESIGN: An open-label, single-center, prospective study in which all participants received the treatment condition.

METHODS: tianeptine was administered at 12.5 mg 3 times a day for 12 weeks. Subjects were evaluated at pretreament and at, week 2, 4, 8, 12 and 16.

20 subjects were screened and 15 subjects, who met the inclusion criteria, were recruited.

Tinnitus minimum masking level (MML), The Tinnitus Handicap Inventory (THI), OH NO Tinnitus annoyance scale, Clinical Global Impression - Improvement scale were administered. The presence of side effects was investigated.

Three outcome variables were selected in this preliminary analysis: MML,THI and tinnitus annoyance scale. Data was obtained by subtracting baseline score´s from week 12's scores. Data was interpreted on an intention to treat analysis.

RESULTS: Changes on THI scores ranged from 12 to 80 points at 12 weeks , mean value 42.53 (Std = 20.69) (p=.833).

Changes on tinnitus annoyance scale: ranged from 1 to 10 points at 12 weeks, mean value 5.87 (Std=2.56 (p=.012).

Changes on tinnitus magnitude: MML (15/15 patients) ranged from 7.6 to 86 dB (mean 27.57 dB, std=19.69) at baseline and from 2 to 26 dB (mean= 11.95 dB, std=7.99dB) at 12 weeks (8/15 patients) (p=006).

Side effects were……, but were uncommon.

CONCLUSION: these results indicate that tianeptine is a promising drug to mitigate tinnitus. Effects on tinnitus magnitude were impressive. A randomized controlled trial is necessary, using criteria that could identify subgroups of tinnitus patients who are likely responsive to this medication.

Individual data:

Tinnitus Annoyance Scale (0-10)
Tinnius Handicap Inventory (THI)
Minimum Masking Level (MML)

P21. MULTISENSORY CONGRUENCE TREATMENT FOR TINNITUS

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Background: It has been demonstrated that sensory stimuli have the ability to influence the perception of stimuli in another modality, and that the presence of congruent cross-modal features facilitates attentional control towards the incoming stimulus.

We performed two studies with multisensory stimulation based on the hypothesis that rhythmical congruency of cross-modal stimuli helps to target attention away from their tinnitus

Methods: Two experiments were executed in patients with chronic, non-pulsatile tinnitus. The first study included 18 patients who all underwent 3 different sessions (duration of 10 minutes) of sensory stimulation: 1) stimulation of the vestibular system by a rocking pillow, 2) auditory stimulation by a sea wave sound and 3) the combination of the rocking pillow and sea wave sound.

The second study consisted of 7 male patients, who received multisensory stimulation (10 sessions of 30 minutes) consisting of visual and auditory triggers in combination with somatosensory stimulation consisting of transcutaneous electrical stimulation of the C2 dermatome (6 Hz, 2 mA, ISI 3).

Results: The first study performing rhythmically congruent multisensory stimulation by the rocking pillow and sea wave sound demonstrated a significant decrease in tinnitus loudness and annoyance, with a more pronounced effect compared to solitary auditory or vestibular stimulation. But neither tinnitus loudness nor annoyance was decreased by the combination of visual, auditory and C2 stimulation in the second study.

Conclusion: Currently, we cannot conclude that multisensory stimulation is an effective treatment option for tinnitus, although is suggests that drawing attention away from the tinnitus sound by rhythmically congruent cross-modal sensory stimuli is a treatment option, but further research is necessary to explore the optimal stimulation design.

P22. A UNIVERSITY BASED TINNITUS MANAGEMENT PROGRAM: STRUCTURE AND EXPERIENCE

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The aim of this poster is to share knowledge and experience gained over 15 years since establishment of a tinnitus program within an existing university clinic. We will share the structure and content of our program, including patient flow, services and treatments offered, and statistics on subscription to the various services/treatments offered. The intent is to stimulate conversation with others in similar clinical settings, and to offer advice to those in process of starting a clinical service for tinnitus management.

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P23. THE TREATMENT OF DI BARTOLOMEO'S SYNDROME: THE PATULOUS EUSTACHIAN TUBE ANOMALY AND EMERGING PATHOGNOMONIC SYMPTOMS OF AUTOPHONY AND A PLUGGED EAR

Di Bartolomeo, J and Di Bartolomeo, M. (Presenter: Tyler RS)
Ear Foundation, Santa Barbara, CA

Aims/Objectives: To identify the unique clinical symptoms associated with the development of a Patulous Eustachian Tube (PET) disorder and to establish the diagnosis in the clinical examination alone.

Methods: The Food and Drug Administration (FDA) Investigational New Drug (IND) study - included clinical phases I, II and III for a double blind, random study of 160 subjects. Post-clinical trials – included direct patient participation in the social media medical forum, resulting in the identification and treatment of an additional 3,000 patients internationally from more than 20 countries during the past four years.

Results: National Organization of Rare Disorders (NORD) granted PET Orphan Disorder status #96-988. The clinical trial center was established in Santa Barbara CA. Subjects came to enroll in the study from the United States, North America, European nations, Asia, England and Australia that participated in the randomized double-blind study. Results were dramatic and significant relief of their pathognomonic symptom of autophony and associated symptom of a plugged ear, with normal otoscopic examination.

The study resulted in the development of a new generation drug-free treatment which does not require a prescription. The study of the drug-free product continues in a medical forum on the social media managed by a support group of those patients whose patulous eustachian tube disorder was successfully treated under the IND study.

Since this forum was established, over 4,000 inquiries were received and over 3,500 patients were treated with the drug-free product, comprised of essential nutrients, vitamin C metabolites with enhanced antioxidant properties with increased bioavailability achieved in specific manufacturing processes. The results were extremely favorable in over 85% of those who received the product internationally.

Conclusion: The incidence of Di Bartolomeo's Syndrome of autophony and tubal tinnitus unknown prior to the 20th century has emerged during the 21st century as a result of modern medicine, cultural changes, autonomic tubal dyssynchrony in otherwise healthy individuals.

References:

1. *DiBartolomeo JR. A New Medication to Control Patulous Eustachian Tube Disorders. The American Journal of Otology, July 1992, 13:323-327.*
2. *DiBartolomeo JR, Henry DF, DiBartolomeo M. Patulous Eustachian Tube Disorders - A New Nasal Medication. The New Frontiers of Oto-Rhino-Laryngology in Europe, June 1992, 1:219-221.*

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P24. TENSOR TYMPANI SYNDROME (TTTS): ONE CASE

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The Tensor Tympani Syndrome (TTTS) is little known. The typical symptoms may be confused and attributed to other pathologies. TTTS knowledge is important to make a correct diagnosis and treatment.

The tensor tympani muscle's abnormal activity has been described in environment with exposition to sudden and unexpected loud sound (acoustic shock injury)[1] and temporomandibular joint disorders in stressed people. Common symptomatology is observed in otic symptoms like aural pain, tinnitus, vertigo, hyperacusis/ phonophobia, otic fullness sensation and numbness or burning sensation around the ear. Not understanding these symptoms and their prolongation in time will trigger emotional reactions such as anxiety, depression and hypervigilance.

We report a case in which the main symptoms were otic fullness and hyperacusis. Dysfunction of Eustachian tube was diagnostic of and was indicated eardrum tubes. It is the case of a forty eight years old male who presented otic pain, fullness otic, tinnitus and hyperacusis four years ago. These symptoms appeared after exposure to severe gun shot. At that time he had to travel a lot by plane which worsened the symptoms. In addition, he was advised to wear earplugs which worsened the symptoms

even more. After that, he received surgical indication to put an ear ventilation tube.

Method: we follow the department protocol with Questionnaires, Anamnesis, ENT exploration, Audiology study (pure tone audiometry and speech audiometry, tympanometry and discomfort levels).

Two Questionnaires: the Tinnitus Handicap Inventory (THI) obtained six points (no disability) and the Nelting test of hyperacusis (THS) obtained twenty nine points (very serious disabilities). Anamnesis: it is important to note the exposition to sudden noise record, as well as hyperacusis, fullness otic, important labour stress, anxiety reactions to unexpected situations and hypervigilance to environmental sounds. Tinnitus is not significant for him.

Audiology study: normal pure tone audiometry and speech audiometry; tympanogram typo A de Jerger and very high discomfort levels.

Diagnostic. Acoustic shock injury by TTTS.

Treatment: Tinnitus Retraining Therapy (TRT) with Counseling and Sound Therapy.

Counseling: we use Jastreboff's neurophysiologic model1 to explain the peripheral and central auditory pathway, the mechanism of TTTS and stress as a trigger. Sound Therapy: always avoid silent and desensitization therapy[1]. the patient was also referred to a psychosomatic specialist to control stress and anxiety with medical treatment and cognitive therapy.

Follow up: every month or every two months with measurement of discomfort levels until return to normality.

Results: the patient understood his symptoms and the detonator mechanism which led him to calm down. Sound Therapy helped him to correct hyperacusis.

Conclusion: TTTS should be well-known to identify some otic symptoms in order to do the right diagnosis and the proper treatment.

Bibliography

1. *Westcott M. Acoustic shock injury (ASI). Acta Oto-laryngologica 2006; 126:54-58.*

P25. LONG-TERM OUTCOMES OF TINNITUS AFTER TREATMENT OF SUDDEN SENSORINEURAL HEARING LOSS ACCOMPANIED BY TINNITUS

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The aim of this study was to investigate long-term outcomes of tinnitus after steroid therapy in sudden sensorineural hearing loss (SSNHL) accompanied by tinnitus.

Thirty-four patients diagnosed with SSNHL with tinnitus were retrospectively included for this study. All patients underwent systemic steroid therapy and/or intratympanic steroid injection. Clinical and audiological findings, and assessment of tinnitus were performed before and after treatment of SSNHL. Assessment of hearing recovery after treatment was done with Kim's and Siegel's criteria.

The study group consisted of 17 male and 17 female patients. The ages of all patients ranged from 19 to 81 years (mean age, 49.8 years) and the mean follow-up period was 16.5 months. Eight patients (23.5%) had dizziness and medical treatment for tinnitus was done in all patients. Final hearing after treatment evaluated by the two criteria was that complete recovery was approximately 30% and no recovery approximately 40%. Patients showing the poor recovery of final hearing in both Kim's and Siegel's criteria revealed significantly poor global subjective tinnitus score ($p<0.016$ and $p<0.033$, respectively). There was a high correlation between the grades of initial hearing in SSNHL and Kim's criteria ($p<0.029$). However, there was no significant correlation between the grade of initial hearing in SSNHL and global subjective tinnitus score.

Successful treatment results of SSNHL may assure the favorable long-term control of tinnitus.

P26. CLINICAL STUDY ON PATIENT'S DISABILITY IN THE CASE OF UNILATERAL SUDDEN SEONSORINEURAL HEARING LOSS AND TINNITUS

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Introduction; Sudden sensorineural hearing loss (SSNHL) is defined as sudden sensorineural hearing loss of 30 dB or worse in 3 consecutive speech frequencies within 3 days. Tinnitus has been reported to accompany SSNHL in 70–90% of patients. Some patients with sudden sensorineural hearing loss and tinnitus (SSNHL/TN) are not recovered despite full medical therapy. In the early days of SSNHL/TN, most patients concern about unilateral hearing loss. This may result from sudden loss of advantages form binaural hearing. However, quite a few patients whose SSNHL/TN is not recovered are frustrated by residual tinnitus. Some reports support this situation, showing that a sizeable portion of patients with unilateral hearing loss do not perceive the anticipated benefits of the hearing aid (as a result, binaural hearing) and that these may be better served with a unilateral hearing without a hearing aid. Contrary to hearing loss, patients with unilateral tinnitus suffer similarly with those with bilateral tinnitus.

Aims/Objectives; This study aimed to evaluate patient's disability/discomfort which he/she suffers after sudden loss of unilateral hearing as well as attack of tinnitus in the daily living life.

Methods; After MRI, patientswith idiopathic SSNHL/TN were included into the study. Patients with SSHNL with no initial tinnitus or Meniere's disease were carefully

excluded from this study. All of recruited patients were treated with 5 day-schedule treatment including oral administration of steroids (1mg/Kg of body weight) and vasoactive drugs; carbogen; and intravenous administration of dextran. They were further treated with stellate ganglion block for 1 months and oral intake of vasoactive drugs for 3 months. The hearing improvement was determined by comparing the four-tone average (arithmetic mean) of thresholds at 0.5, 1, 2, and 4 kHz on pure-tone audiometry before and 3 months after the treatment. The degree of the hearing recovery was calculated with the use of Siegel's criteria. Tinnitus was subjectively evaluated by tinnitus handicap inventory (THI) before and 3 months after the treatment.

Results; This study demonstrated that there was a discrepancy between hearing improvement and tinntus improvement. However, THI score was significantly improved in hearing improvemet (+) group than in hearing improvemet (-) group. This study showed that THI score was significantly improved at 3 months compared with that before treatment. This study also showed that many patients sufferred from sequeled tinnitus rather than uniaural hearing 3 months after treatment although they concerned about unilateral hearing loss in the early days of SSNHL/TN.

Conclusion; This study suggests that tinnitus in one ear may be more anxious than discomfort from uniaural hearing. Clinicians must try to improve patient's hearing loss in earlier days of SSNHL/TN but they should keep in mind that some patients are troubled with severe tinnitus at the end.

P27. PETROSQUAMOSAL SINUS IN THE TEMPORAL BONE AS A CAUSE OF PULSATILE TINNITUS: A RADIOLOGICAL DETECTION

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Objective: To report a newly evidenced cause of venous pulsatile tinnitus (PT) - the petrosquamosal sinus in the temporal bone with dehiscent cortical plate.

Methods: The case of a 45-year-old woman has presented with an incapacitating objective PT in the left ear for 10 years and undergone dual-phase contrast-enhanced CT, MRI, and DSA.

Results: The venous phase CT showed a petrosquamosal sinus in the left temporal bone that originated at the junction between the transverse and sigmoid sinuses, and traveled in the left temporal bone. The form bifurcation was demonstrated at the anterior end of the petrosquamosal sinus, without anterior communications. A dehiscent cortical plate around the petrosquamosal sinus and an extensive pneumatized temporal bone filled with air were also found. DSA confirmed the presence of the petrosquamosal sinus. The manifestation of the petrosquamosal sinus on DSA resembled that on CT, but the petrosquamosal sinus was not demonstrated on MRI. The symptom of PT disappeared after reconstruction surgery for dehiscent cortical plate.

Conclusion: the petrosquamosal sinus in the temporal bone with dehiscent cortical plate is a newly described treatable cause of PT. Contrast-enhanced CT is recommended as the primary diagnostic tool with the suspicion of the disease. The surgical treatment of such a lesion is an effective and safe method.

P28. SIGMOID SINUS DIVERTICULUM AND PULSATILE TINNITUS: ANALYSIS OF CT SCANS FROM 15 CASES

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Objective: To examine the CT characteristics of sigmoid sinus diverticulum accompanied with pulsatile tinnitus (PT).

Methods: Fifteen PT patients with sigmoid sinus diverticula proven by surgery were recruited after consenting. CT images of 15 patients were obtained and analyzed, including features of diverticula, brain venous systems, integrity of the sigmoid plate, and the degree of temporal bone pneumatization.

Results: Sigmoid sinus diverticulum in the 15 patients located on the same side of PT. Diverticula originated at in the superior curve of sigmoid sinus in 11 patients and the descending segment of sigmoid sinus in 4 patients. Sigmoid sinus diverticula focally eroded into the adjacent mastoid air cells in 12 patients and mastoid cortex in 3 patients. Among 8 patients with unilateral dominant brain venous systems, the diverticula were seen on the dominant side in 7 patients and non-dominant side in 1 patient. In contrast, the other 7 patients showed co-dominant brain venous systems, with 3 presenting diverticula on the right side and 4 on the left. More notably, dehiscent sigmoid plate on the PT side was demonstrated in all patients. In addition, temporal bone hyper-pneumatization exhibited in 9 patients, while good and moderate pneumatization showed in 3 patients respectively.

Conclusion: Dehiscent sigmoid plate and extensive temporal bone pneumatization are two important imaging characteristics of the PT induced by sigmoid sinus diverticulum.

P29. HYPERACUSIS AND OTHER INNER EAR DISORDERS ARE IMPROVING AFTER IRRADIATION WITH PHOTOBIOSTIMULATING LASERS

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Background: There are several theories about pathophysiological mechanisms involved in hyperacusis as an inner ear disease. Authors discuss errors in the regulating processes of amplification of hearing cells. Other theories about the disorder are based upon central sound processing at subcortical level. There are also discussions about the role of certain substances that could activate neurotransmitters that could increase both nervous system cell activity and sound perception. A prospective study of a group of patients who were suffering from several inner ear disorders (Morbus Menière, Tinnitus and other disorders) was made with laser irradiation therapy based upon a photobiostimulation energy protocol. All patients were suffering from different grades of hyperacusis that was measured with a pure tone level audiometer using sound signals, each lasting 0.2 seconds. Previously Zazzio (1) reported in 2010 a conclusion about the positive effect on pain thresholds for all hyperacusis patients treated with a multitherapy based on laser therapy.

Materials and method: Fifty-eight (58) patients were treated twice a week with some dose of low level laser light. A laser device with four laser probes - two emitting intensity or irradiance of 90 mw/cm2 of 650 nm red light wavelength and two probes emitting 300 mW/cm^2 of 808 nm. Near infra red light - were used. The laser probe tips were placed inside the hearing canal. A standard treatment protocol for at least six weeks was used.

Results: Hyperacusis was significantly improving in all patients and we also found that the Auditory Dynamic Range seems to be the best measurement of correlation between the improvement of patient symptoms and the status of cochlear homeostasis. Among hyperacusis patients 98% of the observations have a large improvement of auditory capacity and 78.9% of them reached normal discomfort levels (no hyperacusis) without any statistical correlation between etiologies of disorders. Six weeks of laser light therapy is at least what is required to get significant results.

Conclusion: After therapy all patients had an improvement or a total recovery both on their hyperacusis and often also on other hearing symptoms and disorders. Irradiation of the cochlea with a specific dose of light laser energy produces an obvious improvement in hyperacusis and other auditory disorders. This can be evaluated by comparing the Audiometric Dynamic Range before and after the treatment period. The results confirm that hyperacusis as a disorder is more susceptible to a poor cochlear condition than of other known neurophysiological processes. The role of photobiology effects and Laser Photo-Therapy (LPT) involved in the cochlear homeostasis opens a new approach for the management of hyperacusis and other inner ear disorders.

(1)Zazzio M. Pain threshold Improvement for chronic hyperacusis patients, a prospective clinical study. Photomed Laser Surg. 2010 Jun. 28(3):371-7.

FRIDAY
MAY 17, 2013

09:00 - 10:15 a.m.
PLENARY TALKS

9:00 - 9:40 a.m. – Keynote Speaker
SOUND THERAPY – RELIEF OR TREATMENT: A CLINICAL PERSPECTIVE

GD Searchfield, New Zealand
Section of Audiology and Centre for Brain Research, The University of Auckland, New Zealand

Background/Aims – A tinnitus sound therapy is: the therapeutic use of any sound to alter tinnitus in a positive way. Sound therapies are commonly used alongside psycho-education in audiologically based treatments. The use of sound in the management of tinnitus is not without a number of controversies as to: its merit, mechanism(s), and application. The aim of this review is to consider existing and emerging evidence for sound's ability to relive or treat tinnitus, and present one evidence-informed sound therapy protocol.

Methods – Review of recent psychoacoustic and psychometric evidence for the effect of sound on tinnitus perception, cognition and reaction.

Results – Sound therapy can provide immediate relief and in many cases acts as a treatment. Evidence for sound therapy has not, historically, been strong, but new research is beginning to address this. Psychoacoustic models of tinnitus and sound therapy appear to have fallen out of favour since the emergence of neurophysiological models; however, results are presented that support a psychophysical model of tinnitus sound therapy that incorporates: signal detection, attention, memory and the individual psychology of patients (1).

Conclusion – Sound therapy is beneficial to many patients, but it is not a cure in its current form. An evidence-informed clinical protocol based on adapation level theory (1) is introduced.

