



4th International TRI Tinnitus Conference Frontiers in Tinnitus Research

June 8th - 11th, 2010, Dallas, Tx, USA

Program and Abstract Book

Program and Abstracts

Fourth International TRI Tinnitus Conference Frontiers in Tinnitus Research

Organized by the
Tinnitus Research Initiative Foundation
and
The University of Texas at Dallas

Organizing Office

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The organizers want to thank the people who have helped organize this Conference, especially Beth Keithly in Dallas, and Susanne Staudinger and Sylvia Dörner-Mitschke in Regensburg.

OBITUARY

CARLOS HERRAIZ PUCHOL † March 2010



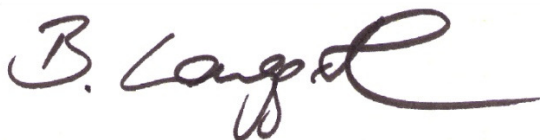
Just before Easter we received the terrible news of the tragic death of our friend and colleague Carlos Herraiz Puchol. He lost his life at the end of March in a motorcycle accident.

As one of the leading tinnitus experts in Spain, Carlos aimed to provide the best possible care for his tinnitus patients. At the same time, he always looked for new and innovative treatments of tinnitus. With these ambitions he joined TRI already in 2006. Within TRI he was always one of the most creative clinicians, motivated to translate knowledge from basic research into a clinically useful application. His research activities were always clinically oriented and encompassed a broad field, including methodologic studies for the assessment of treatment, the

benefits of somatosensoric interventions, pharmacologic treatment and auditory training. He was actively involved in the TRI Tinnitus Clinic Workgroup and contributed many chapters to the book "Tinnitus. Pathophysiology and Treatment" as well as to the new book "Textbook of Tinnitus". He also represented Spain in the EUTi, the European Federation of Tinnitus Associations. Carlos was always a very special person, modest, open minded, energetic and friendly. With his optimism he inspired and motivated colleagues around him.

We are grateful and proud that we had the privilege to work with him and to have him as a friend.

We will miss his joyful presence.

A handwritten signature in dark ink, which appears to read "B. Langguth". The signature is fluid and cursive, with a long, sweeping horizontal stroke at the end.

Berthold Langguth
Chairman of the TRI Executive Committee

Welcome to Dallas

As the host for the Fourth International TRI Tinnitus Conference I welcome you to Dallas. The three previous conferences in this series of tinnitus conferences were organized by the Tinnitus Research Initiative, which is now the Tinnitus Research Initiative Foundation. The Tinnitus Research Initiative Foundation and The University of Texas at Dallas are the organizers of Conference in Dallas.

As you will see from the Program, this Conference offers a broad coverage of research on the pathology of different forms of tinnitus, as well as coverage of treatments on the cutting edge.

It is a great pleasure to introduce you to Dallas. The city with its surrounding communities and sister city, Fort Worth, create a sprawling Metroplex with about 6.5 million inhabitants. The Metroplex has a rich cultural life featuring the Dallas Symphony Orchestra, the Meyerson Symphony Center, Dallas Museum of Art with Nasher Sculpture Garden, and the Kimbell Art Museum in Fort Worth.

The area is the site for many education and training institutions including large universities such as our co-organizer, The University of Texas at Dallas. Other universities in Dallas are UT Southwestern Medical School, Southern Methodist University and Dallas Baptist University.

Many large corporations have their home in the Dallas-Forth Worth area. Well-established firms including Kimberly Clark, J.C. Penny, Exxon Mobil, Texas Instruments and American Airlines and a variety of newer technology corporations have their North American headquarters here. In 2009, 25 area businesses were Fortune 500 companies. Dallas-Forth Worth is fifth among metropolitan areas for Fortune 500 companies.

The Dallas-Forth Worth International Airport is the third busiest airport in the World in terms of aircraft movements with nearly 1800 flights per day, with nonstop flights to 134 domestic and 37 international destinations; it is the eighth in terms of passenger traffic.

The University of Texas at Dallas (UTD) was established 40 years ago; it is a part of The University of Texas System of state schools. UTD has approximately 450 faculty and more than 15,000 enrolled students. UTD has seven schools, the Schools of Arts and Humanities, Behavioral and Brain Sciences, Economics, Political & Policy Sciences, Interdisciplinary Studies and the Erik Jonsson School of Engineering & Computer Science, all offering BA, MA, MS and PhD degrees. The academic programs cover wide areas. The Callier Center for Communication Disorders established 1962, became a part of the School of Behavioral and Brain Sciences in 1975. Recently The Center for Brain Health was created as a part of the School of Behavioral and Brain Sciences.

I hope you will enjoy your visit to Dallas and that the Conference will give you new aspects on tinnitus and perhaps it will give you new ideas about studies of tinnitus and about the treatments of patients with this enigmatic disease.

Aage Møller
Dallas, June 2010

Announcing the X International Tinnitus Seminar:



X International Tinnitus Seminar

March 16 to 19, 2011

Florianópolis - Santa Catarina - Brazil

Dear colleague,

Brazil has been elected to host the next International Tinnitus Seminar during the last 2008 meeting held in Sweden. It is the first time such an event takes place in Latin America.

We are pleased to announce the X International Tinnitus Seminar to be held in March 16 to 19, 2011 at the Resort of Costão do Santinho, situated in the paradisiacal island of Florianopolis, Santa Catarina, Brazil (www.its2011brazil.com.br)

The event will host the world's health community with a common interest in tinnitus. It will be a great opportunity to share and discuss related topics and a mind opening experience to new ideas.

Along with an exciting scientific program we are also organising a unique cultural experience of the warm and friendly "Brazilian way".

Your invaluable presence will help us to make this an unforgettable event full of new knowledge and fun.

We look forward to welcoming you to Brazil in March 2011.

Prof Tanit Ganz Sanchez, MD, PhD

President of ITS 2011

Claudia Barros Coelho, MD, PhD

President of the Scientific Committee

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OVERVIEW SCIENTIFIC PROGRAM

	June 8 th	June 9 th		June 10 th		June 11 th	
08:00 - 09:00 a.m.		PLENARY TALK: Thalamocortical Dysrhythmia and Tinnitus Rodolfo Llinás		PLENARY TALK: Synaptic Physiology of Cochlear Hair Cells: Afferent Signaling Paul Fuchs		PLENARY TALK: Tinnitus and Neural Plasticity Larry Roberts	
09:00 - 10:00 a.m.		PLENARY TALK: Do Sensory Cortices Process More than One Sensory Modality During Perceptual Judgements? Ranulfo Romo		PLENARY TALK: Tinnitus and Psychiatric Comorbidity Berthold Langguth		PLENARY TALK: Increase in Gain in the Central Auditory System and Tinnitus Arnaud Norena	
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----							
10:30 a.m. - 12:30 p.m.		Pathophysiology of Tinnitus A Norena, D De Ridder	Somatosensory Tinnitus TG Sanchez	Behavioural Therapy M Mazzoli	TMS / VNS A Londero	Sound Therapy G Searchfield	Pharmacologic Treatment of Tinnitus AB Elgoyhen
12:30 a.m – 1:30 p.m.-----LUNCH -----LUNCH -----							
01:30 - 03:30 p.m.		POSTER SESSION	POSTER SESSION		Electrical Stimulation to the Brain and to the Ear A Möller	Perceptual Training G Searchfield	
			Specific Forms of Tinnitus: T Kleinjung	Animal Models R Salvi			
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----							
04:00 - 06:00 p.m.		Neuroimaging in Tinnitus: Mechanisms and Networks F Husain	Design of Clinical Trials M Landgrebe, WH Martin	The TRI Flowchart for Patient Management B Langguth	Animal Models R Salvi	Imaging N Weisz	Audiologic Assessment R Roeser New Hypotheses JM Lainez
06:00 - 07:00 p.m.	OPENING LECTURE: The Role of the Hippocampus in Tinnitus and Hearing Richard Salvi <i>Welcome Cocktail</i>	MEETING: Is there a need for an international tinnitus society?					
08:00 p.m.				BANQUET			

DETAILED SCIENTIFIC PROGRAM

Tuesday, June 8th	
06:00 - 07:00 p.m.	<p>Opening lecture: The Role of the Hippocampus in Tinnitus and Hearing</p> <p style="text-align: center;">Richard Salvi</p> <p style="text-align: center;"><i>Welcome Cocktail</i></p>

Wednesday, June 9th		
08:00 - 09:00 a.m.	Plenary Talk: Thalamocortical Dysrhythmia and Tinnitus Rodolfo Llinás	
09:00 - 10:00 a.m.	Plenary Talk: Do Sensory Cortices Process More than One Sensory Modality During Perceptual Judgements? Ranulfo Romo	
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----		
10:30 a.m. - 12:30 p.m.	Pathophysiology of Tinnitus A. Norena / D. De Ridder R. Levine: The brainstem and tinnitus: adjustments to the dorsal cochlear nucleus tinnitus hypothesis D. De Ridder et al.: Auditory cortex involvement in Tinnitus S. Vanneste: A network approach for understanding tinnitus pathophysiology B. Langguth: The involvement of nonauditory brain regions in tinnitus N. Weisz: Analyzing network activity: implications for tinnitus research	Neuroscience and Clinical Research on Somatosensory Tinnitus T.G. Sanchez R. Bürgers et al: Temporomandibular joint and masticatory muscle disorders in patients with tinnitus T.G. Sanchez: Deactivation of myofascial trigger points is effective to control somatosensory tinnitus S. Shore: Neural basis of somatosensory influence on tinnitus Q. Yang et al: Abnormalities of vergence eye movements in somatic tinnitus J. Zhang: Electrical suppression of tinnitus
12:30 - 01:30 p.m.-----LUNCH-----LUNCH-----LUNCH-----		
01:30 - 03:30 p.m.	POSTER SESSION	
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----		
04:00 - 06:00 p.m.	Neuroimaging in Tinnitus: Mechanisms and Networks F. Husain E. Diesch: Altered inhibitory processes in Tinnitus: MEG studies D. Hall et al: Challenges and rewards of brain imaging in tinnitus F. Husain et al: Neural network differences in tinnitus and hearing loss: An fMRI study J. Melcher et al: Is the frontal lobe involved in tinnitus? A structural MRI study L> Haab et al: Event-Related Potentials as Correlates of Attentional Binding in Tinnitus: Some Insight from Neurodynamical Multiscale Modeling	Design of Clinical Trials M. Landgrebe / W.H. Martin P. Davis, S. Ransdell: Meta-Analysis of Current Tinnitus Treatments M. Koller et al: Which changes in the THI score are clinically relevant? M. Landgrebe et al: The Tinnitus Research Initiative (TRI) database: A new approach for delineation of tinnitus subtypes and generation of predictors for treatment outcome W.H. Martin et al: Fatal experimental design flaws in clinical trials of tinnitus interventions B. Schmidt: Bringing a Tinnitus Medication to Market: Challenges for the Pharmaceutical Industry
06:00 - 07:00 p.m.	MEETING: Is there a need for an international tinnitus society?	

Thursday, June 10th		
08:00 - 09:00 a.m.	Plenary Talk: Synaptic Physiology of Cochlear Hair Cells: Afferent Signaling Paul Fuchs	
09:00 - 10:00 a.m.	Plenary Talk: Tinnitus and Affective Disorders Berthold Langguth	
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----		
10:30 a.m. - 12:30 p.m.	Behavioural Therapy M. Mazzoli H. Argstatter et al: The Heidelberg Model Music therapy in chronic tinnitus – treatment outline and neuroscientific evaluation M. Mazzoli et al: Mindfulness based stress reduction (MBSR) intervention in tinnitus therapy L. McKenna: A cognitive therapy model of tinnitus distress K. Peterson: 10 dilemmas in clinical work with tinnitus sufferers - Why neurophysiology and psychology should join forces in research and clinical practice H-P. Zenner: Psychophysiological treatment of tinnitus	TMS / VNS A. Londero M. Landgrebe et al: rTMS for the treatment of tinnitus: Results of a large randomized sham controlled trial T. Kleinjung et al: Strategies for enhancement of temporal rTMS in tinnitus patients I. Lorenz et al: Transcranial Magnetic Stimulation as a Treatment of Chronic Tinnitus: A Critical View of the Status Quo and a New Therapy Approach J.F. Piccirillo et al: Low-frequency rTMS over the left temporoparietal area for bothersome tinniuits N. Weisz, I. Lorenz: The Quest for the Magic Bullet against tinnitus: can sound stimulation aid in improving the spatial accuracy of rTMS S. Vanneste: Correlation between tDCS, TMS and TENS: are some brains more responsive than others to neuromodulation K. Engineer et al: Reversing Pathological Neural Plasticity to Treat Tinnitus
12:30 - 01:30 p.m.-----LUNCH-----LUNCH-----LUNCH-----		
01:30 - 02:30 p.m.	POSTER SESSION	
02:30 - 03:30 p.m.	Specific Forms of Tinnitus T. Kleinjung F. Bast et al: Otosclerosis and Tinnitus – Effect of the laser-assisted stapedotomy on preoperativ cases of tinnitus M.E. Hoffer et al: Blast Induced Tinnitus D. Roitman: Lightning and tinnitus, Three new cases of tinnitus resulting from lightning T.G. Sanchez et al: Auditory hallucinative phenomenon, tinnitus and hearing loss: truth or myth?	Animal Models R. Salvi B.J. Farley, A. Norena: Auditory cortex voltage-sensitive dye imaging reveals spatiotemporal patterns of spontaneous and evoked neural activity at high resolution A. Fryatt et al: Altered voltage-gated sodium channel expression following moderate sound exposure in rat spiral ganglion neurons Th. Imig et al: Unilateral sound damage causes an increase in single unit spontaneous activity in the inferior colliculus of freely moving rats S. Voytenko, A. Galazyuk: Sound-triggered suppression of spontaneous firing in central auditory neurons and residual inhibition of tinnitus T. Kitahara et al: Behavioral and molecular combined animal studies for visualization of phantom tinnitus S. Hébert, P. Fournier: From rats to humans: Validation of the acoustic gap startle paradigm to objectify tinnitus E. Lobarinas: The effects of Tonabersat and Cyclobenzaprine on Noise Induced Tinnitus in rats J.G. Turner et al: Effects of Neramexane in a Mouse Model of Tinnitus C. Wu et al: Screening of Investigational Tinnitus Drugs Using Cultured Auditory Cortex Networks
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----		
04:00 - 06:00 p.m.	The TRI Flowchart for Patient Management M. Koller: Introduction: Medical Guidelines T. Kleinjung: History / Clin exam / Audiol measurements De Ridder: Pulsatile tinnitus T. Kleinjung: Tinnitus and conductive hearing loss L. Del Bo: Tinnitus and sensorineural hearing loss A. Londero: Tinnitus and vertigo J.M. Lainez: Tinnitus and headache	Animal Models R. Salvi ... Continuation

	M. Landgrebe: Tinnitus and psychiatric comorbidity T.G. Sanchez: Somatosensory tinnitus G. Searchfield: Auditory stimulation B. Langguth: Pharmacotherapy M. Landgrebe: Cognitive behavioural therapy D. De Ridder: Neurostimulation	
<i>BANQUET</i>		

Friday, June 11 th		
08:00 - 09:00 a.m.	Plenary Talk: Tinnitus and Neural Plasticity Larry Roberts	
09:00 - 10:00 a.m.	Plenary Talk: Increase in Gain in the Central Auditory System and Tinnitus Arnaud Norena	
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----		
10:30 a.m. - 12:30 p.m.	Sound Therapy G. Searchfield M. Bergholm et al: Internet-based acoustic therapy (IBAT) for tinnitus patients G. Searchfield et al: The effect of fractal sounds on tinnitus perception P.A. Tass et al: Long-lasting tinnitus relief achieved by acoustic coordinated reset stimulation - Clinical investigation: Phase I - Prospective clinical investigation on the acoustic stimulation with the “coordinated reset of neural subpopulations” in the treatment of chronic Tinnitus L. Del Bo et al: Passive Auditory Stimulation by MP3: results after 6 months. B. Raymond et al: The New Zealand experience with a new sound therapy concept L. Del Bo et al: Passive Auditory Stimulation by a prototype of hearing aid that implements the high-pitch auditory stimulation. O. Dyrlund: High frequency dual sound generator combination instrument for tinnitus sound therapy.	Pharmacological Treatment of Tinnitus A.B. Elgoyhen C. Coelho: Cyclobenzaprine to treat chronic tinnitus: results of a 16 weeks prospective open-label trial M. Egler et al: Physicians' assessment of tinnitus treatment options in Europe and the US R. Figueiredo et al: Effects of Caffeine in tinnitus: preliminary data O. Meeus et al: Administration of the combination Clonazepam – Deanxit as a treatent for tinnitus
12:30 - 01:30 p.m.-----LUNCH-----LUNCH-----LUNCH-----		
01:30 - 03:30 p.m.	Electrical Stimulation to the Brainand to the Ear A. Möller D. De Ridder: Electrical brain stimulation for tinnitus E. Simon et al: Epidural electrical auditory cortex stimulation in the managment of chronic unilateral disabling tinnitus: first results of the pilot study "Electin" J. Zhang et al: Auditory Cortex Electrical Stimulation to Suppress Tinnitus: An Animal Model J.E. Chang et al: Variability in Tinnitus Suppression via Electric Stimulation A. Kleine Punte et al: Electrical promontory stimulation to predict tinnitus suppression after cochlear implanatation A. Kleine Punte et al: Cochlear Implantation as a durable tinnitus treatment in patients with single-sided deafness	Perceptual Training G. Searchfield D. Hoare et al: The effects of auditory training on tinnitus perception and intrusiveness: a systematic review L.E. Roberts, D. Bosnyak: Augmentation of cortical representations for sound in the tinnitus frequency region and its effects on tinnitus G. Searchfield, K. Wise: Attention Process Training for Tinnitus I. Viaud-Delmon et al: Virtual reality protocol for Tinnitus
-----Coffee Break (30 min)-----Coffee Break (30 min)-----Coffee Break (30 min)-----		
04:00 - 06:00 p.m.	Imaging N. Weisz K.L. Hyde et al: A Voxel-Based-Morphometry Study of Structural Brain Differences in Unilateral Tinnitus A. Maudoux et al: Resting state auditory network in tinnitus patients: a fMRI study D. Bosnyak, L.E. Roberts: The relation between the amplitude of the 40-Hz auditory steady-state response and the tinnitus percept suggests abnormal neural activity during tinnitus but not during residual inhibition. A. Dimitrijevic et al: Electrophysiological correlates of tinnitus and tinnitus suppression	Audiologic Assessment R. Roeser M. Sereda et al: The relationship between tinnitus pitch and audiometric variables: A meta analysis J. Smurzynski et al: Distortion product otoacoustic emissions in normally hearing patients with unilateral tinnitus O. Warusfel et al: Virtual Reality for Tinnitus therapy: Tinnitus recreation method X. Zhou et al: Loss of Cochlear compression is predictive of Tinnitus for subjects with mild to moderate hearing loss New Hypotheses J.M. Lainez

	H. Okamoto et al: Detrimental effects of extensive portable music player usage on population-level frequency tuning in human auditory cortex H. Stracke et al: Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity	K. Brookler, N. Gilston: Molecular biology of tinnitus: Cytokine and Endocrine Causes D. De Ridder: Allostasis as a mechanism for tinnitus chronification M. Murase: Towards a New Synthesis: Health and Disease
End of the Conference		

Posters

June 09, 2010 01:30 – 02:20 p.m.	
Assessment Questionnaires	
R Görtelmeyer et al	Development and Psychometric Validation of the Attention and Performance Self Assessment Scale (APSA) in tinnitus patients
US Korbel et al	Intercultural Validation of the Tinnitus Handicap Inventory 12 (THI-12)
O Meeus et al	Independency of variables in a tinnitus population
Audiological Assessment	
B Chaudhury et al	Individual Profiling of Tinnitus Perception by developing Interactive Tinnitus Analyzer Software
P Nee et al	Comparing an Online Tinnitus Examination to a Tinnitus Exam in a Research Environment
HJ Shim et al	Hearing abilities at high frequency in patients with tinnitus
Clinical Trials	
M Koller et al	THI score changes over the course of therapy and patient's subjective perception of tinnitus change
Epidemiology	
R Figueiredo et al	Incidence of tinnitus in teenagers and young adults mp3 players users
D Roitman, A Aspinwall	Survey Online about Tinnitus and hyperacusis, via our website
Health System	
Ph Gander et al	A survey of Audiology departments across England: Referral pathways
D Hoare et al	A survey of Audiology departments across England: Tinnitus assessment, treatment and outcome measures
J Lim et al	Experience of a tinnitus counseling clinic in Singapore
Pathophysiology	
J Ylikoski et al	Stress reaction in patients with acute noise induced tinnitus
H-P Zenner	The sensitization model for acquired centralized tinnitus
N. Catz, A.J. Norena	Changes in the cortical spectro-temporal receptive fields induced by notched stimuli
L Lagemann et al	Frequency tuning in chronic tinnitus patients

June 09, 2010 02:30 – 03:30 p.m.	
Case Reports	
Z Komacek, et al	Unilateral Tinnitus – The Only Symptom of a Large Vestibular Schwannoma
JJ Song, JW Koo,	Recording and analysis of pulsatile tinnitus in dural sinus diverticulum
P Winkler	Early intervention in sudden onset tinnitus
Others	
G Reul, M. Malusevic	American Tinnitus Association : Our Mission To Cure Tinnitus

Somatosensory Tinnitus	
E Biesinger et al	Qigong for the treatment of tinnitus. A randomized controlled pilot study
M Estola	Muscular tension and tinnitus. An experimental Trial of Trigger Point Injections on Tinnitus
R Levine et al	Continuous auricular electrical stimulation quiets the tinnitus of the somatosensory pulsatile tinnitus syndrome
SN Park	Clinical Characteristics and Therapeutic Responses of Muscle Origin Tinnitus
C Rocha, TG Sanchez	Efficacy of myofascial trigger point deactivation for tinnitus treatment
V Vielsmeier et al	Tinnitus and temporomandibular joint disorders – a special subgroup of tinnitus patients?
Special Forms of Tinnitus	
G Baracca et al	Botulinum toxin treatment for objective tinnitus caused by palatal myoclonus
AC Binetti, et al	Tinnitus in Vestibular Migraine
P Gao, Y Jin	New Pathogen and Therapy - In 17 Cases of Chronic Conductive Tinnitus
J-W Koo	Recording and analysis of pulsatile tinnitus in dural sinus diverticulum
H-J Lee	Evaluation of Tinnitus in the patients with Meniere's Disease
SN Park	A Case of Palatal Myoclonus Associated with Orofacial Buccal Dystonia

June 10, 2010 01:30 – 02:30 p.m.	
Auditory Stimulation	
G Baracca et al	Customized Sound Therapy for Tinnitus
D Choy	Sequential phase shift sound cancellation RX predominant tone tinnitus
M Nakagawa	A Study of Music Therapy using “1/f-fluctuation sounds” for Tinnitus patients
CW Newman, SA Sandridge	Benefit from and economic value associated with two alternative sound therapy tinnitus management options
M Piskosz	Clinical application of a new Tinnitus Sound Generator (TSG) device
VS Rothholtz et al (pres. author: KM Reavis)	Tinnitus Suppression by Low-Rate Modulated Sounds
SA Sandridge, CW Newman	First year findings of three-year study of long-term benefits of neuromonics treatment
M-W Suh et al	Specific Effects and Prognostic Factors of Hearing Aids on Tinnitus
Brain Stimulation	

SJ Burger	rTMS for the treatment of tinnitus: Are there clinical parameters which predict the therapeutic response and what happens with responders over longer follow-up periods ?
K Ogawa	Repetitive transcranial magnetic stimulation for treatment of chronic tinnitus. -Clinical and experimental study
M. Landgrebe	Clinical improvement after repetitive transcranial magnetic stimulation is accompanied by changes in gray matter detected by voxel-based morphology
Cochlear Implant	
M Cosgarea et al	Tinnitus after cochlear implantation
A Kleine Punte	Electric acoustic stimulation and tinnitus
Neurofeedback	
B Richmond et al	Developing a Brain Computer Interface (BCI) for Neuromodulation of Tinnitus Disability
Nutrition	
K Prasad et al	Micronutrients in Prevention and Improvement of Standard Therapy in Tinnitus
Animal Pathophysiology	
J Suchland, M Kössl	Effects of local salicylate application on inferior colliculus neuronal activity in vivo
Pharmacology	
M.A. Lopez-Gonzalez et al	Oral glycine inhibits cortical activity in tinnitus patients
MA Lopez-Gonzalez et al	Wine and histamine in tinnitus
AK Shukuryan et al	Treatment of tinnitus in hypertensive patients

Abstracts of Oral Presentations

TUESDAY JUNE 08, 2010

**06:00 - 07:00 p.m.
OPENING LECTURE**

ROLE OF THE HIPPOCAMPUS IN TINNITUS AND HEARING LOSS

Richard Salvi (salvi@buffalo.edu), Suzanne Kraus, Sneha Hinduja, Senthilvelan Manohar, Ed Lobarinas, Dan Stolzberg, Guang-Di Chen and Wei Sun
Center for Hearing and Deafness and Dept. Communicative Disorders and Sciences, University at Buffalo, Buffalo, NY 14214

Tinnitus typically emerges following the onset of hearing loss induced by acoustic overstimulation, ototoxic drugs or aging. In some individuals, the tinnitus is mild and manageable, but for others, tinnitus can be extremely loud, intrusive and debilitating. What differentiates debilitating tinnitus from its benign form remains largely a mystery. Jasterboff suggested that non-auditory brain regions such as the limbic system contribute to the severity of tinnitus by linking the emotional and memory regions of the brain to the auditory pathway. The neural generators that give rise to phantom sound of tinnitus and its emotive components are currently the subject of intense study. There is growing evidence from human brain imaging studies that aberrant neural activity in the central auditory system as well as non-auditory centers are correlated with the perception of tinnitus. In earlier PET imaging studies with patients who could voluntarily modulate the loudness of their tinnitus with an oral-facial maneuver, we found that changes in tinnitus loudness were not only strongly correlated with altered neural activity in classical auditory areas such as the auditory cortex and medial geniculate but also the left hippocampus and surrounding limbic regions. Although the

hippocampus lies outside the classical auditory pathway, animal studies indicate that the hippocampus responds to sounds. Interestingly, the hippocampus is one of two unique regions of the brain where large numbers of stem cells persist into adulthood. Roughly 9000 new cells are born in the rat hippocampus each day and most of these differentiate into neurons which become functional integrated into the hippocampus and surrounding regions. Tinnitus has long been known to be associated with stress and depression; both of these conditions have shown to down regulate cell proliferation and neurogenesis in the hippocampus. Antidepressant drugs, which upregulate hippocampal neurogenesis, sometimes provide relief of symptoms in tinnitus patients with very loud tinnitus and depression. To elucidate the potential role of the hippocampus in tinnitus, we present data from animal models that show a link between stem cell proliferation and ototraumatic conditions that induce tinnitus. The anticancer drug, cisplatin frequently induces tinnitus and also increases spontaneous activity in the dorsal cochlear nucleus. Surprisingly, cisplatin also causes cell death in the hippocampus and significantly decreases stem cell proliferation and neurogenesis in this non-auditory region. High intensity noise exposures not only induce tinnitus and increase spontaneous activity in the dorsal cochlear nucleus, but also affect the hippocampus. Remarkably, unilateral noise exposures that damage just one cochlea significantly reduce cell proliferation in the hippocampus and suppress neurogenesis. Studies are currently underway to determine if the noise and cisplatin-induced changes in hippocampal neurogenesis are in anyway linked to tinnitus, depression or memory and whether these changes can be prevented or reversed.

Supported by TRI and NIH (R01DC009091, R01DC009219)

WEDNESDAY JUNE 09, 2010

8:00 - 10:00 a.m. PLENARY TALKS

8:00 - 9:00 a.m.

THALAMOCORTICAL DYSRHYTHMIA AND TINNITUS

Rodolfo R. Llinás, MD, PhD

Dept. Physiology and Neuroscience, NYU School of Medicine

Tinnitus, and auditory dysfunction of central or peripheral origin, is characterized by the perception of auditory noise, most commonly a whistling or a roaring sound, in the absence of an objective physical sound source. While it is now universally accepted that central tinnitus is a disconnection syndrome the underlying neuronal mechanism is presently unresolved. Indeed, central tinnitus provides a unique opportunity to define the intrinsic neuronal and ionic mechanisms capable of supporting such stable auditory hallucination. Very likely mechanisms relate to recurrent thalamocortical resonance known as thalamocortical dysrhythmia. This presentation will address such possibility.