1. *Searchfield, G. D., Kobayashi, K., & Sanders, M. (2012). An adaptation level theory of tinnitus audibility. Front Syst Neurosci, 6, 46. doi:10.3389/fnsys.2012.00046.*

9:40 - 10:15 a.m. – Keynote Speaker
SOUND THERAPY – THE BASIC NEUROSCIENTIST'S PERSPECTIVE

A Norena
Aix-Marseille University, France

Sound therapy has long been recognized as a potential means to alleviate tinnitus. Nowadays, it is still a popular approach as it seems natural to use sounds to interfere with the putative causes and/or consequences of tinnitus and it is relatively easy to administrate. A first approach is to mask tinnitus with various external sounds presented in the tinnitus, contralateral or both ears. This approach improves tinnitus condition in some subjects, as tinnitus subjects may prefer hearing a (neutral) masking sound rather than tinnitus (which is often associated to negative beliefs : "tinnitus is the symptom of severe disease", for example). One notes, however, that tinnitus masking is not intended to treat the origins/causes of tinnitus, but rather its consequences (the tinnitus percept and its related distresses). More recently, other sound therapies, inspired by the discoveries made in the field of neurosciences, have been developed to target the origins of tinnitus. All these approaches share the assumption that tinnitus may result from central changes (triggered by sensory deprivation) and that these central changes can be reversed so as to restore a near-normal central organization (not accompanied by tinnitus). These methods differ from each other, however, by the specific action they are intended to produce on the central auditory system. Indeed, while some approaches are intended to normalize the cortical tonotopic map organization, others are aimed at reducing cortical hypersynchrony or cortical hyperactivity. In my talk, I will present an overview on sound therapies, emphasizing the hypothetical origins of tinnitus which motivated these approaches, i.e. the spectro-temporal characteristics of the « therapeutic » acoustic stimulus. The limitations of this class of methods to alleviate tinnitus will also be discussed.

10:45 a.m. - 12:45 p.m.
SESSION 7: Neurostimulation
Chairs: D De Ridder, T Kleinjung

STRIATAL NEUROMODULATION EFFECTS ON TINNITUS

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Background: Deep brain stimulation (DBS) of the basal ganglia is emerging as a candidate therapeutic modality for tinnitus, a phantom sensory disorder manifested by auditory percepts in the absence of external correlates. The predominant neuromodulatory treatment approach is to alter central auditory dysfunctional hyperactivity, plastic change or synchronized oscillations that may underlie tinnitus perception. An alternative treatment approach is to modulate phantom auditory gating function of the dorsal striatum.

Objective: To demonstrate DBS of the dorsal striatum modulates perception of auditory phantoms.

Methods: Two acute human electrical stimulation experiments in area LC, a locus of the caudate nucleus positioned at its anterior body, were performed in 7

interactive adult subjects undergoing surgery to treat movement disorders. Tinnitus loudness was rated on a 0 to 10 scale, sound quality was described qualitatively, and spatial location was referenced to the ears.

Results: Short-term area LC stimulation suppressed tinnitus loudness to a nadir of at least 2 and controllably triggered new phantom tones, clicks, and frequency modulated sounds. Current results suggest the dorsal striatum may play an important role in gating potential auditory phantoms for perceptual awareness. A conceptual basal ganglia model of phantom percept gate control is proposed.

Conclusion: Striatal dysfunction may be a critical feature of bothersome tinnitus. DBS neuromodulation of area LC to treat auditory phantoms could confer healthy restrictive dorsal striatal gate function to reject potential auditory phantoms. Clinical trials are needed to evaluate safety and efficacy of long-term area LC neuromodulation for tinnitus.

THE CINGULATE CORTEX AS TARGET FOR TINNITUS TREATMENT

Dirk De Ridder[1], Kathleen Joos[2], Jan Ost[2], Pieter Van Looy[2], Sven Vanneste[2]

[1] *Dept of Surgical Sciences, University of Otago, New Zealand*
[2] *BRAI²N, University Antwerp, Belgium*

The cingulate gyrus is a phylogenetically old structure interposed between the basal ganglia/thalamus and cortex. It consists of at least 4 subdivisions, each with another function or functions. It has been suggested that the dorsal part of the anterior cingulate gurys (dACC) is a hub involved in emotion, cognition, motivation and autonomic responses.

In tinnitus, the subgenual/pregenual ACC have been implicated in noise-canceling, the pregenual/rostral ACC is involved in the amount of time the tinnitus is perceived and the dACC in distress and chronification of tinnitus. The PCC seems to be involved in cognitive aspects of distress and tinnitus characteristics (pure tone/noise-like tinnitus).

In view of its involvement it makes sense to consider the cingulate cortex as a target for neuromodulation in tinnitus.

It has been shown that double cone coil TMS (AC/DC TMS) can target the dACC. In tinnitus, single session AC/DC TMS can transiently improve tinnitus loudness and distress in a frequency specific manner, and a better effect can be obtained in more patients with repeated sessions. It has also been shown that the tinnitus suppressing effect of bifrontal tDCS is mediated via the pregenual/rostral ACC.

The results of 2 implants targeting the ACC will be described as well as the results of sLORETA neurofeedback targeting the PCC (BA30).

Based on these results the involvement of the ACC in tinnitus will be discussed.

RTMS FOR THE TREATMENT OF TINNITUS: A RANDOMIZED CONTROLLED MULTICENTRIC STUDY

Landgrebe M[1], Joachim Cordes, Andreas Fallgatter, Jacqueline Höppner, Frank Padberg, Carlos-Schönfeldt-Lecuona, Stefan Wolf, Göran Hajak, Peter Eichhammer, Berthold Langguth

[1] *Department of Psychiatry, Psychosomatics, and Psychotherapy, Sozialstiftung Bamberg, Germany*

Introduction: Chronic tinnitus is a frequent disease accompanied in many cases by high morbidity and reduction in quality of life. Despite its high incidence, treatment remains elusive. Aggregated research over the last years has contributed to a deeper understanding of the neurobiological basis of chronic tinnitus and point to the involvement of auditory and non-auditory brain areas. Repetitive transcranial magnetic stimulation (rTMS) is able to non-invasively modulate brain activity. Pilot studies indicate a potential therapeutic effect of rTMS in tinnitus patients, however, sample sizes were small so far. The aim of this study was to evaluate the efficacy and safety of rTMS in tinnitus in a large patient sample.

Methods: 7 study centers participated in this randomized, placebo-controlled trial. From February 2008 until May 2011 a total of 154 patients were enrolled and received 10 sessions of either verum or sham 1Hz-rTMS over the left primary auditory cortex. Effects on tinnitus and accompanying psychiatric symptoms were evaluated using a variety of standardized rating scales (tinnitus questionnaire (TQ), tinnitus handicap inventory (THI), beck depression inventory, etc.).

Results and conclusions: rTMS treatment was well tolerated in all patients. In the primary outcome (change of the TQ-score baseline vs. day 12) no significant difference between both study arms was observed. During the follow-up period, a trend to superiority of verum rTMS could be observed, which did not reach statistical significance. This study shows, that 1Hz-rTMS over the left primary auditory cortex is not superior to placebo treatment.

AUDITORY CORTEX STIMULATION TO SUPPRESS TINNITUS: MECHANISMS AND PARAMETERS

Jinsheng Zhang[1,2], Hao Luo[1], Edward Pace[1], Xueguo Zhang[1], John Moran[1]

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[2] *Department of Communication Sciences & Disorders, Wayne State University College of Liberal Arts & Sciences, Detroit, Michigan, USA*

Numerous treatments such as drugs, noise-masking, Tinnitus Retraining Therapy, Neuromonics, and electrical or magnetic stimulation of the somatosensory structures, vagal nerve, cochlea, cochlear nucleus, prefrontal cortex, and auditory cortex (AC), have yielded variable results, mainly due to limited understanding of the mechanisms underlying tinnitus and its treatments. The AC is a major player subserving tinnitus perception and is frequently targeted for stimulation via AC electrical stimulation (ACES), transcranial magnetic stimulation (TMS) and

direct current stimulation (tDCS). Active clinical studies have shown that ACES, TMS, and tDCS have acute and long-lasting suppressive effects. The drawbacks of most studies are that cortical regions are stimulated instead of etiology-based specific loci and the lack of understanding of the involved mechanisms.

To understand the mechanism of ACES-induced tinnitus suppression, optimize ACES, and improve TMS and tDCS, we established a rat model of ACES and multi-structural electrophysiology. Our results demonstrated that ACES suppressed both tonal and noise tinnitus. The induced tinnitus suppression was accompanied by variable changes in spike firing rate, bursting, neurosynchrony and the tonotopic map. Specifically, following ACES of low-middle frequency loci, the hypersynchrony in tinnitus(+) rats was broadly decreased but was drastically decreased in stimulated and adjacent recording channels. This decrease was accompanied by increased synchrony within the inferior colliculus (IC) and dorsal cochlear nucleus (DCN). When examining inter-center spontaneous synchrony coefficients, we found that the AC IC, AC DCN and IC DCN synchrony was more robust in tinnitus(+) than tinnitus(-) rats. We also found that ACES at 1 pps induced significant reduction in AC IC synchrony and insignificant changes in AC DCN and IC DCN synchrony in both tinnitus(+) and tinnitus(-) rats. The reduction in the AC IC hypersynchrony was greater in tinnitus(+) than tinnitus(-) rats. However, 10 pps ACES did not induce as robust suppression as 1 pps ACES, which is consistent with clinical studies. Furthermore, we found that ACES improved the tuning of the DCN, IC and AC of tinnitus(+) rats and CF-tone-driven I/O functions of AC and IC neurons.

Taken together, the results suggest that the etiology of tinnitus involves structures at different levels and could be mediated by gating and gain control between cortical and subcortical centers; that synergetic down-regulation of synchronized firing in AC neurons and up-regulation of synchrony to enhance neural processing in subcortical neurons may suppress unwanted tinnitus-related activity; that inter-center hypersynchrony may contribute to the etiology of tinnitus; and that improving central auditory processing contributes to tinnitus suppression. The results from the animal model are important for identifying etiology-based stimulation strategies using ACES, which are helpful to improve the efficacy of other clinical tools for cortical stimulation such as TMS and tDCS.

HEAD-TO-HEAD COMPARISON OF TRANSCRANIAL RANDOM NOISE STIMULATION, TRANSCRANIAL AC STIMULATION AND TRANSCRANIAL DC STIMULATION FOR TINNITUS

Kathleen Joos[1], Felipe Fregni[2], Dirk De Ridder[3] & Sven Vanneste[1]

[1] *Translational Neuroscience, Faculty of Medicine, University of Antwerp, Belgium.*
[2] *Laboratory of Neuromodulation, Harvard Medical School, USA.*
[3] *Department of Surgical Sciences, University of Otago, New Zealand.*

Tinnitus is the perception of a sound in the absence of an external sound stimulus. This phantom sound has been related to plastic changes and hyperactivity in the auditory cortex. Different neuromodulation techniques such as TMS and tDCS have been used in an attempt to modify local and distant neuroplasticity as to reduce tinnitus symptoms. Recently, two techniques of pulsed electrical stimulation using weak electrical currents - transcranial alternating current stimulation (tACS) and transcranial random noise stimulation (tRNS) - have also shown significant neuromodulatory effects. In the present study we conducted the first head-to-head comparison of three different transcranial electrical stimulation (tES) techniques, namely tDCS, tACS and tRNS in 111 tinnitus patients by placing the electrodes overlying the auditory cortex bilaterally. The results demonstrated that tRNS induced the larger transient suppresive effect on the tinnitus loudness and the tinnitus related distress as compared to tDCS and tACS. Both tDCS and tACS induced small and non-significant effects on tinnitus symptoms, supporting the superior effects of tRNS as a method for tinnitus suppression.

10:45 a.m. - 12:45 p.m.

SESSION 8:
Tinnitus Pathophysiology: The Auditory Pathway
Chairs: A Norena, R Salvi

SOUND-TRIGGERED SUPPRESSION OF BACKGROUND ACTIVITY IN AUDITORY NEURONS: IMPLICATIONS FOR RESIDUAL INHIBITION OF TINNITUS

S.V. Voytenko, R.J., Longenecker, A.V., Galazyuk.
Northeast Ohio Medical University, Department of Anatomy and Neurobiology, Rootstown, Ohio, USA

Tinnitus can be suppressed briefly following the offset of an external sound. Although this phenomenon, termed “residual inhibition,” has been known for four decades, its underlying cellular mechanism remains unknown.

Our recent work has shown that spontaneous firing in auditory neurons can be suppressed following the offset of an external sound. Since abnormally high spontaneous firing has been linked to tinnitus we hypothesize that sound-triggered suppression of this firing may be the underlying mechanism of residual inhibition. The goal of this research was to determine whether basic characteristics of sound-evoked suppression of

spontaneous firing resemble basic features of residual inhibition.

Methods: This study was conducted on CBA/CaJ mice. Twelve control mice and four mice with behavioral signs of tinnitus were studied. Tinnitus was induced with a narrowband noise centered at 12.5 kHz and 116 dB SPL unilaterally for 1 hour under general anesthesia (Ketamine/Xylazine). Tinnitus was assessed with gap-induced prepulse inhibition of the acoustic startle reflex. Extracellular recordings were performed in the inferior colliculus (IC) in awake restrained animals. Pure tones at neurons' characteristic frequency and/or wideband noise sounds (5 or 30 seconds duration) were presented in the free-field. Firing rates of IC neurons were measured before, during, and after sound presentation.

Results: The vast majority of IC neurons (about 80%) showed spontaneous activity. The firing rates of the neurons in control (unexposed) animals ranged from 0.5 to 110 pulses/s (5 pulses/s, median). Consistent with the results of previous studies, the firing rate in the animals with behavioral signs of tinnitus was greatly increased compared with controls. However, this increase was evident only in the IC contralateral to the exposed ear, whereas the firing rates of neurons in the ipsilateral IC were similar to the control animals. In control animals, about 85% of neurons exhibiting spontaneous firing suppressed their firing following sound offset. This suppression increased with sound duration and lasted an average of about 40 seconds when a sound 30 seconds in duration was presented. The suppression duration also increased with sound level. Interestingly, IC neurons exhibited significantly longer suppression in response to pure tones at the neuron's CF than to wideband noise. If the same sound stimulus was presented several times, the duration of the suppression became increasingly shorter with each presentation. The mice with behavioral signs of tinnitus exhibited sound-triggered suppression similar to that seen in control animals.

Conclusion: The basic characteristics of neuronal suppression in the IC resemble the basic features of residual inhibition of tinnitus. This result strongly suggests that suppression is an underlying mechanism for residual inhibition. Further research is necessary to confirm this by developing a residual inhibition animal model.

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CELL PROLIFERATION IN THE RAT COCHLEAR NUCLEUS FOLLOWING NOISE EXPOSURE.

Zheng, Y. , McNamara, E., Aitken, P. and Smith, P.F*
Dept. of Pharmacology and Toxicology, School of Medical Sciences, and the Brain Health Research Centre, University of Otago, Dunedin, New Zealand.

Background and Aims: Many areas of the brain respond to trauma with an increase in cell proliferation. In neurogenic areas, this may lead to neurogenesis; in other areas it may be an indication of inflammation. We sought to investigate the effects of a type of noise exposure that has been demonstrated to cause tinnitus, on cell proliferation in the cochlear nucleus (CN).

Methods: Rats were exposed to either a 16 kHz, 115 dB pure tone, unilaterally via a speculum inserted into the external auditory canal, for 1 h under anaesthesia, or a sham exposure procedure for the same period of time. In the noise-exposed and sham groups, animals were allowed to recover for 24 h (n = 4 and 5, respectively), 48 h (n = 5 and 5, respectively), 72 h (n = 3 and 5, respectively) or 4 weeks (n = 5 and 3-4, respectively). In order to quantify cell proliferation, 150 mg/kg bromodeoxyuridine (BrdU) was injected (i.p.) 2 h before sacrifice. For newborn cell survival, the same dose of BrdU was injected at 72 h following noise exposure and the rats were sacrificed at 4 weeks after BrdU injection. BrdU immunohistochemistry and stereological cell counting were used to quantify the number of cells expressing BrdU in the ipsilateral and contralateral CN at the various time points.

Results: In the exposed animals, there was a large and significant increase in the number of BrdU-positive cells in the ipsilateral CN at 72 h post-exposure, compared to sham controls (ANOVA treatment x time interaction: $F(2,21) = 28.00$, $P \leq 0.000$). A similar increase was observed in the contralateral CN at this time point, in noise-exposed animals (treatment x time interaction: $F(2,19) = 16.20$, $P \leq 0.000$). However, by 4 weeks post-BrdU injection, this increase in BrdU-positive cells had disappeared in both the ipsilateral and contralateral CN ($P \geq 0.05$ for both sides).

Conclusions: It is possible that the increase in BrdU expression by cells in the bilateral CN following noise exposure is an inflammatory response to the trauma, which may be implicated in the pathogenesis of tinnitus. However, immunohistochemical analysis of the CN at 24, 48 and 72 h post-exposure showed no significant change in interleukin-6 (IL-6) expression compared to sham controls. We are currently investigating the expression of cyclo-oxygenase 1 (COX-1) in the CN following noise exposure. If the increase in cell proliferation is accompanied by an inflammatory response and is implicated in the aetiology of tinnitus, anti-inflammatory drugs may be one avenue for effective drug therapy for the condition.

Supported by the Deafness Research Foundation of New Zealand and the New Zealand Neurological Foundation.

*presenter

NOISE TRAUMA INDUCED DEVELOPMENT OF SUBJECTIVE TINNITUS: PREDISPOSITION AND PREVENTION

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Aims and Objectives: Dysfunction of the inner ear as caused by presbyacusis, injuries or noise traumata may result in subjective tinnitus, but not everyone suffering from one of these diseases develops a tinnitus percept and vice versa. The reasons for these individual differences are still unclear and may explain why different treatments of the disease are beneficial for some patients but not for others. In a hearing impaired animal model we here for the first time compare behavioral and neurophysiological data in specimen with (T) and without (NT) a tinnitus percept that may elucidate why some individuals do develop subjective tinnitus after noise trauma while others do not.

Methods: A total of 35 male Mongolian gerbils (Meriones unguiculatus) were used in this study. An acoustic trauma (2 kHz, 115 dB SPL, 75 min) in deep ketamine-xylazine-anesthesia was used to induce a frequency specific hearing loss (HL) in all animals and the subsequent development of a tinnitus percept in most animals (cf. below). HL was quantified using auditory brainstem response (ABR) and behavioral audiometry (prepulse inhibition (PPI) modulated auditory startle response (ASR)). In addition, two different forms of gap-noise paradigms were used to demonstrate the existence of possible tinnitus percepts and to give a rough estimate of the perceived tinnitus frequencies [cf. 1]. Responses of single and multi-units in primary auditory cortex field AI to tones were recorded before and during multiple recording sessions after the acoustic trauma.

Results: Although noise trauma induced a similar permanent HL in all animals, tinnitus did develop only in about 75% of these animals. NT animals showed higher overall cortical and auditory brainstem activity before noise trauma compared to T animals; that is, animals with low overall neuronal activity in the auditory system seem to be prone to develop tinnitus after noise trauma. Furthermore, T animals showed increased activity of cortical neurons representing the tinnitus frequencies after acoustic trauma, whereas NT animals exhibited an activity decrease at moderate sound intensities by that time. Spontaneous activity was generally increased in T but decreased in NT animals. Plastic changes of tonotopic organization were transient, only seen in T animals with complex temporal dynamics and vanished by the time the tinnitus percept became chronic. As these tonotopic changes in AI and changes in evoked rates at BF were transient in the T animals whereas the increases in spontaneous discharge rate and discharge rate at high, tinnitus-related frequencies persisted beyond one week post trauma, we believe that the latter are the neurophysiological correlates of the tinnitus percept rather than the former.

We propose a model for tinnitus prevention that points to a global inhibitory mechanism in auditory cortex that may prevent tinnitus genesis in animals with high overall activity in the auditory system, whereas this mechanism seems not potent enough for tinnitus prevention in animals with low overall activity.

1. Turner JG, Parrish J. Am J Audiol, 2008; 17:S185-192.

ROLES OF HOMEOSTATIC AND SENSORY MAP PLASTICITY IN HEARING LOSS-INDUCED TINNITUS

Yang S, Jackson W, Weiner B, Zhang LS, Miyakawa A, Gibboni R and Bao S
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Aims/Objectives: Hearing loss-related tinnitus is thought to be caused by elevated spontaneous activity in the neurons of the auditory pathway. Homeostatic and sensory map plasticity have been proposed as mechanisms underlying hearing loss-induced increase in spontaneous activity. We investigated hearing loss-induced tinnitus in two gene knockout (KO) mice with either impaired homeostatic plasticity (the TNFα KO) or sensory map plasticity (the FMR1 KO), to assess their contributions to the phantom perception.

Methods: TNFα and FMR1 KO mice and their respective wildtype controls underwent unilateral noise-induced hearing loss (NIHL, 8kHz, 112dB, 2 hours). A putative tinnitus behavior was measured using a gap detection task 1-5 days before, and 2 and 10 days after NIHL. Homeostatic and sensory map plasticity were examined electrophysiologically. In addition, homeostatic down regulation of GAD65 was also measured in both KO mice and their wildtype controls.

Results: TNFα KO mice had normal cortical map plasticity, but impaired homeostatic regulation of cortical activity and less homeostatic down regulation of GAD65. They showed no impairment in gap detection 10 days after NIHL. FMR1 KO mice were impaired in cortical sensory map plasticity. However, they exhibited stronger impairment in gap detection than their wildtype controls 10 days after NIHL.

Conclusion: Our results suggest that, while homeostatic plasticity may contribute to NIHL-induced tinnitus, sensory map plasticity is probably not required for the hearing loss-induced phantom perception.

1:45 - 3:15 p.m.

SESSION 9: Epidemiology and Prevention Chair: D Hall

NON-OTOLOGIC RISK FACTORS OF 'SIGNIFICANT' TINNITUS: 10-YEAR TRENDS FROM A NESTED CASE-CONTROL STUDY IN THE UK

Deborah A Hall[1], Carlos Martinez[2], Christopher Wallenhorst[2], Don McFerran[3]

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

[2] *PharmaEpi, Frankfurt, Germany*

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Background: Tinnitus assessment and management within the NHS is challenging and the current healthcare system probably utilises its resources inefficiently. A better understanding of risk factors associated with developing tinnitus can inform better allocation of public health resources or target prevention campaigns. This study reports analysis of risk factors for developing a 'significant' tinnitus (sigT) - defined as a recording of tinnitus within GP practice with a requirement for additional health-care resources.

Some population studies have already suggested risk factors including otologic conditions (hearing loss and middle ear infections), head and neck injuries, generalised health status (such as history of smoking), anxiety and depression. But not all reports confirm these risk factors, and interpretation is complicated by different definitions of tinnitus. In addition, the set of factors making up the model affects the adjusted odds ratio (OR) estimates for individual risks.

We have conducted a more extensive analysis of the risk factors for developing sigT than has been achieved hitherto. Here, we report on findings for the non-otologic risk factors.

Methods: We constructed a comprehensive model with 40 putative risk and protective factors according to a broad search of the previous literature. The model included 40 factors: i) Otological disorders (infectious, neoplastic, labyrinthine, other, ii) Use of ototoxic medications, iii) Neurological disorders, iv) Traumatic disorders, v) Orofacial disorders, vi) Systemic disorders (infectious, cardiovascular, cerebrovascular, rheumatological, immune-mediated disease affecting the inner ear, endocrine and metabolic conditions, mood disorders), and vii) general population health factors.

Observational data for NHS patients in England was accessed from two sources: (1) Clinical Practice Research Datalink (CPRD), a primary care database for England and (2) Hospital Episode Statistics (HES), the national statistical data warehouse for England of the care provided by NHS hospitals and for NHS hospital patients treated elsewhere. Two cohorts of all eligible patients were identified between January 2001 and December 2011: an incident sigT cohort with no prior recording of hearing loss or 'non-significant' tinnitus (n=10,157) and a control cohort matched on year of birth, gender, GP practice and index day with no previous sigT (n=39,472). In a case-control analysis, adjusted ORs were estimated using conditional logistic regression for the 40 factors.

Results: Increased risk is indicated by an adjusted OR>1, with confidence intervals that do not overlap with 1. Preliminary results suggest migraine, temporomandibular joint disorder, use of cardiovascular drugs, carotid artery disease, history of rheumatoid arthritis, anxiety, use of non-steroidal anti-inflammatory drug and socioeconomic status, indicating increased risk.

Decreased risk (protection) is indicated by an adjusted OR<1. Again, early results are preliminary but suggest that current smoker, body mass index deviating from optimal weight and pregnancy might be protective.

Conclusion: Using observational data from a large UK population cohort, we report evidence on a large population cohort which sometimes supports, and sometimes contradicts, previous findings. Although preliminary, our findings add important new evidence to open fresh debate on tinnitus risk factors and underpinning mechanisms for its etiology.

TINNITUS AMONG TEENAGERS: SIMPLE FACTS LEADING TO CHRONICITY. WHAT CAN WE DO?

Tanit Ganz Sanchez[1,2], Fernanda Moraes[1], Juliana Casseb[1], Jaci Cota[1], Márcia Kii[1,2], Katya Freire[2]

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Background/objectives: Tinnitus is increasing worldwide. Our previous research with children aged 5 to 12 years showed that 37.7% had tinnitus (19% annoyed). Such alarming data motivated this present research with teenagers because they are more likely to present early ear symptoms due to modern life and they tend not to use ear protection. The objectives of this study are: 1) to estimate the frequency of tinnitus in teenagers and its main characteristics; 2) to propose strategies to future intervention, so as to have this age group better enrolled in early treatment.

Methods: 350 teenagers - aged 11 to 17 years – studying in a private school were invited to participate. So far, after parents´ authorization, 170 students (61.1% males; mean age 14.2 years) underwent a specific questionnaire (targeting tinnitus and potentially risky leisure habits) plus medical and audiological evaluations (otoscopy, pure tone audiometry up to 16kHz, and Loudness Discomfort Levels). The teenagers who have tinnitus were additionally submitted to VAS (0 to 10) for annoyance, as well as to loudness/pitch matching and minimum masking levels. Evaluations were performed within the school and always by the same team of ENTs and audiologists.

Results: According to the questionnaire, 93 teenagers (54.7%) have or have had tinnitus in the past 12 months. Among them, 51.1% notice it preferably or exclusively for hours to a few days after leaving noisy environments, but they do not use ear protection nor decrease the time spent with these leisure activities. There was a high

predominance of bilateral and symmetrical tinnitus (78.5%) and 58.8% did not feel jeopardized at all by the symptom (mean value of VAS for annoyance was 3.57). Out of these 93 students who reported tinnitus, 49 (28.8%) were able to reliably measure pitch and loudness matching inside the acoustic booth, while the other 44 (25.9%) could not detect their tinnitus at the moment of such evaluation. Considering this evaluation, tinnitus pitch varied from 0.25 to 16kHz, predominating between 10 and 12 kHz. Loudness varied greatly from 1 to 29dBSL, with a mean value of 6.9dBSL in the right ear and 7.1 in the left one. There was no statistical difference between right and left ears ($p>0.05$).

Conclusions: This study pointed out to many facts towards chronicity of tinnitus among the teenagers: 1) the surprisingly high frequency of occurrence (54.7% through questionnaire and 28.8% through pitch/loudness matching); 2) the high relation with exposure to loud music in their self-evaluation; 3) the low impact on their daily life (low mean score in VAS), which does not motivate to use ear protection nor to spontaneously seek for early investigation and treatment. In addition, most tinnitus pitches were reliably matched with extended high frequencies (>8 kHz), which are not routinely evaluated by most professionals. In order to break this vicious cycle and enhance the chance of treating and preventing further damage to periphery and central auditory pathways, a more active campaign of awareness should be exhaustive targeted to this age population, including parents at home and teachers at school.

NOISE-INDUCED SYMPTOMS IN A YOUNG POPULATION

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Background: Tinnitus is perceived by 5 to 15% of the adult population. In addition, approximately 9% of the population suffers from hyperacusis, which is very often associated with tinnitus. In an earlier epidemiological study we obtained prevalence data of noise-induced symptoms in adolescents and young adults by use of a questionnaire. In a group of 4000 students, 74.9% often experienced temporary tinnitus after loud music exposure. 18.3% already experienced a permanent tinnitus. In contrast, most students held a neutral attitude towards noise and the use of hearing protection was very limited (< 5%). In the present study we performed individual measurements on young adults in order to assess these symptoms more in detail and to examine the audiological characteristics of young people.

Methods: A group of 80 university students (mean age: 22.35 ± 1.95 years old) underwent a full audiological examination. Audiological testing consisted of: pure-tone audiometry from 125 Hz to 16 kHz, speech-in-noise testing, harmonic/disharmonic intonation testing, and otoacoustic emissions. In addition, the validated Dutch hyperacusis questionnaire (HQ) was filled out by all students as well as the Tinnitus Questionnaire (TQ) (only by students perceiving tinnitus permanently).

Results: 19.4% of the students had hyperacusis according to the HQ. Participants with hyperacusis showed significantly worse hearing thresholds at 4 kHz ($p= 0.035$) and 6 kHz ($p= 0.013$). A permanent tinnitus was perceived by 15% of the total group while 62.5% reported temporary tinnitus after recreational noise exposure. No differences in hearing thresholds were apparent between the tinnitus group and the non-tinnitus group. 17.5% of the students (14 out of 80 students) showed a noise notched configuration on the audiogram at 3, 4 or 6 kHz but this was not significantly different in the tinnitus and non-tinnitus group. Students without tinnitus performed significantly better on speech-in-noise tests than students with tinnitus. The presence of hyperacusis was very strongly ($\chi = 0.76$; $p= 0.025$) positively associated with the presence of permanent tinnitus. Students perceiving tinnitus also showed lower TEOAE 's at 2.8kHz ($p= 0.013$) and lower DPOAE's at 6000Hz ($p= 0.021$).

Conclusions: Hyperacusis and tinnitus seem to be as prevalent in a young population as in an adult population. The strong association between the two symptoms was confirmed by the present study. The study results showed a large prevalence of noise-induced symptoms in young people, temporary as well as permanent. As a result, the focus should be on preventing such noise-induced damage in the future.

Acknowledgements: This research was financially supported by the Stavros Niarchos Foundation and a TOP-BOF mandate of the University Antwerp

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PROGRESSION OF TINNITUS-RELATED DISTRESS IN PATIENTS WITH CHRONIC TINNITUS IN A 6 YEAR PERIOD

Wallhäusser-Franke E[1], Ziegler J[1], Goebel G[2], Hiller W[3], Flor H[4], Lux-Wellenhof G[5], Delb W[1,6]

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5 Frankfurt, Germany , 6 ENT-practice, Kaiserslautern, Germany

Background/Aim: From patient reports there is evidence that tinnitus-related distress may change in patients with chronic subjective tinnitus. We combined data from two large scale self-report surveys with an interval of six years to find out which factors including therapies may influence a change of tinnitus-related distress.

Methods: In 20041 and 20102 self-report questionnaires were sent to all registered patient members of the German Tinnitus Association (Deutsche Tinnitus-Liga, DTL). Data from 4995 questionnaires in 2004 and from 4705 questionnaires in 2010 were entered into the data base. In both questionnaires tinnitus-related distress was recorded with the German Mini Tinnitus Questionnaire (MTQ)1. In addition, the questionnaires contained items regarding tinnitus characteristics, subjective tinnitus loudness, and accompanying problems like hearing impairment, hyperacusis, and vertigo. In 2010 several scales addressed depressivity, anxiety and somatic

symptom severity, and the participants were questioned about therapies that had been carried out.. The results from the 1301 participants who provided data in both surveys are presented.

Results: Already in 2004, 98.5% had their tinnitus since more than 1 year. Between 2004 and 2010, the overall average change of tinnitus-related distress was -0.88 (MTQ, range: 0-24). We concentrated on the subgroup (G1) with an improvement of at least 5 points in the MTQ (n=192), and the subgroup (G2) with an aggravation of at least 5 points (n=114).

In G1, 39.1% had the subjective impression that tinnitus-related distress had decreased, and 30.2% thought that the tinnitus had become louder. From 2004 to 2010 the percentage with hyperacusis (12 to 6%) and vertigo (38 to 25%) decreased considerably. Noteworthy were the advantageous mental health indicators in G1. In 2010, average scores for depressivity, anxiety and somatic symptom severity were lower and resilience was higher than in the other groups. In G1, 80% attended at least one somatic therapy and 55% participated in at least one psychological therapy. For 41% no therapy had helped, 8% benefitted most from somatic therapies, whereas 38% benefitted most from psychological therapies. .

In G2, 48% had the subjective impression that tinnitus-related distress had worsened, the percentage with relevant hyperacusis nearly doubled since 2004, and the percentage with vertigo increased from 24 to 30%. In the 2nd survey, a hallmark of G2 was the high level of depressivity, anxiety and somatic symptom severity together with low resilience. 86% utilized at least one somatic therapy while 52% participated in at least one psychological therapy. 52% indicated that no therapy helped them, while for 11% somatic therapies and for 24% psychological therapies helped best.

Conclusion: Presently, it is more likely that tinnitus patients benefit from psychological therapies. Moreover, the possible occurance of depressivity, anxiety and somatisation should be monitored in chronic tinnitus patients in order to initiate psychological therapies before relevant aggravation of tinnitus-related distress occurs.

1. *Hiller W, Goebel G. Arch Otolaryngol Head Neck Surg. 2006;132:1323-1330.*
2. *Wallhäusser-Franke E, Brade J, Balkenhol T, D'Amelio R, Seegmüller A, Delb W. PLoS One, 2012; 7:4*

1:45- 03:15 p.m.

SESSION 10: Posttraumatic Tinnitus Chairs: J Zhang, S Hébert

TRAUMA ASSOCIATED TINNITUS

Peter M. Kreuzer[1], Michael Landgrebe[1,3], Veronika Vielsmeier[2], Tobias Kleinjung[4], Dirk De Ridder[5], Berthold Langguth[1]

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Abbreviations: TBI=traumatic brain injury; HL=hearing loss; AV=arteriovenous; CD=carotid dissection; CCF=carotid-cavernous fistula; OChD= ossicular chain disruption;

Conflicts of Interest and Source of Funding:

P.K. received travel grants by the European Psychiatric Association, Servier, Pfizer, and Astra Zeneca.

M.L. received travel grants, consultancy and speaker honoraria from Servier, Lundbeck and Lilly.

V.V. is supported by the Tinnitus Research Initiative.

T.K. is supported by the Tinnitus Research Initiative.

DDR is supported by the Tinnitus Research Initiative, Antwerp University TOP Project and has received consultancy fees from SJ Medical Neurodivision.

B.L. is supported by the Deutsche Forschungsgemeinschaft, the American Tinnitus Association and the Tinnitus Research Initiative, he received consultancy and speaker honoraria from Autifony, ANM, Astra Zeneca, Merz, Novartis, Pfizer, Lundbeck and Servier.

Background: Up to 53% of individuals suffering from traumatic brain injuries (TBI) develop tinnitus.

Objective: To review the current literature on trauma-associated tinnitus in order to provide orientation for the clinical management of patients with trauma-associated tinnitus.

Materials: A systematic literature search has been conducted in pubmed-database applying the search terms posttraumatic tinnitus and trauma-associated tinnitus. Results have been complemented by related studies, book chapters and the authors' clinical experience.

Results: Mechanical, pressure-related or noise-related head traumata, but also neck injuries and emotional trauma can cause tinnitus. Exact diagnosis is essential. Disorders such as ossicular chain disruption, traumatic eardrum perforation or perilymphatic fistula can be surgically treated. It should also be considered that pulsatile tinnitus can be a sign of life-threatening disorders such as carotid-cavernous fistulas, arteriovenous malformations and carotid dissections. Also posttraumatic stress disorder should be taken into consideration as a potential contributing factor.

Conclusions: There is an evident mismatch between the high incidence of trauma-associated tinnitus and scarce literature on the topic. A consistent and – at best – standardized assessment of tinnitus- and hearing-related sequelae of trauma is recommended both for the improvement of clinical care and for a deeper understanding of the various pathophysiological mechanisms of trauma-associated tinnitus.

TRAUMA-ASSOCIATED TINNITUS: AUDIOLOGICAL, DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Peter M. Kreuzer[1], Michael Landgrebe[1,2], Martin Schecklmann[1], Susanne Staudinger[1], Berthold Langguth[1] and the TRI Database Study Group*

* **Veronika Vielsmeier, Tobias Kleinjung, Astrid Lehner, Timm B. Poeppl, Ricardo Figueiredo, Andréia Azevedo, Ana Carolina Binetti, Ana Belén Elgoyhen, Marcelo Rates, Claudia Coelho, Sven Vanneste, Dirk De Ridder, Paul van de Heyning, Florian Zeman, Markus Mohr, Michael Koller.**

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Background: Tinnitus can result from different etiologies. Frequently, patients report the development of tinnitus after traumatic injuries. However, to which extent this specific etiologic factor plays a role for the phenomenology of tinnitus is still incompletely understood. Additionally, it remains a matter of debate whether the etiology of tinnitus constitutes a relevant criterion for defining tinnitus subtypes.

Objective: By investigating a worldwide sample of tinnitus patients derived from the Tinnitus Research Initiative (TRI) Database we aimed to identify differences in demographic, clinical and audiological characteristics between tinnitus patients with and without preceding trauma.

Materials: A total of 1.606 patients were investigated. Assessment included demographic data, tinnitus related clinical data, audiologic data, the Tinnitus Handicap Inventory, the Tinnitus Questionnaire, the Beck Depression Inventory, various numeric tinnitus rating scales, and the World Health Organisation Quality of Life Scale (WHOQoL).

Results: Our data clearly indicate differences between tinnitus patients with and without trauma at tinnitus onset. Patients suffering from trauma-associated tinnitus suffer from a higher mental burden than tinnitus patients presenting with phantom perceptions based on other or unknown etiologic factors. This is especially the case for patients with whiplash and head trauma. Patients with posttraumatic noise-related tinnitus experience more frequently hyperacousis, were younger, had longer tinnitus duration, and were more frequently of male gender.

Conclusions: Trauma before tinnitus onset seems to represent a relevant criterion for subtypization of tinnitus. Patients with posttraumatic tinnitus may require specific diagnostic and therapeutic management. A more systematic and – at best - standardized assessment for hearing related sequelae of trauma is needed for a better understanding of the underlying pathophysiology and for developing more tailored treatment approaches as well.

The study was supported by the Tinnitus Research Initiative/TRI (www.tinnitusresearch.org).

A NEUROPSYCHOLOGICAL PROFILE OF BLAST INDUCED TINNITUS

JL Woodard, PE May, MA Sugarman, AL Norman AT Cacace
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Aims/Objectives: In humans, blast-induced tinnitus, concussion-induced tinnitus, and tinnitus induced by blast + concussion are complex entities that are not clearly understood. Our approach to studying this area includes neuropsychological assessment, magnetic resonance imaging, and behavioral and electroacoustic auditory studies. To date, the largest sample we have accumulated is from the group where tinnitus is induced from exposure to blasts. In this study, we investigated relationships between various performance indexes on measures from a computerized neuropsychological battery and indexes of severity and impairment associated with blast-induced tinnitus.

Methods: Sixteen participants (one female) between 26 and 73 years of age (mean age=51.5 years) have been studied to date. Using the computerized neuropsychological testing program (ANAM), there are a number of variables that can be investigated. The principal dependent variables are 1) Median Reaction Time (RT) to Correct Responses; 2) Percent Correct (Accuracy); and 3) Standard Deviation of RT to Correct Responses (SDRTC) to investigate patterns of intra-individual variability. Cognitive measures from ANAM include 1) Simple RT (SRT), repeated twice to evaluate for fatigability; 2) Procedural (Choice) RT (PRO); 3) Mathematical Processing (MTH); 4) Matching-to-Sample (Working Memory; MTS); 5) Code Substitution (Processing Speed; CDS); and 6) Code Substitution

Delayed (delayed incidental recall; CDD). Tinnitus measures included audiometric sensitivity averaged across four frequencies, tinnitus loudness in decibels, and scores from the Tinnitus Handicap Questionnaire (THQ). The mean THQ total score for the sample was 49.1±18.8.