9:00 - 10:00 a.m.

DO SENSORY CORTICES PROCESS MORE THAN ONE SENSORY MODALITY DURING PERCEPTUAL JUDGEMENTS?

Ranulfo Romo

*Instituto de Fisiología Celular - Neurociencias
Universidad Nacional Autónoma de México Mexico City*

Recent studies have reported that sensory cortices process more than one sensory modality, challenging the long lasting concept that they process only one. However, both the identity of these multimodal responses and whether they contribute to perceptual judgments is unclear. We recorded from single neurons in somatosensory cortices and primary auditory cortex while trained monkeys discriminated, on interleaved trials, either between two tactile flutter stimuli or between two acoustic flutter stimuli, and during discriminations sets that combined these two sensory modalities. In these tasks, monkeys must compare the second stimulus to the memory trace of the first stimulus, and must postpone the decision until a sensory cue triggers the motor report. We found that primary somatosensory cortex is exclusively associated with sensory encoding of tactile flutter, and that primary auditory cortex is also exclusively associated with sensory encoding of acoustic flutter. These results suggest that multimodal encoding and perceptual judgments occur outside primary sensory cortices. Consistent with this observation is the fact that frontal lobe neurons encode information about the acoustic and tactile flutter stimuli during the stimuli, working memory and decision making periods of these tasks. We think that our results are worth of consideration for understanding the functional organization of sensory and frontal lobe cortices in multimodal sensory processing and perceptual judgments.

10:30 a.m. - 12:30 p.m. SYMPOSIUM

Pathophysiology of Tinnitus A. Norena / D. De Ridder

THE BRAINSTEM AND TINNITUS: ADJUSTMENTS TO THE DORSAL COCHLEAR NUCLEUS TINNITUS HYPOTHESIS

Robert Levine (Robert_Levine@MEEI.harvard.edu)

Massachusetts Eye and Ear Infirmary, Boston, MA 02114

A fundamental unanswered question regarding tinnitus and hearing loss, is why, with any degree of hearing loss some people develop tinnitus and others do not. Even with total hearing loss, 80% of people develop tinnitus, but 20% do not. The current tinnitus dorsal cochlear nucleus (DCN) disinhibition hypothesis cannot account for this fact, since it predicts tinnitus whenever auditory nerve fiber spontaneous activity diminishes.

However, the addition of (1) the concept of a neural threshold for tinnitus and (2) consideration of type I and type II inputs to the DCN separately, as excitatory and inhibitory to DCN output respectively, leads to a modification of the DCN hypothesis. Whether any degree of hearing loss will result in tinnitus will depend upon the relative interplay in changes in the degree of excitation and inhibition caused by Type I and Type II nerve fiber dysfunction relative to the neural threshold for tinnitus.

These modifications of the DCN hypothesis can now account for (1) one in five people not developing tinnitus despite a total hearing loss and (2) cochlear nerve transection abolishing tinnitus for some people but not for others.

Because (1) inhibition from Type II nerve fibers is mediated by GABA and (2) benzodiazepines potentiate GABA, quieting of tinnitus by benzodiazepines may be from potentiation of Type II nerve fiber DCN inhibition.

AUDITORY CORTEX INVOLVEMENT IN TINNITUS

Dirk De Ridder, Elsa van der Loo, Sven Vanneste, Mark Plazier, Paul Van de Heyning

TRI Tinnitus Clinic Antwerp, Belgium

Introduction: Non-pulsatile tinnitus is the auditory perception of a sound without an external or environmental source and can be considered an auditory phantom percept. It can result in considerable distress in 20% of people affected by it. It has recently become clear that tinnitus intensity and tinnitus distress are generated by different but possibly partially overlapping networks.

The auditory cortex can be subdivided into a primary (A1), secondary (A2) and association cortex (A3). In animals this corresponds somewhat to the auditory cortex, belt and parabelt areas.

Based on data from consciousness research in the visual and somatosensory systems it is likely that A1 activity in itself might not result in a conscious auditory percept.

Methods and materials: a literature research on tinnitus and PET, fMRI, EEG, iEEG, MEG is performed revealing

data that can be integrated into a coherent concept of auditory cortex activity in tinnitus.

Results: the auditory fMRI BOLD signal correlates positively with gamma band activity and negatively with theta and alpha activity. In tinnitus, auditory cortex BOLD is decreased ipsilaterally to the sound percept, but only for the tinnitus pitch, not for other pitches. In PET studies tinnitus correlates with either increased left auditory cortex activity or contralateral auditory cortex activity. In MEG increased auditory cortex gamma band activity is associated with decreased alpha and increased theta. The same results can be found in intracranially recorded EEG activity. EEG research suggests that auditory cortex gamma band activity correlates to the intensity of the tinnitus, and that gamma activity is increased bilaterally in both A1 and A2 in tinnitus patients in comparison to controls. This suggests that lateralization of the tinnitus percept might not depend on the auditory cortex activity.

EEG studies do not demonstrate a difference in auditory cortex activity in women and men suffering tinnitus, nor in tinnitus type (noise-like tinnitus vs pure tone tinnitus).

The auditory cortex activity recorded by MEG relates to intrusiveness, but this is not replicated in EEG studies. This suggests that the distress network (amygdala-dACC-insula-sgACC-parahippocampal area) and the tinnitus intensity network could possibly overlap in the auditory cortex, or that distress modulates auditory cortex activity.

In chronic tinnitus, MEG and EEG studies show that the involvement of the auditory cortex changes in time, both spectrally and with regards to connectivity, suggesting that tinnitus is the result of a continuing dynamic reorganization of a complex tinnitus network.

Conclusion: the auditory cortex is but a node participating in a dynamic system of multiple integrated tinnitus networks, each representing another aspect of the phantom sound percept. Auditory cortex activity might only be involved in tinnitus intensity coding and pitch representation. It could be modulated by the amount of tinnitus distress.

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Based on data from consciousness research in the visual and somatosensory systems it is likely that A1 activity in itself might not be sufficient to result in a conscious auditory percept.

Methods and materials: a literature research on tinnitus and PET, fMRI, EEG, iEEG, MEG is performed revealing data that can be integrated into a coherent concept of auditory cortex activity in tinnitus. To further elucidate the relevance of gamma band activity in the auditory cortex for tinnitus intensity and its modulation, a log-transformed gamma band current density was calculated in 160 tinnitus patients for both the left and right DLPFC (BA9, BA46), Primary Auditory Cortex (BA40, BA41), Secondary

Auditory Cortex (BA21, BA22), and Parahippocampal area (BA27, BA29). To permit calculation of no tinnitus in the sample for improved correlation analysis and to analyze the brain areas involved in the on/off tinnitus switch, 78 people without tinnitus were included in the study as well (NTE database).

Results: A linear regression analysis with DLPFC (BA9, BA46), Primary Auditory Cortex (BA40, BA41), Secondary Auditory cortex (BA21, BA22), and Parahippocampal area (BA27, BA29) for both the left and right side as independent variables and tinnitus loudness (Numeric scale from 0 (no tinnitus) to 10 (as loud as I can imagine)) as dependent variables revealed a significant model ($R^2 = .16$; $F(16,222) = 2.59$, $p < .001$) and revealed a significant effect ($p < .05$) for Primary Auditory Cortex (BA41 left and right and BA40 left). No other Brodmann area obtained significance.

A logistic regression with DLPFC (BA9, BA46), Primary Auditory Cortex (BA40, BA41), Secondary Auditory cortex (BA21, BA22), and Parahippocampal area (BA27, BA28) for both the left and right side as independent variables and the presence of tinnitus (yes or no) as dependent variables yielded a significant model (Nagelkerke $R^2 = .42$; $\chi^2(16) = 88.76$, $p < .001$). Further analysis revealed a significant effect ($p < .01$) for the right Parahippocampal area (BA27 right, BA29 right). No other Brodmann areas were significant. Important to note is when the auditory regions were excluded from the model, also of the right DLPFC (BA9, BA 46) became significant ($p < .01$). If we however excluded the DLPFC regions the auditory regions did not become significant.

Discussion: The auditory fMRI BOLD signal correlates positively with gamma band activity and negatively with theta and alpha activity. In auditory stimulus presentation the BOLD signal in the primary auditory cortex correlates to the stimulus intensity. In tinnitus, auditory cortex BOLD is decreased ipsilaterally to the sound percept, but only for the tinnitus pitch, not for other pitches. In PET studies tinnitus correlates with either increased left auditory cortex activity or contralateral auditory cortex activity. In MEG increased auditory cortex gamma band activity is associated with decreased alpha and increased theta. The same results can be found in intracranially recorded EEG activity. EEG research suggests that auditory cortex gamma band activity correlates to the intensity of the tinnitus, and that gamma activity is increased bilaterally in both A1 and A2 in tinnitus patients in comparison to controls.

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In chronic tinnitus, MEG and EEG studies show that the involvement of the auditory cortex changes in time, both spectrally and with regards to connectivity, suggesting that tinnitus is the result of a continuing dynamic reorganization of a complex tinnitus network.

Conclusion: the auditory cortex is but a node participating in a dynamic system of multiple integrated tinnitus networks, each representing another aspect of the phantom sound percept. Auditory cortex activity might only be involved in tinnitus intensity coding and pitch representation. Its activity could be modulated by the amount of tinnitus distress. The DLPFC, parahippocampal area and the auditory regions are likely correlated with

each other (i.e. multicollinearity), with the DLPFC and parahippocampal area modulating the amount of gamma band activity in the auditory cortex.

A NETWORK APPROACH FOR UNDERSTANDING TINNITUS PATHOPHYSIOLOGY

Sven Vanneste & Dirk De Ridder

TRI Tinnitus Clinic & BRAIN, University Hospital Antwerp, Belgium

The complex functional organization and connectivity in the human brain is incompletely understood. Recently, topological measures based on graph theory have provided a new approach to analyze large-scale cortical networks. These methods have been applied to connectivity data on nonhuman species, and cortical networks have been shown to have small-world topology, associated with high local and global efficiency of information transfer. Functional networks derived from functional magnetic resonance imaging and magnetoencephalographic data have shown the same organizational properties of the healthy human brain, consistent with similar results reported in anatomical networks derived from diffusion tensor imaging. Here we show, using graph theory on resting state EEG data in 163 healthy volunteers and 163 tinnitus patients, that the groups differ in their brain topology, derived from region of interest analysis (i.e. 82 areas) of the current density for the different frequency bands (i.e. δ , θ , α , β , and γ). For healthy volunteers all cortical divisions shared scale free topology and efficient wiring. However for tinnitus patients the topology of functional organization differs and other hubs emerge. These hubs are consistent with data from other imaging techniques such as functional magnetic resonance imaging, positron emission tomography, voxel based morphometry and magnetoencephalography. We propose that the topological differences between the healthy cortex and the cortex of tinnitus patients may represent the outcome of different functional brain organization. The findings might benefit the understanding of the pathophysiology of tinnitus and could potentially lead to new neuromodulation treatments.

INVOLVEMENT OF NONAUDITORY BRAIN AREAS IN TINNITUS

B. Langguth¹, M. Landgrebe¹, T. Kleinjung², D. De Ridder³

¹*Department of Psychiatry, Psychosomatic and Psychotherapy, University of Regensburg, Germany*

²*Department of Otorhinolaryngology, University of Regensburg, Germany;*

³*TRI Tinnitus Clinic & BRAIN, University Hospital Antwerp, Belgium*

Early neuroimaging studies have demonstrated altered activity of the auditory cortex in tinnitus patients. These findings together with animal studies have moved the focus of tinnitus research from the ear to the auditory cortex. However, the auditory cortex is but one of the areas involved in the generation of the phantom sound. Functional imaging studies have demonstrated that both the tinnitus sound percept and the tinnitus related distress are network properties of different, possibly overlapping networks.

Activation of the auditory cortex alone is not sufficient for generating a sound percept. Rather co-activation of the "attention network" consisting of frontal and parietal brain areas is needed for generating a conscious percept. Tinnitus distress in turn depends on co-activation of areas involved in emotion regulation such as the amygdale-hippocampal area, the cingulate cortex or the insula.

Thus tinnitus research is maturing, evolving from a pure 'ear problem' to an 'auditory cortex problem', to a 'static network problem' into a 'dynamic multiple parallel network problem'. This implies that targeting the auditory cortex alone with neurostimulation techniques will not be sufficient. Recent TMS studies combining frontal and auditory cortex stimulation is but one example of application of these new insights.

10:30 a.m. - 12:30 p.m.

SYMPOSIUM

**Neuroscience and Clinical
Research on Somatosensory
Tinnitus
T. G. Sanchez**

TEMPOROMANDIBULAR JOINT AND MASTICATORY MUSCLE DISORDERS IN PATIENTS WITH TINNITUS

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Gerhard Handel¹ (gerhard.handel@klinik.uni-regensburg.de),

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Objectives: The literature contains conflicting evidence if the relationship between temporomandibular joint and masticatory muscle disorders (TMD) and tinnitus is causal or coincidental. The present prospective clinical study was conducted to evaluate the prevalence of TMD, tinnitus, and co-occurrence of both symptoms and to investigate the effect of dental functional therapy on tinnitus symptoms.

Methods: 951 patients of the Department of Prosthetic Dentistry were asked for perceived tinnitus symptoms. Patients with TMD and simultaneous tinnitus (n=30; 3.2%) were included in the study. The baseline examination comprised detailed functional analysis of the temporomandibular joint (TMJ) and the masticatory muscles, examination and diagnosis according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD), determination of the Helkimo clinical dysfunction index, and a tinnitus questionnaire (Tinnitus Handicap Inventory/THI). All patients received dental functional therapy (distraction splint or Michigan splint and physiotherapy). The effects of the functional therapy on the TMD and the tinnitus symptoms were examined after three to five months.

Results: The prevalence of tinnitus was found to be 8-fold higher in patients with TMD (36.6%) than in patients without TMD (4.4%). Functional TMD therapy resulted in significant effects (improvement or total remission) on pain of TMJ or masticatory muscles (in 82% of the affected patients), on TMJ clicking (69%), and on limited vertical range of mandible motion (50%). Apart from that, functional TMD therapy resulted in an improvement of tinnitus symptoms in 11 of 25 patients (44.0%).

Conclusions: The results of this prospective clinical study demonstrate a significant correlation between tinnitus and TMD. The observed treatment outcome suggests that dental functional therapy may have a positive effect on TMD and in approximately half of the patients improves the perceived tinnitus distress.

DEACTIVATION OF MYOFASCIAL TRIGGER POINTS IS EFFECTIVE TO CONTROL SOMATOSENSORY TINNITUS

Tanit Ganz Sanchez, MD, PhD

*Otolaryngology Department of University of São Paulo
School of Medicine and Instituto Ganz Sanchez*

Our interest in somatosensory tinnitus started after watching Levine's presentation in 1999. We decided to evaluate our own casuistry of patients, reaching similar high prevalence of tinnitus modulation by forceful maneuvers of head and neck muscles¹, and demonstrating that most maneuvers elicited a reliable pattern of modulation. In the meanwhile, we also had the opportunity to cure a patient with gaze-evoked tinnitus through a specific training using her own modulation pattern², as well as some other patients with myofascial trigger points in muscles of the head, neck and shoulder girdle. So, patients with somatosensory tinnitus started to be seen as a subgroup, needing different approaches than the ones applied to help the conventional cases of tinnitus.

In this symposium, we will show the connections between tinnitus and trigger points and the efficacy of the deactivation of such trigger points and a home exercise program for the relief of tinnitus in patients with myofascial pain syndrome. Using a double-blind randomized placebo controlled clinical trial, we were able to provide evidence that:

- the deactivation of such trigger points was more effective to decrease tinnitus parameters (loudness, number of sounds, and score of THI, $p < 0,001$), as well as all pain-related variables (intensity, algometer value and amount of trigger points, $p < 0,001$).
- the side of the ear with the (worst) tinnitus is correlated with the side of the body with (worst) pain, and the more the pain is relieved, the more the tinnitus is improved ($p = 0,013$)
- tinnitus modulation upon palpation of trigger points was frequent in both experimental and control groups (75.7% e 83.3% respectively). Even though such phenomenon did not influence the prognosis of the treatment, we noticed that patients who showed an immediate modulation by diminishing of tinnitus intensity upon such palpation had better prognosis for reaching more tinnitus relief after treatment ($p = 0,002$).

NEURAL BASIS OF SOMATOSENSORY INFLUENCE ON TINNITUS

S. Shore

*Kresge Hearing Research Institute, University of Michigan,
Ann Arbor*

Tinnitus patients are able to modify their tinnitus by manipulating somatic regions of the head and neck, such as in jaw clenching. Many patients also can attribute their onset of tinnitus to somatic insults in the head and neck region. These observations have led to the hypothesis that "somatosensory tinnitus" can occur through an alteration of firing rate in cochlear nucleus (CN) neurons by somatosensory neurons of the head and neck. Here, we present anatomical and physiological substrates for somatosensory influences on tinnitus and provide evidence that somatosensory influences on CN firing patterns are significantly altered following noise-induced hearing loss.

Building on previous results that showed correlations between increased spontaneous rates (SR) and behavioral evidence of tinnitus, we extend these findings to demonstrate that the specific neurons showing increased SRs are primarily those that receive excitatory

somatosensory inputs (Shore et al., 2008). These findings support the view that tinnitus can no longer be considered an exclusive disorder of the auditory system, but it is rather an expression of neural plasticity encompassing reactions of multisensory neurons to changes in their external environment. The enhanced responsiveness of CN neurons to trigeminal stimulation, combined with immunochemical evidence of increased glutamatergic inputs from non-auditory regions (C. Zeng et al., 2009), suggests a compensatory response from the somatosensory system that occurs to balance the loss of excitatory input from the auditory nerve.

ABNORMALITIES OF VERGENCE EYE MOVEMENTS IN SOMATIC TINNITUS

Q. Yang¹, M. Vernet¹, C. Orssaud², P. Bonfils³, Z. Kapoula¹, A. Londero³

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Oculomotricity problems have already been demonstrated by orthoptic testing in patients with subjective tinnitus. This study examines with objective recordings vergence eye movements in patients with somatic tinnitus (i.e. patients with ability to modify their subjective tinnitus percept by various movements such as jaw, neck, eye movements or skin pressure). Vergence eye movements were recorded with the Eyelink II video system in 15 (23-63 years) control adults and 19 (36-62 years) subjects with somatic tinnitus. 1) accuracy of divergence but not of convergence was lower in subjects with somatic tinnitus than in control subjects; 2) vergence duration was longer and peak velocity was lower in subjects with somatic tinnitus than in control subjects; 3) there was no significant difference of vergence latency between these two groups. Such deficits could be attributed to dysfunction of related vergence areas in brain particularly for cerebellum and brainstem involved in control of accuracy and peak velocity of vergence. Tinnitus and vergence dysfunction could be both manifestations of mild cortical-brainstem-cerebellar syndrome including abnormality of cross-modality interactions between vergence eye movements and auditory signals.

ELECTRICAL SUPPRESSION OF TINNITUS

J. Zhang

Laboratory of Auditory Prostheses Research, Department of Otolaryngology-Head and Neck Surgery and Department of Communication Sciences & Disorders, Wayne State University College of Liberal Arts & Sciences, Detroit, MI

Somatosensory electrical stimulation has been used clinically to suppress tinnitus, but this approach has not been developed as an effective treatment. Experiments delivering electrical current to the basal part of the pinna on DCN activity of both control and tone-exposed animals showed interesting results: there was more suppression than excitation during and after stimulation in both control and tone-exposed groups. At higher levels of current, there was a significantly higher suppression after stimulation than during stimulation for both groups, and there was also

higher degree of suppression during and after stimulation in exposed animals than in controls.

Based on this work, we are testing the suppressive effects of electro-acupuncture on tinnitus. Through assessments of visual analogue scales and a verbal retrospective rating scale, it has been reported that acupuncture can yield different results in treating tinnitus, including long-term or transient relief of tinnitus, noise reduction, suppression of otoacoustic emissions and improved sleep. It has been shown that local points around the pinna are usually more effective than the distal points, and combination of the local acupoints and distal acupoints has been mostly used for the treatment. In addition to identifying the effective acupoints, the operating modes of acupuncture mainly consisted of manual acupuncture, laser acupuncture and electroacupuncture, and it appears the electro-acupuncture may provide relatively more robust therapeutic effect than manual acupuncture.

Although acupuncture yields suppressive effects on tinnitus, the therapeutic effect varies greatly, ranging complete remission of tinnitus to no effect, and sometimes exacerbating tinnitus. This prompts an immediate question as to which acupoints should be used. It is also unknown which types of combination of acupoints will yield superior suppression of tinnitus. Taken together, we predict that stimulation of only certain acupoints can activate certain pathways, leading to robust suppression of tinnitus.

04:00 - 06:00 p.m.
SYMPOSIUM
Neuroimaging in Tinnitus:
Mechanisms and Networks
F. Husain

**ALTERED INHIBITORY PROCESSES IN TINNITUS:
MEG STUDIES**

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Introduction: Tinnitus is a hyperexcitability disorder brought about by a reduction of inhibitory processes and gain increase at several stages of the auditory system. However, neither the auditory afferent pathways of the two hemispheres nor the within-hemisphere frequency channels of the auditory system are independent of one another. Rather, they may be thought of as a multi-stage network involving inter-hemispheric, within-hemisphere lateral, and recurrent inhibition. It would be of some interest to establish non-invasive indicators of distinct inhibitory processes and their alteration in tinnitus. Here, we use the method of multiple modulation frequency auditory steady-state responses to study the interaction of the responses to two or more simultaneous auditory input streams.

Methods: The steady-state auditory evoked magnetic field was studied in tinnitus patients with chronic tinnitus and healthy controls using both binaural and monaural stimulation paradigms. Stimuli were AM-tones with different carrier frequencies. In the binaural paradigm, stimuli equated in carrier frequency, but differing in modulation frequency, were simultaneously presented to the two ears. In the monaural paradigm, single AM-tones were presented in a single presentation condition and superpositions of three AM-tones differing in carrier and modulation frequency were presented in a multiple presentation condition. Modulation frequency-specific steady-state response (SSR) components were recovered by bandpass filtering. Source Hilbert amplitude and the

slope of source amplitude, i.e. the change of amplitude over time, were computed selectively for each carrier and modulation frequency.

Results: In the binaural paradigm, in both hemispheres the source amplitude of the response was larger for contralateral than ipsilateral input. In non-musicians with tinnitus, this laterality effect was enhanced in the hemisphere contralateral and reduced in the hemisphere ipsilateral to the tinnitus ear, especially for the tinnitus frequency. The hemisphere-by-input laterality dominance effect was smaller in musicians than in non-musicians. In both patient groups, source amplitude change over time, i.e. amplitude slope, was increasing with tonal frequency for contralateral input and decreasing for ipsilateral input. However, slope was smaller for musicians than non-musicians. In patients, source amplitude was negatively correlated with the MRI-determined volume of the medial partition of Heschl's gyrus. In the monaural paradigm, in multiple mode SSR amplitude was reduced in healthy controls, but increased in tinnitus patients when compared with single mode.

Conclusions: Tinnitus patients show an altered excitatory-inhibitory balance reflecting the downregulation of inhibition and resulting in a steeper dominance hierarchy among simultaneously active processes in auditory cortex. Direction and extent of this alteration are modulated by musicality and auditory cortex volume. Compared with single mode, in multiple modes SSR amplitude is reduced in healthy controls, but increased in tinnitus patients. These alterations of the excitatory-inhibitory balance observed in tinnitus thus far suggest that tinnitus may also exert an influence on auditory spatial attention and auditory stream segregation, as both the salience maps involved in spatial attention and the forward masking mechanisms involved in auditory stream segregation are based on inhibitory interactions.

Research is supported by DFG grant Di497/3-2.

CHALLENGES AND REWARDS OF BRAIN IMAGING IN TINNITUS

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The primary motivations for studying the neural substrates of tinnitus in humans have been to demonstrate objectively its representation in the central auditory system, to develop a better understanding of its diverse pathophysiology and to examine the functional interplay between sensory, cognitive and affective systems. Experimental studies comparing small groups of people with and without tinnitus have succeeded in demonstrating the central representation of tinnitus in the auditory system and have defined brain centres, such as the limbic system, involved in the emotional aspects of the disorder. Together these findings represent a significant advance in tinnitus research over the past decade or so.

Nevertheless, a number of challenges remain. We recently undertook a broad review of the neuroimaging literature and reported somewhat inconsistent results in the literature, even for those studies reported from the same laboratory (Adjamian et al., 2009). Perhaps one of the main methodological difficulties for this type of research concerns achieving control over inter-subject variability. This issue is fundamental. From a statistical point of view, a significant difference between a tinnitus and non-tinnitus group requires the 'between-group' variability to be reliable

greater than the 'within-group' variability. Experimental results are limited when the variance components are poorly estimated (e.g. when the sample size is small) or when the within-group variability is relatively large. Variability from one person with tinnitus to the next is well-known and has been attributed in part to the complex nature of the disorder, with its diverse aetiology and symptoms. One way to seek control is to select tinnitus participants according to some well-defined set of inclusion and exclusion criteria, such as degree of hearing loss, tinnitus severity and presence of comorbid symptoms such as hyperacusis (e.g. Melcher et al., 2009).

In our review, we also remarked that some studies have failed to advance our understanding of the mechanisms of tinnitus because it remains possible that the abnormal activation in people with tinnitus is less related to the fact that these people hear a phantom sound than it is to some other variable that was not matched between groups. Decisions taken during the experimental design can help to reduce the variability between tinnitus and control groups. For example, in their review article, Lanting and colleagues (2009) concluded that groups should be closely matched for characteristics such as hearing loss, age and gender. It is imperative that effects potentially attributable to tinnitus are not confounded by deafness, since hearing loss is the central factor that drives reorganisational changes in the central auditory system.

My talk expands on the theme of variability using illustrative examples taken from fMRI and MEG studies of patients with tinnitus and/or hearing loss.

References:

Adjamian P, Sereda M, Hall DA. (2009) The mechanisms of tinnitus: Perspectives from human functional neuroimaging. *Hearing Research*. 253: 15-31.

Lanting CP, de Kleine E, van Dijk P (2009) Neural activity underlying tinnitus generation: Results from PET and fMRI. *Hearing Research* 255: 1–13

Melcher JR, Levine RA, Bergevin C, Norris B. (2009) The auditory midbrain of people with tinnitus: Abnormal sound-evoked activity revisited. *Hearing Research*, 257: 63-74.

NEURAL NETWORK DIFFERENCES IN TINNIUS AND HEARING LOSS: AN FMRI STUDY

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One of the challenges in studying chronic tinnitus is the effect of hearing loss. Hearing loss causes reorganization of the central auditory processing pathways and associated areas in the brain, possibly leading to tinnitus. However, not everyone with hearing loss has tinnitus and about 10% of those with tinnitus have normal hearing. In the present study, our goal was to study the neural bases of tinnitus, possibly related to attention, and dissociate them from those of hearing loss.

We used functional magnetic resonance imaging (fMRI) to study auditory processing in persons with bilateral hearing loss and tinnitus (TIN), with bilateral hearing loss without tinnitus (HL), and with normal hearing without tinnitus (NH; defined as less than 25 dB loss at all measured frequencies). To examine group differences in the neural bases of auditory processing, we employed pure tones

and sweeps in a delayed-match-to-sample task. We scanned 8 TIN, 7 HL and 9 NH using an EPI clustered acquisition paradigm in a 3T GE scanner. All subjects had normal hearing up to 2000Hz and all stimuli were low-pass filtered at 2000Hz so that the groups could hear them equally well. The task trials were presented in pseudo-random order with rest trials interspersed. Image volumes were realigned, co-registered to a high-resolution structural image, normalized into standard stereotactic space and smoothed. Multi-subject fixed effects analysis was performed in SPM5 with a threshold of $p < 0.05$ FWE corrected.

For all three groups, a network of brain regions including the primary and non-primary auditory cortices was activated to a greater extent during discrimination of sweeps and tones compared to rest. Performance was similar among all three groups – accuracy was above 90%. On average, the tinnitus group differed from the hearing loss group in having greater activation of the superior temporal, supramarginal and parahippocampal gyri for the task compared to rest. The non-tinnitus groups (hearing loss and normal hearing) exhibited increased activations in the middle frontal gyrus, middle temporal gyrus, and inferior parietal lobule for the task compared to rest. The results suggest that the attentional network, consisting of regions in the parietal and frontal cortices, was activated to a lesser extent by the tinnitus group compared to either one of the non-tinnitus groups. We compared the groups directly which confirmed the above result: decreased activation in the parietal and frontal lobes in the participants with tinnitus compared to both HL and NH groups. Our results suggest that the engagement of the attentional network may be one of the key differences between individuals with chronic tinnitus and hearing loss and those with hearing loss without tinnitus.