Results: Left ear audiometric sensitivity averaged across four frequencies was significantly ($p<.04$) related to performance accuracy on the MTS task ($r=-.53$, working memory). Audiometric sensitivity in both ears was marginally significantly related ($p< .08$) to performance accuracy during MTH (mathematical processing, r's = -.45 for each ear). Tinnitus loudness in decibels was significantly ($p<.05$) associated with MTH performance accuracy (r = -.51). Median RT on CDS (processing speed) was significantly ($p< .02$) related to audiometric sensitivity in both ears (r's = .62 and .58 for left and right ears, respectively). Similar findings were observed for median RT on PRO (choice RT): r's=.53 and .57 for left and right ears, respectively. Intra-individual variability in RT on CDS (processing speed) was significantly ($p<.05$) associated with audiometric sensitivity in each ear (r's=.56 and .50 for left and right ears, respectively. Intra-individual variability during the simple reaction time task (SRT) was significantly ($p < .03$) related to tinnitus loudness ($r=-.70$), and impairment on the THQ (Social, Emotional, and Behavioral subscale, $r=.61$; Total Score, $r=.54$).

Conclusion: Our results suggest that several aspects of computer-based cognitive performance are associated with tinnitus severity. Specifically, variations in audiometric sensitivity appears to be related to performance accuracy, RT, and intra-individual variability on measures of processing speed, as well as on simple reaction time and math processing performance. Our results for patients with blast-induced tinnitus are consistent with prior research on patients with chronic tinnitus. Slowed RT, increased RT variability, and lower accuracy may be associated with difficulty inhibiting attention to distracting tinnitus signals.

BLAST-INDUCED TINNITUS AND ITS RELATED TRAUMATIC BRAIN INJURY

Jinsheng Zhang[1,2], Hao Luo[1], Jessica Ouyang[1], Laura Lepczyk[1], Edward Pace[1], Xueguo Zhang[1], Gulrez Mahmood[1], Srinivasu Kallakuri[3], Huichao Lu[3], Wei Zhang[1], Michael S. Zheng[1] and John M. Cavanaugh[3]

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Blast shock waves can affect structures with air-fluid interfaces, making the middle and inner ear susceptible to damage. Studies indicate that about 50% of combat personnel exposed to blast trauma developed tinnitus. Often co-occurring with traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD), tinnitus is currently the number one service-related disability affecting military personnel, resulting in over one billion dollars in annual disability compensation. The underlying mechanisms of tinnitus are largely unknown, which has contributed to the lack of reliable treatments. Given the health and economic impact surrounding tinnitus and its related TBI, it is important to investigate its pathophysiology so effective treatments can be developed.

To investigate the mechanisms of blast-induced tinnitus and related TBI, our lab has developed a rat model by using multidisciplinary techniques such as behavioral assays, electrophysiology, immunocytochemistry, MRI-DTI and MEMRI. Our studies demonstrated that blast-induced tinnitus occurred at all frequency bands (noise tinnitus) immediately after blast exposure, which tended to shift to high frequencies (tonal tinnitus) over time. Blast exposure also resulted in loss of consciousness as shown by prolonged duration to surface right. Electrophysiologically, early onset hyperactivity was found in the dorsal cochlear nucleus (DCN) and inferior colliculus (IC), which then shifted to delayed hyperactivity in the auditory cortex (AC). This implies that blast-induced early onset tinnitus may be related to hyperactivity in the brainstem whereas delayed tinnitus may be attributed to hyperactivity in the AC. MEMRI studies showed that blast increased $Mn2+$ accumulation in the auditory brainstem and basolateral nuclei of the amygdala but decreased accumulation in the anterior cingulate cortex. Blast exposed rats also showed significant long lasting astroglial up-regulation identified by glial fibrillary acidic protein immunoreactivity and diffusive axonal injury detected by silver impregnation. The above pathological changes may have contributed to the psychological sequelae of blast-induced tinnitus, TBI and possibly PTSD.

INVESTIGATING THE BRAIN "CONNECTOME" OF BLAST-INDUCED TINNITUS: SOME INITIAL OBSERVATIONS OF A RESTING-STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING (RS-FMRI) CONNECTIVITY ANALYSIS

AT Cacace, Y Ye

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Aims/Objectives: To investigate whole brain connectivity under the effects of tinnitus following blast over pressures using resting state functional magnetic resonance imaging (RS-fMRI) connectivity analysis. Research has shown that single or multiple exposures to blasts can produce complex and heterogeneous changes in the brain. Consequently, it is not surprising that the entity of blast-induced tinnitus and associated neural activity in the central nervous system is poorly understood. Therefore, to improve this state-of-affairs, methodological strategies capable of global functional analysis are needed. RS-fMRI represents one of several contemporary neuroimaging-based paradigms which can assess the spontaneous activities of both whole-brain and particular regions-of-interest (ROI), and can lead to the development of testable hypotheses to advance the knowledge base in this area.

Methods: We applied RS-fMRI connectivity analysis to 13 adults with blast-induced tinnitus and compared results to 7 normal controls without tinnitus. RS-fMRI data were collected on a Siemens Verio 3T scanner using an

Gradient Echo EPI sequence with following scanning protocol: TR/TE = 2500/30 ms, 3.3 x 3.3 x 3.3 mm3 isotropic voxels, and 43 axial slices to cover the whole brain. For preprocessing, all functional images were first co-registered and normalized to Montreal Neurological Institute (MNI) space, 6 movement parameters generated during co-registration were regressed out, then data were detrended to remove baseline drifting, low-pass filtered (0.01~0.08 Hz), and spatially smoothed using a Gaussian filter with 6 mm full width at half maximum. To calculate the correlation matrix, 90 brain regions from the Automated Anatomical Labeling (AAL) atlas, also in MNI space, were used as a ROI to extract the corresponding signal time courses, and then the autocorrelation coefficient between every pair of the ROIs were calculated to create the correlation matrix for each subject.

Results: While the patterns of correlation coefficients in the connectivity matrix were similar between the two groups, the overall connectivity level was notably higher in the blast vs. the normal control group. Interestingly, connectivity between the thalamus and occipital lobe, inferior frontal lobe and cuneus and between cuneus and occipital lobe was significantly higher in the blast group. While the inter-subject deviation of the correlation coefficients was similar for both groups, in the area of occipital lobe, cuneus, and fusiform areas, very low inter-subject variation was observed. These results suggest elevated whole-brain connectivity for the blast-induced tinnitus group, while certain brain regions were more affected than others.

Conclusion: The generalized increase in connectivity may be consistent with neurophysiologic studies of tinnitus, where increases in neural hyperactivity, neural synchrony across brain areas, and other factors could have an influence on these results. Keep in mind however, that the blast wave becomes a compression wave in the brain, inducing various structural and neurobiochemical effects on the whole-brain scale. Therefore, blast-induced differences in connectivity analysis may be a unique entity, in large part because modality specific (auditory) effects may not necessarily be the only sensory modality or brain area/pathway affected under these circumstances. Lastly, we emphasize that a larger sample size is needed to validate and extend these results.

3:45 - 5:15 p.m.
PLENARY TALKS

3:45 - 4:30 p.m. – Invited Speaker

CBT BASED TINNITUS TREATMENT: A STEPPED CARE APPROACH

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Usual care practice in treating tinnitus still consists of fragmentized audiological rehabilitation primarily, with optional counselling resulting in costly prolonged referral trajectories. Presently a novel treatment protocol, combining elements from TRT and CBT-t in a 2 stepped-care framework is proposed. A stepped-care approach is a framework for organizing health services with a gradual increase in the intensity of the care at each level. Evidence was recently found in a large randomized controlled trial that this specialised tinnitus treatment protocol, versus care as usual, was effective as well as cost-effective. (Cima, et al., 2012; Maes, Cima, Vlaeyen, Anteunis, & Joore, 2013)

Results: Results firmly supported the primary hypotheses. This study demonstrates that our novel specialized stepped-care tinnitus treatment is more effective than care as usual not only in decreasing tinnitus annoyance, disability, tinnitus related negative thoughts and fears, and general negative affect, but also in a clinically relevant increase in general health.

Explaining results

Moreover, Tinnitus related fear was found to largely explain the benefits of this stepped care approach, and treatment seemed to be beneficial for both mild and more severely affected patients. Where the largest group of patients were effectively treated within a fairly short period of time, since patients with mild tinnitus complaints, received step-1 treatment only, and were included in all analyses, and more severe suffering patients entered an additional step 2. Effectiveness the specialised tinnitus treatment protocol was established throughout the whole group.

The CBT based treatment protocol: A stepped care approach

The specialised care treatment protocol, and the rationale behind the included treatment elements will be introduced during the conference

Cima, R. F. F., Maes, I. H., Joore, M. A., Scheyen, D. J. W. M., El Refaie, A., Baguley, D. M., et al. (2012). Specialised treatment based on cognitive behaviour therapy versus usual care for tinnitus: a randomised controlled trial. The Lancet, 379(9830), 1951-1959.

Maes, I. H., Cima, R. F. F., Vlaeyen, J. W., Anteunis, L. J., & Joore, M. A. (2013). Tinnitus: A Cost Study. Ear and Hearing.

4:30 - 5:15 p.m.

TREATMENT WITH A TINNITUS-FOCUSED COCHLEAR IMPLANT

Richard Tyler, Shelley Witt, Andrew Keiner, Eveling Rojas, Jin Jun Hyung, Ann Perreau, Camille Dunn, Bruce Gantz, Marlan Hansen, Smita Agrawal and Kurt Walker
Dept of Otolaryngology-Head and Neck Surgery and Communication Sciences and Disorders, Iowa City, IA, The University of Iowa, Rich-tyler@uiowa.edu

Electricity presented to the cochlea likely has one of the best opportunities for treating tinnitus. First, we review early laboratory trials demonstrating the range of analog and pulsatile stimuli that can be effective. We include observations on different depths of electrodes. Second, we review data from patients with a hearing implant but who also have tinnitus, including studies with unilateral deaf patients. Third, we highlight important observations from recent laboratory trials comparing the effectiveness of different stimuli. Finally, we discuss options and share data for field trials with stimuli specific for tinnitus. We conclude that there will soon be a range of cochlear implants to treat tinnitus. This will include strategies interleaved with electrodes to code speech, tinnitus stimuli running in the background of speech-coded stimuli, and a short basal electrode.

Support from the Action on Hearing Loss, Tinnitus Research Initiative, and Cochlear Corporation.

05:15 - 06:30 p.m.
POSTER SESSION II

Sound Treatment
guided by
G Searchfield

P30. TINNITUS PERCEPTION FOLLOWING MIDDLE EAR IMPLANTATION FOR MIXED AND CONDUCTIVE HEARING LOSS

Roberta Marino[1,2], Dayse Tavora Vieira[1,3], Gunesh P Rajan[1] (Presenter: Vesna Maric)

1 Otolaryngology, Head and Neck Surgery Unit, School of Surgery, The Universtity of Western Australia
2 Specialist Hearing Services, Mt Hawthorn, Australia
3 Medical Audiology Services, West Perth, Australia

Background: The aim of this study was to measure tinnitus perception in a group of patients after Vibroplasty using the Vibrant Soundbridge (VSB) middle ear implant for mixed and conductive hearing loss. To date, there is no study of VSB outcomes which have examined the benefits of device use on tinnitus perception. Yet according to the literature, 35% of people affected by some form of conductive loss have tinnitus 1.

Methods: Subjects enrolled in this study could not derive benefit from conventional hearing aids because of conditions directly affecting the coupling of hearing aids or moulds with the ear canal or the severity of the hearing loss. The Tinnitus Reaction Questionnaire2 (TRQ) was used to assess the impact of tinnitus distubance on the subjects' well being, emotions, and lifestyle. The TRQ was completed before and after surgery in order to compare the post-operative outcomes. A single-subject, repeated measures design was employed. All VSB fittings were based on hearing thresholds results and were not set to mask tinnitus.

Results: A total of 10 patients (7 females and 3 males) were included in the study. Average age of subjects at surgery was 55.45 (SD: +/- 15.84, range of 25.97 - 78.55) years. The mean hearing loss in the implanted ear using the four frequency average of air conduction thresholds was 68.25dB (SD: +/- 18.12dB). The average bone conduction thresholds were 22.75dB (SD: +/- 10.26) in the implanted ear. Of the 10 subjects, 4 had significant tinnitus perception pre-operatively (average score of 55.25 on the TRQ) which diminished in 3 of the 4 subjects (average score of 30.5 post-operatively).

Conclusion: The VSB application in our cohort of patients with mixed or conductive hearing loss, significantly decreased tinnitus perception for the majority of subjects experiencing tinnitus pre-operatively.

1. *Holgers, K M and Hakansson, B. E V (2002), Sound stimulation via bone conduction for tinnitus relief: a pilot study, International Journal of Audiology 2002; 41: 293-300.*
2. *Wilson PH, Henry J, Bowen M, Haralambous G: Tinnitus Reaction Questionnaire : Psychometric properties of a measure of distress associated with tinnitus. J Speech Hear Res 1991 ;34: 197-201*

P31. INTRACOCHLEAR ELECTRICAL STIMULATION TO SUPPRESS TINNITUS – TOWARDS A TINNITUS IMPLANT

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Aims/Objectives: Previous studies seem to show that tinnitus can be suppressed by intracochlear electrical stimulation, providing possibilities for development of a tinnitus implant. However, there is limited literature on optimizing electric stimulation[1]. The current study systematically explores and optimizes two stimulation parameters: current level and anatomical site inside the cochlea.

Methods: Eleven CI-recipients with unilateral or bilateral tinnitus-complaints participated in a single blinded randomized trial. Subjects were included based on their score on the Tinnitus Handicap Inventory (THI > 16). The pitch matched electrode was found using a two-alternative forced-choice method. Standard clinical software was used to convert the input, an audio file on a mp3-player, into parameter-specific electric stimulation of the auditory nerve. Based on scarce literature, it was hypothesized that subthreshold and thus inaudible current levels suppress tinnitus to a lesser extent than above-threshold stimulation[2]. Furthermore, it was hypothesized that tinnitus suppression is optimal when applying narrow-band pitch-matched electrical stimulation. Experiments were ethically reviewed and approved by the Medical Ethics Committee of Maastricht University/academic hospital Maastricht.

Results: Preliminary results show that the majority of subjects experience significant tinnitus suppression during intracochlear electrical stimulation. In one subject tinnitus even remained suppressed up to three days after electrical stimulation of the auditory nerve. Adaptation could be observed in some patients, even at larger stimulus levels. Suppression could not be observed at subthreshold levels, in line with expectations. Although some patients experience better suppression at larger stimulus levels, optimal parameters appear patient-specific. No clear relation could be observed between tinnitus suppression and stimulus type or location.

Conclusion: Most patients appear to experience tinnitus suppression by intracochlear electrical stimulation, which opens up possibilities for development of a tinnitus implant. Stimulus parameters appear patient-specific, which underlines the importance of optimization on an individual basis.

[1] Chang JE, Zeng FG. Frontiers in Systems Neuroscience. Tinnitus suppression by electrical stimulation of the auditory nerve. 2012. Vol.6: Art.19.
[2] Battmer RD, Heermann R, Laszig R. HNO. Suppression of tinnitus by electric stimulation in cochlear implant patients. 1989. Vol. 37 No. 4: 148-52.

P32. SOUND THERAPY OF TINNITUS BASED ON THE EQUALIZATION OF THE HEARING LOSS CURVE: A MULTICENTER STUDY

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Aims/Objectives. A multicenter study of Sound Therapy of tinnitus, based upon the neuroauditive stimulation of the auditory system with stimuli equalized by the patient hearing loss, is presented. The study is motivated by the encouraging results obtained in a preliminary trial with ten patients where 80 % reported an improvement of their tinnitus perception (Herraiz et al., 2011). Partial objectives include: Assessment of the tinnitus response (frequency, intensity, distress and masking level (MML)), description of actuation mechanisms, Indication criteria, comparison of results of treatment groups with control group (placebo), and comparison of results with different stimuli (random, tone-pips and tone-burst sequences).

Methods. A double-blind multicenter study is designed including three treatment group (random, tone-pip and tone-burst) and a control (placebo) group. Patients are sorted to each group randomly. Stimuli for the treatment groups include compensation for the hearing loss curve of the patients. Stimuli for the control group patients can be also random noise, tone-pip or tone-burst sequences, but do not include any compensation. The calculation of the stimulus for each patient is carried out by a Matlab GUI (Diges et al., 2013). The customized stimulus is given to the patients in wav format, together with a prescription: listening the sound barely below its tinnitus level, one hour per day, during two months. A complete exploration is carried out to the patients, before the treatment, just finished and three months later, including: ORL exploration (tonal, air and bone audiometry, logoaudiometry, high frequency audiometry, binaural balance, tympanometry, ipsi- and contralateral stapedial reflex, DPOAE and Dead Regions Test), Tinnitus exploration (sound intolerance threshold, acuphenometry (frequency, intensity, MML)), Residual inhibition, and Handicap exploration (THI, VAS,THS-GÜT, HANDS, ..).

Inclusion criteria: Patients from 18 to 65 years old, with more than one moth tinnitus time, THI > de 20%, moderate to severe hyperacusis according to THS, tinnitus pitch of 4, 6, 8 kHz, or higher, hearing loss at high frequencies, including presbiacusis, evolved acoustic thrauma, high pitch HANS, barothrauma, secondary HANS due to ototoxicity, and head trauma.

Exclusion criteria: Patients with severe psychiatric history, Meniere disease, acute sudden deafness, and Cochlear hydrop.

Results/Discussion: We expect to corroborate the preliminary results obtained with a limited simple of patients (Herraiz et al., 2011). In order to get statistical significance, we expect to recruit a minimum of 75 patients per group. The clinical relevance of the trial will be obtained comparing the average THI, VAS and NML of the four groups, before, after, and after+three months the treatment be applied.

Diges, I., Rodriguez, A., Cobo, P., Harguindey, A. (2013). Graphical User Interface (GUI) for the sound therapy of tinnitus. Tinnitus Research Initiative Conference, Valencia (Spain).

Herraiz, C., Diges, I., Cobo, P., Noreña, A., Hernández, J., Aparicio, J.M., (2011). Enricehd acoustic environment with spectrum matched to the patient hearing loss curve for tinnitus sound therapy. International Tinnitus Seminar, Florianopolis (Brasil).

P33. GRAPHICAL USER INTERFACE (GUI) FOR THE SOUND THERAPY OF TINNITUS

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Aims/Objectives. Different sound therapies for tinnitus treatment have been proposed that claim comparable treatment benefits despite the use of different sound signals. This seems to suggest that the efficacy of the sound therapy does not depend on the stimuli properties. However, since acute tinnitus is an aberrant homeostatic plastic product of a decreased sensory input to the auditory system, we claim that the best sound stimulation is one that selectively compensates (equalizes) such diminished input (Schaette and Kempter, 2006). The aim of this work is to implement three stimuli that satisfy this condition in a Graphical User Interface (GUI).

Methods. The three stimuli included in the GUI have a frequency spectrum matched to the patient hearing loss. One of them consists of a random noise equalised by the hearing loss curve. The other two are sequences of tones burst or pip of random frequency, within the patient audible frequency band, each one with amplitude proportional to the hearing loss at that frequency. Thus, these tones, which are based in the enriched acoustic environment (EAE) previously used in trials with hyperacusis patients (Noreña and Chery-Croze, 2007), stimulate sequentially the patient auditory system compensating for his hearing loss. Unlike other sound therapies, the one proposed here is customized for each patient. It is designed specifically for each one after a previous exhaustive auditory exploration.

Results. Once the hearing loss curve has been carefully assessed, the stimulus, which can be a continuous random sound or a sequence of tones, is calculated accordingly. The resulting sound is given to the patient in an easily playing format (MP3, CD) together with a prescription (minutes/day, duration), and a date for following-up.

Conclusion. A GUI which facilitates the prescription of a personalized sound therapy for tinnitus has been designed. The specialist introduces the hearing loss curve of the patient and chooses the parameters of the sound stimulus. After that, the GUI provides the sound signal in a usual playing format.