Supported by the NIDCD Intramural Research Program, UIUC, and the Tinnitus Research Consortium

IS THE FRONTAL LOBE INVOLVED IN TINNIUS? A STRUCTURAL MRI STUDY

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Objective: Test for abnormalities of brain structure in tinnitus subjects.

Background: Phantom perception of sound is just one of many symptoms plaguing the tinnitus patient, others being sleep disturbance, anxiety, and disrupted concentration, for instance. The latter, non-auditory problems imply a role for brain centers outside the classical auditory system in the clinical problem of tinnitus. Imaging studies do also. For instance, reports of diminished alpha-band activity in spontaneous neuromagnetic recordings suggest a failure of the brain to default normally to a resting state [1]. Recent fMRI data from our group have shown elevated sound-evoked activity in auditory cortex specifically related to tinnitus, which we speculate may reflect sustained over-attention to the auditory domain mediated by attentional networks. Examinations of brain structure have also suggested involvement of non-auditory areas in tinnitus, but not consistently, possibly because of insensitivity of the particular analysis method employed [2,3]. The present study is undertaking a re-examination of brain structure in tinnitus subjects by means of a complementary approach

Methods: To date, 12 subjects have undergone behavioral testing and structural imaging. Six were patients with bilateral tinnitus recruited through the Mass. Eye and Ear tinnitus clinic. The remaining 6 subjects reported no tinnitus. Both ears of all subjects met the

following threshold criteria at octave intervals from 250 Hz through 8 kHz: ≤ 25 dB HL for 5 of 6 frequencies and, ≤ 30 dB at the remaining frequency. Imaging at 3T included a magnetization-prepared rapid gradient echo scan (MPRAGE; resolution: 1x1x1 mm).

Image analysis entailed (1) automated identification of 148 cortical areas and 14 subcortical structures in individual subjects and (2) subsequent comparison of the volume and, for cortex, gray matter thickness, of each identified region between tinnitus and non-tinnitus subjects [4-6]. A Bonferroni correction was applied to the resulting p-values (Student's t-test) to account for the ~160 comparisons made.

Results: While no structure showed statistically significant differences between tinnitus and non-tinnitus groups, one region, the right inferior frontal sulcus (IFS) showed a trend ($p = 0.06$). The trend was for differing volume (tinnitus 2481 ± 103 mm³; non-tinnitus 3305 ± 121 ; mean \pm SEM), not gray matter thickness, indicating that the difference was in IFS surface area.

Discussion: The results suggest a role for the right, inferior frontal lobe in tinnitus. This region is part of the of the ventral attentional network, a right-lateralized network believed to control mainly involuntary orientation to novel stimuli, something the tinnitus percept may be misconstrued to be. While preliminary, the results are intriguing.

1. Weisz N., Moratti S. et al., (2005) PLoS Medicine 2: 546-553.
2. Muhlau M., Rauschecker J.P. et al. (2006) Cerebral Cortex 16: 1283 – 1288.
3. Landgrebe M., Langguth B. et al. (2009) NeuroImage 46: 213-218.
4. Desikan R.S., Cabral H.J. (2009) Brain 132: 2048-2057.
5. Sigalovsky I.S., Fischl B., Melcher JR (2006) NeuroImage 32: 1524-1537.
6. Fischl B., Salat D.H. et al. (2002) Neuron 33: 341-355.

EVENT-RELATED POTENTIALS AS CORRELATES OF ATTENTIONAL BINDING IN TINNITUS: SOME INSIGHT FROM NEURODYNAMICAL MULTISCALE MODELING

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It is widely accepted that central mechanisms play a crucial role in the tinnitus decompensation. However, the relative importance and significance of individual mechanisms is hard to judge from the available empirical human and animal data. It is even harder to estimate their interplay in the attentional fixation to tinnitus and in the process of decompensation. Computational multiscale modeling offers a tool to identify key mechanisms and their complex interplay across spatiotemporal scales, ranging from the analysis of neuronal plasticity marker proteins to metabolic and electromagnetic imaging in humans. Understanding the significance of scale specific parameters and their interactions is necessary for the design of therapeutic interventions from a clinical point of view.

We will present a neurodynamical multiscale model of attentional binding in tinnitus which allows the simulation of

event-related potential (ERP) data. The model is based on an auditory stream selection scheme, a computational implementation of the widely accepted hypothesis that the hippocampus acts as a comparator, and corticothalamic circuitry which has been described for attentional binding before. The large-scale electrophysiological effects of the oscillatory hippocampal interactions with corticothalamic loops are quantitatively represented by a neural field model. As long as no temporal synchronization of the two input signals occurs at the level of this comparator, the incoming auditory stream receives attentional resources by thalamocortical circuitry. Matching of the new auditory signal with memory signals might be prevented by the influence of the amygdala, which is heavily involved in the processing of emotionally relevant stimuli. Thus emotional value of a stimulus, in particular that of a negative valence, is thought to bind attentional resources. In the model this is represented by an endogenous stream weight. This might explain why distress associated with subjective tinnitus is tightly coupled to the inability of decompensated patients to habituate to their phantom perception. In accordance to the model, empirical data suggest that habituation deficits are likely due to the activation of brain areas, which are only indirectly involved in auditory processing, such as the limbic system.

Computational simulations using the model are compared to multicenter experimental ERP data related to attention and habituation in tinnitus patients which were categorized with respect to their distress levels and control subjects. We show that the model predicts the instantaneous phase stability of single-trial auditory ERP sequences (N1/P2 range) which has recently been suggested as an objective measure of tinnitus decompensation and "early" attentional binding. Apart from our own ERP data and the electroencephalographic scale, the predictions of the model are in accordance to several studies at the molecular, network, and metabolic scales.

Altogether our model reflects neural correlates of attentional binding in tinnitus as represented by EPRs and is in accordance to published imaging studies on tinnitus. It reinforces the role of attention in the tinnitus decompensation using arguments at different neurofunctional scales.

The present model still contains simplifications as the field of multiscale modeling of tinnitus is still at its start. However, it provides a computational framework and novel tool for further interdisciplinary research.

04:00 - 06:00 p.m.
SYMPOSIUM
Design of Clinical Trials
M. Landgrebe / W.H. Martin

META-ANALYSIS OF CURRENT TINNITUS TREATMENTS

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Evidence-based clinical practice is an increasingly important goal for the modern-day tinnitus specialist. While statistical significance is often reported, the clinical significance of any post-therapy changes is often unclear. The use of meta-analysis can create a common measure of a study's effect size, which essentially provides a "level playing field" for a meaningful comparison of the clinical significance of the various treatments. Meta-analysis is

particularly relevant to clinicians as it involves the calculation that constitutes a rating of the consistency of response to treatments, and so best relates to a patient's general perception of improvement. The effect size is obtained by numerous means, with the simplest being calculating the mean change over therapy, divided by the standard deviation. However, this meta-regression methodology has very rarely been applied in the tinnitus arena. It appears to have only been conducted on several studies of CBT or Ginko Biloba, but not across different treatments.

The presentation will be the first report of an ongoing project to rank the scientific rigor of current tinnitus treatment studies and compare their outcomes in absolute terms that may be useful to practicing clinicians. It is initially limited to randomized &/or well controlled studies that were recently published in peer-reviewed medical journals. To maximize reliability, they also need to utilize well-established psychometric and/or audiometric measures. As the studies report their final post therapy data at different times, the resulting data needs to be displayed in table form to enable meaningful analysis of results at each time point. Objective audiometric pre/post measures like LDLs and MMLs are a useful common index for comparison of neuroplastic change, but they currently tend only to be reported in the more comprehensive recent studies. Long-term measures of post-therapy sleep, relaxation and concentration are relevant, but rare.

The present analysis includes the following techniques; CBT, TRT with Noise Generators, TRT with Hearing Aids, Neuromonics Tinnitus Treatment, Open Fit Hearing Aids, High Frequency Hearing Aids, Counseling, Memantine, Ginko Biloba, Piribedil, and Electrical Stimulation. Unfortunately, many other recent publications surveyed had lacked sufficient scientific rigor to be utilized in this analysis, but more new publications of sufficient quality will be included up to the conference opening.

Initial analysis indicates that the effect size of studies using hearing aids or pharmaceuticals tends to be low when all enrolled subjects are accounted for. As electrical stimulation currently only tends to be effective for a smaller subset of patients, its effect size also suffers accordingly. TRT studies can be effective, but it tends to require more than twice the elapsed time and twice the clinician time to achieve similar results to Neuromonics. CBT appears to be efficient at helping patients change their attitude towards their tinnitus, but more objective data on changes in audiological aspects, such as loudness discomfort, is currently lacking.

It is hoped that this ongoing project may help identify some of the strengths and weaknesses of the state-of-the-art of clinical research, and introduce some vital perspective in understanding relative clinical effects of tinnitus treatments.

WHICH CHANGES IN THE THI SCORE ARE CLINICALLY RELEVANT?

M. Koller et al.

Center for Clinical Studies, University Hospital Regensburg

Objective: The Tinnitus Handicap Inventory (THI) is a validated and widely used questionnaire for evaluating tinnitus severity. For the design of clinical studies it is important to know which changes in THI score are seen as clinically relevant for patients. Therefore, the aim of this study is to evaluate which change in the THI score indicates that patients are actually feeling better.

Methods: A good statistic to estimate the minimal change in the THI score which is relevant for the patient is the effect size according to Cohen. By means of the Clinical

Global Improvement Questionnaire (CGI) patients specify on a scale from 1 (very much improved) to 7 (very much worse) how their tinnitus changed since the beginning of treatment. Calculating the effect sizes for different combinations of the CGI scores an estimation for a patient relevant effect size can be made.

Results: For this study we enrolled 131 patients out of the TRI data base subdivided in the following 4 groups: Group1: CGI 1, 2, 3 i.e. feeling at least minimally better or better, group2: CGI 3 i.e. feeling just minimally better, group3: CGI 4 i.e. no change, group4: CGI 5, 6, 7 i.e. feeling at least minimally worse. The effect sizes for each of the groups were: Group1: $d=0.91$, group2: $d=0.72$, group3: $d=0.23$, and group4: $d=0.24$.

Conclusion: A considerable difference between the effect sizes of group2 and 3, i.e. between the perception of a minimal improvement and no change of the tinnitus was observed. Therefore an effect size of $d=0.7$ can be seen as clinically relevant for the patient. Based on our data, ΔTHI (i.e. THI baseline - last visit) has an estimated standard deviation of $SD_{diff}=17$ and the correlation in THI between baseline and last visit is $\rho=0.75$. Using Cohen's formula for the effect size, a difference of 8 points of the THI score can be seen as a clinical relevant change for the patient.

THE TINNITUS RESEARCH INITIATIVE (TRI) DATABASE: A NEW APPROACH FOR DELINEATION OF TINNITUS SUBTYPES AND GENERATION OF PREDICTORS FOR TREATMENT OUTCOME

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Tinnitus, the phantom perception of sound, is a frequent disorder that causes significant morbidity. Tinnitus represents a heterogeneous condition. There are different treatment options available from which some patients benefit. However the same treatment fails in other patients, 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 a specific 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.

As mentioned before, an individualized treatment approach based on the specific clinical profile of each patient would be highly desirable. Performing clinical trials according to standardized methodology and pooling the data in a database should facilitate both clinical subtypisation of different form of tinnitus, and identification of promising treatments for different types of tinnitus. This would be an important step towards the goal of individualized treatment of tinnitus.

Such a database containing tinnitus patients, which have been characterized using a standardized set of tinnitus measures (e.g., psychoacoustic measures, questionnaires) and undergo different treatments, is at present not available. Within the framework of TRI such a

database has been established with the primary objectives of : (1) collecting a standardized set of data on patient characteristics, treatments, and outcomes from tinnitus patients consulting specialized tinnitus clinics all over the world (at present 13 centers in 8 countries), (2) delineating different subtypes of tinnitus based on these systematically collected data and (3) identifying predictors for individual treatment response based on the clinical profile. Starting in 2008, the database already contains data from more than 400 patients. Every clinical researcher is invited to contribute patient data to this database. The only precondition is that patient assessment and outcome measurement have to be performed according to the database standard. The service in return is a systematic analysis of these data, but also the possibility to describe the data in the context of other therapeutic interventions and the identification of patient characteristics which are predictive for positive treatment outcome.

FATAL EXPERIMENTAL DESIGN FLAWS IN CLINICAL TRAILS OF TINNITUS INTERVENTIONS

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Tinnitus remains an elusive condition with a myriad of manifestations, degree of resulting impairment and few treatments beyond those addressing obvious active disease processes that trigger the phenomena. A simple online literature search reveals evidence of nearly 200 clinical trials that have been performed in an attempt to find effective treatments. Most studies fail to recognize the heterogeneity of the condition and design studies in a way that will identify subgroups that may respond to treatment. Most studies also fail to consider confounding factors such as tinnitus severity, duration prior to the onset of the study, stability, effects of concurrent medications or other interventions, subject emotional factors and the challenge of meaningful outcomes measures. Enriched enrollment design has not been used in clinical trials for tinnitus but may provide a means to systematically identify true responders to and intervention and define predictive factors as to whether or not an individual will be likely to respond to the specific intervention. This presentation identifies the challenges facing clinical investigators studying tinnitus and presents a model for experimental design that may prove useful to those conducting clinical trials for tinnitus.

BRINGING A TINNITUS MEDICATION TO MARKET: CHALLENGES FOR THE PHARMACEUTICAL INDUSTRY

Bernd Schmidt, Wittnau, Germany

Developing a medicine for subjective tinnitus is like cutting a path through a jungle. Currently there is no globally

approved medication for systemic treatment of tinnitus on the market, there are no specific development guidelines available from regulatory authorities and there is no trodden regulatory pathway to marketing authorization like in most other indications, that can be followed by the pharmaceutical industry.

All the facts above put the development of a pharmaceutical treatment of chronic, subjective tinnitus in the commercially high risk category, counterbalanced only by the high unmet medical need and the rewards in case of a successful market entry.

With the evidence of tinnitus being a phantom auditory tone involving subcortical and cortical areas when becoming chronic, drug development for subjective tinnitus may be carried out in analogy to the rules and regulations for some CNS-disorders, like e.g. neuropathic pain, a condition involving central sensitization as well.

Following the standard process of drug development, for a New Chemical Entity, after identification of suitable pharmacological targets, a preclinical program is carried out thought to be predictive for the approached indication. For tinnitus currently the available animal models mimic only some aspects of the complex human situation, modelling mainly sensation, not suffering. Due to the lack of an effective human medication, retrospective validations of the existing models are not feasible yet.

After preclinical identification of a development candidate, a toxicology program, drug formulation work, clinical pharmacology studies and exploration of maximally tolerated doses in healthy volunteers, a proof-of-concept study in patients is initiated. For subjective, chronic tinnitus still there is no validated surrogate marker enabling a company to make a rapid go-decision, or decide against further development. Therefore, the next step, a proper phase-II dose finding study, has to involve a considerable number of patients for sufficient length of drug exposure.

Given that the phase-II study had provided a clear dose-response profile for preliminary effectiveness, then contact to regulators are intensified in order to discuss and lay out a development plan for the pivotal phase-III program as basis for later approval. Agreement has to be obtained on study endpoints accepted globally, particularly on which aspects of the whole spectrum of subjective chronic tinnitus are measured by which validated instruments.

Finally, assuming the minimum of two large pivotal studies in the approached indication has been completed successfully, all the long-term toxicology studies have shown no negative results and the regulatory bodies have allowed the drug to enter the market, a last hurdle is waiting.

The novel tinnitus medication has to prove its pharmacoeconomic value compared to other existing therapy strategies, in order to be reimbursed at a price that offsets on average 7-12 years of development time and 400-800 millions of USD development costs for a novel drug.

**06:00 - 07:00 p.m.
MEETING**

Is there a need for an international Tinnitus Society?

THURSDAY JUNE 10, 2010

8:00 - 10:00 a.m. PLENARY TALKS

8:00 - 9:00 a.m.

SYNAPTIC PHYSIOLOGY OF COCHLEAR HAIR CELLS: AFFERENT SIGNALING

Paul Albert Fuchs

Otolaryngology, Head and Neck Surgery, and the Center for Sensory Biology, Johns Hopkins University School of Medicine

Advances in molecular, cellular and genetic methods have enhanced our knowledge of hair cell physiology in the past two decades. This paper will summarize recent findings on hair cell transmitter release obtained by intracellular ('patch-clamp') recording from afferent dendrites in the micro-dissected rodent organ of Corti. Intracellular recording from terminal dendrites adjacent to ribbon synapses have confirmed that hair cells release glutamate to activate AMPA-type ionotropic receptors in type I afferent neurons. An unexpected observation was that individual ribbons simultaneously release multiple vesicles to produce large, suprathreshold synaptic events in the afferent fiber. Multivesicular release occurs with equal probability independent of the overall rate of release. That is, hair cell depolarization raises the probability of release, but not the amplitude distribution of synaptic events ('non-binomial' release). Individual ribbons within a single hair cell appear to have different release dynamics, perhaps reflecting the number, or open probability of voltage-gated calcium channels at each active zone. Intra-terminal recordings from type II afferents beneath outer hair cells show that these too are activated by glutamate binding to AMPA-type receptors. Additionally, type II afferents are highly sensitive to ATP, at least in the neonatal cochlea. Despite the fact that individual type II afferents contact dozens of outer hair cells, total synaptic transfer is an order of magnitude less than that from the single ribbon to a type I afferent, for equivalent patterns of excitation. These observations support the hypothesis that type II afferents are designed to respond only to very loud, perhaps traumatic levels of sound.

9:00 - 10:00 a.m.

TINNITUS AND AFFECTIVE DISORDERS

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Tinnitus is often accompanied by affective disorders, especially in severe forms of tinnitus. Affective disorders, together with personality factors, play an important role in creating the distress experienced by many individuals with tinnitus.

The exact relationship between tinnitus and comorbid depression may vary from patient to patient. Depression may either evolve as a consequence of tinnitus, depression may represent a risk factor for the development of tinnitus, both disorders may result as a consequence of another causal event (e.g. trauma) or they may just co-occur accidentally.

There is an overlap between brain structures involved in depression and tinnitus, explaining the frequent co-

occurrence of both disorders. Furthermore Tinnitus is associated with neuroendocrine alterations, which are characteristic for depressive disorders.

Affective disorders in patients with tinnitus should be efficiently treated. Depression can occur in the context of various psychiatric disorders and the etiology has to be considered in the treatment plan. Treatment options include primarily pharmacological (e.g., antidepressants) and psychotherapeutic (e.g., cognitive behavioral therapy, tinnitus retraining therapy) approaches. In patients with severe depression the treatment plan has to include management of risk of suicide as a potentially life threatening complication.

10:30 a.m. - 12:30 p.m. SYMPOSIUM Behavioural Therapy M. Mazzoli

THE HEIDELBERG MODEL MUSIC THERAPY IN CHRONIC TINNITUS – TREATMENT OUTLINE AND NEUROSCIENTIFIC EVALUATION

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Background: Music therapy according to the Heidelberg Model extends the therapeutic spectrum of treatment options in chronic tinnitus. A compact form of music therapy was applied over five consecutive days. Advantages of this form of music therapy are the integration of acoustic and psychotherapeutic modules into specific music therapeutic techniques including active exercises (resonance practice, musical training of attention focussing and tonal intonation) as well as receptive techniques (tinnitus desensitization, psycho-physiological training, tinnitus-landscape).

Methods & Results: Improvements were observed by measuring difference of global tinnitus load by Tinnitus Questionnaire (TQ), psycho-physiological measurements and cortical evoked response audiometry (CERA). Additionally the neuro-functional base for this form of treatment was evaluated by means of MRI. Several multidisciplinary studies with more than n = 150 participants account for the effectiveness of this therapy form. The results indicate that the therapy is highly advantageous in terms of treatment duration, effectiveness, and follow-up stability compared with customary interventions. Recent models of tinnitus pathophysiology argue for pathologic binding of attention and emotion to the tinnitus sound. Our clinical findings gave evidence for decay of the phantom noise itself. Voxel

based morphometry (VBM) revealed changes in grey matter (GM) of patients' brain between two structural MRI scans before and after therapy. In tonal tinnitus (tinnitus has an identifiable frequency) especially anatomical alteration of limbic, striatal and prefrontal structures was observed whereas in noise-induced tinnitus the imaging techniques demonstrated neuroplastic changes in putamen and insula. Psychophysiological measurements indicate cardiovascular influences on noise-induced tinnitus but not tonal tinnitus.

Discussion: Overall music therapy was able to influence the microanatomical configuration of neural structures as are known for tinnitus pathology. Brain imaging data confirm the top-down-model of tinnitus generation. Therapy success depends on the sound quality of the tinnitus; therefore any treatment should consider this.

MINDFULNESS BASED STRESS REDUCTION (MBSR) INTERVENTION IN TINNITUS THERAPY

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Objectives: To verify the efficacy of MBSR in reducing both stress and annoyance associated with tinnitus and tinnitus itself (loudness, pitch). To identify and tailor specific techniques within the MBSR based interventions for tinnitus patient. To establish objective measurements of tinnitus and tinnitus improvement by MBSR interventions with EEG measurements (alpha/delta ratio).

Methods: 60 patients have been enrolled in 3 different centers participating in the study. Tinnitus and annoyance have been assessed by means of audiometric evaluation (pitch and loudness match, MML, discomfort level etc.), questionnaires (THI, TQ, VAS) and EEG measures of alpha/delta waves ratio. The have attended a 2 hrs/week x 8 week course in mindfulness based stress reduction techniques and were re-evaluated afterwards.

Results: most patients reported a better ability to relax and to control tinnitus during periods of increased annoyance of tinnitus (70%). Some patients experiences periods of absence of tinnitus (10%). Alpha waves have significantly increased after treatment in most subjects.

Conclusions: MBSR can be a valid support therapy for tinnitus therapy.

A COGNITIVE THERAPY MODEL OF TINNITUS DISTRESS

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There has been formal recognition of the importance of psychological factors in tinnitus distress for almost three decades. Many studies have demonstrated the efficacy of psychological treatments in this context. Nonetheless, it still remains for a coherent psychological model of tinnitus distress to be proposed. This paper proposes a structured

cognitive behavioural model of tinnitus distress. The model suggests that overly negative thoughts provoke arousal and distress and this in turn provokes selective attention and monitoring of tinnitus and related physical and psychological sequelae. These have the effect of maintaining the detection of tinnitus and of reinforcing the negative thoughts. It is also proposed that selective attention leads to a distortion in the perception of tinnitus, an effect that further provokes the overly negative interpretation of tinnitus. The negative evaluation of tinnitus involves cognitive distortions that provoke behavioural responses to keep the individual safe from perceived threat. These safety behaviours also maintain the overly negative thoughts and so further fuel the feed back loops that are centred around these thoughts. The individuals historical belief system influence the type of overly negative thoughts that are produced. Research evidence is cited for each of the components of the proposed model. The evidence supporting the component parts is drawn from by audiological, psychological and neuroscience studies. While a small number of psychological models have been proposed this is distinct in that it is precise and is in keeping with the latest theories within clinical psychology. The proposed model is a clinically relevant tool.

10 DILEMMAS IN CLINICAL WORK WITH TINNITUS SUFFERERS - WHY NEUROPHYSIOLOGY AND PSYCHOLOGY SHOULD JOIN FORCES IN RESEARCH AND CLINICAL PRACTICE

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Ideally, the treatment of choice should always be based on the etiology in each individual patient. No doubt, tinnitus is a medical condition and should be treated as such. In clinical studies neurophysiological based treatments have shown promising results the last decade. Psychological treatment, usually cognitive therapy, is often recommended in comorbid cases, in which the tinnitus suffering is presented in conjunction with symptoms of depression and/or anxiety. Additionally, psychological treatment is often suggested as an alternative, in cases where the patient either doesn't respond to or is non-compliant to the neurophysiological based treatment.

Aim: The aim of this review is to highlight some of the gaps that exist between psychology and neurophysiology in clinical practice. It is argued that neurophysiological as well as psychological factors are at play in tinnitus, and that an effective treatment approach needs to integrate these aspects. Some suggestions on how the two fields could synthesize their respective bases of empirical knowledge are outlined in terms of ten dilemmas.

1. Habituation versus receptor adaptation. Is long-term habituation to tinnitus reaction achievable without the involvement of frontae cortex?
2. Unlearning of CS-US associations versus establishing new, inhibitory associations. Why are negative affective reactions so resistant to habituation?
3. Subconscious mechanisms versus preconscious cognition. Is conscious awareness a required prerequisite for mental processes?
4. What can we promise but blood, sweat and tears? Should prognostic information be tailored to heighten the patient's acceptance and commitment to treatment, or should the clinician take an optimistic approach for motivational boosting?
5. Where to go from the Empathy Pit? Validating the patients' emotional reactions and prior experiences of

losses and failures, versus expressing a strong belief in the patients' coping resources? (Stay friends and stay put or move forward?)

6. The problem with symptom overlap between depression and tinnitus related complaints. When to treat what? Depression is known to block habituation processes on the one hand, while the tinnitus exhausts the patient on the other.

7. Patient autonomy versus therapist's authority. What we know versus what we openly express to the patient, and how this inconsistency can cause problems.

8. The change-resilient patient versus the overwhelmed patient? Does it matter what perspective we take on the problem of non-adherence to treatment?

9. The Eye of the Tiger. Should the tinnitus problem be confronted head on vigilantly, or is attention distraction the way to go?

10. Psychological treatment: The end or the beginning? What the cognitive therapist needs to know to be useful.

PSYCHOPHYSIOLOGICAL TREATMENT OF TINNITUS

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Background: Pharmacological treatment of tinnitus can not be considered as well established. Thus, reducing tinnitus severity through a behavioral therapy is emerging as a key therapeutic goal.

Methods: 286 patients suffering from persistent and stable tinnitus for 3 months or longer participated in this controlled clinical multicenter study. The study investigated the efficacy and safety of a standardized treatment involving individual cognitive behavioural therapy (CBT). 120 patients waiting to be treated served as controls. Therapy was standardized using manualized procedures within the setting of a specifically designed disease management program (DMP). The primary outcome measure was the tinnitus change score (TCS) using a 8-point numeric verbal rating scale. Secondary outcome measures were tinnitus severity determined by the tinnitus questionnaire score (TQS) as well as the tinnitus loudness score (TLS) and the tinnitus annoyance score (TAS) using 6 and 8-point numeric verbal rating scales. From multivariate ranks a composite endpoint was formed of these four validated variables.

Results: The primary outcome differed significantly ($P < 0.0001$) between treated and waiting patients. The same was true when univariate scores were considered. The primary efficacy variable TCS revealed the efficacy of treatment with an odds ratio (OR) of 3.4 (CI 2.6 to 4.5). 84 % of the treated patients showed a TCS improvement, while only 22 % did so in the waiting control. The secondary outcome measures TQS, TLS and TAS improved in the treatment group significantly more than in the control group. In the therapy group TQS was reduced by 50 % from a median of 27 to 13.5, whereas in the control group no median TQS change was observed.

Conclusions: A structured tinnitus specific CBT using standardized tinnitus specific interventions can be a safe and effective individual therapy for the treatment of patients suffering from tinnitus for at least 4 months (clinicaltrials.gov, PRS identifier number: NCT 00719940)

10:30 a.m. - 12:30 p.m. SYMPOSIUM TMS / VNS A. Londero

RTMS FOR THE TREATMENT OF TINNITUS: RESULTS OF A LARGE RANDOMIZED SHAM CONTROLLED TRIAL

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Tinnitus affects 10% of the population, its pathophysiology remains incompletely understood, and treatment is elusive. Both animal models and functional imaging data in tinnitus patients indicate that tinnitus is associated with increased neuronal activity, increased synchronicity and functional reorganisation in the auditory cortex. Imaging data further suggest the involvement of nonauditory areas such as the frontal cortex or the limbic system. Targeted modulation of these brain areas by repetitive transcranial magnetic stimulation has been proposed as a new therapeutic approach for chronic tinnitus.