1. *Noreña, A.J., Chery-Croze, S. (2007). Enriched acoustic environment rescales auditory sensitivity.NeuroReport 18: 1251-1255.*
2. *Schaette, R., Kempter, R. (2006). Development of tinnitus-related neuronal hyperactivity through homeostatic plasticity*

after hearing loss: a computational model. Eur. J. Neurosci., 23: 3124-3138.

P 34. NEUROMONICS TINNITUS TREATMENT – EXPERIENCE AT NATIONAL UNIVERSITY HOSPITAL, SINGAPORE

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The challenge in managment of tinnitus is the heterogenous symptoms manifested such as auditory, attentional and emotional disturbances (David. B., 2002, Susan et al 2011).

This study aims to document the distress levels assoicated with Tinnitus using the Tinnitus Reaction Questinnaire and to document the efficacy of Neurmonics Tinnitus treatement (NTT).

Retrospective analysis of case records of twelve patients who underwent Tinnitus treatement was performed. A total of twelve patients who reported unilateral tinnitus were included in this study (nine males and three females). Age range of these patients was between 45-68 years and an average of 57.8 years.

Subjects underwent audiometric testing (250-12.5KHz), Otoscopy, Tympanometry, Minimum masking levels (MML), Loudness discomfort levels (LDL) and Residual inhibition (RI) and fitted with Neuromonics. TRQ was administered at four stages to assess the progress made by patients at pre-treatment, two months, four months and at six months post treatment. TRQ was utilized to asses the psycological distress associated with Tinnitus on a Likert 5 point grading scale. TRQ scores ranged between 0 – 104 indicated the severity of disturbances, namely no handicap (<17), mild (18-36) moderate (38-56) and severe (>58). Out of 12 subjects eleven subjects were diagnosed with severe handicap and one subject diagnosed with a mild handicap at pre-treatment stage. Descriptive statistics and repeated measures of ANOVA were utilized to analyze the data.

Progress was achieved in each individual in the domains of Tinnitus awareness and disturbance.

TRQ scores six months post NTT reflected a significant reduction on pairwise comparisons. (2 months = 11.69, 4 months = 8.23 and 6 months = 6.19) Overall all subjects reported reduced tinnitus disturbances at post NTT clinical reviews.

The time of usage of NTT was analysed with repeated measures of ANOVA. The mean usage of the device decreased from initial high of 280 minutes to 200 minutes.

Mean score analysis of three different subscales (represented by question groups on TRQ) on emotional, Functional and Catastrophic aspects also indicated marked improvements. This was similar to literature reported elsewhere.

Our clinical unit was able to determine the efficacy of NTT as a tinnitus management tool during this study and it was observed all twelve patients exhibited prognosis.

Challenges faced during the study were language based, since few of the subjects required translation of English from family members.

The authors acknowledge that NTT is not the only method of treatment for Tinnitus provided the heterogeneity of the symptoms exhibited. This is an attempt to develop and document the nascent Tinnitus management program available in the region and add to existing literature of tinnitus management in Asian context.

REFERENCES

David, B. (2002). New Developments in Hearing and Balance, British Medical Bulletin, 63(1), 195 -212.

Davis, P.B., Paki, B., & Hanley, P.J. (2008). Treatment of tinnitus with a customized, dynamic acoustic neural stimulus: underlying principles and clinical efficacy, Trends in Amplification, 12(3), 1-2.

Dayse, TV., Robert, E., Gemma Ivey., Stuart Miller., (2011). A Multicentre study on the long term benefits of tinnitus management using Neurmonics Tinnitus treatment. International tinnitus Journal 16(2) 111-7.

Susan, H., Nigel, P.G. (2011). Narrative Review of Tinnitus and its impact. Biological Research for nursing, 13 (1), 97 -108.

Wilson, P.H., Henry, J., Bowen, M., & Harlambous, G. (1991). Tinnitus Reaction Questionnaire: Psychometric properties of a measure of distress associated with tinnitus. Journal of Speech and Hearing Research, 34, 197-201.

P35. PERCEPTUAL ATTENTION TRAINING IN TINNITUS TREATMENT

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BACKGROUND: Tinnitus is the conscious awareness of sound without an external, driving sound source. Growing evidence suggests that cortical and subcortical regions associated with memory, emotion and attention may be involved in tinnitus' pathophysiology (1). Although the exact mechanism(s) are not yet fully understood it has been proposed that these structures contribute to tinnitus' salience and annoyance. Perceptual attention training may therefore represent a viable therapeutic intervention in the treatment of tinnitus.

AIMS: Ascertain the effect of an auditory training paradigm on attention and tinnitus.

METHODS: Thirty one participants with tinnitus were recruited. An experimental group (N = 15) performed 20 consecutive daily sessions (30 min) of "Terrain", a computer-based auditory attention training game. A control group (N = 16) trained using a visual task (Tetris). An Auditory-Visual Multiprocessing Test (AVMT) (Comprehensive Attention Battery®) was assessed before and after training together with the Tinnitus Handicap Inventory (THI) and Tinnitus Functional Index (TFI).

RESULTS: Significant reductions in reaction time of hits were observed for visual ($F1, 14 = 21.962$, $p < 0.001$), auditory ($F1, 14 = 9.612$, $p = 0.008$), and mixed ($F1, 14 = 13.679$, $p = 0.002$) tasks of the AVMT in the experimental (Terrain) group following training. This effect was coupled with clinically significant improvements in TFI and THI

measures. There was no significant change in reaction time, TFI or THI with the control (Tetris) game.

CONCLUSIONS: An auditory attention training task improved executive attention in participants with tinnitus. Importantly, this improvement was associated with a reduction in tinnitus' handicap and effect on patients' lives. New attention based strategies incorporating sensory interaction are proposed.

1. *Golm D, Schmidt-Samoa C, Dechent P, Kröner-Herwig B. Neural correlates of tinnitus related distress: An fMRI-study. Hear Res. 2013;295(0):87-99.*

P36. FOLLOW-UP OF CR-NEUROMODULATION THERAPY WITH TINNITUS CHARACTERIZATION USING A NUMERIC SCALE FOR THE TINNITUS SPECTRUM

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Background: Tinnitus, a phantom perception of sound, is connected with abnormal neural synchrony in the central auditory system. Coordinated reset (CR) therapy induces a long-lasting desynchronization of tinnitus-related neural synchrony. However, a properly performed matching of the CR tones to the patient's individual tinnitus is mandatory for the CR therapy to be effective. This type of adaptation/pitch match relies on subjective psychoacoustic measurements. The aim of the present study is to analyze the efficiency of the CR therapy using a numeric scale in the tinnitus spectrum (TS) determination and to reveal correlations between the spectrum and the therapy outcome.

Materials and Methods: The following method is used to determine the dominant tinnitus frequency of a patient. First, tones between 500 Hz to 13 kHz in steps of 500 Hz are presented to the patient, who can adjust the tones' loudness. For each frequency the patient assesses the similarity of the actual tone to his own tinnitus on a numeric scale from 0 to 10. By this simple tone matching we obtain the patient's TS defined as the graph of the numeric similarity scale versus frequency. Second, starting from a preset tone, the patient has to identify the tone closest to his tinnitus by adjusting the tone's frequency. The preset (3 to 5) tones are selected from the dominant frequencies of the TS. Third, the patient performs pairwise comparisons of the resulting 3-5 frequencies, which can differ from the dominant regions of the TS, to obtain the best fit to his tinnitus. The resulting frequency is further pairwise compared to the most dominant frequencies of the TS. The pairwise search ends when the patient unambiguously selects one frequency. The stimulating tones of the CR neuromodulator are then programmed based on this frequency.

An acoustic CR neuromodulator was used to stimulate all patients for 4–6 hours every day, while the control was scheduled monthly for a period of 6-7 months. The therapy effectiveness is evaluated based on a standardized tinnitus questionnaire (TQ).

Results and Conclusions: The introduction of a numeric scale in the TS allows to subjectively assess the dominant frequency region(s) and its (their) character. The measured tinnitus spectra were rather broad including several dominant frequencies. With our method, the patient's dominant tinnitus frequency within an a priori defined threshold can be precisely determined. CR-induced spectral changes and, in particular, extinction of dominant frequencies in the TS can well be monitored with the introduction of a numeric scale. The CR therapy-induced tinnitus pitch alteration is in correlation with the changes in the TS. The TQ value has decreased for all patients within half year, which illustrates both the improvement of the patient's tinnitus and the efficiency of the CR neuromodulation therapy.

In conclusion, the determination of the patient's tinnitus frequency, which has a subjective and individual character, is important for the CR therapy effectiveness. The presented method allows both for an effective and patient-specific calibration of the CR therapy and for an assessment of spectral changes in the patient's tinnitus.

P37. PLAYING AND LISTENING TO TAILOR-MADE NOTCHED MUSIC: THE EFFECTIVENESS OF MULTIMODAL AND UNIMODAL MUSICTRAINING IN TINNITUS THERAPY

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Chronic tinnitus is a symptom that affects the quality of life in 1-3% of the general population. The generation and maintenance of tinnitus is based on maladaptive auditory cortex reorganization that can be reversed to a certain degree by behavioral training. Previous studies demonstrated that short-term and long-term musical training can induce functional plasticity in the human auditory cortex. Listening to modified („notched") music which contains no energy in the frequency range surrounding the individual tinnitus fequency can inhibit the neuronal activity in the auditory cortex corresponding to the center-frequency of the notch. Further, music making was shown to be one of the most powerful stimulator for brain plasticity. In this MEG-study non-musician tinnitus patients who either played or listened to tailor-made notched music for two months were investigated. We evaluated the effectiveness of tailor-made notched music training in the multimodal (playing) and unimodal (listening) modality. Both groups reported a reduction of tinnitus handicap, but only the unimodal listening group showed a significant reduction of tinnitus-related auditory activity and reported an alleviation of tinnitus loudness, consciousness and distress. These findings indicate that auditory cortex reorganization is mainly dependent on the auditory input; additional integration of the somatosensory and visual system seem to rather disturb the process of reorganization of auditory cortex in the tinnitus patients. In summary, listening to notched music can reverse the maladaptive reorganization of a specific cortical area and is a low cost, practical and more effective treatment for non-musician tinnitus patients than multimodal music training.

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P38. CENTRAL MECHANISMS OF TINNITUS DISTRESS

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Aims: The known cause of subjective tinnitus is a dysfunction of the auditory system. This dysfunction likely leads to changes in activity of different brain regions. In this work, we studied possible causes responsible for a generation of central tinnitus or intensification of tinnitus perception in context of affective stress.

Methods: Ten tinnitus patients and 10 age- and gender-matched healthy controls were included in this study. Pseudo-randomized, four acoustic stimuli were presented via headset to all subjects: 1) pleasant chimes, 2) unpleasant beeps, 3) neutral words, 4) significant affective words. During the presentation, MRI was performed to determine the regions of brain activated by signals and the activation patterns. MRI data were functionally analyzed with the SPM package and correlated with psychometric scores obtained from all subjects.

Results: The comparison of activation patterns between tinnitus patients and controls yielded significant differences in limbic regions, prefrontal areas and in the auditory cortex. Obtained activation patterns correlated with the tinnitus-induced and emotional distress.

Discussion: Our findings support the notion about the interaction between limbic, prefrontal and auditory systems. Of special importance seems to be the emotional and review process. We propose an existence of tinnitus cortical distress network. Specific components of this network (limbic and prefrontal cortex as associative center of attention control and negative feedback loops in tinnitus and temporal regions) may play an important role in generation and amplification of central tinnitus.

P39. NEUROIMAGING IN PATIENTS WITH CRONIC TINNITUS UNDERWENT ACUPUNCTURE TREATMENT

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Aims/Objectives: Tinnitus is characterized by a perception of sound in the absence of an external auditory stimulus, which treatment is still a challenge. Recent evidence reports that central nervous system mechanisms are involved in the generation of tinnitus, with abnormal brain functional activity in front of the symptom. Acupuncture is a promising proposal, but there are few studies proving its benefits towards tinnitus.

Methods: A randomized double-blind clinical trial (RCT) was performed to investigate the effect of acupuncture in regional brain blood flow in 34 subjects with tinnitus and normal audiometry, submitted to placebo or active acupuncture intervention (n=17). Clinical evaluation consisted of Tinnitus Handicap Inventory (THI). All subjects underwent a 99mTc-ethylcysteinate dimer single-photon emission computer tomography (99mTcECD-SPECT) exam before and after twelve acupuncture sessions. Data was analyzed with Statistical Parametric software using small volume correction. Regression models were built to analyze the effects of the RCT and baseline assessments for each outcome and patient's status in each group were included as covariates.

Results: Decrease of left parahippocampal gyrus (MNI: -22 -6 -22, pFWE<0.05) perfusion after active acupuncture treatment and reduction in the THI score in the active acupuncture group were also observed [β (standardized), THI = -0.390, p = 0.028].

Conclusion: These findings suggest the parahippocampal gyrus is involved in the pathophysiology of tinnitus and that its activation can be modulated by acupuncture, decreasing the impact of tinnitus in patient's life.

P40. SHORT-TERM PLASTICITY OF THE AUDITORY CORTEX IN TINNITUS PATIENTS

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Introduction: Listening to notched music for 3h on three consecutive days leads to temporary changes in the tuning of neurons in the human auditory cortex (1). This short-term plasticity is discussed in terms of an increased activation of neurons corresponding to the frequency bands around the notch leading to a greater lateral inhibition (LI) of the neurons corresponding to the center frequency of the notch. Since a lack of LI in the auditory cortex seems to play a major role in the manifestation of tinnitus perception, the induction of increased LI is assumed to result in a reduction of tinnitus perception. These mechanisms were already demonstrated in long-term studies measuring the effect of notched music on the tinnitus perception and its neural correlates. However, the direct effects and time course of stimulation with notched music on the auditory cortex in tinnitus patients has not been investigated so far.

Objectives: The aim of this study is to investigate the impact of a massive stimulation with notched music on the primary and secondary auditory cortex of tinnitus patients. The induced functional deafferentation of the notched area is expected to result in a reduction of the

activity of the hyperactive neurons representing the tinnitus frequency (TF). Furthermore we want to gain new insights into the impact of other cortical regions on the mechanisms of short-term plasticity in the auditory cortex of tinnitus patients.

Methods: Ten subjects suffering from chronic tonal tinnitus, a TF in the frequency range between 1 kHz and 8 kHz and without severe hearing loss (≤ 55 dB HL between 125Hz and 8kHz) participated in the study. The subjects listened for 3 hours on three consecutive days to notched music with a notch-bandwidth of ½ octave centered at the tinnitus frequency. Before and immediately after exposure to the notched music, neural activity was measured by magnetoencephalography (MEG). The stimulation in the MEG comprised two different sound stimuli with the test tone representing the individual TF and a control tone of 500Hz far away from the tinnitus frequency. Both stimuli with carrier frequencies equal to the individual TF or the control frequency had a duration of 1000 ms and were presented binaurally in a randomized order. The first 300 ms were sinusoidal eliciting the N1m response, whereas the last 700 ms were 40 Hz amplitude modulated (modulation depth of 100%), generating the auditory steady state response (ASSR). MEG recordings were analyzed in time windows of the N1m and the ASSR, respectively. Additionally, five minutes of spontaneous activity were recorded.

1. Pantev C, Wollbrink A, Roberts LE, Engelien A & Lütkenhöner B . Brain Res., 1999; 842: 192-199.

P41. STRUCTURAL CHANGES IN RELATION TO TINNITUS DISTRESS: A VBM STUDY

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Objectives: Chronic tinnitus affects about 5% of the population. Up to 17% of those persons experience severe distress due to the condition. They suffer from negative mood, sleep difficulties and concentration problems. Tinnitus in general is associated with neuroplastic changes. Several studies examined those changes using voxel based morphometry. There is evidence for differences in frontal, limbic and auditory regions in tinnitus patients. However, the results are heterogenous. Previous studies included tinnitus patients with or without hearing loss, individuals without tinnitus, but with hearing loss and healthy controls with neither tinnitus nor hearing loss. Since limbic and frontal regions seem to play a significant role in persons who experience distress due to the phantom sound, our study focused on this distress.

Methods: We used voxel-based morphometry to assess structural MRI scans of 45 persons with tinnitus and 21 healthy control participants without tinnitus. None of the participants had a hearing loss > 30 dB at 2 kHz or in more than one frequency between 0.5 and 3 kHz. Gray matter volume was correlated with tinnitus related distress, depression, anxiety, tinnitus loudness and average hearing loss.

Results: First data will be presented.

P42. PATHOLOGICAL OSCILLATIONS IN HYPERACUSIS BRAIN EVEN WITHOUT SOUND STIMULI: A HYPERRESPONSIVENESS NETWORK WITH PARADOXICALLY INACTIVE AUDITORY CORTEX

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Objectives: Although hyperacusis, a hyperresponsiveness to non-noxious auditory stimuli, is a sound-evoked symptom, possible resting-state pathologic oscillations in hyperacusis brain have never been explored. By comparing 17 tinnitus participants with hyperacusis (T+H+) and 17 without hyperacusis (T+H-), we aimed to explore characteristic resting-state cortical activity of hyperacusis.

Methods: The T+H+ and T+H- groups, strictly matched for all tinnitus characteristics to exclude tinnitus-related cortical changes, were compared using resting-state electroencephalography source-localized activity complemented by functional connectivity analyses.

Results: Correlation analysis revealed that hyperacusis questionnaire score was positively correlated with the orbitofrontal cortex (OFC) beta power, the right auditory cortex (AC) alpha1 power, and the dorsal anterior cingulate cortex (dACC) beta1 power. Compared to the T+H- group, the T+H+ group demonstrated increased beta power in the dACC, OFC and increased alpha power in the right AC) Region of interest analyses including 17 normal controls further confirmed that these differences originated solely from relatively increased power of the T+H+ group, not from a relative power decrease of the T+H- group. Also, the T+H+ group showed increased connectivity between the OFC/dACC and the AC as compared to the T+H- group.

Conclusion: The beta power increase in the OFC/dACC may indicate increased vigilance leading to increased startle reflex. Additionally, increased alpha power in the AC may reflect an adaptive top-down inhibition against sound stimuli probably mediated by the increased beta power of the OFC. The OFC/dACC, also frequently found to be activated in analogous diseases such as allodynia/hyperalgesia, may compose a hyperresponsiveness network.

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P43. MINDFULNESS-AND BODY-PSYCHOTHERAPY-BASED GROUP-TREATMENT OF CHRONIC TINNITUS: A RANDOMIZED CONTROLLED PILOT STUDY

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Background: Tinnitus, the perception of sound in absence of an external acoustic source, impairs the quality of life in 2% of the population. Since in most cases causal treatment is not possible, the majority of therapeutic attempts aim at developing and strengthening individual coping and habituation strategies. Therapeutic interventions that incorporate training in mindfulness meditation have become increasingly popular in the treatment of stress-related disorders. Here we conducted a randomized, controlled clinical study to investigate the efficacy of a specific mindfulness- and body-psychotherapy based program in patients suffering from chronic tinnitus.

Methods: Thirty-six patients were enrolled in this pilot study. The treatment was specifically developed for tinnitus patients and is based on mindfulness and body psychotherapy. Treatment was performed as group therapy at two training weekends that were separated by an interval of 7 weeks (eleven hours/weekend) and in four further two-hour sessions (week 2, 9, 18 and 22). Patients were randomized to receive treatment either immediately or after waiting time, which served as a control condition. The primary study outcome was the change in tinnitus complaints as measured by the German Version of the Tinnitus Questionnaire (TQ).

Results: ANOVA testing for the primary outcome showed a significant interaction effect time by group ($F=7.4$; $df=1,33$; $p=0.010$). Post hoc t-tests indicated an amelioration of TQ scores from baseline to week 9 in both groups (intervention group: $t=6.2$; $df=17$; $p<0.001$; control group: $t=2.5$; $df=16$; $p=0.023$), but the intervention group improved more than the control group. Groups differed at week 7 and 9, but not at week 24 as far as the TQ score was concerned.

Conclusions: Our results suggest that this mindfulness- and body-psychotherapy-based approach is feasible in the treatment of tinnitus and merits further evaluation in clinical studies with larger sample sizes.