We undertook a randomized, double-blind, parallel group, sham-controlled clinical study for investigating the safety and the efficacy of different rTMS protocols for the treatment of tinnitus. 192 adults aged 20-79 years, suffering from chronic tinnitus were randomly allocated to receive either sham rTMS, PET based neuronavigated 1 Hz rTMS over the area of increased metabolic activity in the auditory cortex, 1 Hz rTMS over the left auditory cortex based on 10-20 EEG coordinates or combined 20 Hz rTMS over the left dorsolateral prefrontal cortex followed by 1 Hz rTMS over the left auditory cortex. In all patients treatment was performed over 10 days and outcome was assessed over a follow-up period of 11 weeks after treatment by using the German version of the Tinnitus Questionnaire (TQ). The primary outcome was the comparison of TQ change (baseline versus end of treatment) between treatment arms in the intention-to-treat sample.

rTMS treatment was well tolerated and no severe side effects were observed. All active rTMS treatments resulted in a significant reduction of the TQ as compared to baseline, whereas such an effect was not observed for the sham rTMS group (neuronavigated: $p = 0.03$; left temporal: $p = 0.03$; combined frontal and temporal: $p = 0.002$, sham $p = 0.22$). The comparison between treatment groups failed to reach a significant difference (effect of time: $p < 0.001$; interaction time x group: $p = 0.24$). Separate comparisons of the different active rTMS groups with sham rTMS revealed an almost significant superiority for the combined rTMS protocol ($p = 0.052$), but no significant effects neither for PET based neuronavigated rTMS nor for left temporal low frequency rTMS.

This large study demonstrated the safety and tolerability of rTMS treatment in patients with chronic tinnitus. The primary efficacy variable failed to demonstrate a significant difference between active rTMS and sham rTMS. Moderate beneficial effects have been observed in secondary assessment variables, especially for combined frontal and temporal rTMS. The use of PET based neuronavigated rTMS has shown no superiority as compared to the non-neuronavigated TMS protocols.

STRATEGIES FOR ENHANCEMENT OF TEMPORAL RTMS IN TINNITUS PATIENTS

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There is compelling evidence that the perception of chronic tinnitus is associated with regional changes in cortical excitability. Repetitive transcranial magnetic stimulation (rTMS) over the temporal or the temporoparietal cortex has recently been introduced as a new treatment strategy for tinnitus. The technique has been applied in two different ways in tinnitus patients. Single sessions of high-frequency rTMS have been successful in transient reduction of tinnitus perception whereas repeated sessions of low-frequency rTMS have resulted in longer lasting tinnitus reduction indicating therapeutic potential. However, treatment outcome so far is characterized by high interindividual variability and only moderate effect size.

This presentation reviews different approaches for enhancement of rTMS effects in tinnitus patients. The different strategies include the combined stimulation of non-auditory and auditory brain areas, the variation of stimulation frequencies and intensities as well as the comparison of different firing modes (burst vs. tonic stimulation). Furthermore the value of optimum patient selection is discussed. Another approach consists of a combination of rTMS administration with pharmacological intervention.

Repetition of rTMS treatment in treatment responders seems to be a promising approach for the prolongation of treatment effects. A pilot study suggests further, that treatment effects can be enhanced by combined stimulation of auditory and non-auditory brain areas. Moreover, clinical data like tinnitus duration and the dimension of hearing loss seem to have important impact on treatment effects. Successful enhancement of treatment effects will depend on a more detailed understanding of the neuronal correlates of the different forms of tinnitus and the mechanisms, by which rTMS exerts its effects.

TRANSCRANIAL MAGNETIC STIMULATION AS A TREATMENT OF CHRONIC TINNITUS: A CRITICAL VIEW OF THE STATUS QUO AND A NEW THERAPY APPROACH

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In my talk I critically discuss the status quo of repetitive transcranial magnetic stimulation (rTMS) as a treatment of chronic tinnitus. A great body of research has engaged in various rTMS approaches trying to cure chronic tinnitus. However, most studies have demonstrated only moderate effects regarding the attenuation of tinnitus (~ 20% symptom relief). Furthermore, the results are characterized by high interindividual variability. In this context I will

present data from two rTMS studies: In a parametric study we systematically examined changes in auditory responses (N1, auditory steady state response) measured by means of magnetoencephalography after single-sessions with different transcranial magnetic stimulation paradigms (1 Hz rTMS, individual alpha frequency rTMS, intermittent theta burst stimulation, continuous theta burst stimulation, and sham). We found a distinct reaction pattern of the auditory steady state response and the N1 after rTMS inasmuch as the auditory steady state response was reduced after stimulation, whereas the N1 was slightly enhanced or not changed at all. Moreover, the reduction of the auditory steady state response was strongest after intermittent theta burst stimulation. However, the effect of the active rTMS parameters on tinnitus loudness/distress was rather small. We further conducted a sham-controlled therapy study applying 1 Hz rTMS for ten days. No significant reduction of tinnitus-related distress measured by means of the Tinnitus Questionnaire has been observed. Overall, our studies point to several critical issues when employing TMS as a treatment of chronic tinnitus. One very important issue supported by data from our parametric study is that standard rTMS approaches do not have the spatial resolution to selectively target the overly synchronized neuronal assemblies in the auditory cortex. Such an inaccuracy could contribute to the high interindividual variability, which is consistently reported by rTMS studies and could obscure effects with low sample sizes. In an outlook I will present the current treatment approach from our laboratory focussing on an increase of the spatial resolution of rTMS in chronic tinnitus.

LOW-FREQUENCY RTMS OVER THE LEFT TEMPOROPARIETAL AREA FOR BOTHERSOME TINNITUS

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Several studies have evaluated the effect of rTMS in over 200 tinnitus patients. These studies report reductions in tinnitus severity from low-frequency (1 Hz) rTMS applied to the scalp overlying the primary and secondary auditory cortex. The current study objective was to determine the effectiveness and safety of low-frequency rTMS to the left temporoparietal area in patients with bothersome tinnitus.

Participants were 14 adults between the ages of 42 and 59 (mean 52) with subjective, unilateral or bilateral, non-pulsatile tinnitus duration that ranged from 6 months to 18 years, with a median of 7 years. The median reported tinnitus loudness was 7.5 based on a visual analogue scale of 0 to 10, indicating, respectively very quiet to very loud. Tinnitus interfered with sleep for 13 (93%) participants, and the median Tinnitus Handicap Inventory (THI) score was 51. The stimulation site was over the left temporoparietal area.

This was a cross-over double-blind randomized clinical trial. Participants received 5 stimuli (active rTMS or sham) sessions per week (one per day) for 2 weeks. Low frequency stimulation (1Hz) was administered at 110% of motor threshold for a total of 42 ½ minutes. Pulses (2000 total) were administered over six pulse trains each separated by 90 seconds. The sham magnet was actively driven by the console power system and was identical in physical appearance to the active magnet. The order of active versus sham treatment was counterbalanced and subjects underwent a two-week washout between treatment arms to control for any carry-over treatment effects.

The median (95% CI) reduction in THI score, associated with active treatment was 5 (-14 to 0) points. The median (95% CI) reduction in THI score with sham was 6 (-12 to -2) points. The Primary Efficacy Parameter was the difference in the change in THI active from the change in THI sham [$\Delta(\Delta\text{THI}) = \Delta\text{THI active} - \Delta\text{THI sham}$] and ranged as low as 34 points reduction in THI score after active treatment to an increase of 22 points, with a median $\Delta(\Delta\text{THI})$ reflecting an increase of only 1 point and 95% CI (-6 to 4). There were no changes in secondary outcomes measures between active and sham treatments. There were no serious adverse events and the most common adverse events included jaw twitch and neck or shoulder tightness or twitch.

The results show that low-frequency rTMS to the left temporoparietal area was no more effective than placebo for patients with chronic bothersome tinnitus. A possible explanation for the negative findings is shallow penetration of rTMS stimulation over the temporoparietal area into buried parts of auditory cortex within the Sylvian fissure. Alternatively, treatment with rTMS should be explored in non-auditory cortical regions that also are more directly accessible to stimulation effects.

This research was supported by a grant from the National Institutes of Deafness and Other Communication Disorders (R01 DC009095).

THE QUEST FOR THE MAGIC BULLET AGAINST TINNITUS: CAN SOUND STIMULATION AID IN IMPROVING THE SPATIAL ACCURACY OF RTMS?

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A growing consensus is emerging, that tinnitus is related to hyperactivity within auditory cortical regions. Enhanced neuronal firing and synchronized firing in auditory cortical regions could engage downstream higher-order brain regions responsible for the conscious perception of the tinnitus sound. Conceptually, brain stimulation tools such as rTMS could be an ideal tool for normalizing this abnormal ongoing hyperactivity. Studies of rTMS in the motor system have demonstrated modifications of neuronal excitability outlasting the period of stimulation. Despite significant effects in reducing tinnitus distress usually employing 1 Hz rTMS, the clinical results of this method are only moderate and far from being a "magic bullet". If rTMS is potent in modulating neuronal excitability it is legitimate to ask why this is the case. A strict interpretation might be that the notion outlined above and mainly derived from animal models is incorrect or at least not applicable to humans with chronic tinnitus: indeed an increasing amount of evidence suggests that changes occur with increasing tinnitus duration. However, the strong correlation between the tinnitus frequency spectrum and pattern of hearing loss, implies that even in chronic

tinnitus some forms of tinnitus-relevant neuronal activity should be going on in auditory cortex. Yet, these data also imply that this tinnitus-relevant activity should affect circumscribed regions and not the entire auditory cortex. Our group has recently invested greater efforts in identifying factors of rTMS that may limit its effectiveness in the treatment of tinnitus. In a MEG study investigating various TMS stimulation paradigms we were able to show that the effects are not frequency specific. In the context of tinnitus this means that the modulating effects of current rTMS treatments may not or not only impact hyperactive regions, a feature that would be theoretically desirable. Recent reports have shown TMS effects to be highly dependent on the excitability state of neuronal assemblies. Using so-called adaptation paradigms mostly in the visual domain, research could provide evidence that spatial resolution of single pulse TMS can be greatly improved. The current study in normal hearing controls aimed at investigating whether such a logic can be applied to modulate excitability selectively for distinct sound frequencies using rTMS. For this purpose, two groups of participants listened to either a bandpass or notch filtered noise for 10 minutes before receiving 1 Hz rTMS (1000 pulses). A control group listened to the bandpass filtered noise, however received a sham stimulation protocol. EEG recordings were taken before and after the noise+rTMS treatment, while participants listened to 40 Hz amplitude-modulated tones of varying frequencies. Preliminary analysis indicates that the type of noise has a great and opposing effect on the N1, while the auditory Steady-State response remained unaffected. Compared to sham stimulation, rTMS greatly reduced the sound induced effects, however not for a specific frequency. This result shows that neuronal excitability in auditory cortex can indeed be modulated using 1 Hz rTMS, however sound stimulation as employed in the present study does not improve spatial accuracy.

CORRELATION BETWEEN TDCS, TMS AND TENS: ARE SOME BRAINS MORE RESPONSIVE THAN OTHERS TO NEUROMODULATION

Sven Vanneste & Dirk De Ridder

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Over the last decade researchers became more and more interested in non-invasive neuromodulation techniques as a method for the treatment of tinnitus. The most popular one is transcranial magnetic stimulation (TMS) which is a tool provoking a strong impulse of magnetic field that induces an electrical current which can alter the neural activity at the applied area. Also transcranial direct current stimulation (tDCS) and transcutaneous electrical nerve stimulation (TENS) became more popular. These two latter methods modulate cortical excitability in the brain regions of interest through a weak direct current (DC) or alternating current (AC) respectively. Although these techniques have shown to alter tinnitus significantly, not all patients respond to this treatment. Research already demonstrated that about 50 % of the tinnitus patients respond to TMS or tDCS and only 20 % approximately respond to TENS. In the present research we explore whether some patients are more responsive to neuromodulation than others and verify if different tinnitus characteristics can predict whether a patient will respond or not. We further discuss if the variability of treatment response among patients with tinnitus for non-invasive neuromodulation can reduce the power of clinical trials to demonstrate efficacy and whether this is a challenging factor in the development of the next generation of neuromodulation techniques.

REVERSING PATHOLOGICAL NEURAL PLASTICITY TO TREAT TINNITUS

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Disruption of the normal cortical topography following cochlear damage may be responsible for the phantom sensations typically associated with tinnitus. Although auditory cortex has been implicated in the development and progression of tinnitus, there is as yet no direct evidence for a causal role of cortical map plasticity in the generation of the tinnitus percept. The best method to test whether map plasticity is directly responsible for tinnitus would be to reverse the plasticity and evaluate the perceptual consequence. If plasticity reversal eliminates the pathological sensation, then this approach might also be useful in treating patients. We are currently testing a novel approach using vagus nerve stimulation (VNS) paired with tones to reverse the cortical map distortions observed after noise trauma. VNS triggers the release of neuromodulators known to enhance neural plasticity. Our aim was to pair VNS with tones across the frequency map except for the overrepresented frequencies to reverse the pathological plasticity and reduce or eliminate the tinnitus percept.

Four to six weeks after noise trauma (115 dB SPL 16 kHz octave band), rats were unable to detect a gap at one or more narrowband frequencies. We then paired brief episodes of VNS with tones spanning the rat hearing range but excluding the tinnitus frequency. Three control groups were either passively exposed to the same tones, received VNS alone or received no therapy. After three weeks of daily VNS Tone Pairing, the ability of the rats to detect gaps in the over represented frequencies was restored to pre-trauma levels. These results suggest that pairing multiple tones with VNS can reverse the gap impairment in rats with the presumed tinnitus percept. Using dense microelectrode mapping techniques, we quantified neurophysiology data from primary auditory cortex of the same rats. After VNS Tone pairing, receptive field size, response strength, spontaneous rate and synchrony of primary auditory cortex neurons decreased to pre-trauma levels. This confirms our hypothesis that VNS pairing therapy works by reversing the pathological cortical plasticity generated by noise trauma. These results support the larger hypothesis that plasticity triggered by noise trauma contributes to tinnitus and suggest that reversal of this plasticity could be an effective tinnitus therapy.

2:30 a.m.- 3:30 p.m. SYMPOSIUM Specific Forms of Tinnitus T. Kleinjung

OTOSCLEROSIS AND TINNITUS – EFFECT OF THE LASER-ASSISTED STAPEDOTOMY ON PREOPERATIVE CASES OF TINNITUS

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Background: According to studies on the topic, between 40-80% of otosclerosis patients suffering from hearing loss also suffer from tinnitus on the effected side. For a lot of these patients tinnitus represents a handicap that is just as debilitating as the hearing loss itself. The major goal of the surgical treatment of the otosclerosis is a significant improvement in hearing loss. However a positive side effect is that there are also frequent reports of reduced tinnitus after surgery.

Patients and methods: All patients that underwent laser-assisted stapedotomy between 2004 and 2008 were included in the study. Retrospectively, the tinnitus questionnaire as compiled by Goebel and Hiller was sent to the patients. 34 of 54 patients replied (13 male and 21 female with an average age of 42.9 years). The pre- and postoperative cases of tinnitus were divided into compensated and non-compensated tinnitus. In addition the subclasses emotional and cognitive burden, penetrance of the tinnitus and somatic ailments due to the tinnitus were evaluated.

Results and Conclusions: Over 90% of the patients surveyed suffered from tinnitus pre operation. The tinnitus disappeared or improved in over 50% of the cases after laser-assisted stapedotomy. In addition, the surveyed subclasses also improved appreciably post surgery.

BLAST INDUCED TINNITUS

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Blast exposure has become one of the signature injuries of the current wars in Southwest Asia and an increasingly common issue in the civilian world. The exposure to blast produces a number of effects both on the hearing/balance end organs and on the brain. These effects can produce a unique pattern of audio-vestibular injuries including tinnitus. In this abstract we analyze three groups of patients exposed to blast as follows: early (those seen within 72 hours of exposure), sub-acute (those seen within one month of exposure), and chronic (those seen one month or more after exposure). In particular we focus on tinnitus patterns in these groups demonstrating a changing pattern over time. We highlight how this pattern change affects evaluation and treatment options. In addition, we

supply some basic science foundations that have implications in our broader understanding of tinnitus.

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LIGHTNING AND TINNITUS, THREE NEW CASES OF TINNITUS RESULTING FROM LIGHTNING

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The ears are commonly affected in over 50% of lightning victims causing auditory or vestibular symptoms.

Possible mechanisms may include: flow of electric current through the cochlea, changes in the ear vascular flow, hemorrhage, rupture of the ear drums, and acoustic trauma.

Side ear symptoms of lightning are transient or permanent hearing loss and tinnitus that affect most survivors of lightning strikes, also vertigo has been reported.

Chronic ear infections and partial hearing loss and vertigo occur in half of patients with initial ear injury.

Three new cases of tinnitus secondary to the effects of lightning are reported here, together with details of their treatment and evolution, we also review the literature referred to

AUDITORY HALLUCINATIVE PHENOMENON, TINNITUS AND HEARING LOSS: TRUTH OR MYTH?

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Introduction: Auditory hallucinative phenomenon (AHP) refers to auditory perceptions without acoustic stimuli. It is often considered as a major symptom of psychiatric disorders, but may also occur under many organic conditions (ear and neurological disorders, toxic states, side effect of drugs etc). Although verbal and/or musical hallucinosis associated to hearing loss have been described, none have showed a diagnosis of psychosis. The "release theory" is the most accepted mechanism to explain the physiopathology of AHP. According to it, sensory inputs suppress a large number of nonessential information, including previous memory; when these sensory inputs decreases, the perception-bearing circuits will be disinhibited, resulting in re-experienced memory. The aim of this study is to characterize the AHP in otologic patients through an interdisciplinary point of view.

Methods: All consecutive patients from the Tinnitus Research Group of University of São Paulo Medical School complaining about AHP were enrolled in a 3-year period. They underwent a thorough evaluation by the same interdisciplinary team: otological, neurological and psychiatric examination, as well as pure tone audiometry, electroencephalography (EEG), Tinnitus Handicap Inventory (THI), Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCDI-I).

Results: Seventeen patients with AHP complaints were evaluated (15 women; mean age 62.5±16.9 years). The type of AHP was musical in 11 (64.7%), verbal in 3 (17.6%) and mixed in 3 (17.6%) patients. All subjects had a preserved contact with reality, being aware that no one else could hear such sounds. The context of musical AHP was often reported as pleasant, reactivating past memories, although the repetition of such phenomenon was considered as annoying for 100%. All subjects had tinnitus and hearing loss, which were bilateral in 94.1% of the cases. The total THI score varied from 22 to 96 (mean 77.42). The degree of hearing loss was mild or moderate in 5 (29.4%), severe in 4 (23.6%) and profound in 8 (47.0%) subjects. The time of onset of either hearing impairment or tinnitus was similar (mean 15.63±13.21 and 17.5±14.58, respectively), but the mean onset time of AHP was 10.52±11.4 years later than the deafness onset. On the neurologist evaluation, just 3 subjects (17.6%) had epilepsy. On the other hand, the psychiatric evaluation showed 12 (70.6%) subjects with some degree of depression: subclinic in 2 (11.7%), major in 6 (35.3%) and psychotic depression in 4 (23.5%), while 5 (29.4%) individuals didn't have any established psychiatric diagnosis.

Conclusion: Auditory hallucinative phenomenon comes to light separately (secondary to ear or neurological disorders) or as part of psychiatric symptoms (depression). It can be associated to tinnitus and hearing loss, not necessarily in profound or long term deafness. It is dominant in women and usually starts much later than the otological symptoms. The musical type was the most common AHP and all subjects had a preserved contact with reality, indicating that AHP might be more common than usually investigated.

**02:30 - 3:30 p.m. and
04:00 – 06:00 p.m.
SYMPOSIUM
Animal Models
R. Salvi**

AUDITORY CORTEX VOLTAGE-SENSITIVE DYE IMAGING REVEALS SPATIOTEMPORAL PATTERNS OF SPONTANEOUS AND EVOKED NEURAL ACTIVITY AT HIGH RESOLUTION.

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Phantom perceptions in tinnitus are hypothesized to be produced by abnormal spatiotemporal patterns of spontaneous neural activity in auditory cortex. Characterizing these patterns in detail would benefit from a population recording method with high spatial as well as temporal resolution, such as voltage-sensitive dye optical imaging. However, this method has not yet been extensively applied to the study of auditory processing. We report the results of measuring spontaneous activity, as well as evoked activity in response to pure-tone acoustic stimuli, in the auditory cortex of the anesthetized guinea pig, using optical imaging with the voltage-sensitive dye

RH1691. For evoked activity, data acquisition trials were synchronized with the ECG, and performed while artificial respiration was temporarily blocked, in order to mitigate spurious noise caused by cortical movement artifacts. Stimulation with a pure-tone, relative to no stimulus, resulted in population responses in putative primary auditory cortex which were initially spatially restricted and later more broadly distributed. Temporally, the responses were characterized by an initial increase in fluorescence relative to baseline which peaked at approximately 30 ms after stimulation, followed by a decrease in fluorescence peaking at approximately 80 ms. Voltage-sensitive dye imaging thus provides a method to monitor spatiotemporal patterns of activity over a large spatial extent of auditory cortex, and is a promising means to compare abnormal spontaneous activity following acoustic trauma, to normal sound-evoked activity patterns.

ALTERED VOLTAGE-GATED SODIUM CHANNEL EXPRESSION FOLLOWING MODERATE SOUND EXPOSURE IN RAT SPIRAL GANGLION NEURONS

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Depending on its duration and intensity, exposure to intense sound can result in varying degrees of functional deficit in the auditory periphery including hearing loss and tinnitus. Recently, experimental evidence has shown that following moderate noise exposure, more subtle derangement of the sensorineural apparatus may contribute the earlier stages in development of auditory deficit (Kujawa and Liberman, 2009). This subtle damage is manifest as swelling and degeneration of the synapses and dendrites of spiral ganglion neurons (SGN). The SGNs provide the afferent innervation of the hair cells and express a unique subset of voltage-gated sodium channels (VGSC) that are essential to their physiological role in sound processing (Fryatt et al., 2009). Interestingly, in models of neuropathic pain, similar neuronal axotomy is accompanied by altered voltage-gated sodium channel (VGSC) expression, leading to neuronal hyperactivity.

In this study, a moderate acute noise model consisting of a 15kHz single tone at 110dB SPL delivered in two sessions, each lasting 2 hours, in adult Wistar rats was used. Evoked auditory brainstem responses (ABR) were utilised to measure hearing deficit at 12, 16, 24 and 30kHz. This protocol produced a significant yet mild mean ABR threshold elevations of approximately 15-20dB at 24 and 30kHz ($p < 0.005$ and $p < 0.001$ respectively; $n=8$). However, there were no accompanying changes in suprathreshold transfer function or ABR waveform latency at any frequency.

Quantitative PCR in conjunction with immunohistochemistry was used to study the complement of VGSCs in the SGN between the deafened and control rats. NaV1.1 and NaV1.6 mRNA expression had significantly decreased following sound exposure with about a 30% and 55% decrease respectively ($p < 0.001$), while NaV1.7 mRNA expression had increased by approximately 20% ($p < 0.005$) compared to unexposed animals ($n=7$). Streptavidin-horseradish peroxidase immunohistochemistry extended these findings, revealing significantly increased staining for NaV1.1 along the SGN dendrites ($p < 0.05$; $n=3$) and some indication of increased staining for NaV1.7 in the cell bodies.

These results provide evidence, for the first time, of selective changes in VGSC expression accompanying mild threshold elevation following moderate ototrauma. We hypothesise that early changes could contribute to the generation of perceptual anomalies such as tinnitus

experienced in many sufferers not experiencing profound hearing loss (König et al., 2006).

References

Fryatt AG, Vial C, Mulheran M, Gunthorpe MJ, Grubb BD (2009) Voltage-gated sodium channel expression in rat spiral ganglion neurons. *Mol Cell Neurosci* 42:399-407.

König O, Schaette R, Kempter R, Gross M (2006) Course of hearing loss and occurrence of tinnitus. *Hear Res* 221:59-64.

Kujawa SG, Liberman MC (2009) Adding insult to injury: Cochlear nerve degeneration after "temporary" noise-induced hearing loss. *J Neurosci* 29:14077-14085.

UNILATERAL SOUND DAMAGE CAUSES AN INCREASE IN SINGLE UNIT SPONTANEOUS ACTIVITY IN THE INFERIOR COLLICULUS OF FREELY MOVING RATS

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Tinnitus in humans is often associated with sound damage to the inner ear. Sound damage in rats alters central nervous system activity in specific auditory regions, which may represent a neural correlate of tinnitus. In this study we are evaluating the effects of sound damage on spontaneous discharge of single units in the inferior colliculus of freely moving rats. Male Long Evans rats between 1 and 4 months of age were anesthetized with a ketamine/xylazine mixture and exposed unilaterally to a 16kHz continuous pure tone at 114dB SPL for one hour. One or more days later a stainless steel recording chamber was implanted to allow access to the inferior colliculus. One week after the sound exposure we began electrophysiological recordings. A lightweight microdrive containing up to 8 tungsten insulated microelectrodes was used to record single unit activity. Just prior to recording, the rats were anesthetized with isoflurane and the microdrive was inserted into the recording chamber. Rats were then placed in a plexiglass chamber with a loudspeaker mounted in one wall. The microdrive was connected via a flexible cable to the recording equipment, allowing rats to move freely within the recording chamber. Electrodes were slowly advanced while presenting a noise burst search stimulus. Once a single unit was identified, its spontaneous activity was recorded while the rat sat quietly in the chamber. From each unit we recorded five periods of spontaneous activity lasting 5 seconds each. Following these measurements we tested the response of each unit to noise stimulation by presenting 50 ms noise bursts that varied in intensity between 0 and 70 dB SPL. Finally, we recorded the response of each unit to 50 ms tone pips that varied in frequency between 300 Hz and 100 kHz and in intensity between 0 and 70 dB SPL. We recorded from 9 control animals (206 units) and 10 sound-exposed animals (144 units). The average spontaneous activity in control animals was 14.3 spikes/sec, and in the sound-exposed animals average spontaneous activity was 21.6 spikes/sec. Two-tailed t-tests revealed a significant difference in spontaneous activity between groups ($p < 0.005$). Subsequent experiments will evaluate the locations of these units within cytoarchitectural areas of the inferior colliculus.

These experiments were supported by funding from the Tinnitus Research Consortium, the Department of Defense (PR081241) and the NIH (HD002528).

SOUND-TRIGGERED SUPPRESSION OF SPONTANEOUS FIRING IN CENTRAL AUDITORY NEURONS AND RESIDUAL INHIBITION OF TINNITUS

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Recently we have reported that sound stimuli lasting a few milliseconds duration can suppress spontaneous firing in inferior colliculus (IC) neurons for several hundreds of milliseconds. The primary goals of the present study were: (1) to test whether the duration of this suppression depends on the stimulus duration; and (2) to elucidate the mechanism(s) underlying this suppression. Extracellular responses of IC neurons exhibiting spontaneous firing were recorded in awake CBA/CaJ mice in response to pure tones at the neurons' characteristic frequency, or to broadband noise. Stimuli ranging from 50 - 1500 ms in duration were presented once every 30 sec. A significant majority of IC neurons (93%, 21/23) showed spontaneous firing, ranging from 0.4 - 43 spikes/second (sp/s) with median of 5.2 sp/s. The majority of these neurons (82%, 18/21) showed suppression of spontaneous firing after cessation of the stimulus. The duration of suppression increased with stimulus duration and at the maximal stimulus duration tested (1500ms), suppression ranged from about 50 milliseconds to up to 11 seconds. Duration was largely dependent on the response strength of IC neurons. Neurons showing robust response firing rates during the entire stimulus duration typically exhibited the longest suppression, whereas neurons exhibiting weak response firing rates or onset/offset response patterns typically showed no, or very short (about 50 ms) suppression of spontaneous firing.

The time course of the suppression strongly suggests that metabotropic rather than ionotropic receptors might be responsible for suppression, because the former are known to alter neuronal activity for seconds. We tested the hypothesis that metabotropic glutamate receptors (mGluRs) contribute to the suppression by the recording from the IC neurons exhibiting sound-triggered suppression of spontaneous firing. Drugs targeting mGluRs were injected iontophoretically directly to these neurons. We found that mGluR-targeted drugs can reversibly block the suppression of spontaneous firing in about 60% of neurons exhibiting long-lasting suppression. Hyperactivity or abnormally high spontaneous activity has been linked to behavioral signs of tinnitus, and the duration of the suppression that we observed approximates the duration of residual inhibition in humans; thus sound-triggered suppression of spontaneous firing may be an underlying mechanism of residual inhibition.

Supported by NIH R01 DC00537, and the Research Incentive Research Grant from Northeastern Ohio Universities College of Medicine.