The study is registered with clinicaltrials.gov (NCT01540357).

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P44. CLINICALLY-SIGNIFICANT TINNITUS SYMPTOMS: THE ROLE OF TOP-DOWN COGNITIVE PROCESSES

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Subjective tinnitus is a perception of a sound in the absence of external source or acoustic stimulation and can be classified as an auditory phantom. Frequent triggers are acoustic traumas, drugs and lesion in auditory peripheral and consequences are reduced life quality of approximately 20% of the subjects. One important question is why 80% of the subjects do not present clinically significant symptoms although equally perceiving the phantom sound. Current models condition, or at least emphasize, the role of external events congruently paired with the causal physical event that originated the phantom perception. Our suggesting for explaining negative symptoms related to tinnitus is based on top-down cognitive processes. Integrating behavioral, neuroanatomical and neurofuncional research results, we propose a detailed neurofunctional model whose main structural components are the peripheral auditory system, the thalamus (reticular, medial geniculate and dorsal nuclei), the limbic system (hippocampus, anterior cingulate cortex, amygdala), brain stem (raphe nucleus), basal ganglia (ventral palladium), striatum (nucleus accumbens), and the auditory and prefrontal cortices. Functionally, we assume continuous or intermittent abnormal signal at the peripheral auditory system or midbrain auditory paths. The signal might be perceived or not, depending on availability of attentional resources, and is initially considered irrelevant by the cognitive and emotional systems and consequently receives low valuation scores. This cognitive valuation strengthen the lateral-inhibition noise canceling mechanisms at the mid-brain and thalamus levels are activated[1], leading to ceasing of sound perception and maintenance of the signal evaluation as irrelevant. However, the "sourceless" sound is eventually perceived and can be cognitively interpreted as suspicious and/or an indication of a decease, in which case cortical top-down processes weaken the noise canceling effect and the abnormal signal being considered a relevant stimulus. The consequences are an increase of cognitive and emotional negative reactions, such as depression, observed in part of the tinnitus patients. Negative or positive top-down feedback can be independent of previous experience or association with stimuli similar in nature to the abnormal neural activity that generated the phantom auditory perception. It depends on general personality biases toward negative cognitive interpretation of stimuli, such as the case of people that present hypochondria, generalized anxiety syndrome and/or depression symptoms[2]. 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. *Rauschecker, J.P., A.M. Leaver, and M. Muhlau, Tuning out the noise: limbic-auditory interactions in tinnitus. Neuron, 2010. 66(6): p. 819-26.*
2. *Marciano, E., et al., Psychiatric comorbidity in a population of outpatients affected by tinnitus. Int J Audiol, 2003. 42(1): p. 4-9.*

P45. EFFECTS OF COUNSELING, AMPLIFICATION AND SOUND STIMULATION IN TINNITUS MANAGEMENT

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Sound stimulation combined with appropriate counseling has been reported as an effective way to manage tinnitus distress 1. It has also been reported that hearing aids can independently provide effective tinnitus management for many patients 2 since tinnitus is often associated with hearing loss. Finally, sound stimulation and stress reduction have been shown to be effective in suppressing tinnitus or alleviating its impact on quality of life. Consequently, hearing aids that include a sound generator capable of producing relaxing fractal tones and amplification seem to be an ideal solution for managing tinnitus patients.

The aim of this study is to investigate the effectiveness of a tinnitus management using three consecutive phases, i.e., instructional counseling, amplification and sound stimulation. The intervention period is 6 months.

Subjects with hearing loss and Tinnitus Handicap Inventory (THI) scores >18 that searched for tinnitus management in the Center for Assistive devices and Communication were included in the study. The subjects underwent tinnitus management in three phases: counseling followed by amplification and finally a phase of sound stimulation, where the fractal tones were activated as an additional program in the hearing aids. Each phase lasted in average 2 months.

Twenty five subjects were included in the ongoing study, however 5 subjects withdrew. Most subjects initially reported tinnitus to have a moderate to severe negative impact on their quality of life. The age of the subjects ranged from 48 to 75 years with a mean age of 60. All subjects went through a complete audiological evaluation and filled out the Tinnitus Handicap Inventory (THI) before admission to the study. All subjects were fitted with hearing aids according to their hearing loss, and were given a sound stimulation program containing fractal tones. Subjects were instructed to use the hearing aids several hours per day, and it was recommended that they used the sound stimulation program at a minimum of 2 hours per day. The subjects attended three or more follow-up sessions where they filled out the THI questionnaires. This was done at two months post counseling, two months post hearing aids, and two months post sound stimulation. Additional questionnaires regarding hearing aid and sound stimulation experiences were also filled in.

The results show that the majority of subjects have a clinically and statistically significant reduction in perceived degree of tinnitus and tinnitus-related distress after six months ($p<0.001$). Improvements have been seen at all phases of tinnitus management: counseling ($p<0,001$), hearing aids and sound stimulation ($p< 0,02$). The majority of subjects are very satisfied with the hearing aids (73%) and 80% have evaluated the sound stimulation as satisfactory/very satisfactory. Overall the findings show that a combined approach with counseling and hearing aids that include a sound generator capable of producing fractal tones can be used successfully in tinnitus management.

References:

1 *Newman CW, Sandbridge S, (2009) Tinnitus Treatment. In Montanno JJ, Spitzer JB,eds. Adult Audiologic Rehabilitation. San Diego:plural, 399-444.*
2 *Kochkin S., Tyler R., Born J. MarkeTrak VIII(2011): The Prevalence of Tinnitus in the United States and the Self-reported Efficacy of Various Treatments Hearing Review.18(12):10-27.*

P46. TINNITUS AND HYPERSENSITIVITY TO SOUND, INTEGRAL THERAPY OF TINNITUS ASSOCIATED WITH AUDITORY REHABILITATION (KNASTER METHOD) AND HEARING SYSTEMS

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Overview: Tinnitus is a subjective sensation of sounds that is located in the ears or inside the head. According to some authors is accompanied by 86% of hearing loss and discomfort in 40-45% of cases, even though sound has very low intensity.
It is possible that the hypersensitivity to sound restrict the development of appropriate sound therapy accompanied by hearing aids in cases that require it.
Therefore, this paper attempts to demonstrate improvement of patients with disabling tinnitus and hypersensitivity to sound which has been applied to a mixed technique but complementary, as is the auditory rehabilitation (Knaster method) to train patients to receive and tolerate sound at different intensities.

Objectives: Measure the implementation of the Integral Therapy of Tinnitus and compare the results after application of different therapies through standardized tests.
Measure sound tolerance before and after hearing retraining therapy (Knaster method).

Methodology: It uses a protocol of assessment and monitoring at an early stage and between 4-6 months after the start of therapy.
Rating a sample of 25 patients treated in different centers GAES IAI Las Palmas, Burgos, Tenerife, Pamplona, San Sebastian, Salamanca, Zaragoza, Bilbao, Gijón, León, Santander, Alicante, Madrid and Logroño, under the same method.
Hearing correction was used in cases with hearing loss, however small it may be, sound stimulation with accustomed sounds, counseling and hearing rehabilitation.
The hearing rehabilitation (Knaster method) involves a pantonal noise stimulation at different intensities through phonetic materials aply both, language and noise stimulation, over a period of 15 sessions with headphones.
Is a type of active stimulation where patient must pay selective auditory attention and repeating tasks.
Items: Tests THI, THS, Sheldrake questionnaire, VAS, UCL and Affinity (Interacoustics equipment with Knaster module).

Results: In the sample of 25 patients treated by the interaction of both methods different levels of improvement are obtained, these results were demonstrated by measuring the evaluation tests of tinnitus and sound intolerance.

Conclusion: Discomfort sound rates decrease after 15 training sessions, improving confidence in working with different sounds.
The perception of tinnitus decreases after normalized hearing stimulation.
The rehabilitation of auditory discrimination may encourage the patient's ability to relocate tinnitus attention and reduce their impact and intensity.
The introduction of sound generators favors the discrimination of selective attention to tinnitus.
The combination of current therapies may provide better results in the quality of life of patients with tinnitus.

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P47. CORRELATION TYPE OF MASKER NOISE OF THE MINIMUM MASKING LEVEL AND TINNITUS QUESTIONNAIRE IN CHRONIC TINNITUS PATIENTS

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Objective: The aim of this study is to compare the results of the minimum masking level (MML) with other possible maskers and to analyse their correlation with the Tinnitus Questionnaire (TQ). The second goal of the study is to see if the interaction between loudness matching (LM) and the MML can predict the outcome on the TQ.

Background: MML is a psychoacoustic measurement for evaluating treatment effects in tinnitus patients. Typically a broadband noise is used as masker, but to our knowledge no research is performed yet to the correlation of the MML measured with different masker noises and the subjective outcome measurement TQ.

Method: The MML was measured in 96 patients with a non-pulsatile chronic tinnitus with four different maskers: white noise (MML-WN), speech noise (MML-SN), pure tone of 500 Hz (MMl-500) and at last tinnitus frequency and characteristics (MML-TIN). The MML was expressed in terms of dBHL and dBSL. Furthermore all patients completed the TQ.

Results: A significant moderate correlation between the subscales and total score of TQ and MML-WN (dBHL) was found ($p<0,05$; r=from 0,420 to 0,583). Also a significant, but weak, correlation was found between subscales and total score of TQ and MML-TIN ($p<0,05$; r=from 0,211 to 0,523). MML-WN, MML-SN and MML-TIN and their interaction with LM had a significant, but small, effect on the total score of TQ and his subscales ($p<0,05$; R2= from 0,112 to 0,235).

Conclusions: MML-WN shows the best correlation with the subjective outcome measurement TQ. Also a significant interaction was found of MML-WN and LM on the TQ and his subscales. Nevertheless the effect was too small to conclude that the psychoacoustic tests can predict the outcome on the questionnaire TQ.

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Neurostimulation
guided by
T Kleinjung

P48. EFFECTIVENESS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION TO DIFFERENT CHARACTERISTICS OF CHRONIC TINNITUS

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Objectives: rTMS, the non-invasive neuromodulation intervention, is well documented in literature for treating chronic tinnitus. This study investigates effects of rTMS to different clinical characteristics of tinnitus.

Methods: Forty-one patients were enrolled into this study. We grouped tinnitus patients according to their characteristics and etiologies. The following parameters were included: age, sex, tinnitus laterality, tinnitus duration, tinnitus etiology, subscales of TQ, and the pattern of audiogram. Sessions of 1-Hz ,theta-burst rTMS, and sham stimulation were performed to the patients randomly.

Results: The average tinnitus suppression rate was 64% for the active group. Theta-burst stimulation had a higher but shorter-lasting rate compared with 1-Hz tonic stimulation. Pure tone tinnitus had better improved rate

in both groups. Tinnitus caused by sudden sensorineural hearing hardly revealed response to rTMS. Emotional distress in TQ subscales could achieve the most improved rate. Baseline TQ, patient's gender and age, tinnitus duration and laterality did not influence treatment outcome.

Conclusion: Chronic tinnitus caused by sudden sensorineural hearing loss might results in long-term solid deafferentiation of auditory pathway that made rTMS difficult to modulate. This study concluded that rTMS was not a decisive treatment for chronic tinnitus following with sudden sensorineural hearing loss.

P49. P300 IN THE ASSESSMENT OF CHRONIC TINNITUS PATIENTS FOLLOWING REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

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Objectives: P300 (event-related auditory evoked potential) is associated with processing of stimulus in auditory brain cortex. The aim of this study is to evaluate higher auditory brain function after rTMS in tinnitus patients.

Methods: Twenty-four patients were enrolled and grouped into Group I: Tinnitus patients receiving rTMS (theta-burst) with evident TQ reduction (N=7); Group II: Tinnitus patients receiving pharmacotherapy (N=5); Group III: Normal volunteer adults without tinnitus nor hearing loss (N=5); Group IV: Patients with documented motor disorders treated with rTMS in Neurology Department (N=7). P300 latency and N2P3 amplitude were recorded before and after rTMS (Group I and IV) or 20 minuets time-gap. Binaural 1000Hz (80%) and 2000Hz (20%) tones at rates of 1.1/sec with loudness of 80db were delivered through earphones.

Results: There were significant N2P3 amplitude differences in rTMS intergroups (Group I and IV) and tinnitus intergroups (Group I and II). N2P3 amplitude and P300 latency were both influenced by rTMS in Group I and IV patients.

Conclusion: Our results showed that N2P3 amplitudes were reduced and P300 latency were prolonged in patients with tinnitus treated by rTMS. However, the relationship of inhibitory rTMS and auditory cortex were not completely understood.

P50. TRANSCUTANEOUS VAGUS NERVE STIMULATION IN CHRONIC TINNITUS: A PILOT STUDY

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Background: Vagus nerve stimulation has been successfully used as a treatment strategy for epilepsy and affective disorders for years. Transcutaneous vagus nerve stimulation (tVNS) is a new non-invasive method to stimulate the vagus nerve, which has been shown to modulate neuronal activity in distinct brain areas. In the present study we present data derived from a pilot study applying tVNS to 52 patients with chronic tinnitus (present more than 6 months).

Methods: The study has been conducted in two phases with two different stimulating devices (Cerbomed CM02 and NEMOS). Clinical assessment was based on Tinnitus Questionnaire (TQ), Tinnitus Handicap Inventory (THI), Beck Depression Inventory (BDI), WHO Quality of Life (WHOQOL), and various numeric rating scales (tinnitus loudness, annoyance, discomfort, distractibility, unpleasantness). Primary outcome was the change in TQ from baseline to the final visit. Cognitive capacities (TAP testing) and ECG effects have been monitored closely throughout the study at each visit (Scr/BL, W2, W4, W8, W12/16, W24 (= End of study), W28 Follow-up-visit).

Results: Primary analysis indicated a reduction of 3.7 points with a moderate effect size and 38% responder rate for phase 1. Concerning phase 2 the reduction was 2.8 points and 46% responder rate. Secondary analyses indicated no systematic and significant effects. There was a specific significant reduction for the TQ and the BDI for the first recruitment phase (uncorrected for multiple testing). Clinical global impression (CGI) showed equal number of patients or even a higher number of patients with worsening of symptoms in contrast to patients with amelioration of symptoms. Adverse events (apart from inherent symptoms of transcutaneous vagus nerve stimulation like twitching and feelings of pressure at electrode placement site) included three SAEs (one palpitation episode requiring hospitalization and monitoring of the patient at an ICU, one elective bowel operation which had not been reported by the patient at baseline visit, one noise trauma followed by hospitalization by a firework device). One patient showed a left bundle branch block not present at baseline during the W8 visit, which did not require hospitalization and therefore was not defined as a SAE. Cognitive testing revealed no decline.

Conclusion: Our data demonstrate the feasibility of tVNS in individuals over a period of 6 months. Our data also suggest that tVNS is safe in patients without a history of known cardiac disease. However, effects of tVNS on cardiac rhythm should be carefully monitored and systematically assessed in further studies. There was no

relevant improvement of tinnitus complaints after tVNS treatment.

P51. STRUCTURAL BRAIN CHANGES AFTER 10 SESSIONS OF LEFT TEMPORAL LOW-FREQUENCY RTMS IN PATIENTS WITH CHRONIC TINNITUS

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Objectives: Low-frequency repetitive transcranial magnetic stimulation (rTMS) of the temporal cortex has been shown to significantly reduce tinnitus severity in a subgroup of patients. Furthermore, differences in grey matter volume between tinnitus patients and healthy controls have been observed. However, no study has investigated yet whether rTMS treatment induces structural changes in tinnitus patients. Therefore, this study aims to investigate changes in grey matter volume due to rTMS treatment and their correlation with treatment success.

Methods: 41 patients with chronic tinnitus were treated with rTMS over the left temporal cortex (2000 stimuli, 1 Hz). At three time points (at baseline, day 12 and after a follow-up period of 90 days) high resolution images of the brain were acquired and tinnitus severity was assessed. The VBM toolbox for SPM was used for data analysis.

Results: At day 12, brain changes were detectable in the left temporal pole, the right insula, the right occipital cortex and the left inferior frontal cortex (uncorrected $p < .001$). Correlations of these changes with treatment success were not significant. From baseline to day 90, no changes were visible.

Conclusions: Left temporal rTMS may be able to induce structural brain changes in different regions of the brain. As those structural changes are not correlated with treatment success, the clinical relevance of this effect is questionable.

P52. REPEATEAD COURSES OF rTMS TREATMENT IN PATIENTS WITH CHRONIC TINNITUS

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Several studies have examined the effect of repetitive transcranial magnetic stimulation (rTMS) in chronic subjective tinnitus, mostly treating patients for five to ten sessions. However, there is little information on the effect of repeated rTMS therapies in patients who have and who have not responded to their first treatment. Therefore, the question arises whether repeated courses of rTMS can contribute to the maintenance of treatment effects or may even enhance treatment response. In order to obtain a first impression of the effect of maintenance rTMS, descriptive clinical data of 48 patients are presented.

P53. EFFICACY AND SAFETY OF TRANSCUTANEOUS VAGUS NERVE STIMULATION IN TINNITUS; A CASE CONTROL STUDY

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Objectives: It was recently demonstrated in the rat tinnitus model that tinnitus-related maladaptive neuronal plasticity might be reversed by a combination of vagal nerve stimulation (VNS) and sound. A clinical pilot study in tinnitus patients using implanted VNS paired with sound showed promising results as well. It has been demonstrated by functional MRI and EEG recordings that transcutaneous VNS (tVNS) of the auricular branch of the vagus nerve (ABVN) or Arnold's nerve activates the central vagal pathways in a similar way as implanted VNS. In addition, we have recently shown by magnetoencephalography recordings (MEG) that the auditory cortical responses can be modulated by the application of tVNS. This suggests an access to the auditory system through the vagus nerve. The aim of this study was to investigate therapeutic efficacy and safety of tVNS in tinnitus patients.

Methods: The left ABVN of 30 patients with moderate or severe tinnitus was stimulated with tVNS continuously for 60 min per day for five days. Customized sound (music) therapy was applied simultaneously. Tinnitus loudness and annoyance (VAS), tinnitus handicap inventory (THI) and mini-TQ were registered before and after treatment. WHO-5-point questionnaire was used for the evaluation of general well-being, a. Heart rate was continuously monitored during the treatment sessions.

Results: tVNS seems to consistently reduce the subjective loudness and annoyance of tinnitus. The average scores of THI and mini-TQ were lowered by 20 and 5 points, respectively. Furthermore, tVNS seems to have a clearcut beneficial effect on tinnitus-related stress increasing significantly the patients` coherence and subjective well-being.
Heart rate monitoring during the tVNS treatments showed no cardiac or circulatory effects (e.g. bradycardia) in any of the patients. No adverse effects were observed during subsequent treatments.

Conclusion: A combination of tVNS and tailored ST seems to reduce the severity of subjective tinnitus sensation and the tinnitus-associated distress in tinnitus patients. It is also worth noting that no adverse effects were observed during the tVNS treatments.

P54. COMPARISON OF rTMS OUTCOMES BETWEEN IPSILATERAL AND CONTRALATERAL AUDITORY CORTEX APPLICATION IN UNILATERAL TINNITUS

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We compared the impact of 1Hz repetitive TMS (rTMS) delivered either contralateral or ipsilateral to the symptomatic ear in patients with unilateral chronic tinnitus. Forty patients with unilateral, non-pulsatile tinnitus of 6 months duration or greater who were refractory to medication were enrolled. Patients were randomly assigned to one of two treatment groups: with stimulation at 1Hz applied to the temporoparietal junction either ipsilateral (n=21) or contralateral (n=19) to the symptomatic ear. Six hundred pulses per session were given daily for 5 days. Changes in tinnitus handicap inventory (THI) and self-rating visual analogue scores (VAS) for loudness, awareness, and annoyance were measured and analyzed before, immediately after, and 1 month after treatment. There was no statistically significant difference in the number of patients with improved THI scores between ipsilateral and contralateral stimulation. Additionally, there was no significant difference in decrease of THI and VAS scores between two groups at immediate follow-up and 1 month after rTMS. Finally, significant decreases in THI and most VAS scores were observed 1 month after rTMS in both ipsilateral and contralateral stimulation groups. Daily treatments of 1Hz rTMS applied ipsilateral and contralateral to the side of tinnitus both demonstrated a significant beneficial effect. The laterality of stimulation with 1Hz rTMS may not be a decisive factor in relieving symptoms.

Others
guided by
C Coelho

P55. MISOPHONIA FROM ARISTOTLE TO LEVITIN

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Misophonia is a sound sensitivity disorder which was first identified by Dr. Jastreboff. He described an aberrant, sound induced behavior observed to a sound or a group of sounds, usually in an adolescent population. It is considered to be an auditory disorder, however, according to Dr. Jastreboff; it is not related to auditory pathways; at least not related to the peripheral auditory mechanism.
From a Greek word "miso" meaning dislike, Misophonia represents an auditory phenomenon which manifests itself with a strong dislike of certain sounds which are perfectly acceptable to most people in terms of loudness and pitch. It is often manifested by an uncontrollable, very strong, autonomic and automatic reaction such as rage, fear, anger. Therefore, it would appear that Misophonia results from an abnormally strong reaction of the Autonomic Nervous System (ANS) and Limbic System (LS) to a sound or sounds resulting from enhanced connections between the auditory and LS as well as the ANS. Therefore, the question which begs itself; "is misophonia a learned conditioned response?" or, "Is it hardwired, CNS/ANS systems which have gone a-wry?"
According to private correspondence with Misophonia group members, the "repair" of the systems responsible for Misophonia as suggested by Dr. Jastreboff, has not been very successful.
A new explanation of the Misophonia disorder will be described. It is proposed that the auditory pathways play a more significant role in amplifying the adverse sounds in some patients. In addition, the role of associated, non-auditory systems will be reviewed. Creation of "misophonic loops" and subsequent use of brain plasticity in habituation of such loops will be offered as a treatment option.
The role of the reticular formation, specifically the descending reticular nuclei in the brain which are involved in reflexive behavior such as coughing, chewing, swallowing will be explained. It is also proposed that there is a creation of a very specific auditory attention loop/s which causes additional tuning to the misophonic sounds. Since it appears that such sounds receive "preferential" attention, the role of Cognitive Behavioral Therapy (CBT) may be useful as an additional component in treating misophonia. Levitin's record keeping theory and Aristotle's sensory categorization, as they may be applied to misophonia, will be discussed.
Reverse Progressive Masking (RPM) ©™ is a new method for Misophonia treatment which was developed by this presenter over the last two years. It has been successfully applied in his practice to misophonic patients. There will be a short presentation of a few cases. One case will be reviewed from the onset to the final conclusion.

Levitin DJ, This is your brain on music. Penguin Group, 2006
Guenther RK, Memory. Foundations of Cognitive Psychology, Cambridge: MIT Press, 2002

P56. A NOVEL MECHANISM FOR THE COCHLEAR AMPLIFIER

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Background: Von Bekesy's model of the frequency – place arrangement for analysis of sounds within the cochlea was a remarkable achievement. The amplification of sounds, however, is not explained by his model. It is consensus that positive feedback is applied to the outer hair cells (OHCs) to amplify the motion of the basilar membrane (BM). How the feedback is generated and applied in correct and timely fashion is unclear – especially considering that the stereocilia tips of most outer hair cells are embedded in the overlying tectorial membrane (TM). This work hypothesises a mechanism that requires the OHCs to provide a 'pumping action' similar to that used in electronic parametric amplifiers. This pumping may give rise to lateral vibrations of the fibres of the Organ of Corti (OC) at a frequency equal to the sum of the characteristic frequency (CF) of the underlying BM vibrations and the frequency of the pumping motion.

Method: This model has been formed over more than twelve years by reading relevant texts and journal articles, attending tinnitus conferences and asking questions of some of the notable researchers in the field. The main driving idea is that the cochlea has potentially quantifiable inputs and outputs, so reverse-engineering should be a possibility. Many of the structures within the cochlea resemble the detectors and antenna arrays of radar systems, but in miniature. Where there is functional similarity, it is possible that the same physical laws apply to both. The main precept is that each cochlea may be considered to be a bank of thousands of analogue –to– digital-convertors (ADCs) whose operation is synchronised by a fixed sampling (pump) frequency. Some ideas of Helmholz, Gold and others are re-visited and brought into the digital age. Ultrasonic perception of sounds through bone conduction is also discussed and some supporting experimental results noted.

Conclusions: 1. The auditory – vestibular system is the primary defence system in humans. It must function at all times when awake and, possibly, also when asleep. It must continue to function when there has been significant damage to its constituent parts and when the individual is dis-oriented. The key to all this is timely analysis of the sound field surrounding a person and may require a fast 'clock' signal.

2. Everyone may have tinnitus. For normally hearing people, the pitch could be an inaudible tone or sampling signal with a frequency of around 20 to 25 kHz. If OHC damage occurs, however, then the pitch reduces by an integral factor – e.g. to one half, one third, one quarter or one fifth of the sampling frequency – giving rise to the sensation of tinnitus.

3. At the very least this model of auditory function can be used by GPs, audiologists and others to explain to patients that tinnitus is a natural consequence of OHC malfunction and that it enables the cochlea to continue to transduce and localise sounds despite considerable OHC damage.

P57. OTOSOCIOLOGY: THE CAUSE OF TINNITUS IS OUTSIDE THE EAR IN THE SOCIAL ENVIRONMENT

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Background: Otosociology (1) is a new discipline that poses a new paradigm in tinnitus. The otosociological methodology studies from the ear to the social environment of the person and finds the cause of tinnitus in the social environment. The cause is comprised of conflicts and social tensions along with an inappropriate attitude. Conflicts and social tensions derived from family and work fundamentally. The inappropriate attitude stems from beliefs (knowledge), emotions (feelings) and habits (manners). This causes stress to be the mechanism of action of central neural hyperactivity that generates tinnitus.

Methods: Otosociological methodology (2) studies the tinnitus in five steps: 1. Ear (otorhinolaryngology and audiology), 2. Head (images), 3. Body (somatosensory and organic), 4. Person (personality), and 5. Social environment (social semi-structured interview). Social semi-structured interview finds conditioning factors, triggers factors and temporal link of conflicts and social tensions in the generation of tinnitus.
Otosociological methodology is applied to 50 patients with idiopathic subjective tinnitus.

Results: Of the 50 patients with tinnitus, the causes of tinnitus are conflicts and social tensions in the family and work. The family cause is present in 60% and labor cause in 40% of cases. In the family, from high to low incidence: caretaker of a dependent family, illness of a relative, divorce, death of a relative, own illness, other. In the work, from high to low incidence: unemployment, studies and oppositions, promotion with more responsibility, retirement, work overload, other.

Conclusions: Otosociology finds the cause of idiopathic subjective tinnitus in the social environment of the person

1. *López-González MA, Cherta G, Abrante A, Esteban F. Otology versus Otosociology. INRS Otolaryngology 2012, doi:10.5402/2012/145317.*
2. *López González MA, Abrante A, Esteban F. Find out the cause of tinntus and put treatment. Seville: Publidisa, 2013.*

P58. TINNITUS: NOT ONLY TREATABLE BUT ALSO CURABLE DISEASE

CASE PRESENTATION

Ramiro Vergara
Institution: Fundacion Ciencia y Tecnologia. Bogotá – Colombia. www.funda-cyt.com.

C. H. Patient G. M. female 60 years old. On January 2012, she told Tinnitus on left ear started on November 2011, one week after she returned from holidays at the sea side. She spent one week at the sea side with her husband, her daughter and her son in law. She has never been at the sea side before. She lived a very pleasant holidays and on returning home, one Sunday morning cooking breakfast with her daughter, she had to abandon the kitchen and she couldn't take her breakfast because she felt panic. There was no visible reason for her panic, but it was so intense she couldn't stay alone at bathroom for a shower and three days later tinnitus on her left ear began, similar to crickets. She felt pain on the region around her left ear. Hyperacusys absent.

Background.- No history of hearing impairment. Four children's Mother. Profession: housewife.

Examination.- Normal otoscopy on both ears. Hearing tests: pure tones audiogram: normal. Type A tympanogram on both ears. Acoustic reflex present on both ears. Objective accouphenometry on left ear: frequency at 3.100 Hz, intensity 3 dB. Vital signs normal. Laboratory: blood count and urinalysis normal. Tall 1.58 m, 52 kg weight.

Treatment.- I. One month sketch: 1. Pyridoxine I V 900 mg daily during ten days. 2. Next ten days Pyridoxine orally 2 gr daily. 3. Pyridoxine I V 900 mg daily. After first month treatment tinnitus began to low its intensity; panic was lowering and the same for pain around left ear. Then

a second month sketch was started in the same way than the first and after twenty days tinnitus was absent. Panic lasted three more weeks. II. Psychotherapy sessions once a week. Now nine months after treatment started, tinnitus is absent the same than panic.

Conclusions.- 1. A pleasant experience can generate tinnitus. 2. Panic goes usually accompanying tinnitus. 3. Treatment based on neurophysiologic mechanism of tinnitus is successful.

P59. TINNITUS AMONG TEENAGERS: EXPOSURE TO POTENTIALLY RISKY LEISURE HABITS

Tanit Ganz Sanchez[1,2], Fernanda Moraes[1], Juliana Casseb[1], Jaci Cota[1], Márcia Kii[1,2], Katya Freire[2]

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Background/aim: It is clear that leisure habits of modern life induced an earlier exposure to loud sounds, anticipating cumulative and irreversible auditory lesions. Interestingly, young people often perceive their tinnitus before noticing changes in hearing, except for moments of temporary threshold shift after exposed to noise. Thus, tinnitus in this particular population seems more suitable to be a warning symptom, which could lead for early diagnosis and intervention, so as to avoid further damage to auditory pathways. The objective of this study is to compare the frequency of potentially risky leisure habits between teenagers with and without tinnitus.

Methods: As part of a 3-phase study to be completed in 2 years, we invited teenagers from 11 to 17 years-old to fulfill a specific questionnaire searching for hearing symptoms and detailed information about potentially risky habits during leisure activities, such as noisy environments (parties, shows, pop concerts), ear phones and mobiles. They also underwent medical and audiological evaluations including otoscopy, wax removal, pure tone audiometry up to 16kHz and Loudness Discomfort Levels. Those who have tinnitus were additionally submitted to VAS (0 to 10) for annoyance, as well as to pitch/loudness matching and minimum masking levels. Such complete evaluation was performed in the school by the same team of ENTs and audiologists. So far, 170 teenagers (61.1% males; mean age 14.2 years) were included. Exposure to potentially risky habits was compared between teenagers with tinnitus (Group A, n=93, 54.7%) and without it (Group B, n=77, 45.3%).

Results: The habit of using ear phones was very common among teenagers of Group A (89.2%) and B (92.2%), but there was no significant difference between groups regarding the preferred volume, the number of hours per day and the number of days per week that they use to listen to music. The habit of going to noisy environments was also very common between Group A (82.7%) and B (75.3%), but there was no significant difference between groups regarding the number of hours per day nor the number of days per month that they spend in such environments. However, temporary appearance/increase in tinnitus loudness right after sound exposure was significantly higher in Group A (63.6%) when compared to Group B (34.4%). The habit of using mobiles was also very common among teenagers of Group A (93.5%) and B (96.1%), but there was no significant difference between groups regarding the number of hours per day nor the preferred ear to talk on the phone.

Conclusions: conversely to what was previously expected, the frequency of 2 abstract submissions - TRI 2013 https://email.1und1.de/ox6/v=NpshSGA/detailMail.html[18.02.2013 09:43:09] exposure to potentially risky leisure habits was similar between teenagers with and without tinnitus. So far, the only significant difference between groups is the appearance/increase in tinnitus loudness right after sound exposure. Although this is a temporary phenomenon which is ignored and considered as "normal" by the vast majority of patients, we speculate whether it should be considered a symptom of vulnerability to constant tinnitus.

P60. THE EFFECT OF PREVENTION CAMPAIGNS ON YOUNGSTERS

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Background: As a consequence of loud music exposure, whether through parties or personal listening devices use, symptoms such as hearing loss, noise-induced tinnitus and hyperacusis, increased tremendously over the last years in adolescents and young adults. Noise-induced tinnitus (NIT), even in a transient form, is a sign of overexposure and might therefore be a relevant precursor for future hearing problems. Previously an epidemiological study, conducted at University Antwerp, on 4000 secondary school students (aged 14 to 18 years old) and 250 university students, revealed a prevalence of 74.9% of transient NIT in this young population, with a significant increase of the symptoms with age. Approximately 18% even reported a permanent experience of tinnitus. In contrast, barely 5% used hearing protection (HP) in noisy environments. Assessment of the attitudes towards noise and HP (by use of the 'Youth Attitudes Towards Noise Scale' (YANS) and the 'Beliefs About Hearing Protection and Hearing Loss' (BAHPHL) respectively) showed that adolescents do not see exposure to loud music as risky behavior and therefore do not have the intentions to protect their hearing. In an attempt to increase the awareness of young people and to prevent future noise traumas in this population, the Flemish authorities financed two separate sensitization campaigns. The present study evaluated the efficacy of a certain sensitization program.

Methods: The questionnaire used in the epidemiological study was administered a second time to 1000 adolescents and young adults in March 2012. Following questions were evaluated: was the campaign visible enough?; was there a change in attitudes towards noise?; was there a change in attitudes towards HP?; was there an increase of HP use among young people?

Results: Unfortunately, only a small 10% confirmed to be familiar with the campaign. However, after the sensitization campaigns as well as local initiatives, scores on the YANS and BAHPHL were significantly decreased compared to the previous survey, meaning the attitudes towards noise became more negative. This attitude change also reflected in a large increase of HP use in those students who knew the campaign (+11%) compared to those who were not familiar with the campaign (+1.2%). Those familiar with the campaign were also more inclined to use HP in the future than those who did not knew the campaign.

Conclusion: Adolescents and young adults are not insensitive to sensitization programs. As such, these initiatives should be maintained in the future. Future research should assess whether such campaign have long term effects.

Acknowledgements: We thank the Stavros Niarchos Foundation and a TOP-BOF mandate of the University Antwerp for the financial support for tinnitus research.

SATURDAY
MAY 18, 2013

9:00 - 10:15 a.m.
PLENARY TALKS

9:00 - 9:40 a.m. – Keynote Speaker
TINNITUS: BRAIN CONNECTIVITY AND ITS DYNAMICS

Winfried Schlee
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The human brain activity is in permanent change and dynamically adapts to external and internal demands. Thereby the brain adapts to environmental changes and altered sensory input, it reorganizes itself as an effect of sensory loss or malfunction and also adjusts to brain dysfunctions in case of injuries or infections. This continuous change is largely advantageous and functional in a way that it helps to optimize the information processing and output of the central nervous system. The timeline of this change can be a within milliseconds, from one situation to the other, or within years in the case of age-related changes over the life-span.

The brain activity related to tinnitus is often associated with increased functional connectivity between the auditory cortex, the dorsolateral prefrontal cortex, the orbitofrontal cortex, the insula, the anterior and posterior cingulate cortex (see e.g. [1]). Given the adaptive nature of the human brain, the pattern of functional connectivities in the tinnitus brain is also in perpetual change. In this talk I will review several lines of research investigation this adaptive changes of tinnitus-related brain networks and its behavioral relevance. At first, this comprises connectivity changes as a function of tinnitus duration. Secondly, I will discuss the influence of age on the tinnitus perception and the associated brain networks. As a third point I want to tackle the largely underinvestigated topic of short-term changes in tinnitus perception. Tinnitus patients report that their tinnitus perception can change from one situation to the other. How often does that happen and is it a regular pattern? What are the reasons for this variation? Is this moment-to-moment variation of tinnitus perception related to the dynamic changes in functional brain connectivity? What are the methodological limitations in assessing moment-to-moment tinnitus variation and how can they be solved? I will try to answer some of these questions and show some first attempts in investigating the moment-to-moment tinnitus variation.

References

Song J-J, De Ridder D, Schlee W, Van de Heyning P, Vanneste S. Neurobiol Aging. 2013; 34(7): 1853–1863.

9:40 - 10:15 a.m. – Invited Speaker
PULSATILE TINNITUS

Dirk De Ridder
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Pulsatile tinnitus, in general, is not related to pathology of the auditory system. Two main types of pulsatile tinnitus exist: arterial heart beat synchronous pulsatile tinnitus and venous respiratory synchronous pulsatile tinnitus. The arterial pulsations are most likely transmitted to the cochlea via the cerebrospinal fluid, a mechanism similar to what has been proposed as an explanation for bone conduction. The arterial and venous pulsations are normally suppressed via somatosensory-auditory interactions involving the dorsal cochlear nucleus. Arterial pulsations are possibly also dampened by venous plexuses surrounding the carotids and vertebral arteries. The main causes of pulsatile tinnitus are related to abnormal blood vessels, either arterial or venous. Examples are vascular stensosis, aneurysms, arteriovenous malformations or fistulas etc. But also hyperdynamic flow, or turbulence caused by sharply curving vascular loops, duplicated carotids or hypervascularized tumors and large sinuses can be responsible for sound transmission leading to pulsatile tinnitus. Benign intracranial hypertension is another common cause of pulsatile tinnitus.
MRI, CT, or classical angiography are diagnostic tools for pusatile tinnitus. Selective angiography with transient balloon occlusion can be used clinically to correlate radiological findings with the pulsation perception, and guide surgical or non-surgical treatment.
In 15-30% of patients, no cause can be found for the pulsations, even though recently some new causes have been discovered, including somatosensory pulsatile tinnitus, vascular aquaduct compression and a looping carotid artery.
In view of the fact that many causes are treatable pulsatile tinnitus should be investigated thoroughly in each individual. In those patients in whom no cause can be found but are characterized by a marked hearing loss, a trial with hearing aids could be theoretically considered, in order to mask the pulsations transmitted via the cerebrospinal fluid.

10:45 a.m. - 12:45 p.m.

SESSION 11: Neuroimaging of Tinnitus Chairs: A Cacace, S Vanneste

AUDITORY NETWORK CONNECTIVITY IN TINNITUS PATIENTS: A RESTING-STATE FMRI REPLICATION STUDY

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Background: The underlying neural mechanisms of tinnitus have yet to be defined. However, the advent of human neuroimaging methods such as functional MRI (fMRI) is providing new ways of investigating such mechanisms. So far, most fMRI tinnitus studies have focussed on sound-evoked brain activity, but in the case of chronic health conditions such as depression and schizophrenia, there is a growing interest in resting-state brain activity. In one tinnitus pilot study (1), resting-state fMRI data were collected from four patients and six age-matched controls. Preliminary results indicated that "average functional connectivity scores" between paired auditory cortical regions were significantly lower in tinnitus patients than in controls ($p < .05$). This present study aims to replicate and build on this work, using a larger cohort of age, sex and hearing-matched subjects with and without tinnitus.

Methods: Twelve patients (seven male; mean age 66 years) all with chronic, (2 years minimum duration) constant tinnitus participated in the study. We also recruited eleven age and hearing matched controls (eight male; mean age 68 years). Subjects with a history of neurological disorder, hyperacusis or unilateral/asymmetrical hearing loss were excluded. Whole-brain functional images were acquired for each patient during a five-minute period of eyes-closed wakeful rest. The fMRI data were pre-processed using SPM v8. Group level independent component analyses (ICA) were then performed to identify the spatially independent component corresponding to the auditory network. Voxel peaks of resting-state auditory 'activity' were identified from that auditory network component using pre-defined anatomical masks for bilateral primary and secondary auditory cortex. These four peaks were then entered as seed regions for the functional connectivity analyses.

Results: A two sample t-test of the group level auditory network component showed increased functional connectivity in the right supramarginal gyrus and left posterior middle temporal gyrus for the tinnitus group ($p < 0.01$). However, these areas of increased functional connectivity do not survive false discovery rate corrected statistical thresholding. No significant differences were found between the bivariate correlation coefficients or the partial correlation coefficients for any of the paired auditory seed regions.

Conclusions: Results from this present study did not replicate the findings of Kim et al. (2012). An explanation for this conflict may be that Kim et al.'s groups were not well matched in hearing status. This crucial factor could confound results as compensatory mechanisms for hearing loss may differ to those of tinnitus, resulting in differences in functional neural responses (2).