BEHAVIORAL AND MOLECULAR COMBINED ANIMAL STUDIES FOR VISUALIZATION OF PHANTOM TINNITUS

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Objectives: Tinnitus is a non-observable sensation. As such, it is a difficult condition to investigate and, to date, no effective treatment has been developed. To approach this phantom sensation, we aimed to develop a rat behavioral model of tinnitus using salicylate, an active component of aspirin known to induce tinnitus. We also aimed to establish a molecular marker of tinnitus by assessing the expression of transient receptor potential cation channel superfamily V-1 (TRPV1) in the rat auditory pathway during salicylate-induced tinnitus.

Methods: Wistar rats were trained to perform "an active avoidance task". Tests were performed in a conditioning box with an electrical floor which was separated by a low wall. The conditioned stimulus was a 20, 60 or 80 dB SPL pure tone with a frequency of 4, 16 or 40 kHz of 5 sec duration, and the unconditioned stimulus was a 3.7 mA electrical footshock presented for 30 sec at most. The interval between conditioned and unconditioned stimuli was 1 sec. Electrical shocks were stopped when the animal correctly moved to the other side of the box. The inter-trial interval was at least 1 min. The "score" stands for the level of performance assessed by the ratio of how many times the rat correctly moved in response to sound out of 10 trials. Animals were considered to be conditioned when the "score" reached at least 80% in three consecutive sessions. When conditioned, animals were included into main experiments.

The main experiments were performed once a day for five days at the regular hour. Animals received injection of saline on the 1st day and injection of salicylate (400mg/kg, i.p.) from the 2nd to 4th day. On the 5th day, they received no treatment. The behavioral testing protocol consisted of a daily measurement of the "score" and "false positive" responses. The "false positive" responses stand for the number of movement during a silent period, or feeling phantom tinnitus. Trials were randomized and electrical footshocks were only presented if the animal did not move in response to sound. Whatever the results of the "score" and "false positive" responses were, each session included 10 trials and lasted 15 minutes.

In addition, tissues from the auditory pathway were obtained in saline- and salicylate-treated groups. Among these two groups, changes in TRPV1 expression were examined by using real-time PCR and Western blotting.

Results and Conclusion: Animals treated with salicylate presented no significant change in the "score", but significant increase of the "false positive" responses. The number of the "false positive" responses was the highest when the conditioned stimulus was 60 dB SPL and 16 kHz, indicating that animals could experience tinnitus like 60 dB SPL and 16 kHz after salicylate injection. In addition, TRPV1 expression was significantly up-regulated in the spiral ganglion 2h after salicylate injection and this up-regulation together with the increase in the number of "false positive" responses was significantly suppressed by capsazepine (10mg/kg, i.p.), a specific antagonist of TRPV1. This suggests that salicylate could induce tinnitus through activation of TRPV1 in the auditory pathway.

FROM RATS TO HUMANS: VALIDATION OF THE ACOUSTIC GAP STARTLE PARADIGM TO OBJECTIFY TINNITUS

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Background: The acoustic startle reflex is a primitive reflex produced by a sudden and unexpected loud sound. It can be inhibited by inserting a weak sound (a prepulse sound) a few milliseconds before the startle sound. A modified version of prepulse modulation was recently developed to model tinnitus in animals, by using a silent gap rather than a prepulse. In normal rats, the gap decreases the startle reflex, similar to a prepulse. In contrast, in rats with salicylate- or noise- induced tinnitus, there is no inhibition of the startle reflex, presumably because the gap is filled with the tinnitus sound. The lack of inhibition is specific to background noise of frequency close to tinnitus frequency, and is therefore used to objectively demonstrate the presence of tinnitus. We propose that, transposed to human subjects, the startle reflex may provide an effective paradigm to measure tinnitus objectively.

Objectives: In two experiments, we 1) validated the efficiency of the gap to inhibit the acoustic startle reflex, using high- and low- frequency background noise, in normal-hearing human participants, and 2) examined how it compares with inhibition induced by a prepulse.

Methods: Young participants without hearing loss or tinnitus were recruited and were randomly assigned to one of the gap duration condition (50ms, 100ms, 200ms). STARTLE-only trials consisted of a 50ms white noise 105dB(A) burst. GAP trials consisted of a 50ms, 100ms, or 200ms silent gap inserted into either high- or low-frequency background noise set at 65dB(A), followed by a startle sound. PREPULSE trials consisted of either 50ms bursts of low- or highfrequency noise at 65dB(A) presented in quiet, followed by a startle noise. Electromyographic responses of eyeblink amplitude to the three types of stimuli were measured.

Results: Results show that prepulse sounds were very effective in inhibiting the acoustic startle reflex, a finding consistent with previous studies in human subjects. The gap was also effective in inhibiting the reflex, but the effectiveness varied with the parameters used and durations.

Conclusion: The gap-in-background noise paradigm is effective in inhibiting the acoustic startle reflex in normal-hearing subjects, and it is a promising approach to objectively measure tinnitus in humans.

THE EFFECTS OF TONABERSAT AND CYCLOBENZAPRINE ON NOISE INDUCED TINNITUS IN RATS.

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Aims and objectives: To date there are no reliable pharmacological treatments for most forms of tinnitus. However, there is evidence that some forms of tinnitus, such as typewriter tinnitus, respond to pharmacological treatment. The goal of the current project is to evaluate innovative pharmacological therapies for noise induced tinnitus using our tinnitus animal model. Here we present new data on the effects of the neuronal gap junction

blocker Tonabersat and the CNS antispasmodic Cyclobenzaprine on persistent noise induced tinnitus

Methods: We have used the Gap Prepulse Inhibition of the Acoustic Startle (GPIAS) to determine the onset, pitch, and persistence of tinnitus and to evaluate potential pharmacological treatments after a tinnitogenic unilateral high-frequency noise exposure (16 kHz, 123 dB SPL). Animals were first treated with Tonabersat or Cyclobenzaprine. After a one week washout period, subjects were exposed to traumatic noise and measured at 2, 7, 10, and 15 days for the presence of persistent tinnitus. After animals were treated with either Tonabersat or Cyclobenzaprine and the effects on tinnitus were measured using GPIAS.

Conclusions: Preliminary data suggests that chronic treatment with Tonabersat or acute treatment with Cyclobenzaprine was effective in attenuating tinnitus in some animals. Further studies will identify which animals are more likely to respond to either treatment and the duration of efficacy of these compounds.

EFFECTS OF NERAMEXANE IN A MOUSE MODEL OF TINNITUS

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Neramexane is a dual NMDA and alpha9/10 nicotinic receptor antagonist that has shown promising results in a phase II clinical trial for tinnitus and is currently being assessed in wide scale phase III clinical studies. Adult CBA/CaJ mice with noise-induced behavioral evidence of chronic tinnitus (n=12) and controls (n=10) were given 0, 2.5, 5, or 20 mg/kg Neramexane (i.p.) over the course of four consecutive days in a counterbalanced order design. 30-min after dosing (each day) mice were tested for behavioral evidence of tinnitus using an animal model that measures ability to detect silent gaps in an otherwise continuous background sound (Turner et al., 2006). Neramexane i.p. at the 5 mg/kg dose produced a significant (p=0.0006) reduction in behavioral evidence of tinnitus, while no significant changes were observed for any of the dose levels in control mice. Blood plasma studies showed that 5mg/kg i.p. Neramexane in mice (n=3 at each dose) produces plasma levels which are within the typical clinical range.

*Study funded by Merz Pharmaceuticals. J. Turner is a paid consultant to Merz.

SCREENING OF INVESTIGATIONAL TINNITUS DRUGS USING CULTURED AUDITORY CORTEX NETWORKS

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Introduction: Tinnitus or "ringing in the ears" is defined as the perception of sound in the absence of a corresponding external sound. It is often, but not always, associated with hearing loss. Although tinnitus is a common disorder affecting 1 in 100 people in the US there is no specific treatment for tinnitus. Tinnitus is associated with an increase in electrical activity in the cortical areas. As a model for such phenomenon, we used pentylentetrazole

(PTZ), a convulsant drug to cause excitation of neuronal activity (tinnitus-like) in auditory cortex networks (ACNs) growing in vitro on multielectrode arrays (MEA). Further, we evaluated the efficacy of four experimental tinnitus treatment drugs in PTZ-induced activity. The drugs used in this study were: Pregabalin, Gabapentin, L-Carnitine, and Linopirdine. Pregabalin (Lyrica), along with its precursor Gabapentin (Neurontin), are selective Ca channel blockers that form a new class of anti-convulsants, having their therapeutic action on neuropathic pain. L-Carnitine is a prevalent over-the-counter anti-oxidant. Linopirdine, although discontinued in the US, is widely used in Europe as a treatment of pain for its action on potassium channel blockage.

Methods: Dissociated neurons from auditory cortices of mouse embryos were grown on photoetched MEAs with 64 transparent indium-tin oxide electrodes. We induced excitatory tinnitus-like electrical activity in ACNs by applying PTZ to cultures growing on the MEAs. Following this, the ACNs were exposed to various concentrations of Pregabalin, Gabapentin, L-Carnitine or Linopirdine to determine if the activity could be reduced to pre-PTZ level.

Results: Our data show that 1.0 mM PTZ significantly increased activity in the ACNs by potentiating action potential spike rate and burst rate. Results also indicate that Pregabalin, Gabapentin, L-Carnitine, Linopirdine reduced the activity in ACNs to or below their pre-PTZ level, with no overt morphological damage to the neurons. The potency of the drugs was Linopirdine > L-Carnitine > Gabapentin > Pregabalin.

Conclusion: We conclude that ACNs serve as an attractive model for the study of tinnitus-like activity that has as a hallmark increased neuronal excitability with exposure to PTZ. The fact that the drugs used to attenuate the increased firing are already on the market for the treatment of other medical conditions, the ion channel drugs and the antioxidants may prove to be therapeutic for the relief of tinnitus, but only a carefully-controlled clinical trial of these drugs will provide more definitive answers.

04:00 - 06:00 p.m.

SYMPOSIUM

The TRI Flowchart for Patient Management B. Langguth

ALGORITHM FOR THE DIAGNOSTIC AND THERAPEUTIC MANAGEMENT OF TINNITUS

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Tinnitus can be a symptom of a wide range of different underlying pathologies and be accompanied by many different comorbidities, indicating the need for comprehensive multidisciplinary diagnostic assessment. Basic diagnostics should include a detailed case history, assessment of tinnitus severity, clinical ear examination, and audiological measurement of hearing function. For a considerable number of patients, these first diagnostic steps in combination with counseling will be sufficient.

Further diagnostic steps are indicated if the findings of basic diagnostics point to acute tinnitus onset, a potentially dangerous underlying condition (e.g., carotid dissection), a possible causal treatment option, or relevant subjective impairment.

Further diagnostic management should be guided by clinical features. There is increasing evidence that phenomenologic and etiologic aspects determine the pathophysiology and the clinical course of tinnitus. In a hierarchical diagnostic algorithm, the first differentiation should be between pulsatile vs. non-pulsatile tinnitus. In case of non-pulsatile tinnitus, differentiation between acute tinnitus with hearing loss, paroxysmal tinnitus, and chronic tinnitus is recommended. Further diagnostic procedures of constant non-pulsatile tinnitus will depend on concomitant symptoms and etiological conditions. All diagnostic and therapeutic steps should be accompanied by empathic and insightful counseling. The ultimate treatment goal is complete relief from tinnitus. If causally oriented treatment options are available, these should be preferred. However in many cases, only symptomatic therapies can be offered, and then the treatment goal in clinical practice will be defined as the best possible reduction of unpleasant hearing sensations and accompanying symptoms, i.e., to improve quality of life.

FRIDAY JUNE 11, 2010

8:00 - 10:00 a.m. PLENARY TALKS

8:00 - 9:00 a.m.

TINNITUS AND NEURAL PLASTICITY

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Auditory perception is the outcome of neural processing from the cochlea to the auditory cortex and more distal brain regions. It is an important but challenging task to understand the transformations that take place at each stage of the projection pathway and how they relate to hearing, auditory perception, and memory. Neural plasticity is a contributing process in these transformations, which can be imaged (albeit it coarsely) by auditory evoked potentials (EEG) and magnetic fields (MEG) that arise from events occurring at different levels of the central auditory system. Our research using these methods suggests that neural remodeling in the auditory system is driven by the spectrotemporal statistics of the acoustic input in adults as well as in children, such that neural representations become tuned to the sounds that are present in the environment. Attention becomes increasingly important after maturity, but appears to exert its selective effects principally on higher order auditory processing required for complex skill, adaptive behaviour, and memory. Knowledge about these principles may assist in understanding auditory skills as well as disorders of auditory function of which tinnitus is a prime example. Psychoacoustic and brain imaging evidence from our laboratory and from other research groups points to synchronous neural activity in deafferented regions of the auditory cortex as the basis of tinnitus sensations. Whether such activity can be reversed by auditory training is uncertain and one topic to be discussed. We also consider whether understanding tinnitus can provide information about mechanisms that underlie normal auditory perception.

(Research supported by CIHR and NSERC of Canada and the Tinnitus Research Initiative)

9:00 - 10:00 a.m.

INCREASE IN GAIN IN THE CENTRAL AUDITORY SYSTEM AND TINNITUS

Arnaud J. Norena

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Hearing loss is very common in our industrialized societies where cochlear insults resulting from occupational and leisure noise exposure add to the damages caused by aging (presbycusis). It has been largely documented that sensory deafferentation induced dramatic changes at all levels of the central auditory system. We suggest that these central changes result from an adaptive mechanism aiming at maintaining stability of neural responses around a set point level (homeostatic plasticity) and preserving neural coding efficiency. However, as most things in life, nothing comes for free: these central changes may be accompanied by abnormal neural activity underlying tinnitus and hyperacusis. We will present the view suggesting that these central changes induced by sensory

deafferentation may account for the generation of hyperacusis and tinnitus, and will discuss its therapeutic implications.

10:30 - 12:15 SYMPOSIUM Sound Therapy Grant Searchfield

INTERNET-BASED ACOUSTIC THERAPY (IBAT) FOR TINNITUS PATIENTS

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There is a growing consensus that the treatment of tinnitus patients should include counseling and acoustic therapy (AT) (Tyler 2005). Hearing aids (HAs) and noise generators (maskers) have been widely recommended for tinnitus patients for decades. Although HAs are conveniently accessible option for tinnitus patients with hearing impairment, there is little conclusive evidence of efficiency, particularly in silent environment. Similarly the effectiveness and user acceptability of tinnitus maskers has been questioned (Henry 2006).

New successful treatment programs aimed to treat tinnitus patients combine counseling and AT. An integral part of TRT (Jastreboff 1990) is white noise type AT from ear level noise generators. However, according to our clinical experience, TRT-type AT has not been well accepted by our patients. It has also been suggested that AT aimed for desensitization should be customized according to the individual's hearing and tinnitus profile. AT is also an important part of the auditory tinnitus management program (ATM, Henry 2005). This program utilizes CD- or MP3 players and varying non-customized sound sources, preferably water-sounds (Henry et al 2008). Drawbacks of ATM sound therapy are that it is not customized and it leaves to the patient to search for appropriate AT material. The crucial part of the acoustic desensitization protocol, (ADP, Davis et al 1999, 2005) or Neuromonics tinnitus therapy (NTT) (Hanley et al 2008) is music-based, customized AT, which is delivered by specially designed ear level sound generators.

The reported overall efficiency of these sound-based tinnitus therapies varies. Among these, best documented seems to be the NTT (using customized, music-based AT). The wide use of NTT, however, may remain limited especially because of economical reasons.

We have extracted appropriate parts of TRT, NTT and ATM therapies to develop our own modification of tinnitus treatment program since a few years back. This means identification of the patients hearing and tinnitus profiles (auditory testing, tinnitus matching with an equalizer) and design of customized AT material. When we have offered customized AT material to our patients packed in CDs or

MP3 players or memory sticks we have noticed that the best way of providing AT material to individual patients might be via the internet. We also noted that the testing and customization that we are doing individually to our patients, can also easily be performed via internet. These observations have been the basis for starting the internet-based acoustic therapy (IBAT) project.

In IBAT we use music and nature sounds customized according to individuals tinnitus and hearing profiles. Our aim is also to utilize the benefits that music therapy is providing for stress treatment. At the first stage, IBAT is available for professional clients.

THE EFFECT OF FRACTAL SOUNDS ON TINNITUS PERCEPTION

Grant Searchfield, Daniel Kim, Kei Kobayashi

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Tinnitus has the potential to develop into a chronic condition strongly influenced by the psychological state of the sufferer. There is some evidence that suggests relaxation therapy may be effective in reducing the intrusiveness of tinnitus. Music is often used as a relaxation aid. The psychological benefits of music include relaxation and calming effects. The effects of different music types on tinnitus perception have been reported (Hann et al., 2008). Most people prefer music that has a calming effect and complexity that can redirect attention from tinnitus to the music. A hearing aid has recently been released which offers fractal sounds as a programmable option for users. The fractal sounds are proposed to promote relaxation, which might in turn have some benefits for users with tinnitus. The hearing aid software creates a random, harmonic tone or chime, based on a fractal mathematical algorithm so that the 'music' is similar to itself without being repetitive. The sounds are played taking account the individual's level of hearing loss. The aim of this study was to determine whether, and how, fractal sounds affect tinnitus perception. The methods of Hann et al., 2008 were used with the substitution of fractal sounds for music. Study participants were asked to complete a set of standard Tinnitus and Health Questionnaires to assess how they perceived their tinnitus. Participants were also required to complete several visual analog scales (Tinnitus annoyance scale [TAS]; stimulus annoyance scale [SAS] and semantic association scales [SeAS]) during the presentation of the sounds. Individual and average ratings will be presented along with a critique of fractal sound use for tinnitus management.

References:

1. Hann, D, Searchfield, G. D., Sanders, M., & Wise, K. 2008. Strategies for the selection of music in the short-term management of mild tinnitus. *Australian and New Zealand Journal of Audiology*. 30(2): 129-140.

LONG-LASTING TINNITUS RELIEF ACHIEVED BY ACOUSTIC COORDINATED RESET STIMULATION - CLINICAL INVESTIGATION: PHASE I - PROSPECTIVE CLINICAL INVESTIGATION ON THE ACOUSTIC STIMULATION WITH THE "COORDINATED RESET OF NEURAL SUBPOPULATIONS" IN THE TREATMENT OF CHRONIC TINNITUS

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The aim of this trial is to confirm the efficacy and safety of the coordinated reset neurostimulation technology and to measure the improvement of the QOL (quality of life) by reducing the Tinnitus-Symptoms of the patient. These objectives will be assessed by the standardized criteria of the Tinnitus Questionnaire (TQ) and perceived tinnitus loudness; annoyance and the effect of tinnitus on life were assessed through the Visual Analog Scale (VAS) with and without stimulation.

Study design: Eligible patients were randomized to five therapy groups, G_1: stimulation for 4 - 6 hours a day, 4 tones per sequence, G_2: stimulation for 4 - 6 hours a day with 12-tone sequences, G_3: stimulation for 4 - 6 hours a day, 4 tones per sequence with a signal controlled by EEG measurement, G_4: stimulation for 1 hour a day with 4 tones per sequence, G_5: stimulation with placebotone.

A total of 63 patients were included and are followed up for clinical relevant change of tinnitus at 0- 1- 4- 8- 12 - 16 - 42 weeks. An interim analysis was performed on a total of 45 patients after 12 weeks of treatment.

When analyzing the mean TQ total score over the 12 weeks treatment there was an important improvement in total score, especially visible for treatment groups I and III. Before treatment, mean TQ score in G_I = 44.4 and for G_III = 45.3, while after 12 weeks of treatment these scores were 32.0 and 28.3 respectively, showing an improvement of approximately 15 points.

A clinically significant reduction on VAS scores was obtained after 12 weeks treatment for both groups, both for off stimulation as well as for comparison between off and during stimulation. The improvement after 12 weeks was approximately 25 points for VAS off stimulation. Stimulation improved the VAS even further about 20 points additionally as compared to off stimulation at 12 weeks.

We observed a major improvement of hearing ability measured by the audiogram (hearing threshold) and calculated as Pure Tone Averages over the 12-week treatment. Before treatment the mean hearing threshold of G_I and G_III was 8.94 Db and 17.81Db for HdB1 and 6.10 Db and 11.05 Db for LdB respectively. After the 12 weeks of treatment the audiometrical measurements showed mean values of 4.38 Db and 1.94 Db for HdB1 G_I and G_III, while for LdB values were -1.50 Db and 4.90 Db respectively. Overall, the improvement is on average about 6 Db for both groups. This is consistent with the hearing improvement of > 5 Db over the whole frequency range (500-10.000 Hz) in both groups.

Furthermore, the Tinnitus tone frequency improved dramatically over the 12-week period: this clinical important improvement of at least 70% was achieved for G_I and G_III.

Our results suggest that acoustic CR stimulation provides an effective tinnitus therapy. CR induced Tinnitus relief is accompanied by a decrease of tinnitus frequency and an improvement of hearing.

Final 16 w FU data will be presented at the conference.

PASSIVE AUDITORY STIMULATION BY MP3: RESULTS AFTER 6 MONTHS

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Our clinic in Milan belongs to the Passive Auditory Stimulation (PAS) Work Group and we cooperate for the International Project "Innovative auditory stimulation as enhancer of brain plasticity in tinnitus therapy". The theory is that high pitch auditory stimulation could induce neuroplasticity and reverse the neural correlates of tinnitus. Our goal is to evaluate a new auditory stimulation treatment by an MP3-based ear level device. This therapy includes a close-to-thresholds high-pitch auditory stimulation therapy combined with an environmental relaxing sound.

In order to evaluate the PAS results, 20 tinnitus patients were recruited: 10 patients followed the new therapy for six months and 10 (but one was lost during follow up) followed a control treatment based on the sole environmental relaxing sound. The Tinnitus Handicap Inventory (THI) was administered to the patients before at the beginning, after 3 and 6 months of therapy.

The initial score was 42 ± 21.83 in PAS group and 44 ± 21.76 in control group, so no significant difference was present between the two groups at the beginning. After 3 months of therapy the score was 32 ± 20.27 in the first group and 37 ± 17.33 in the second. Finally, after 6 months, the scores were 27 ± 11.88 and 31 ± 6.39 respectively. No significant differences were found either between the two groups and during the time in each group. The most probable cause is the restricted number of patients in each group.

To analyze together the data from all work group clinics is necessary in order to evaluate the PAS usefulness in tinnitus treatment once and for all.

THE NEW ZEALAND EXPERIENCE WITH A NEW SOUND THERAPY CONCEPT

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Tinnitus is widely believed to be the consequence of auditory system reactive plasticity to auditory pathology. Hearing aids, masking and auditory habituation sound therapies have been shown to be useful adjuncts to counselling for tinnitus. Our understanding of central plasticity processes has increased and digital storage and signal processing has progressed; this now enables the use of more complex sound stimulation paradigms for tinnitus treatment. This study reports initial clinical trial results of a treatment based on the plasticity research of Norena and Eggermont (1). The findings are part of a

multi-centre study of this innovative treatment concept. The benefits and shortcomings of the New Zealand experience with this treatment approach will be discussed.

[1] Norena AJ, Eggermont JJ. Enriched acoustic environment after noise trauma reduces hearing loss and prevents cortical map reorganization. *J Neurosci.* 2005;25(3):699-705.

PASSIVE AUDITORY STIMULATION BY A PROTOTYPE OF HEARING AID THAT IMPLEMENTS THE HIGH-PITCH AUDITORY STIMULATION

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The International Project "Innovative auditory stimulation as enhancer of brain plasticity in tinnitus therapy" is based on the theory that high pitch auditory stimulation could induce neuroplasticity and reverse the neural correlates of tinnitus. In our tinnitus clinic in Milan, we tested for six months the Passive Auditory Stimulation (PAS) by an MP3-based ear level device. Now, our new aim is to evaluate the PAS by a prototype of hearing aid that implements the high-pitch auditory stimulation.

As in the MP3 version, the therapy includes a close-to-thresholds high-pitch auditory stimulation therapy combined with an environmental relaxing sound. The instrument consists of an amplification part with advanced signal processing such as multi band wide dynamic range compression, digital feedback suppression and noise reduction, and an advanced dual sound generator part. The bandwidth of the instrument is extended to approx 9.5 kHz.

In order to evaluate the results of the PAS with the new hearing aid, 10 tinnitus patients were recruited among October and December 2009. They will follow the new therapy for six months and they'll draw up the Tinnitus Handicap Inventory (THI) and the Visual Analogue Scales (VAS) before at the beginning, after 3 and 6 months of therapy.

During the meeting the results will be present.

HIGH FREQUENCY DUAL SOUND GENERATOR COMBINATION INSTRUMENT FOR TINNITUS SOUND THERAPY

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Background: Tinnitus is a serious condition reducing the quality of life for a large number of people. In 2008 Del Bo et al. reports promising results by integrating a sound generator with a number of innovative new features in an open ear combination hearing instrument. The aim of this paper is to describe a newly developed high frequency combination open ear prototype device with a dual sound generator. The first sound generator providing white noise with modulation and frequency shaping for relaxation and the second being a therapeutic sound generator producing tone pips.

Methods and Results: The instrument consists of an amplification part with advanced signal processing such as multi band wide dynamic range compression, digital feedback suppression and noise reduction, and an advanced dual sound generator part. The bandwidth of the instrument is extended to approx 9.5 kHz.

The first sound generator included a number of unique features; a white noise sound generator with flexible frequency shaping capabilities; manual control of the noise level; a random amplitude modulation feature and an environmental steering feature.

The second sound generator is based on the theory that high pitch auditory stimulation could induce neuroplasticity and reverse the neuro-physiological modifications that develop after hearing impairment in the neural auditory pathways and that can be considered a plausible cause for tinnitus (Norena and Eggermont 2005 and 2006).

The stimulus signal consists of short tone pulses presented with random frequencies in the frequency range from 1 kHz to 9.5 kHz with the possibility to low pass and high pass limit the frequency range. The level of the individual tone pulses can be preset e.g. to exceed the auditory threshold of the subject with a specified number of decibels.

Conclusion: A detailed description of the prototype and technical specifications will be presented.

10:30 a.m. - 12:30 p.m.
SYMPOSIUM
Pharmacologic Treatment of
Tinnitus
A.B. Elgoyhen

CYCLOBENZAPRINE TO TREAT TINNITUS: A PRELIMINARY 16-WEEK PROSPECTIVE OPEN-LABEL TRIAL

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BACKGROUND: Cyclobenzaprine is a tricyclic pharmacological agent with central muscle relaxant properties. The mechanism of action is unclear but cyclobenzaprine is likely to increase norepinephrine release, inhibit serotonin 5-HT_{2A}, 5-HT_{2C} and muscarinic acetylcholine receptors. Therefore, it might influence tinnitus mediated by these neurotransmitters as well as somatosensory tinnitus.

OBJECTIVE: Collect preliminary data to determine if a further controlled study is warranted to assess cyclobenzaprine to treat tinnitus.

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

METHODS: The dose of cyclobenzaprine was up titrated from 15 mg to 30 mg per day over the first 4 weeks and then down titrated from week 12 to 14. Subjects were evaluated at screening/baseline, week 2, 4, 8, 12 and 16.

30 subjects were screened and 15 subjects, who met the inclusion criteria, were recruited to this trial. The sample counted on 7 males and 8 females, mean age 54.6 years (STD= 11.3 years). Tinnitus duration ranged from 8 to 504 months, mean duration 172 months (STD = 148 months)

Tinnitus minimum masking level (MML), The Tinnitus Handicap Inventory (THI), Tinnitus Impairment Questionnaire (TBF 12), Clinical Global Impression - Improvement scale (CGII), Beck Depression Inventory and SF-36 were administered. The presence of side effects was investigated.

Two outcome variables were selected in this preliminary analysis: THI and MML. Results were obtained by subtracting baseline from week 12's scores. A positive response to treatment was considered with ≥ 20 points reduction on THI and a decrease of ≥ 5 dB on MML. The highest baseline MML scores between both ears were selected.

RESULTS: Changes on tinnitus handicap: THI scores ranged from 20 to 80 points at baseline, mean value 47.57 (STD= 18.11) and from 0 to 58 points at 12 weeks, mean value 23.86 (STD = 17.91) ($p < .000$).

57.1% of the subjects (8/14) were classified as responders and presented a mean decrease of -34.0 points (STD= 7.17) on THI. Non-responders had a mean decrease of -10.00 (STD= 5.51) ($p < .000$).

Changes on tinnitus magnitude: right ear's MML ranged from 15 to 66 dB, mean value= 43.17 dB (STD=16.7dB) at baseline and from 16 to 59 dB, mean value= 41.17 dB (STD=11.9 dB) at 12 weeks ($p=0.5$). Left ear's MML ranged from 24 to 70 dB, mean value= 46.83 dB (STD=15.47 dB) at baseline, and from 17 to 63 dB, mean value 42.92 dB (STD=12.88 dB) at 12 weeks ($p=0.1$)

58.3% of the subjects (7/12) were classified as responders and presented a mean change on MML of -11.57 dB (STD= 6.87 dB). Non-responders had a mean change on MML of 3.6 dB, (STD= 4.44 dB) ($p=0.001$).

Changes on tinnitus pitch, in most cases to a lower frequency, were observed in 5 subjects. A possible hypothesis to this finding might be that this medication induced changes on neural firing pattern.

Some side effects were common (constipation and dry mouth), but most of the subjects tolerated well, except for one subject that dropped out on week 8.

CONCLUSION: these results indicate that cyclobenzaprine is a promising drug to treat tinnitus. A randomized controlled trial is necessary, using criteria that could identify subgroups of tinnitus patients who are likely responsive to this medication.

This research was supported by TRI Pharmacological Work Group

PHYSICIANS' ASSESSMENT OF TINNITUS TREATMENT OPTIONS IN EUROPE AND THE US

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Objective: To evaluate present tinnitus treatment options and identify country- and physician- specific differences.

Methods: A structured online-survey was conducted by DocCheck Research with 712 tinnitus-treatment experienced physicians. These were selected as 50% general practitioners (GPs) and 50% ear-nose-throat specialists (ENTs) from the US, Germany, UK, France, Italy and Spain.

Results: For acute tinnitus, GPs and ENTs tend to employ pharmaceutical treatment as first line therapy, with the exception of the UK and US. In the UK and US, ~40 to 55% of patients are not actively treated. In contrast, in the other countries this proportion is a maximum of one fifth.

For chronic tinnitus, both GPs and ENTs report a strong reduction in the use of pharmaceutical medication compared with acute tinnitus treatment. In the US and the UK, more acoustic equipment and tinnitus retraining therapy is applied compared to the other countries. The proportion of treated chronic patients in the UK and US is sharply increased compared to acute tinnitus.

In the pharmaceutical treatment of acute tinnitus, there is a wide diversity between countries. Anti-vertigo drugs and systemic corticosteroids are most commonly used in all countries except Germany, where rheological infusion treatment dominates (>90%).

For chronic tinnitus, anti-vertigo products are also used, but the proportion of antidepressants is increasing. There is a tendency towards using a greater variety of options than for the acute form.

Generally, the present treatment options are evaluated very critically regarding efficacy: In all countries 80-90% of doctors state problems with treatment.

Conclusions: There are country- and physician-specific treatment differences for acute and chronic tinnitus therapy. Despite a large variety of treatment options, both GPs and ENTs complain of an inadequate success rate with existing treatments.

Acknowledgments: This study was conducted by DocCheck Research and funded by Merz Pharmaceuticals.

EFFECTS OF CAFFEINE IN TINNITUS: PRELIMINARY DATA

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Introduction: Caffeine consumption has been related to tinnitus worsening for many years. Neurophysiological background for this effect is probably related to caffeine blockage of adenosinic inhibitory receptors at the brain, but caffeine effects on outer hair cells contractions may also account.

Aim: To evaluate the effects of caffeine intake reduction on tinnitus, with a validated questionnaire (THI) and a visual analog-scale (VAS).

Material and method: 23 patients with tinnitus as the main complaint, who took more than 150 ml of coffee (around 150 mg of caffeine) per day, were enrolled. Conductive and mixed hearing losses, as well as vascular, muscular and somatosensorial tinnitus were excluded. A Brazilian Portuguese version of THI and a VAS scale ranging from 1 to 10 were applied before and after reduction of caffeine intake. Patients with THI less than 16 were excluded, and THI variations of 20 points or more were considered as improvement or worsening.

Results: 3 patients dropped out. Of the remaining 20, 5 (25 %) had their tinnitus improved and nobody had tinnitus worsened. 2 patients had a strong effect on THI scores (56 and 50 points). Overall average results were a reduction of 9.4 points in THI (median: 5 points) and 0.85 point in VAS (median: 1 point).

Conclusions: From these preliminary data, we may conclude that caffeine intake reduction has a slight effect on tinnitus, but may have some dramatic effects on specific cases. Further data with a bigger sample, may determine which subtype of tinnitus is more prone to benefit from caffeine reduction. Caffeine reduction should still be recommended for the tinnitus patients at the first visit.

ADMINISTRATION OF THE COMBINATION CLONAZEPAM – DEANXIT AS A TREATMENT FOR TINNITUS

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Present study investigates the combination of clonazepam (Rivotril®) and Deanxit® intake for relief of tinnitus complaints, respecting a double blind placebo-controlled approach for Deanxit in a cross-over set up. Significant tinnitus reduction was seen after intake of the combination clonazepam – Deanxit while no differences in tinnitus could be demonstrated after the administration of clonazepam – placebo. This was true for all patients according to following parameters: time patients are aware of the tinnitus (p=0.026) and the visual analogue scale for tinnitus annoyance (p=0.024). Though tinnitus reduction was recorded as modest, this paper provides valuable data to be used as foundation for further analysis on the effect of clonazepam and Deanxit in tinnitus treatment.

01:30 - 03:30 p.m.

SYMPOSIUM

Electrical Stimulation to the Brain
and to the Ear

A. Møller

ELECTRICAL BRAIN STIMULATION FOR TINNITUS

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Introduction: tinnitus is a prevalent symptom, responding poorly the pharmacological treatment. Non-invasive transcranial magnetic stimulation, transcranial direct current stimulation and invasive auditory cortex stimulation (iACS) via implanted electrodes into the primary or overlying the secondary auditory cortex have been developed to treat severe cases of intractable tinnitus. Recently the frontal cortex has also been evaluated as a potential target for rTMS and the first implant has been performed.

Methods: A series of 43 patients who benefited transiently from two separate placebo-controlled TMS sessions were implanted with auditory cortex electrodes and 1 patient with a frontal cortex electrode. Targeting is based on BOLD activation evoked by tinnitus-matched sound using fMRI-guided neuronavigation.

Results: only 1 in 3 patients respond to iACS with tonic stimulation. Of the 2/3 non-responders, however half benefit from a newly developed burst stimulation. In total 1 out of 3 remain unaffected by the iACS. Average tinnitus reduction is close to 50% for the entire group. Burst stimulation is capable of suppressing tinnitus in more patients and better than tonic stimulation, especially for noise-like tinnitus. For pure tone tinnitus there are no differences between the two stimulation designs. Average improvement for pure tone tinnitus is better than for noise-like tinnitus and worst for a combination of both pure tone and noise-like tinnitus. TMS does not predict response to iACS, but in iACS responders a correlation between the amount of TMS and iACS exist. Gender, age or tinnitus duration do not influence treatment outcome.

For frontal cortex stimulation a gradual improvement is noted in time, with an average reduction from 8/10 for intensity and distress to 5/10 and 3/10 for distress respectively after one year of stimulation.

Conclusion: iACS might become a valuable treatment option for severe intractable tinnitus. Preliminary results of the first frontal cortex electrode warrant further exploration of this target.

A better understanding of the tinnitus network and stimulation designs is required before this technique can be routinely applied.

EPIDURAL ELECTRICAL AUDITORY CORTEX STIMULATION IN THE MANAGEMENT OF CHRONIC UNILATERAL DISABLING TINNITUS. FIRST RESULTS OF THE PILOT STUDY « ELECTIN »

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Introduction: Subjective tinnitus can be very disabling when they are chronic. As in deafferentation pain, the pathophysiological basis for chronic tinnitus could be due to an aberrant cortical reorganization following a peripheral auditory deafferentation. The pilot study "ElecTIN" was designed to evaluate, in patients with unilateral chronic tinnitus resistant to treatment: (i) the effectiveness of epidural electrical auditory cortex stimulation (EEACS) of the auditory cortex to reduce or eliminate the tinnitus, (ii) the predictive value of efficiency of repetitive transcranial magnetic stimulation (rTMS) and (iii) the practical feasibility of such a protocol.

Material and Methods: Two patients with unilateral chronic tinnitus (one right and one left, for over 20 years) have already benefited from this protocol. First, an active or sham rTMS was applied next to the auditory cortex, contralateral to tinnitus (1 and 10 Hz). Then, we proceeded to the EEACS and the adjustment of individual stimulation parameters to obtain maximum efficiency. We then completed a randomized double-blind controlled assessment, with a cross-over after eight weeks of active or sham stimulation. Finally, the patient had to choose "blindly" between the two positions tested (active or sham) for a 12 weeks "pseudo-open" period.

Results: After rTMS sessions, no significant change in subjective intensity of tinnitus (on Visual Analogic Scale (VAS)) or in the multidimensional questionnaire ("Subjective tinnitus severity scale" and "Tinnitus handicap questionnaire") was found. Both patients were implanted, using a neuronavigation system and intraoperative electrophysiological recordings of auditory cortical responses, for the positioning of electrodes.

In the first patient, there was no significant difference found between "active" and "sham" periods. However during the "pseudo-open" period (active position), an efficacy of EEACS was found, with a 30% decrease of the VAS and an improvement of all scores on questionnaire.

For the second patient, the EEACS had a 70% efficiency on VAS. Due to a scar problem, the EEACS system had to be removed after a month with a rebound effect on tinnitus intensity and a return to baseline. Eighteen months later, the EEACS was reimplanted using the same technique of electrode placement, with an efficiency of over 50% on VAS of the intensity of tinnitus in active stimulation.

Conclusion: Our work confirms the technical feasibility of EEACS, with a bimodal positioning of electrodes, in the treatment of unilateral chronic tinnitus. Moreover, it suggests a dissociation between the therapeutic efficacy of rTMS and that of EEACS. Finally, it is the first description of a procedure for re-implantation in the EEACS for tinnitus. Obtaining a similar efficacy in both procedure and a return to baseline during the interval without stimulation are important arguments in favor of the real effectiveness of EEACS.

AUDITORY CORTEX ELECTRICAL STIMULATION TO SUPPRESS TINNITUS: AN ANIMAL MODEL

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Several clinical groups have recently demonstrated that brain stimulation such as auditory cortex electrical stimulation (ACES) has yielded promising results in suppression of patients' tinnitus (e.g., Howard 04; De Ridder 06; Fenoy 06; Friedland 07; Seidman 08; Litre 09). However, large variability in the efficacy of ACES-induced suppression across individuals has hindered its development into a reliable therapy. Due to ethical reasons, many issues cannot be comprehensively addressed in patients. In order to explore effective stimulation targets and identify optimal stimulation strategies, we have developed a rat model to test for suppression of tinnitus following ACES and investigate the modulatory effects of ACES on neural activity in the dorsal cochlear nucleus (DCN), inferior colliculus (IC) and auditory cortex (AC), which have been implicated in the etiology of tinnitus. Our immediate goal is to investigate how the related neural network operates and how ACES modulates neural activity along the auditory axis with regard to tinnitus generation and its suppression.

First, our results demonstrated that ACES of all frequency bands (all channel stimulation), low- or high-frequency bands (selective channel stimulation), and core and belt regions (selective channel stimulation) significantly suppressed behavioral evidence of tinnitus. The induced

suppression occurred during and after ACES. Post-ACES suppression lasted for 24-48 hours. Post-ACES of belt and low-frequency regions tended to yield more suppression than stimulation of core and high-frequency regions. We also observed that continued ACES yielded more post-ACES suppression, suggesting that chronic ACES may be more potent in modulating the adverse neural plasticity. All the collected data thus far demonstrate that our animal model of ACES is a valid model for in-depth investigation of the mechanisms underlying ACES-induced suppression of tinnitus and tinnitus itself.

Second, we observed that ACES improved hearing detection, which coupled with the relief of tinnitus. If validated, the data may help explain the etiology of tinnitus. That is, manifestation of tinnitus may result from an unmasking process as a result of compromised hearing.

Third, electrophysiological data demonstrated that ACES induced complex responses in the DCN and IC, including suppression, excitation and no change which can be moderate and significant, lasting or short lived, but with more susceptibility to ACES in exposed animals than in controls. This indicates that the mechanisms underlying ACES-induced modulation of tinnitus are rather complex.

Finally, ACES suppressed more coherence in the DCN than in the IC, suggesting that the neuronal coherence in the DCN contributes to the origin of neural correlates of tinnitus. The fact that ACES enhances interactions between different regions of the DCN and IC suggests that suppression of tinnitus may involve balancing neural activity and adjusting neural information flow at least along the auditory axis. Our eventual goal is to identify optimal targets for electrical stimulation or other optimal approaches to suppress tinnitus. We will use the findings from the animal model to promote advanced clinical investigations and stimulate development of strategies for effective suppression of tinnitus through neuromodulation.

VARIABILITY IN TINNITUS SUPPRESSION VIA ELECTRIC STIMULATION

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Objective: Electric stimulation of the cochlea has been shown to suppress tinnitus, but the parameters of an effective electric stimulus remain unexplored. Furthermore, a clear distinction needs to be drawn between tinnitus masking and suppression, as they utilize different mechanisms. It has been reported that both high-rate pulse trains (4800pps) and low-rate pulse trains (20-200 pps) delivered to the cochlea can produce complete tinnitus suppression (Rubenstein et al. 2003; Zeng et al. presentation at 2007 ARO).

Methods: Here we explore a large parametric space of electric stimuli and measure its effect on tinnitus suppression. Stimulation rate, electrode place, and loudness of the stimuli were varied and delivered to the cochlear implant for a total of six minutes. Subjective loudness of tinnitus as well as of the stimulus was assessed in thirty (30) second intervals. A total of twelve cochlear implant subjects with tinnitus have participated in our study to date.

Results: Seven out of the twelve subjects achieved tinnitus suppression greater than 30% (<30% suppression could be attributed to a placebo effect), with six subjects

experiencing complete suppression during electric stimulation. Preliminary analysis of the data, however, indicates no trends across stimulation rate, place, or level.

Conclusion: The present results suggest that electric stimulation via a cochlear implant can be an effective therapeutic for those suffering from tinnitus; however, the effective suppression stimulus varies greatly among individuals.

Acknowledgement: Work supported in part by the American Tinnitus Association.

ELECTRICAL PROMONTORY STIMULATION TO PREDICT TINNITUS SUPPRESSION AFTER COCHLEAR IMPLANTATION

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Background: Suppression of tinnitus by auditory stimulation was first reported in 1947 by Saltzman and Erner. Since then many successful reports of tinnitus suppression have been published. In some cases however, tinnitus suppression is not possible with auditory stimulation due to severe to profound sensorineural hearing loss. In these cases, electric stimulation of the cochlea can provide relief of tinnitus. Electrical Promontory Stimulation (EPS) as tinnitus treatment seems to be a promising tinnitus treatment, providing significant tinnitus relief. Research on promontory stimulation shows at least temporary and partial tinnitus suppression. Promising research shows some relief of tinnitus in approximately 82% of patients, and longer-term tinnitus suppression in 45% of these patients (Di Nardo et al., 2009). Rubenstein et al. 2003 also described the effect of EPS on tinnitus and this effect should be investigated with an implantable device.

Methods: 19 patients with severe tinnitus and unilateral deafness underwent EPS prior to cochlear implantation. The short-term effect on tinnitus was assessed during and immediately after the stimulation. The predictive value of EPS on tinnitus suppression after cochlear implantation was investigated.

Results: 8/19 patients (42%) experienced a reduction of tinnitus during EPS. Complete tinnitus suppression (100%) was obtained in 7/8 of these patients. In 11/19 patients (58%) EPS had no effect on tinnitus. 18/19 patients however, experienced significant tinnitus suppression after cochlear implantation.

Conclusions: Electrical Promontory Stimulation can significantly reduce tinnitus and even completely suppress tinnitus, at least during electrical stimulation. However, EPS was less effective in suppressing tinnitus than cochlear implantation.

Tinnitus suppression during EPS did not reliably predict tinnitus relief obtained with cochlear implantation in these patients.

COCHLEAR IMPLANTATION AS A DURABLE TINNITUS TREATMENT IN PATIENTS WITH SINGLE-SIDED DEAFNESS

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Background: Severe tinnitus can seriously impair patients in their activities in daily life and reduce the quality of life of these patients. The aim of this prospective clinical study was to assess the long-term effects of Cochlear Implantation (CI) on tinnitus in patients with single-sided deafness and ipsilateral incapacitating tinnitus.

Methods: 23 subjects participated in this study. Patients suffered from severe tinnitus of more than 6/10 on a Visual Analogue Scale due to unilateral deafness. Cochlear Implantation was performed with a COMBI 40+ M electrode or a PULSAR CI100 FLEXsoft electrode, with the electrode fully inserted into the scala tympani. Twelve of these subjects had normal hearing (NH-group) on the contralateral side, and eleven used a hearing aid (HA-group) contralaterally. Tinnitus assessment consisted of a tinnitus loudness estimation by means of a Visual Analogue Scale (VAS) and a Tinnitus Questionnaire (TQ) that was conducted pre-implantation and at regular intervals up to 48 months post implantation (n=14). Subjective improvement in daily situations was evaluated using the Speech Spatial and Qualities (SSQ) Hearing Scale.

Results: All 23 patients reported a subjective benefit after cochlear implantation. Tinnitus loudness reduced significantly after cochlear implantation from 8.9 to 2.7 on the VAS (of 0-10). Also the TQ total score decreased significantly, the mean tinnitus degree decreased from severe to mild. The amount of tinnitus loudness reduction remains stable up to 4 years after cochlear implantation.

Conclusions: Cochlear Implantation is a successful treatment of severe tinnitus in patients with single-sided deafness. The effect of cochlear implantation on tinnitus suppression is significant. Long-term results up to 48 months after cochlear implantation also suggest CI's provide durable tinnitus relief in these patients.

01:30 - 03:30 p.m. SYMPOSIUM Perceptual Training G. Searchfield

THE EFFECTS OF AUDITORY TRAINING ON TINNITUS PERCEPTION AND INTRUSIVENESS: A SYSTEMATIC REVIEW

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A systematic review is a summary of research that uses explicit methods to select and critically appraise primary studies, applying explicit criteria to assess their quality. Here we present a systematic review of the literature which examines the effects of auditory perceptual training with active sound tasks on the psychoacoustic characteristics, and perceived intrusiveness, of tinnitus. From Pub Med, Cambridge Scientific Abstracts, and Web of Science database searches for 'tinnitus and learning' or 'tinnitus and training', ten from an initial 316 publications were identified that contained an active auditory training task and participants who had tinnitus. Each publication was reviewed independently by two reviewers, data was extracted, and study quality was assessed. Data synthesis was not possible however due to the variations in paradigm and outcome measures used in the different studies. Considered independently, nine out of ten studies reported some form of statistically significant change after auditory training in individuals with tinnitus, either a change in validated questionnaire score, a self-report of improvement, or a change in tinnitus spectrum, matched loudness or minimum masking level. When rating quality (study design, evidence of bias, level of reporting, standard of controls and external validity), nine of the 10 studies were rated as containing either low or moderate levels of evidence for an effect of auditory training on tinnitus. Only one study met the criteria for high level evidence.

Our systematic review therefore identifies a need for further randomized controlled trials to rigorously evaluate the potential clinical benefit of auditory training.

AUGMENTATION OF CORTICAL REPRESENTATIONS FOR SOUND IN THE TINNITUS FREQUENCY REGION AND ITS EFFECTS ON TINNITUS

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Most individuals with tinnitus have significant residual hearing in the tinnitus frequency region (TFR) despite threshold shifts in this region. This study asks whether training for sounds in the TFR remodels cortical representations for sound equally in tinnitus subjects compared to age matched controls, and whether such training modifies tinnitus percepts at the trained frequency. The latter result could happen, if auditory training removed a population of neurons from network behavior supporting the tinnitus percept. We also contrast the effect on tinnitus

of training in the TRF with training on a concurrent visual discrimination task designed to draw attention away from and to suppress the auditory modality. Results will be reported on both questions.

ATTENTION PROCESS TRAINING FOR TINNITUS

Kim Wise and Grant Searchfield

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Tinnitus is associated with abnormal attention processes (1) that may contribute to its resistance to habituation. Reducing tinnitus' attention-capturing properties may facilitate improvement in tinnitus. The main aim of the study was to determine the effectiveness of Auditory Process Training (APT) (2, 3) in reducing tinnitus. APT is a cognitive rehabilitation program originally designed to address attention deficits following brain injury. The APT materials consist of a group of tasks that exercise different components of attention including focused, sustained, selective, alternating, and divided attention. The program tasks place increasing demands on complex attention control and working memory systems. Exercises include listening for descending number sequences, alphabetizing words in an orally presented sentence and detecting targets with the presence of distracter noise. It was hypothesised that aberrant attention processes contribute to tinnitus perception and that APT should reduce tinnitus-related distress. Three groups of participants: Tinnitus sufferers, controls (no tinnitus, but matched for hearing loss) and otologically-normal participants; were compared for performance on a computer based attention battery (Comprehensive Attention Battery (CAB™)). Participants with tinnitus then undertook APT-II training in a crossover design with a non-intervention control period. Preliminary results will be presented which suggest that tinnitus is associated with abnormal attention processing and attention training for tinnitus sufferers may address such deficits.

References:

1. Cuny, C., Norena, A., El Massioui, F., & Chery-Croze, S. 2004. Reduced attention shift in response to auditory changes in subjects with tinnitus. *Audiol. Neurotol.* 9: 294-302.
2. Sohlberg, M. M. and C. A. Mateer 1987. Effectiveness of an attention-training program. *Journal of Clinical & Experimental Neuropsychology* 9(2): 117-30.
3. Sohlberg, M. M., K. A. McLaughlin, et al. 2000. Evaluation of attention process training and brain injury education in persons with acquired brain injury. *Journal of Clinical & Experimental Neuropsychology* 22(5): 656-76.

VIRTUAL REALITY PROTOCOL FOR TINNITUS

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The clinical patterns of tinnitus are similar to those observed in chronic pain following amputation where conditioning techniques using virtual reality have been shown both to be theoretically interesting and effectively useful. **This analogy led us to develop an innovative**

set-up with dedicated auditory and visual 3D virtual reality environments in which unilateral subjective tinnitus sufferers are given the possibility to voluntarily manipulate an auditory and visual image of their tinnitus (tinnitus avatar). If the patient manages to transfer his subjective auditory perception to the tinnitus avatar, it could allow him to gain agency for the movement they see and hear, which would contribute to tinnitus treatment by promoting cerebral plasticity. We will describe the theoretical framework and set-up adjustments required by this attempt to adapt virtual reality techniques to subjective tinnitus treatment. Therapeutic usefulness is currently being validated by a controlled clinical trial. We will present how virtual reality is accepted by the patients and to which point they manage to immerse themselves in the virtual environments.

04:00 - 06:00 p.m.
SYMPOSIUM
Imaging
N. Weisz

A VOXEL-BASED-MORPHOMETRY STUDY OF STRUCTURAL BRAIN DIFFERENCES IN UNILATERAL TINNITUS

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Introduction: The precise neural bases of tinnitus remain elusive, but it likely involves both peripheral and central mechanisms [1]. In particular, studies using Voxel-Based-Morphometry (VBM) have revealed that individuals with tinnitus have decreased gray matter (GM) concentration in a subcallosal region and, increased GM in the posterior thalamus [2] relative to normal controls.

In addition, a recent study found that individuals with tinnitus have a reduced GM volume in the primary auditory cortex (Heschl' gyrus) ipsilateral to the tinnitus ear [3]. However, no study has investigated white matter (WM) differences in tinnitus. Here, we used VBM to investigate both GM and WM concentration differences in tinnitus sufferers relative to age-matched normal controls.

Methods: Eleven adults with unilateral chronic subjective tinnitus (6 left ear, 5 right ear) participated in the present study. The MRI data for the five participants with right unilateral tinnitus were 'flipped' (i.e. right to left hemisphere) to control for the effect of tinnitus ear side and to increase the statistical power of our analyses. Eleven controls were matched to the tinnitus group in age and education. T1-weighted volumes were acquired for all participants on a Siemens 3T MRI scanner. A group comparison at each voxel in the brain was performed using the general linear model to identify brain regions that differed in terms of GM or WM concentration between tinnitus participants and controls. Results were thresholded using a priori random field theory cluster thresholding at $p < 0.05$ level.

Results: As in Mühlau et al. (2006, ref#2), tinnitus participants had decreased GM concentration relative to

controls in a subcallosal area ipsilateral to the tinnitus ear. In addition, tinnitus participants had increased WM concentration in the lateral aspect of the primary auditory cortex contralateral to the tinnitus ear. However, when hearing loss was controlled for, this latter difference disappeared, whereas the decreased GM concentration in the subcallosal area ipsilateral to the tinnitus ear remained. The tinnitus group also had decreased GM concentration in the planum temporale ipsilateral to the tinnitus ear.

Conclusion: Overall, the present findings are partially consistent with previous studies showing structural brain changes in tinnitus [2]. In particular, the decreased grey matter in the subcallosal area ipsilateral to the tinnitus ear, a brain region associated with negative emotions, is uniquely associated with the presence of tinnitus.

References:

1. Eggermont, J.J. and L.E. Roberts, The neuroscience of tinnitus. *Trends Neurosci*, 2004. 27(11): p. 676-82.
2. Muhlau, M., et al., Structural Brain Changes in Tinnitus. *Cereb Cortex*, 2006. 16(9): p. 1283-8.
3. Schneider, P., et al., Reduced volume of Heschl's gyrus in tinnitus. *Neuroimage*, 2009. 45(3): p. 927-39.

RESTING STATE AUDITORY NETWORK IN TINNIUS PATIENTS: A FMRI STUDY

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Introduction and aim: Classically, functional MRI studies focus on the change of blood oxygenation level-dependent (BOLD) signal in response to external stimuli or when doing a task. Recently, increased focus has been directed to the study of the brain's baseline activity (the resting state). Through examination of spontaneous fluctuations in the functional MRI BOLD signal, past studies have shown that it was possible to identify consistent resting-state networks that have a functional relevance (Damoiseaux et al., 2006). Default mode network or networks involved in visual, motor, language, and auditory processing can be consistently found in healthy subjects. The aim of our study was to assess if there was a difference between the resting state auditory network in tinnitus patients compared to that of healthy controls.

Material and method: We studied 7 tinnitus subjects and 8 healthy volunteers. Resting-state BOLD data were acquired on a 3T-MRI scanner (Siemens). None of the tinnitus subjects or the healthy volunteers had neurological or psychiatry disease history. fMRI data were preprocessed and analyzed using the "Brain Voyager" Software package (R Goebel, Brain Innovation, Maastricht, The Netherlands). Data analysis was based on Independent Component Analysis (ICA) which decomposed the BOLD signal in thirty components. The auditory component time course was subsequently used as predictor in a Random Effect General Linear Model (GLM) analysis. Because of the limited number of subjects, we used a threshold of $p < 0.05$ uncorrected.

Results and conclusion: The primary auditory cortex, secondary auditory cortex and thalamus showed a greater activity in tinnitus patients as compared to healthy volunteers during resting state.

References:

- Damoiseaux, J. S., Rombouts, S. A., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., Beckmann, C. F., 2006. Consistent resting-state networks across healthy subjects. *Proc Natl Acad Sci U S A*. 103, 13848-53.

THE RELATION BETWEEN THE AMPLITUDE OF THE 40-HZ AUDITORY STEADY-STATE RESPONSE AND THE TINNIUS PERCEPT SUGGESTS ABNORMAL NEURAL ACTIVITY DURING TINNIUS BUT NOT DURING RESIDUAL INHIBITION.

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Current research suggests that the tinnitus sensation is associated with synchronous neural activity that develops in primary auditory cortex (PAC) as a consequence of this area having lost input from the ear owing to hearing impairment. For some subjects, tinnitus may be briefly suppressed by presentation of a masker. After the cessation of the masker the residual inhibition (RI) of tinnitus may last up to 30s. Functional brain activity in PAC can be measured either during tinnitus or during RI by presenting brief 40-Hz amplitude modulated (AM) tones. These stimuli evoke an auditory steady-state response (ASSR) in the EEG whose cortical sources localize to the region of PAC. As the neurons in PAC are tonotopically arranged, the AM stimulus will selectively activate neurons tuned to its carrier frequency. The amplitude of the ASSR is thought to reflect the number of cortical neurons that represent the stimulus. We theorize that if neurons in the tinnitus frequency region are participating in synchronous oscillatory networks generating the tinnitus percept, they will be unavailable to represent the incoming AM stimulus if its carrier frequency is in the tinnitus frequency region. During RI, the synchronous activity will be suppressed and these neurons will become available to represent the stimulus. To address this question, we compared ASSR amplitude when measured in tinnitus with ASSR amplitude measured during RI.