References

1. *Kim, JY. , Kim, YH. , Lee, S. , Seo, JH. , Song, HJ. , Cho, JH., & Chang, Y. Int J Audiol, 2012; 51: 413-417.*
2. *Husain, FT., Pajor, NM., Smith, JF. , Kim, JH. , Rudy, S. , Zalewski, C. , Brewer, C., and Horwitz, B., PLos ONE, 2011; 6 (10), 1-12.*

EVALUATION OF RESTING STATE BRAIN FUNCTIONAL ACTIVITY IN PATIENT WITH TINNITUS BY FUNCTIONAL MAGNETIC RESONANCE IMAGING

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Background: Recently, increasing evidences have indicated that neural hyper-activity in the central auditory system might be involved in the neuropathophysiology of tinnitus. However, until now, only few studies have performed Blood oxygenation Level Dependent-Functional magnetic resonance imaging (BLOD-fMRI) in patients with tinnitus. The purposes of the current study were (1) to investigate the changes in the firing pattern of neurons in the central auditory system and (2) to contribute objective clues for the clinical diagnosis and treatment of tinnitus.

Methods: To compare the changes in the firing pattern of neurons in the central system in 45 patients with tinnitus and 37 healthy volunteers by means of the standard BLOD-fMRI scan sequence. Among the tinnitus patients, 24 were men and 21 were women. 11 suffered from left-sided tinnitus, 19 had right-sided tinnitus, and 15 had bilateral tinnitus. Among the control group, 21 were men and 16 were women. Subjects of the control group were normal hearing adults with no previous history of tinnitus and otologic disease. The two groups had similar sex and age distribution.

Results: (1) The firing pattern of neurons of the central auditory system in patients with tinnitus was abnormal: such as pons, bilateral medial geniculate body, superior temporal gyrus and so on. (2) Irrespective of the presence of tinnitus, in the auditory system, functional hyper-activity areas of subcortex were predominantly right-hemispheric; on the contrary, the ones of cortex were left-lateralized (left superior temporal gyrus). (3) Intriguingly, the non-auditory systems, such as the limbic system, visual cortex and anterior frontal association

cortex were involved in the process of tinnitus showing differential BLOD signal.

Conclusions of the study: In the resting state, asymmetrical and distinguished functional outcomes depended on differential change pattern of neurons activation in the cortical and the subcortical structures of the auditory pathway in patients with tinnitus owing to lateralization of activity. Although, brain region developed such abnormal change independent of the side of the tinnitus. On the other hand, there was significant difference on signal intensity change between patients with lateralized tinnitus and patients with symmetrical tinnitus.

Keywords: tinnitus; resting state; BLOD fMRI; auditory system; non-auditory systems

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FUNCTIONAL CONNECTIVITY BETWEEN PRIMARY AUDITORY CORTEX, COGNITIVE CONTROL AND DEFAULT MODE NETWORKS IN TINNITUS AND HEARING LOSS

J. R. Melcher and I. M. Knudson
Mass. Eye and Ear Infirmary, Harvard Medical School

B**ackground and Aims:** This study compared functional connectivity (FC) arising from primary auditory cortex (PAC) between people with tinnitus and non-tinnitus control subjects. FC is measured as a temporal correlation of activity between brain areas. Here, FC was examined using fMRI during a "resting" (i.e., undriven) state. Given the emotional and cognitive elements of the tinnitus condition, we asked two questions: (1) Does PAC activity show FC with brain areas typically engaged during executive and/or emotional processes such as those forming two major networks of brain function: a cognitive control network (CCN) and default mode network (DMN)? (2) Does FC differ between tinnitus and control subjects?

Methods: Subjects in three groups were tested. NH-control subjects (n=10; 6 men; 44-60 yrs) had clinically normal/ near-normal thresholds and no tinnitus. NH-tinnitus subjects (10; 8; 44-61) had tinnitus and mean threshold matched to the NH-control goup. HF-tinnitus subjects (11; 9; 47-62) had bilateral, high-frequency hearing loss and tinnitus. To control for sex, in addition to age and threshold, the men of each group were considered separately, in addition to considering the full groups.

fMRI images of the entire brain were acquired in brief clusters (<1 s) separated by ~8 s. The fMRI data were temporally high-pass filtered (0.0016 Hz). The first five principal components of the overall signal time course in CSF and in white matter, and the first component for the gray matter, were removed from the fMRI data by regression. Signal vs. time in left and right PAC was cross-correlated with the signal in each voxel of the brain resulting in a spatial map of correlation coefficient. PAC was defined in individual subjects as the gray matter of first Heschl's gyri of each subject.

Results: PAC of all three subject groups showed the expected positive FC (i.e., positive correlations) with auditory areas of the ipsilateral and contralateral temporal lobe,

PAC also showed positive FC with areas in the CCN: supplementary motor area (SMA), preSMA and anterior cingulate cortex. There was no difference among groups in FC to these areas.

PAC of the three subject groups also showed negative FC (negative correlations) with areas comprising DMN: precuneus/posterior cingulate cortex (PCC), right and left parietal lobe and, medial prefrontal cortex.

The full subject groups did not show significant differences in FC to DMN areas, but the male subset did. Specifically, the NH-control group showed significantly more negative correlation with PCC than the HFL–tinnitus group, for both left and right PAC seeds (cluster-level FWE-corrected $p<0.01$). Left PAC correlations with MPFC were also more negative in NH-controls (cluster-level FWE- corrected $p=0.06$). The NH-tinnitus group, like the HF-tinnitus group, showed less negative correlation with the PAC seeds compared to NH-controls.

Conclusions: The results suggest a conduit by which exogenous auditory information can interact with the endogenous signals of the default mode network and suggest that this conduit may not operate normally in those with tinnitus, and especially those with hearing loss and tinnitus.

Funded by NIH/NIDCD and the Tinnitus Research Consortium.

FUNCTIONAL NEAR-INFRARED SPECTROSCOPY IN TINNITUS

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Background: In recent years, human neuroimaging enhanced the understanding of neural mechanisms of tinnitus. However, each neuroimaging technique has specific limitations. Here, we firstly provide data in tinnitus from functional near-infrared spectroscopy (fNIRS) - an optical, not magnetic approach to measure blood oxygenation level dependent signals. fNIRS is a valid and reliable method with limited spatial resolution, but was shown to be capable to measure activity in auditory cortex.

Methods: White noise was presented in an event-related (40 x 1.75s with 12-14s breaks) and block-wise (12 x 20s with 20s breaks) manner in 37 patients with tinnitus and 33 healthy controls. The fNIRS probe-sets (2 x 22 channels) were placed over temporal areas. Patients received treatment with repetitive transcranial magnetic stimulation (rTMS).

Results: Preliminary analyses indicate that tinnitus was associated with increased oxygenation in the right auditory cortex in contrast to controls. rTMS induced normalisation of hyperactive right-auditory oxygenation.

Conclusions: fNIRS is capable to add relevant information to sound evoked activity in auditory cortex. Future

studies might be able to add more precise knowledge of auditory cortex activity with respect to the laterality and the character of the tinnitus percept. fNIRS might also be valuable in measuring brain areas which are challenging measureable by functional magnetic resonance imaging, i.e., orbital-frontal cortex due to susceptibility artefacts. In addition, further research should concentrate on resting state measurements or on combined fNIRS-EEG measurements obliterating the limitations of both techniques.

TOWARDS AN OBJECTIVATION OF TINNITUS: MACHINE LEARNING APPROACH OF RESTING STATE ELECTRICAL BRAIN ACTIVITY CAN DETECT THE PRESENCE OF TINNITUS

Sven Vanneste[1], Kathleen Joos[1] & Dirk De Ridder[2]
[1]. *Department of Translational Neuroscience, Faculty of Medicine, University of Antwerp, Belgium.*
[2]. *Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, New Zealand.*

Non-pulsatile tinnitus is a perception of sound in the absence of an external sound source, to de differentiated from objectively observable pulsatile and pseudo-pulsatile tinnitus, generated in the body by turbulence of blood flow or muscle contractions. Non-pulsatile tinnitus a purely subjective form of tinnitus as it can only be observed by the person who has tinnitus. It would be highly desirable to diagnose the presence or absence of tinnitus in an objective way. Recently, scientists have developed machine learning techniques that can learn to recognize patterns by classifying seen data, taking into account their statistical variation. These algorithms can subsequently be applied to unseen data. In other words, based on the known properties learned from the trained data, these algorithms can predict whether the pattern corresponds to the presence or absence of tinnitus. We therefore combined EEG with machine learning to develop a brain-based electrophysiological signature for the presence or absence of tinnitus. Hundred and fifty-three tinnitus EEGs and 264 healthy controls are used as training sets, and the predictability of the presence of tinnitus is trained using a support vector machine. Using the support vector machine yields better predictive results than using Bayesian inference learning, with a correct predictability of approximately 90%. These results suggest that it might become possible in the near future to diagnose the presence or absence of tinnitus based solely on an EEG oscillatory signature.

10:45 a.m. - 12:45 p.m.

SESSION 12:
Tinnitus Pathophysiology: Interaction between Auditory and Non-Auditory Pathways
Chairs: AB Elgoyhen, A Møller

STRESS CHANGES THE PROTEIN EXPRESSION IN AUDITORY PATHWAY

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Aims: We have previously demonstrated that the emotional stress induces auditory hypersensitivity and gene expression changes in the auditory system of Wistar-Harlan rats (1, 2). Here, we studied stress-induced changes in protein expression in the auditory system of Wistar-Hannover rats. In particular, we studied proteins involved in the phenomena of neuroplasticity.

Methods: The rest were stressed as previously described in detail (1, 2). Immediately after finishing the stress as well as 3h, 6h, 24h and 7 days later, we measured auditory brainstem responses. In addition, we collected blood and tested the serum for presence of corticosterone, brain-derived nervous factor (BDNF) and tumor necrosis factor-alpha (TNF-α) using commercial ELISA. The auditory tissues (cochlear nucleus, inferior colliculus and auditory cortex) were lysed in the RIPA buffer, the lysate was subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and the resolved proteins were immunoblotted with antibodies specific for AMPA2, AMPA3, Syt1, Syt12, BDNF and Arc1.

Results: ABR indicated lowering of hearing threshold as soon as 3h after finishing stress. This hypersensitivity reached plateau 24h later and was still statistically significant after one week. Six hours after finishing stress, the concentration of BDNF, TNF-α and corticosterone rose significantly, as compared to control animals. Stress induced upregulation of all studied proteins in the auditory cortex. This upregulation was significant immediately after stress up to 24h later.

Conclusion: Our findings support the association of emotional stress with changes in the auditory system of rats that happen on gene expression and protein expression levels. Interestingly, we found differences in the post-stress auditory reactions between two different strains of rats (Wistar-Harlan and Wistar-Hannover) suggesting genetic factor(s) regulating the type and length of auditory response. Temporary fluctuation of corticosterone in serum of stressed animals is in agreement with the activation of hypothalamus-pituitary-adrenal axis. Increase in circulating systemic BDNF and TNF-α suggests possible damage/regeneration processes in the CNS as well as systemic pro-inflammatory reaction, both potentially affecting auditory pathways. Taken together, emotional stress induces strain-specific modulation of auditory function in rats. This modulation

is accompanied by temporary changes in the expression of genes and proteins essential for the process of neuroplasticity in auditory tissues.

1. *Mazurek B, Haupt H, Klapp BF, Szczepek AJ, Olze H., Neurosci Lett. 2012: 40-5*
2. *Mazurek B, Haupt H, Joachim R, Klapp BF, Stöver T, Szczepek AJ., Hear Res. 2010:55-63*

NEURAL ALTERATIONS IN OUTSIDE THE CLASSICAL AUDITORY PATHWAY AFTER TREATMENT WITH TINNITUS INDUCERS: NOISE AND SALICYLATE

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Center for Hearing and Deafness, University at Buffalo, Buffalo, NY 14214, USA

Background: Debilitating tinnitus is thought result from the confluence of aberrant neural activity within the classical auditory pathway as well non-auditory regions of the brain involved with emotion, memory and attention. While much effort has been devoted to identifying abnormal activity within the classical auditory pathway, comparatively little is known about the neurophysiological changes that occur in non-auditory loci putatively linked to the perception or reaction to tinnitus.

Methods: Here we report on the electrophysiological changes seen in the lateral amygdala (LA), the auditory region of the striatum (Str), hippocampus (Hi), and cingulate cortex (Cg) after high level exposure to salicylate or noise, well known inducers of tinnitus. Results: The LA, involved in fear conditioning, receives inputs from both auditory thalamus and auditory cortex. High doses of salicylate shifted the frequency receptive fields (FRF) of many neurons in the LA towards the mid-frequency region, consistent with the pitch of salicylate-induced tinnitus and the tonotopic map reorganization seen in the auditory cortex. Exposure to intense noise (16-20 kHz or 10-20 kHz) enhanced neural responses near the low-frequency edge of the hearing loss in some, but not all, exposed animals. Expansion of tonotopic map at the transition region could enhance the perception of tinnitus. The Str, previously identified as a “gate” for the perception of tinnitus in humans, also receives inputs from the auditory thalamus and cortex. Consistent with the LA, salicylate shifted the FRF of many Str neurons to the mid-frequencies, consistent with the pitch of salicylate-induced tinnitus. However, exposure to intense noise failed to induce significant FRF shifts or tonotopic map reorganization in the Str. The Hi, which is involved in memory and spatial navigation, responded weakly to acoustic stimulation in controls; however, after salicylate treatment auditory responses were greatly enhanced. However, the Cg, which is involved in memory formation and executive function, was unaffected by high-doses of salicylate.

Conclusions: Our results indicate that two well-known inducers of tinnitus, salicylate and noise, can induce profound changes outside the classical auditory pathway. The LA seems to be involved in both the salicylate- and noise-induced tinnitus whereas the Str appears to be involved in salicylate-induced tinnitus, but not noise-induced tinnitus. Finally, our results suggest that the Hi may also be involved in salicylate-induced tinnitus, whereas the Cg does not. Supported in part by grants from NIH (R01DC009091; R01DC009219) and ONR (N000141210731)

PERSISTENT SOMATOSENSORY EFFECTS ON DORSAL COCHLEAR NUCLEUS NEURONS DIFFER PRIOR TO AND FOLLOWING COCHLEAR DAMAGE AND TINNITUS-INDUCTION

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Background/Objective: Robust functional connections from peripheral and brainstem somatosensory neurons to the cochlear nucleus (CN) provide a substrate for auditory-somatosensory integration (Zeng et al., J. Neuroscience, 2012). Previously, we have shown that preceding auditory with somatosensory stimulation can result in long term suppression in normal animals, but long term potentiation in animals with tinnitus (Dehmel et al, J. Neuroscience, 2012). Our objective here was to explore long-term synaptic plasticity as a dominant underlying mechanism for persistent bimodal effects on dorsal cochlear nucleus (DCN) neurons in normal and noise-damaged animals with and without evidence of tinnitus.

Methods: Single and multi-unit recordings were obtained from normal and noise-damaged guinea pigs using 4-shank multichannel silicon electrodes. ABRs were performed to assess threshold shifts and input-output functions. Gap-induced inhibition of the startle reflex was used as a measure of frequency-specific tinnitus. By altering the order and time interval between auditory and somatosensory stimulation, we examined the hypothesis that persistent somatosensory effects are stimulus timing dependent and change with tinnitus induction.

Results: Following unilateral cochlear damage that induced temporary threshold shifts (TTS) and behaviorally-verified tinnitus, persistent bimodal enhancement prevailed over persistent bimodal suppression at particular auditory-somatosensory stimulation intervals, while persistent bimodal suppression dominated at other somatosensory-auditory stimulation intervals. Furthermore, the effective intervals and orders observed after tinnitus induction were significantly different from those observed in control animals and noise-damaged animals without tinnitus.

Conclusions: These findings indicate that stimulus timing dependent plasticity underlies long-term auditory-somatosensory integration and that the rules governing this integration are altered in animals with tinnitus. These findings pave the way for treatments based on reversal of tinnitus-induced neural plasticity in central auditory structures.

TINNITUS AS SIDE EFFECT: A DRUG-TARGET NETWORK ANALYSIS

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Instituto de Investigaciones en Ingeniería Genética (CONICET) Argentina[1], Department of Pharmacology, School of Medicine, University of Buenos Aires[2], University of Regensburg, Department of Psychiatry and Psychotherapy, Germany[3], Unit of Neurosurgery, Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, New Zealand[4], Brai²n, TRI & Department of Neurosurgery, University Hospital Antwerp, Belgium[5]

Background: A wide variety of approaches have been used in an attempt to delineate the neural correlates of tinnitus. These range from experiments in animal models to brain imaging studies in humans. However, the exact mechanisms underlying this phantom perception are still unknown. A new approach can be based on the availability of large drug databases which include tinnitus as a side effect.

Methods: In order to explore the tinnitus target space, we built and analyzed a drug-target network based on compounds that elicit tinnitus as side effect. A total of 300 drugs with side effect tinnitus were extracted from the SIDER 2 database. We subsequently looked for all reported molecular targets of these drugs in a manually curated database that was generated with information downloaded from the DrugBank and PDSP Ki databases. Using Cytoscape 3 for network data integration and analysis, we generated a bipartite 'drug–target network'.

Results: Of the 300 total drugs, 181 formed a giant component, the largest connected component of the network. Within it, two distinct modules were relevant: one that included central nervous system acting drugs and the other cyclooxygenase inhibitors. A third isolated component included cardiovascular acting drugs, mainly angiotensin converting enzyme inhibitors. The target network also displayed a main giant interconnected component which included molecules from different gene families. Only cyclooxygenase 2, cyclooxygenase 1, ACE (angiotensine converting enzyme), 5HT1A (serotonine type 1A receptor), SLC6A4 (serotonin transporter), SCN5A (sodium channel protein type 5 subunit alpha) were significant above random. These findings recapitulate the fact that tinnitus might be both of peripheral and central origin, being the cyclooxygenases most likely linked to a cochlear site of genesis and 5HT1A, SLC6A4 and SCN5A to a central mechanism. In order to further validate these results we generated drug-target networks with drugs that produce either hearing loss or hyperacousis as side effects, two symptoms that sometimes accompany tinnitus. Similar to that observed in the tinnitus network, cyclooxygenases were enhanced above random in the hearing loss network, suggesting a peripheral site of action of cyclooxygenase inhibitors. On the contrary, whereas the cyclooxygenases were not present in the hyperacousis network they shared with tinnitus 5HTA1, SLC6A4, SCN5, recapitulating the proposed central origin of hyperacousis.

Conclusions: These results indicate that high-throughput electronic-biology approaches based on in silico data mining of existing databases and integration of this information through network analysis can further help understand tinnitus and related disorders. In addition, it might aid towards the design of better pharmacotherapies.

1:45 - 3:15 p.m.
PLENARY TALKS

1:45 - 2:30 p.m. – Keynote Speaker
TINNITUS AND STRESS

Hébert, S.
École d'orthophonie et d'audiologie, Université de Montréal, Qc, Canada

It is generally recognized that stress may act as a trigger of tinnitus or as an amplifier of tinnitus loudness. Yet data to support this claim is scarce. Our experimental studies involving cortisol analyses, a stress-related hormone, support an association between tinnitus and long-term stress. In particular, in tinnitus there is an increased sensitivity of the hypothalamus-pituitary-adrenal (HPA) axis to cortisol-mediated negative feedback. Such HPA axis disturbance has been described in other clinical populations such as patients with chronic fatigue syndrome and burnout. Moreover, recent population studies systematically demonstrate an association between symptoms of long-term stress and increased prevalence of hearing loss and tinnitus. In particular, emotional exhaustion has been identified as a stronger predictor of both tinnitus presence and severity than traditional risk factors, e.g. noise at work, sex and hearing loss. Altogether these findings have implications on treatment options for individuals suffering from severe tinnitus, suggesting that personalized stress level assessment may be considered as an integral part of the design and implementation of preventive and proactive interventional strategies targeting hearing problems.

2:30 - 3:15 p.m.
CLOSING REMARKS
TINNITUS: A TREATABLE DISEASE

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KEY DATES

Call for abstracts open	15 May 2013
Registration open	Late August 2013
Call for abstracts close	1 November 2013