Three groups (tinnitus subjects – mean age 59 years, age matched controls, and young controls – mean age 19 years) listened to noise maskers (30s duration, centre frequency 5 kHz) known to produce RI in the tinnitus group. Following the masker, 12 probe tones (40-Hz AM, 500ms duration) with a carrier frequency of either 5 kHz or 500 Hz (between subjects) were presented over 30s. After a quiet period, the procedure was repeated for a total of 20 presentations. This trial series was preceded by an identical series, except that 30s of silence was presented in place of the masker. The 5 kHz probe was designed to evoke activity from neurons within the tinnitus frequency region, while the 500 Hz probes would activate neurons outside this region. Comparison of the two trial series allowed evaluation of the ASSR amplitude in the presence and absence of the tinnitus percept. 128 channel EEG was recorded and the ASSR evoked by the last 16 AM cycles of the probe was collapsed into one cycle whose amplitude was computed via FFT.

ASSR amplitude was higher in both the tinnitus and the age-matched control group compared to young non-tinnitus controls, consistent with the hypothesis that ASSR amplitude reflects changes in intracortical inhibition associated with aging. When ASSR amplitude was contrasted between tinnitus and residual inhibition in the tinnitus group, an enhancement in residual inhibition was

found. ASSR amplitude did not differ between these two conditions (post-silence and post-masking) in the non-tinnitus controls.

These findings favour the hypothesis that reduced ASSR amplitude during tinnitus reflects the participation of neurons in synchronous tinnitus networks, as ASSR amplitude is reduced during tinnitus and returns to normal during RI.

(Supported by CIHR and NSERC of Canada and the American Tinnitus Association.)

ELECTROPHYSIOLOGICAL CORRELATES OF TINNITUS AND TINNITUS SUPPRESSION

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Background: Event-related potentials (ERP) and auditory steady-state responses (ASSRs) were examined in tinnitus sufferers with and without tinnitus suppression in response to multiple stimuli. We have identified a group of tinnitus subjects in whom we can suppress tinnitus using modulated pure tones. Suppression differs from masking because the stimulus is softer and at a different frequency from the tinnitus, its response requires a longer time to develop (seconds to minutes) and lasts after the suppressor is turned off (minutes to hours). This suggests that tinnitus suppression is generated beyond the cochlea at central levels. We thus reasoned that cortical ERP recordings in these subjects using a within-subject design will help us understand the neurophysiology underlying tinnitus and its suppression. One potential mechanism associated with tinnitus involves abnormal cortical plasticity arising from lateral disinhibition. We reasoned that the effects of disinhibition can be quantified by measuring ASSRs to multiple stimuli and comparing them to the responses to single stimuli. Preliminary data are presented.

Methods: Experiment 1 – cortical responses were measured to frequency-sweep stimuli that were distant or near the pitch-matched tinnitus. Recordings were performed with and without suppression. Responses were quantified using N100/P200 peak amplitude/latency measures, brain source analysis, and event-related synchronization/desynchronization of on-going brain oscillations. Experiments 2 - Recordings using three ASSR stimuli, presented separately or simultaneously, were conducted (i.e., three different modulation rates and three different carrier frequencies near the pitch-matched tinnitus frequencies) in tinnitus sufferers and normal hearing controls. ASSR amplitude responses to multiple stimuli were compared to those of frequencies at single presentation. The three carrier frequencies were chosen to be less than one octave apart in order to examine the effects of lateral inhibition.

Results: Experiment 1 – The most striking effects observed were that N100 responses in the tinnitus suppressed state showed larger responses when compared to the non-suppressed state. No such effect was seen in subjects in whom suppressor stimuli were ineffective. With successful suppression, the radial component of the region dipole source was greatly enhanced. Differences in the scalp topography of the

alpha rhythm were seen in suppressed versus non-suppressed state. Experiment 2 – The most striking effect was that multiple stimuli resulted in enhanced ASSRs compared to the single-stimulus. In contrast, non-tinnitus controls showed the expected suppression of multiple ASSRs (given the small separation in carrier frequency).

Conclusion: These results demonstrated electrophysiological differences related to tinnitus and its suppression. Experiment 1 suggests that cortical differences associated with successful suppression can be objectively measured. Suppression likely involves novel cortical areas resulting in altered inhibitory networks. Experiment 2 suggests that altered cortical plasticity in tinnitus may be associated with altered local inhibitory networks arising from lateral excitation or disinhibition.

Significance: The preliminary data suggests that there are subtypes of tinnitus with different degrees of suppression. Moreover, the different degrees of suppression can be objectively measured using electrophysiology, suggesting that different cortical networks are engaged when suppression is successful.

DETRIMENTAL EFFECTS OF EXTENSIVE PORTABLE MUSIC PLAYER USAGE ON POPULATION-LEVEL FREQUENCY TUNING IN HUMAN AUDITORY CORTEX

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Nowadays portable music players enable almost everyone to listen to favorite music whenever and wherever he wants. The problem is that the volume setting of the players is often extremely high due to the environmental noise and/ or the appetite for music. However, continuous exposure to loud sounds can damage our auditory system (i.e., tinnitus, hearing loss, hyperacusis, etc.). In the present study, we examined the effects of regular portable music player usage on the population-level frequency tuning in the human auditory cortex. By means of magnetoencephalography (MEG), we examined two groups of young people (exposed vs. non-exposed), who were matched in age, gender, and hearing thresholds. The participants in both groups showed no behavioral deficit in their hearing capabilities. During the MEG measurements, we presented pure tones as test stimuli simultaneously with and without band-eliminated noises, which contained a spectral notch (either 1/4, 1/2, or 1 critical band width) around the test stimulus frequency. Attention was distracted from the auditory modality by means of a visual task. The results demonstrated that the source strength of the N1m response, with latency around 100 msec, depended on the type of simultaneously presented band-eliminated noise: the wider the spectral notch in the band-eliminated noise, the larger the N1m response in both groups. However, particularly in case of the narrow band-eliminated noise condition, the attenuating effects of the simultaneous masking sounds were stronger in the exposed compared to the non-exposed group. These results indicate that the population-level frequency tuning was duller in the exposed compared to the non-exposed group. This duller frequency tuning can be interpreted in terms of potential damages of the inhibitory system within the auditory pathway. We conclude that regular and extensive use of portable music players, especially at high intensity, might subliminally damage the inhibitory neural networks in the auditory system, and may lead to hearing loss and tinnitus in long term.

LISTENING TO TAILOR-MADE NOTCHED MUSIC REDUCES TINNITUS LOUDNESS AND TINNITUS-RELATED AUDITORY CORTEX ACTIVITY

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Our previous magnetoencephalography (MEG) study [1] demonstrated that auditory cortex neuronal activity evoked by a test frequency can be significantly attenuated by listening for several hours to so-called "notched music", which contains a spectral gap centered exactly at this test frequency. We hypothesized that the attenuation is a consequence of lateral inhibitory neural activity originating from notch-edge neurons.

The tinnitus perception is supposedly associated with maladaptive auditory cortex reorganization. Maladaptive cortical plasticity has been shown to be reversible by behavioral training. In order to establish a neurophysiologically motivated music training procedure for chronic tinnitus, we recruited patients suffering from chronic (> 12 months) tonal tinnitus with tinnitus frequencies below 8 kHz and without severe hearing loss. We motivated these patients to listen to pleasant (since self-chosen), tailor-made notched music (which did not contain energy in the frequency band of one octave width surrounding the individual tinnitus frequency) for approximately two hours per day over the course of one year. In contrast to comparable patients, who had listened to pleasant placebo music, the target patients experienced a significant reduction (~ 25% on average) in subjective tinnitus loudness. Moreover, also tinnitus-related auditory cortex neuronal activity was significantly reduced in the target patients, but not in the placebo patients. The change in tinnitus loudness correlated positively with the change in tinnitus-related auditory cortex evoked activity [2].

In a follow-up study, we investigate whether noticeable improvements in tinnitus loudness could already be achieved by means of a similar, but much shorter (i.e. 5 consecutive days) and more intensive (i.e. 6 hours per day) notched-music training. The music modification procedure was slightly refined in order to include also patients with tinnitus frequencies beyond 8 kHz. For evaluation purposes, tinnitus loudness is assessed psychometrically and audiometrically, and spontaneous and tinnitus-related evoked neuronal activity is measured by means of magnetoencephalography (MEG).

The results and their implications for the understanding and the treatment of chronic tinnitus are discussed.

1. Pantev C, Wollbrink A, Roberts LE, Engelen A, Lütkenhöner B. Short-term plasticity of the human auditory cortex. *Brain Res.* 1999 Sep 18;842(1):192-9.

2. Okamoto H, Stracke H, Stoll W, & Pantev C. Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity. *Proc Natl Acad Sci USA.* 2010 Jan 19;107(3):1207-1210

04:00 - 06:00 p.m. SYMPOSIUM Audiologic Assessment R. Roeser

THE RELATIONSHIP BETWEEN TINNITUS PITCH AND AUDIOMETRIC VARIABLES: A META ANALYSIS

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Two theories of tinnitus (TI) generation predict different relationships between the dominant TI pitch and hearing loss. If the primary cause of TI is due to expansion within the brain of the frequency representation at the edge of hearing loss then the dominant tinnitus pitch is likely to be related to that edge frequency. On the other hand, if the primary cause of TI is due to changes in the synchrony of neuronal activity within the deafferented region, then the dominant tinnitus pitch is more likely to fall within the region of hearing loss with no specific relationship to the shape of the audiogram.

Studies to date offer contradictory results. While some TI patients match the pitch of their TI to the edge frequency, others show no relationship between the TI pitch and the audiogram. More recent studies report a broad TI spectrum which typically falls within the area of hearing loss. Objective calculation of the audiometric variables seems to be crucial for exploring the relationship between TI pitch and audiogram. Methodological differences resulting from lack of agreed procedures contribute to differences in results and make the studies hard to compare. Many studies have used a pitch-matching procedure whereby the dominant TI pitch is matched to an external sound, usually a single-frequency tone. However, this method yields highly variable results and test-retest reliability is poor. For example, if patients experience a broadband TI percept they may be unable to accurately match their TI to an external tone. Another issue is that the magnitude and slope of hearing loss is typically assessed up to 8 kHz, but considering that high-frequency hearing loss is common in TI patients, assessment of hearing up to 16 kHz is preferable.

Here we explore the relationship between audiogram shape and TI pitch in 67 TI patients. Hearing levels were assessed up to 16 kHz and we used a new method (broken-stick fitting) for assessing slope, degree and edge of hearing loss objectively and independently of the frequencies tested. A computerized 'Tinnitus Tester' was used for measuring pitch and bandwidth characteristics of the TI. We tested for a relationship between audiogram shape and TI pitch within different subgroups of TI patients categorized by different slopes of hearing loss, different tinnitus bandwidth etc. In addition to correlation analysis, we apply a more rigorous multiple regression analysis, which allows us to explore the relationship between a number of audiometric variables and the TI pitch.

In general, the dominant TI pitch fell within the area of hearing loss, consistent with the disrupted synchrony model of TI. There were no further systematic relationships

between audiometric variables and TI pitch when all TI patients were considered as a single group. However, in the subgroup of patients with a narrow TI bandwidth, we found a significant correlation between the edge of hearing loss and TI pitch. However, even in that group TI pitch was sometimes over an octave away from the edge of hearing loss thus not fully supporting the expansion model.

DISTORTION PRODUCT OTOACOUSTIC EMISSIONS IN NORMALLY HEARING PATIENTS WITH UNILATERAL TINNITUS

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Some tinnitus patients do not show any hearing loss in the conventional audiogram, i.e., for frequencies up to 8 kHz. One of several postulated models of tinnitus without a measurable hearing loss was supported by findings that tonotopic map changes resulting in tinnitus can still occur in the absence of peripheral hearing loss (Noreña et al., *Nat Neurosci*, 2006). Thus, some forms of tinnitus may arise from peripheral pathology which may not be detected on the conventional audiogram. Several studies showed that, despite the similarities in the audiograms, distortion product otoacoustic emissions (DPOAEs) were abnormal in tinnitus patients when compared to non-tinnitus controls (e.g., Ozimek et al., *J Acoust Soc Am*, 2006). Those data suggested that outer hair cell (OHC) damage in some of tinnitus patients with clinically normal audiograms may be too small to be detected by standard audiological procedures but already above differential sensitivity of DPOAE testing. It has been postulated that OHC impairment in the most basal region reduces contribution to more apically generated DPOAEs (e.g., Dreisbach et al., *J Am Acad Audiol*, 2008). The extended high-frequency (EHF) audiometric data (>8 kHz) are limited for tinnitus patients (e.g., Knudson et al., *TRI Meeting*, 2009). The present study evaluated DPOAEs and EHF thresholds in normally hearing patients reporting unilateral tinnitus. Thus, each subject acted as their own control. Data were collected for 51 subjects who had hearing thresholds <20 dB HL from 0.25 to 8 kHz and <70 dB HL at 10, 12.5, 14, and 16 kHz. Thirty-nine subjects reported unilateral tinnitus in left ear (Group 1) and 12 subjects in right ear (Group 2). The DP-grams were measured in the 0.5-8 kHz range using 65/55-dB SPL primaries. For Group 1, median audiometric thresholds in the left ears were significantly higher than those in the right ears at all four EHF. Mean DPOAE levels of the left ears were lower than those of the right ears for frequencies above 0.75 kHz. A paired-comparison test of DPOAEs of each patient's right and left ear revealed significant differences at 1.5, 2, 3, and 6 kHz. For Group 2, median audiometric thresholds in the right ears were higher than those in the left ears at 12.5, 14, and 16 kHz. Mean DPOAE levels of the right ears were lower than those of the left ears for frequencies above 2 kHz. However, due to a small sample size in Group 2, audiometric and DPOAE data did not reach statistical significance. In summary, the results suggest that: 1. impairment in the most basal region reduces more apically generated DPOAEs; 2. patients with unilateral tinnitus and normal hearing on the conventional audiogram are likely to demonstrate asymmetrical EHF hearing, in contrast to the data of Knudson et al. (2009); 3. tinnitus generation may arise from OHC impairment revealed by DPOAEs but not by conventional audiometry, and 4. OHC impairment indicated by DPOAE reduction may be present together with other subclinical pathologies resulting in tinnitus, e.g., loss of normally high-threshold spiral ganglion cells.

Study supported by grants from Tinnitus Research Initiative and The International Center of Hearing and Speech, Poland.

VIRTUAL REALITY FOR TINNITUS THERAPY: TINNITUS RECREATION METHOD

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As a first step to a protocol involving virtual reality for tinnitus therapy, an acoustic modelisation of the perceived tinnitus has to be established. The spectral characterization of subjective tinnitus and the creation of a credible tinnitus auditory image is not a straightforward process. To do so, the signal has to match the spectrum and intensity of the tinnitus percept. Thanks to custom-made software a training procedure teaches the patients frequency and loudness matching. Then, by means of a similar graphical interface, patients are asked to adjust a sound played into their contra lateral ear so that it matches their tinnitus in frequency and loudness. It should be noted that for some patients, fitting the frequency and loudness parameters of the tinnitus avatar could even lead to the perception of a tinnitus image located in the middle of the head. This observation reveals that a fusion process can occur between the subjective unilateral tinnitus and the avatar stimulus presented in the contra lateral ear. This method has been used on 140 patients suffering from unilateral tinnitus, who were overall satisfied with the selected methodology.

LOSS OF COCHLEAR COMPRESSION IS PREDICTIVE OF TINNITUS FOR SUBJECTS WITH MILD TO MODERATE HEARING LOSS

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Tinnitus correlates strongly with hearing loss. However, not all subjects with hearing loss have tinnitus and not all tinnitus subjects have significant hearing loss. We previously hypothesized that tinnitus is the result of a gain-adaptation mechanism that when confronted with degraded peripheral input increases neuronal gains such that spontaneous neuronal activity is perceived as a phantom sound. Following this hypothesis we expected that loss of cochlear compression would accentuate the deficits of mild hearing loss, leading to a stronger tinnitus percept. To assess peripheral processing, we measured distortion product otoacoustic emissions (DPOAEs) with high frequency resolution (160 points per octave) as well as audiograms measured using band-pass noise (resolution of 6 points per octave). All measures were obtained in the frequency range of 1 kHz to 8 kHz (N=9), or 11 kHz (N=34) for 28 tinnitus subjects and 15 non-tinnitus subjects with similarly matched hearing loss.

Estimates of cochlear compression were determined for each frequency as the difference in the DPOAE levels measured with the 75 and 55 dB SPL primary levels. Hearing thresholds and compression estimates were averaged over the range from 4 kHz to 11 kHz (excluding frequencies where hearing loss was found to be 50 dB SPL or more as DPOAEs are less detectable at beyond this level of hearing loss). Receiver-operator curve (ROC) analysis shows that for this sample of subjects, prediction of tinnitus based on the audiogram alone is inadequate (area under the ROC of $Az=0.57$). When using compression as an additional diagnostic criterion, prediction improves significantly ($p=0.03$, $Az=0.76$). Preliminary results also show that for a subset of subjects the tinnitus spectrum can indeed be predicted purely from these physiological measures ($p<0.05$). This data suggests that some individuals with mild to moderate hearing loss may have tinnitus precisely because they have a loss of cochlear compression as compared to their non-tinnitus counterparts.

**04:00 - 06:00 p.m.
SYMPOSIUM
New Hypotheses
JM Lainez**

MOLECULAR BIOLOGY OF TINNITUS: CYTOKINE AND ENDOCRINE CAUSES

**Kenneth H Brookler, MD (kbrooklermd@mac.com),
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Neurologic Associates, PC, 111 East 77 Street, NY, NY 10075

Tinnitus emanates from damaged outer hair cells of the inner ear in many patients. It is perceived at the cerebral level. If the trigger site for these damaged hair cells can be modulated by reducing the adverse effects of Tumor Necrosis Factor- α (cytokine load) and controlling endocrine factors, then the perception of tinnitus can be reduced.

Damaged hair cells (or what is conventionally known as sensory hearing loss) may be reversible. Altered hair cells can be measured using specialized high frequency audiometry and outer hair cells can be measured by objective Otoacoustic Emission testing, even in the absence of functional hearing loss.

Cytokine and/or endocrine causes have consistently shown to be the cause for many patients presenting with tinnitus. These patients may or may not have had sensory hearing loss. Once identified and treated, these patients have found their tinnitus to diminish or disappear completely.

Otic capsule (capsular) otosclerosis is an osteoclast driven disorder that produces Tumor Necrosis Factor- α (TNF- α) as a by-product of osteoclastogenesis. Osteoclastogenesis occurs when circulating macrophages are converted to osteoclasts by an inciting inflammation. TNF- α is toxic to hair cells. The bisphosphonate group of drugs target osteoclasts resulting in a reduction or elimination of TNF- α production. Patients, whose high-resolution thin slice axial computerized tomography demonstrated the radiologic evidence of capsular otosclerosis, were treated with bisphosphonates and in many cases their tinnitus symptoms were alleviated.

The most common endocrine disorder is related to abnormalities of either insulin and/or blood sugar. Elevated insulin levels with corresponding alterations in blood sugar can be identified by the five-hour glucose tolerance test with simultaneous insulin levels. Patients presenting with tinnitus who underwent a five-hour glucose tolerance test

frequently revealed abnormal test results. Aside from clear findings of diabetes or hypoglycemia, the most common finding was elevated serum insulin levels and sufficient fluctuations in the blood sugar that could adversely affect the function of the hair cells. Elevated insulin levels (hyperinsulinemia) or insulin resistance is the precursor of Type 2 diabetes. Experimental animals that develop Type 2 diabetes demonstrate evidence of mitochondrial abnormality in skeletal muscle. The hair cells are units of actin and myosin whose mitochondria may be vulnerable to alterations in blood sugar and insulin produced by diet. Nutritional management of these glucose tolerance findings can reverse the effect of poor blood sugar and/or insulin levels and reduce or eliminate their tinnitus symptoms. Some patients presenting with tinnitus will often describe changes in their "ringing" based on foods consumed in their diet.

The underlying molecular biology, endocrinology and clinical examples of diagnosis and treatment of 759 patients with tinnitus will be presented.

THE USE OF ULTRASOUND IN THE TREATMENT OF TINNITUS

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Tinnitus is a disorder that affects nearly 50 million people in the United States and 135 million in Europe. Approximately 80% of these patients find that they have learned to just ignore their tinnitus. However, this leaves nearly 20% of the population, who suffer from tinnitus, as being nearly completely debilitated by its effect. They find it difficult to go to sleep at night, concentrate, and often report that it interferes with their hearing.

A number of years ago, a theory was postulated (Jastreboff, 1990) that tinnitus may be stored in the brain as a memory. The analogy used was similar to that of Phantom Limb syndrome. In Phantom Limb syndrome, patients who have been amputated often perceive a sensation that the limb still is attached, and even some patients perceive pain even though the limb is no longer present. The theory proposed by Jastreboff (1996), postulates that the perception of tinnitus is transferred and stored in the brain even after the generator source no longer exists. His theory was very logical and related well to other sensory systems. However, until recently there was no hard data to substantiate up his hypothesis.

More recently, Lockwood and Salvi et al. (1998), utilizing PET scans, found that an area of the limbic system was more active, in patients suffering from tinnitus than in patients, who did not experience the disorder. Other investigators have added to our knowledge regarding the location of tinnitus in the brain. Wang H, et. al (2001) investigated the relationship between tinnitus and glucose metabolism in auditory cortex and whether positron emission tomography (PET) could be an objective tool in measuring tinnitus function. They concluded that as a new path in research, PET has provided an objective evidence for tinnitus and may be used as a potential tool in objectively measuring tinnitus. More recently (Holmes, 2007) used QEEG and found results similar to the PET studies.

Ultrasound Treatment

Over the past five years we have conducted a number of studies using ultrasound. A piezoelectric transducer (amplitude $<100\text{mV/cm}^2$) was placed on the mastoid and stimulated for one minute. Nearly 75% of the patients treated experienced either total or partial relief of their symptoms. The length of time varied from 3.5 minutes to as long as 17 days. However, 25% of these patients found

no relief after treatment. One possible hypothesis may be, that the ultrasound frequency stimulation is generating sub-harmonics that may be arriving at the location of the stored tinnitus at nearly 180° out of phase. This could possibly be causing a phase cancellation effect and thus reducing the amplitude of the perceived tinnitus. After a period of time, the tinnitus may become synchronous again, and the perception of the tinnitus returns back to its pre-treatment levels.

NEW HYPOTHESIS: ALLOSTASIS AS A MECHANISM FOR TINNITUS CHRONIFICATION

Dirk De Ridder

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Introduction: Recently, the idea of allostasis, defined as the adaptive process for actively maintaining stability (homeostasis) through change, has been introduced in medicine. It has been shown that allostatic mechanisms are controlled by the brain. Homeostasis relates to the mechanisms that maintain stability within the physiological systems and hold all the parameters of the organism's internal milieu within limits that allow an organism to survive. Allostasis, on the other hand, relates to the maintenance of stability outside of the normal homeostatic range, where an organism must vary all the parameters of its physiological systems to match them appropriately to chronic demands, for example, by resetting the system parameters at a new set point. Drug addiction is hypothesized to involve a change in drug reward set point and reflects an allostatic, rather than a homeostatic, adaptation (i.e., outside the normal set point). The idea proposed is that allostasis by resetting of auditory 'silence reference' is involved in chronification of tinnitus.

Methods and materials: The brain areas controlling allostasis are retrieved via a medline search. These areas are subsequently compared to those brain areas specifically involved in chronic tinnitus and tinnitus distress, and a pathophysiological working model is constructed for tinnitus chronification.

Results: In stress the amygdala and the prefrontal cortex as well as the ACC and insula are suggested as allostasis regulating brain areas. Based on parallels between addiction and pain it has been suggested that in chronic pain the concomitant tolerance (adaptive decreases of the drug's efficacy) and hyperalgesia might be the result of the development of a new allostatic equilibrium.

Discussion: Conceptually, in chronic tinnitus, a new allostatic equilibrium could develop, resulting in hyperacusis and persistence of the phantom sound. The dorsal ACC is involved in adaptive decision making and value evaluation by adapting its activity when a new piece of information is witnessed, reflecting its salience for predicting future outcomes by utilizing dopamine reward prediction error signals, but only when something can be learned. Thus, the dorsal ACC might be involved in resetting this equilibrium. Metaphorically speaking, the dorsal ACC attributes salience to the phantom sound and resets its equilibrium allostatically so that the sound remains consciously perceived via resetting the parahippocampal auditory gating (see other abstract from same author). The right dACC thus resets the parahippocampal sensory gate and via the dACC-DLPFC connections, the DLPFC can

subsequently modulate auditory cortex activity. The dACC-insula connections result in increased intensity perception of the auditory cortex activity, analogous to what has been described for pain. Therefore a stimulus that would normally not be perceived consciously will be so as long as the dACC-insula reference has been reset.

TOWARDS A NEW SYNTHESIS: HEALTH AND DISEASE

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Usually, we used to consider health and disease are opposed phenomena based on the traditional dichotomy. Health and disease are, however, should be considered as merely the different aspects of the same living process. This must be similar to the complementary principle originally proposed by Neils Bohr. In other words, there must be a simple principle among diverse life phenomena such as cancer, neurodegenerative disorder, normal development, aging, and even evolution.

In the present paper, attempts are made to integrate various concepts in living things leading to a unified view of life itself including a variety of disorders. One important point is the role of epigenetic variations and resultant selection. Of course, we are very familiar with successive rounds of genetic variations and selections, which must be essential to evolution in ecological systems as Charles Darwin proposed in 1859. However, when we are thinking about the origin and development of disease states, genetic variations are not necessarily present. Just like learning or associate memory formation, cancer evolution occurs without genetic mutations at some developmental stage. Cancer can epigenetically adapt to new internal environment. Through interdisciplinary perspectives, common features among diverse phenomena are discussed.

References:

Masatoshi Murase: Environmental pollution and health: an interdisciplinary study of the bioeffects of electromagnetic fields, *SANSAI: An Environmental Journal for the Global Community*. Kyoto University No.3, 1-35 (2008)

Masatoshi Murase and Ichiro Tsuda (eds.) *Proceedings: What is Life? The Next 100 Years of Yukawa's Dream*, Progress of Theoretical Physics Supplement No.173, 1-370 (2008)

Organized International Workshops by Masatoshi Murase:

"What is Life?" in 2007

<http://www.yukawa.kyoto-u.ac.jp/contents/seminar/archive/2007/ny2007/>

"What is Creativity?" in 2008

<http://www.yukawa.kyoto-u.ac.jp/contents/seminar/archive/2008/yitp-w-08-11/>

"What is Evolution?" in 2009

<http://www.yukawa.kyoto-u.ac.jp/contents/seminar/archive/2009/yitp-w-09-14/ev2009/index.html>

Abstracts of Poster Presentations

POSTER PRESENTATION JUNE 09, 2010, 01:30-02:30 P.M

Assessment Questionnaires

DEVELOPMENT AND PSYCHOMETRIC VALIDATION OF THE ATTENTION AND PERFORMANCE SELF ASSESSMENT SCALE (APSA) IN TINNITUS PATIENTS

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Background: Attention and performance problems are frequently reported by tinnitus patients [Hallam 2004] because of their "ear noise" which is reported to be always present (by many patients with chronic tinnitus). It seemed to be necessary to develop a validated self-rating scale to measure attention and performance problems in a more objective way.

Methods: An item pool was created from various neuropsychological scales [Scholz 2006, Reason 1993, Broadbent et al. 1982, Volz-Sidiropoulou et al. 2007] measuring attention and performance. The 99 items pool was reduced to a final version of 30 items by removing duplicate, similar and irrelevant items. During this process, draft versions of the APSA were tested with 44 volunteers, four of whom were suffering from tinnitus. These volunteers were encouraged to comment on item content and response options.

The final version of 30 items was developed in German. Then it was translated and linguistically validated for six languages including English, French, Spanish, Portuguese [Montigny et al. 2009].

The psychometric validation study was conducted in the USA, Mexico, Germany; the following analysis was conducted on US data only. Five participating sites (two ENT clinics, two clinical research sites, one private practice) recruited more than 200 volunteers in the age of 24-75 years. They had subjective, persistent tinnitus which lasted for at least 3 months. The volunteers had no concomitant symptoms of otological or neurological disease and had not received any kind of pharmacological or non-pharmacological treatment during the previous month that might interfere with tinnitus.

At baseline, the volunteers filled in a set of questionnaires. This was repeated at a follow-up assessment after 2-4 weeks.

The APSA was tested for reliability and convergent validity in comparison with the Tinnitus Handicap Inventory 12 [Greimel et al. 2000, Görtelmeyer et al. 2009], a Tinnitus Rating Scale (TRS), a Tinnitus Severity Scale (TSS), the sleep questionnaire SF-B [Görtelmeyer 1986], and the Hospital Anxiety and Depression Scale (HADS) [Zigmond and Snaith 1983].

Results: Data from 176 volunteers was analyzed; overall, 55% were female, the mean age was 56 (SD=10) years. The mean HADS scores were 7 for the anxiety subscale and 4 for the depression subscale. About 55% of the study population had been suffering from tinnitus for more than 3 years. The intraclass reliability coefficient was 0.89 for the total score and Cronbach's alpha with all items was 0.92. A

principal components analysis revealed one strong main factor and up to 6 specific factors with low explained variances. The results justify the calculation of an APSA total score. This total score correlated highest with impact on life from the TRS ($r=0.41$) and the THI-12 total score ($r=0.55$).

Conclusions: The test-retest reliability was very good for the APSA total score. Convergence with the THI-12 total score and the impact on life item of the TRS was moderately high. This indicates that APSA can measure attention and performance in a manner which is not fully achieved by the tinnitus scales and therefore adds additional value in assessing subjective tinnitus.

DEVELOPMENT OF A TINNITUS EVALUATION SOFTWARE PROGRAM

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A tinnitus evaluation software program was developed to assist clinicians and researchers acquire clinical data on tinnitus patients in an organized and efficient manner. There are five versions of the program; 1) Research, 2) Clinical, 3) Express, 4) Super Express, and 5) Follow-up. The Research version is the most complete. It accumulates; patient demographics, insurance information, clinical history, review of 600 prescription medications, review of 50 medical conditions, Tinnitus Handicap Inventory, Beck Depression Inventory, Beck Anxiety Inventory, quantifies patient's; location, frequency, intensity and masking level of their tinnitus, generates a report for the medical record and is downloadable to a server for data analysis. After the Research version, each of the four subsequent versions contains fewer components. The fifth version (Follow-up), records quantifiable changes to tinnitus after treatment (location, frequency, intensity, masking, perception and duration of treatment benefits).

Little is known about tinnitus, as it varies greatly from patient to patient. Etiologies, acoustical perceptions, psycho-social impacts, and quality of life issues are just some of the variables that contribute to the complexity of describing the impact of tinnitus among different individuals. There are other complicating factors such as medical conditions and prescription medications that also may impact on the variable listed above. Some patients may describe their tinnitus as a noise or a tone, and some report hearing both noise and tone. Often, there may be more than one variable contributing to a patient's tinnitus.

This software program was developed to assist clinicians in gathering information in a systematic manner, using the same measurements. If data were collected by many clinicians, with the ability to share a pooled database, then more robust statistical analyses could be applied to the database as the number of subjects increased. The net result could lead to the development of better treatments if we were able to identify contributing variables.

This presentation will detail each of the components contained in each version of the software. Hopefully, this presentation will result in a discussion of the measurement components and perhaps lead to an expanded protocol that could be integrated into a modification of the current software program.

INTERCULTURAL VALIDATION OF THE TINNITUS HANDICAP INVENTORY 12 (THI-12)

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Background: The THI and THI-12 are frequently used scales in tinnitus research [Greimel et al. 2000, Newman et al. 1996]. So far, no international comparative validation for the THI-12 has been performed.

Method: The present study was conducted in France, Germany, the Netherlands, Mexico, Poland, Spain, and the USA at a total of 21 sites (clinics, ENT units, research institutes) and with at least 40 volunteers from each country. The volunteers included had subjective uni- or bilateral tinnitus that was persistent (i.e. never absent for more than 24 consecutive hours) and had been present for at least 3 months; they had no concomitant symptoms of otological or neurological disease, had not received any kind of pharmacological or non-pharmacological treatment during the previous month that might have had interfered with tinnitus, and were aged 20–77 years. At baseline, the volunteers filled in a set of questionnaires. This was repeated at a follow-up assessment after 2–4 weeks (\pm 2 days).

The THI-12 was tested for reliability, intercultural comparability and convergent validity in comparison with a Tinnitus Rating Scale (TRS), a Tinnitus Severity Scale (TSS), the sleep questionnaire SF-B [Görtelmeyer 1986], the Attention and Performance Self-Assessment (APSA) scale [Montigny et al. 2009], and the Hospital Anxiety and Depression Scale (HADS) [Zigmond and Snaith 1983].

Results: More than 550 volunteers participated in this validation study, 523 were analyzed. From these, 47% were female, and the mean age was 52 (SD=11) years. The mean HADS scores were 7.5 for the anxiety subscale and 5 for the depression subscale. About 50% of the study population had been suffering from tinnitus for more than 3 years.

The psychometric properties for the THI-12 such as reliability (retest, internal consistency) were found to be comparably good between countries. For all of these, the intraclass reliability coefficient ICC(2,1) was above 0.8 for the total score in all countries, and Cronbach's alpha with all items was above 0.8.

Principal component analysis with orthogonal rotation (VARIMAX) resulted in 2–4 factors. These reflect some cultural differences in the factorial validity. Intercultural differences exist, but the results of the convergent-validity analysis indicate that the THI-12 can successfully grade the severity of tinnitus in all countries.

Conclusion: The reliability (retest and internal consistency) of the THI-12 total scale is very good in all countries. Based on the item loading patterns in the PCA, the intercultural comparability is acceptable. Overall, the THI-12 can be used as a diagnostic instrument, and its results can be used as a metric to demonstrate effects of treatment in international trials.

INDEPENDENCY OF VARIABLES IN A TINNITUS POPULATION

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While no general consensus exists in the international literature on how to assess and measure tinnitus, guidelines for tinnitus patient assessments and tinnitus outcome measurements have already been proposed by the Tinnitus Research Initiative. Given the fact that no investigations were yet performed investigating the relation between different tinnitus measurements tools, we decided to investigate the relationship between different assessments of tinnitus and tinnitus related complaints in order to provide a compact list of complementary measurements able to independently assess different aspects of self-perceived tinnitus and disease specific health related quality of life in daily ENT practice. Correlations between different tinnitus assessment tools are hereby presented, as well as a selection of tinnitus assessments expected to provide sufficient tinnitus information in daily ENT practice.

Audiological Assessment

INDIVIDUAL PROFILING OF TINNITUS PERCEPTION BY DEVELOPING INTERACTIVE TINNITUS ANALYZER SOFTWARE

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Introduction: Tinnitus is a conscious perception of phantom sounds in the absence of an external acoustical stimulus. Of the several ways to treat tinnitus, Sound Therapy - Tinnitus Retraining Therapy (TRT) and Tinnitus Masking, is commonly used [4-7, 9]. Unlike TRT, tinnitus therapy is a short term treatment making it a more convenient for patients [10]. Therefore, the proposed work uses Tinnitus masking.

Tinnitus sound varies in terms of loudness and pitch [5, 11- 13] from patient to patient and so does the usefulness of masking therapy. Thus, the main challenge for a clinician is to judge the feasibility of sound masking therapy for a particular tinnitus patient and then generate a customized masker signal.

Measurement of the subjective experiences of tinnitus sufferers is important to recreate the tinnitus sound, to be heard by the clinician and the patient's family, which might be of psychological help to the patient. Additionally, the documented data on acoustical measures is important for assessment and counseling of the patients [1-3]. These reasons necessitate the need for individual profiling of

tinnitus sound for each patient. In the last few years, attempt has been made to automate tinnitus quantification using software programs and the results authenticate their suitability for clinical applications [1, 2].

Objective: This research study proposes to develop software to accurately recreate tinnitus acoustical parameters as perceived by a patient in order to improve the efficiency of masking therapy on that patient.

Proposed scheme: A Tinnitus analyzer has been developed (in MATLAB) for individual profiling and analysis of the perceived tinnitus sound by a patient. The proposed software has 3 main modules – audiogram generator, tinnitus sound generator, and masker analyzer.

Figure 1 – Block diagram of the Tinnitus Software Analyzer

A) Audiogram generator

Loudness is an important parameter to quantify tinnitus, and in this study it has been measured in sensation level (i.e. in reference to the actual hearing threshold at that particular frequency). Hence, this module has been designed to generate the audiogram of the patient.

B) Tinnitus sound generator:

Prior to any successful treatment of a tinnitus patient, it is essential to quantify the perceived tinnitus sound as accurately as possible. This model has been developed to allow the clinician/ patient to:

- 1) Vary frequency and bandwidth of noise and tone components
- 2) Choose a particular ear in case of localized tinnitus
- 3) Mix and match the noise and the tone components
- 4) Measure the loudness of the tinnitus sound
- 5) Save the results digitally for future reference.

C) Masker Analyzer

This module uses the quantified parameters to analyze the feasibility of masking therapy for a particular patient depending on the values of minimal masking level and residual inhibition and then generate the masker signal.

Conclusion: The proposed software can prove to be the state of the art in clinical study of tinnitus due to its ease in portability and use. As a part of the future work, the software will be made available on the internet for flexible accessibility across the globe.

Bibliography

1. James A. Henry, Betsy Rheinsburg, Roger M. Ellingson, "Computer-automated tinnitus assessment using patient control of stimulus parameters", *Journal of Rehabilitation Research & Development*, Volume 41, Number 6A, Pages 871–888, November/December 2004
2. Henry JA, Flick CL, Gilbert A, Ellingson RM, Fausti SA. "Comparison of manual and computer-automated procedures for tinnitus pitch-matching", *J Rehabil Res Dev*. 2004, 41(2):121–38.
3. Henry JA, Meikle MB, "Psychoacoustic measures of tinnitus", *J Am Acad Audiol*. 2000; 11:138–55.
4. R. Trotic, M. Ries, I. Petrovic, R. Rudelic, G. Gudelj and M. Leventic, "Tinnitus – State of the Art and Retraining Therapy", *Acta Clin Croat*, Vol. 42, No. 3, 2003
5. Renee Lokenberg, "Evaluation and Treatment of Tinnitus", Masters thesis, Department of communication Sciences and Disorders, University of Florida
6. "Outline of the Mechanisms of Tinnitus and the Principles of TRT", *Island Hearing Services*
7. Robert J. Olsson, "Self-Directed Tinnitus Sound Therapy Based on the Principles of TRT", www.californiatinnitus.com

8. P. Cariani, A. Oxenham, M. Tramo, "The Auditory System", Harvard-MIT Division of Health Sciences and Technology, www.cariani.com

9. K. Fujimoto, H. Nagashino, Y. Kinouchi, A. Danesh, A. Pandya, "Inhibition of oscillation in a Plastic Neural Network Model of Tinnitus Therapy using Noise Stimulus"

10. S. Kemp and R. George, "Masking of Tinnitus Induced by Sound", *Journal of Speech and Hearing Research* Vol.35 1169-1179 October, 1992.

11. www.ehealthmd.com/library/tinnitus

12. <http://www.tinnitusformula.com/>

13. C. M. Dambra, "Perceived Severity And Its Relationship To The Psychoacoustic Characteristics Of Tinnitus"

COMPARING AN ONLINE TINNITUS EXAMINATION TO A TINNITUS EXAM IN A RESEARCH ENVIRONMENT

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In this study, we compare the results of a tinnitus examination conducted over the internet to a similar examination conducted on the same patients at the Human Neural Plasticity Laboratory at McMaster University in Hamilton, Ontario, Canada.

Each examination takes tinnitus loudness ratings, hearing spectrum measurements, tinnitus spectrum, and residual inhibition measurements from tinnitus sufferers. In the controlled research environment at the Human Neural Plasticity Laboratory, measurements were taken in person using sophisticated audio devices where the audio output properties of those devices were known beforehand. In the online environment, measurements were taken over the internet using commodity home audio components interfacing with personal computers.

The results of each examination method were comparable in their ability to demonstrate a correlation between tinnitus and hearing spectra and approximate a patient's tinnitus loudness, hearing spectrum, and tinnitus spectrum; and induce residual inhibition.

HEARING ABILITIES AT HIGH FREQUENCY IN PATIENTS WITH TINNITUS

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Objectives: In humans, audible frequencies range between 20 Hz and 20 kHz.¹⁶ We have therefore measured hearing thresholds at ultra-high frequency obtained in patients with tinnitus who had normal hearing on classical pure tone audiometry, within a range of 250 Hz~8 kHz. The purpose of this study is to evaluate the ultra high-frequency pure tone thresholds of conventionally normal hearing tinnitus patients comparing with those of normal volunteers.

Patients and Methods: This study was performed in 18 patients (18 ears), each of whom had persistent tinnitus for a minimum of 3 months, a threshold <25 dB HL and threshold differences of < 10 dB between ears at

frequencies of 250 and 500 Hz and 1, 2, 4 and 8 kHz. For each patient, we enrolled 5 age- and sex-matched normal volunteers (10 ears), each of whom had a threshold <25 dB HL and threshold differences < 10 dB between ears at frequencies below 8 kHz. The mean hearing thresholds at 10, 12 and 14 kHz of each tinnitus ear were compared with those of the 10 age- and sex-matched normal ears.

Results: Of the 18 patients with tinnitus, 12 had significantly increased hearing thresholds at more than one of the three frequencies, compared with the normal group. When we assessed results according to frequency, we found that 8 patients had decreased hearing ability at 10 kHz, 10 had decreased hearing at 12 kHz and 7 had decreased hearing at 14 kHz.

Conclusions: In this study, decreased hearing ability was seen at ultra high-frequency in some patients with tinnitus who had normal hearing below 8 kHz. Thus, it is likely that the proportion of patients with tinnitus who had normal hearing within the entire audible range will be smaller than in previous reports.

Clinical Trials

THI SCORE CHANGES OVER THE COURSE OF THERAPY AND PATIENT'S SUBJECTIVE PERCEPTION OF TINNITUS CHANGE

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Objective: The Tinnitus Handicap Inventory (THI) is a validated questionnaire for evaluating actual tinnitus severity and is therefore widely used in clinical practice and research. It seems feasible to use changes in THI scores from baseline (before treatment) to on-treatment or end-of-treatment THI scores as endpoints in clinical studies. However, little is known on how changes in THI scores correspond with patients' subjective perception and reports whether they experienced a change in their tinnitus symptoms.

Methods: A straightforward measure to assess changes in health perception is the Clinical Global Improvement Questionnaire (CGI). Patients indicate on a scale from 1 (very much improved) to 7 (very much worse) how their tinnitus has changed since the beginning of treatment. CGI scores were recorded on week 2, week 4, week 8, last visit. CGI scores were correlated with the respective THI change scores (e.g., CGI week 2 with Δ THI baseline - week 2) using Spearman-Rho Coefficient.

Results: We enrolled 131 patients from 6 different centers for this investigation. According to THI score 9 out of the 131 patients (6.9%) had a slight, 43 (32.8%) a mild, 42 (32.1%) a moderate, 26 (19.8%) a severe and 11 (8.4%) a catastrophic tinnitus at baseline. The THI score at baseline varied from 10 to 100 (mean 45.45, SD 21.34). The correlations between CGI and the respective THI change scores were $\rho = -0.136$ ($p=0.158$) at week 2, $\rho = -0.227$ ($p=0.034$) at week 4, $\rho = -0.273$ ($p=0.017$) at week 8 and $\rho = -0.486$ ($p<0.0001$) at last visit.

Conclusion: It appears that the correlations between CGI and THI change scores increased over time, indicating stronger correspondence between the two self-evaluations. This is the first time that this effect is reported in the literature. It remains to be seen whether this effect can be replicated in future studies or whether it is due to memory effects or due to continuous iteration of filling in the same questionnaires.

Epidemiology

INCIDENCE OF TINNITUS IN TEENAGERS AND YOUNG ADULTS MP3 PLAYERS USERS

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Introduction: Increasing use of mp3 portable players, especially by teenagers and young adults, has been repeatedly associated with hearing loss. Noise-induced hearing loss is supposed to be one of the main causes of tinnitus.

Aim: To compare the incidence of tinnitus between teenagers and young adults mp3 users and non-users.

Subjects and method: 100 patients aged between 15 and 30 years old from Valença Medical School were enrolled, 54 of them regular mp3 users (at least 1 hour of daily use for at least 1 year) and 46 not. They fulfilled a questionnaire concerning tinnitus, including THI, and performed pure tone audiometry, and transient acoustic otoemissions (TAOE). We considered only continuous tinnitus which lasts for at least 6 months.

Results: The incidence of tinnitus amongst non-users was 8.69 %, while in mp3 users group was 27.77 %, a statistically significant difference ($p=0.025$). Average hearing thresholds, considering the average of 3,4 and 6 kHz frequencies of both ears (total of 200 ears), were 10.90 dB in non-users group and 11.56 in the users group. Considering TAOE for both ears in the 2 kHz frequency, we found statistically significant lower levels in the mp3 users group (8.7 dB average) compared with the non-users group (9.83 Db, $p=0.029$). Hearing thresholds for the 8kHz frequency were significantly higher in tinnitus patients who listen to mp3 portable players.

Discussion: The higher incidence of tinnitus amongst the mp3 users corroborates the relationship between noise-induced hearing loss and tinnitus. This fact highlights the need for a prevention strategy amongst teenagers and young adults, and even in children and children's parents concerning the habits of listening to loud music with phones. Conclusion: Tinnitus is more frequent in teenagers and young adults who listen to music in mp3 players in a regular basis. In this study, incidence of tinnitus amongst mp3 players' users was associated with higher hearing thresholds for the 8 kHz frequency.

Key words: tinnitus, hearing loss, acoustic otoemissions, audiometry, mp3 players

SURVEY ONLINE ABOUT TINNITUS AND HYPERACUSIS, VIA OUR WEBSITE

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Since 2004 our private Medical Center, dedicated to patients with tinnitus and Hyperacusis has a Spanish-language website on the internet, where we have a survey with questions about the clinical status of patients who respond via email before to attend their treatment of tinnitus and Hyperacusis in our center.

Every question, except for No. 16, has only two possible answers: yes or no.

The questions are as follows:

A- Personal data:

- Name and Surname,
- Address
- Phone
- E-mail
- Age

B- Tinnitus and Hyperacusis questions:

1. Since when you have tinnitus?
2. Describe briefly how your tinnitus began.
3. Does your tinnitus seem to beat, as with the rhythm of your heart?
4. Do you have good hearing?
5. Do you use hearing aids?
6. You have a hearing loss?
7. Do you have troubles with sound?
8. Does the sounds of everyday life bother you?
9. Are you oversensitive to sound?
10. Does the sound seem to increase your tinnitus?
11. Describe briefly how you began your sensitivity to sound
12. Does your tinnitus interfere with sleep?
13. Does your tinnitus interfere with your work?
14. Does your tinnitus interfere with your recreational activities?
15. Does your tinnitus interfere with your family or partner?
16. What bothers you most, your tinnitus, your hearing loss or your Hyperacusis?

We have since received some 48.000 visits to our website and we received 2400 virtual answers to our survey from tinnitus and Hyperacusis patients; here we review statistically the patients' responses to the 16 questions in our survey.

Health System

A SURVEY OF AUDIOLOGY DEPARTMENTS ACROSS ENGLAND: REFERRAL PATHWAYS

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We surveyed a number of selected audiology staff in 189 National Health Service (NHS) hospital trusts across England asking them about the service they provide for people who have tinnitus. A 36-item questionnaire was sent out to 390 individuals with approximately one third responding. The subset of data presented here describes the perceptions and opinions of audiologists on the patient pathway to and from Audiology.

Referral to Audiology: The most common (59%) referral pathway is from the general practitioner (GP) to the Ear, Nose and Throat (ENT) medical specialist, then to the audiologist based in a hospital setting. Audiologists were asked how appropriately people with tinnitus were referred. In most cases, GP's management was not considered to be appropriate or effective (31%). In contrast, 16% of audiology staff did consider it to be appropriate or effective and 19% thought it was variable.

The NHS patient pathway introduced in December 2008 sets a maximum time of 18 weeks from the point of initial referral up to the start of any treatment necessary for all patients where it is clinically appropriate and where patients want it. All Audiology departments work within this

time frame. In fact, for those people requiring tinnitus care, the majority of cases (45%) take 4-8 weeks to reach the Audiology service and 20% of cases take less than 4 weeks. When asked about the impact of the programme, 57% said that it had changed local procedures for managing tinnitus. Of the remainder, 36% said no and 7% were unsure. For most respondents (56%), the main impact was viewed in a positive way, either by reducing waiting times or raising awareness of the process. Nevertheless, 28% disagreed saying that it either focussed efforts on meeting 18-week pathway targets without considering subsequent management or that it increased work pressure. Main challenges to an efficient referral pathway for tinnitus were considered to be GP or ENT education (36%) and NHS management practices (16%).

Referral from Audiology: Within the NHS, there appear to be limited options for onward referral to specialist care, with only 34% able to access clinical psychology. Most local regions have neither tinnitus support groups (68%) nor long-term support networks (28%).

Although the Department of Health promotes the expansion of the Audiologist's role to encompass competency to deliver counselling and psychological support, only 10% are currently trained to do so. The majority of respondents were in favour of receiving such training, but expressed concerns about limited funding and clinical workload.

A number of general conclusions can be made. Despite some limitations, audiologists generally believe that the NHS tinnitus referral process is effective. However, there is a body of opinion that a good NHS service for people with tinnitus needs to start with appropriate and effective GP referral and, for a small proportion of people, needs to end with suitable psychological support. Education and workforce training and support are ways to achieve these improvements.

A SURVEY OF AUDIOLOGY DEPARTMENTS ACROSS ENGLAND: TINNITUS ASSESSMENT, TREATMENT AND OUTCOME MEASURES

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We surveyed a number of selected audiology staff in 189 NHS trusts across England asking them about the service they provide for people who have tinnitus. A 36-item questionnaire was mailed out to 390 individuals with approximately one third responding. The subset of data presented here describes how tinnitus is assessed and treated, and how the efficacy of treatment is measured. The majority of responders identified themselves as audiologists or hearing therapists. Within their departments, 16% of audiologists and 93% of hearing therapists were considered to specialize in tinnitus.

Assessment: Half of responders used a structured interview format to assess tinnitus, and less than half made use of any sort of standardized tinnitus questionnaire.

Treatment: Routinely, almost all clinicians surveyed offer directive counseling, hearing-aid fitting, sound generators, and some form of tinnitus retraining therapy. Most offer stress management, while less than half offer cognitive behavioral therapy. Only one third reported that they have the option to refer to a psychologist. A minority offer relaxation training or therapy, acceptance and commitment therapy, or sleep hygiene techniques. All responders indicated that they offer combinations of treatments.

When asked what patient characteristics routinely determine the choice of treatment the most significant factors were the audiogram, evidence of anxiety or stress, personality or perceived ability to cope, presence of sleep disturbances, and patient choice. Similar numbers of staff reported either having or lacking resources such as treatment devices, highlighting the differences between NHS departments and the limitations on treatment options.

Measurement of outcome: Treatment outcome assessment is generally unstructured and not standardized within departments. Only one third use a tinnitus questionnaire at this stage.

Perceived efficacy of service: While only 10% identified their department as having a specialized tinnitus team, 72% described their service as being effective. Just 3% described their service as ineffective. In a follow-up question, 38% said they had sufficient resources to provide an effective tinnitus service.

The current provision of an NHS Audiology service for people who have tinnitus is largely delivered on an individualized basis. Nevertheless, there are recurrent themes (e.g. mild or high frequency hearing losses and anxiety as markers for treatment) and preferred assessment and treatment methods (THI, directive counseling, hearing aids). However, there is little standardization across the service, or even within the same department. While a lack of consensus might provide flexibility to meet local demands, it also has drawbacks; it is difficult to ascertain the key standards of best national practice for tinnitus, it makes the process of clinical audit (quality or cost-benefit) difficult, it affects equal patient access to treatments, and it limits the speed of responding to translational research outcomes, such as the speed of adopting new management strategies into clinical practice.

EXPERIENCE OF A TINNITUS COUNSELING CLINIC IN SINGAPORE

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Aim: Tinnitus is a common problem seen in ENT clinics. Up to 15% of outpatients at our clinic have such symptoms. We report the response of patients after management in a tinnitus counseling clinic.

Methods: All patients attending our Tinnitus Counseling Clinic (TCC) from Jan 2008 until Dec 2009 completed a Tinnitus Handicap Inventory (THI) questionnaire as part of the initial assessment and again at the follow-up counseling session. A feedback interview questionnaire was also administered at the follow-up session, when patients were asked if they found the tinnitus counseling useful, and how helpful each of the counseling materials/components were (on a 5-point scale ranging from least to most helpful). The counseling materials consist of information and education components. Patients were further asked if they were 'still seeking a cure for their tinnitus', whether they had 'accepted their tinnitus' and if they wanted to join a tinnitus support group.

Results: From Jan 2008 to Dec 2009, 35% of patients had at least one follow up visit at the TCC. These comprised 115 patients (68 males, 47 females), aged 19-80 years (mean 50.9, SD 13.4 years) who had a follow-up session

ranging from 1 to 12 months (mean duration 2.6 months) after the initial session. The majority (96.5%, n=111) found the initial tinnitus counseling session helpful. The two counseling activities which were most helpful were 'explanation of coping strategies' (mean score 4.45) and showing of 'photos of healthy and damaged hair cells' (mean score 4.36).

The initial overall THI mean score was 38.7 points (SD 24.9), and during follow up it was 16.1 points (SD 18.9). The mean difference between the initial and follow up THI score was 22.6 (95% CI 18.4 - 26.7). At the initial counseling, nearly half (41.8%) of patients were in a moderate to severe THI handicap category. At the follow-up counseling only 13% remained in the moderate-to-severe THI handicap category.

Almost half (47%, n=54) of the patients were 'still seeking a cure for their tinnitus' at the follow up. While 92.2% (n=106) of patients had 'accepted their tinnitus', 40% (n=46) of patients indicated that they wanted to join a tinnitus support group.

Conclusion: The main focus of the tinnitus counseling clinic is minimizing the impact of tinnitus on a patient's life. While only 35% of patients came back for a follow up visit, the majority (96%) of these patients who came for follow up found the counseling useful, with the overall THI score significantly decreased. Having a better understanding of their condition and learning a range of self-help coping strategies can provide assurance to the patient that their tinnitus is not a harmful or dangerous condition, and may have contributed to improvement in THI score.

Pathophysiology

STRESS REACTION IN PATIENTS WITH ACUTE NOISE INDUCED TINNITUS

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Background/aims: Tinnitus and hyperacusis are typically unwanted consequences of the noxious effects of noise/acoustic overstimulation. In some individuals noise-induced tinnitus (NIT) is eliciting a stress response, which is followed by a rapid deterioration of the quality of life. Our aim was to study the occurrence and severity of stress, both as a possible contributing factor as well as an obvious consequence of acute tinnitus.

Methods: Fifty-four patients with acute (symptoms for less than six weeks) NIT were examined by standard otologic methods and comprehensive tinnitus tests. Clinical evaluation included a throughout medical history of stress-related health/mood events. Tinnitus handicap inventory (THI) (Newman et al 1996) was used as the basic tinnitus handicap questionnaire.

Results: Our patients were typically 20- 40 years of age, healthy individuals who had been exposed to loud music (about 80% on patients). Severe stress reaction was demonstrated with THI value higher than 44/100 in more than 60% of patients, in 10% the handicap was catastrophic (THI 72/100 or higher). Tinnitus induced sleep disturbance was present in about 90% of cases. A substantial number of the patients in our study (27%) had chronic compensated (habituated) tinnitus, which exacerbated because of a new acoustic overstimulation.

Only 12 % of our NIT patients had an earlier history of mood disturbances (stress, burn out, depression).

Discussion: Our results support the concept that most patients with acute tinnitus search special care because they have developed a significant stress reaction from tinnitus. Stress reaction can develop within one week to a catastrophic level. Stress led to insomnia which worsened the vicious circle by increasing the tinnitus annoyance. These patients need urgent counseling and stress management. It has been suggested that it is the emotional structure and reduced ability to deal with stressors of affected individuals that makes them susceptible to NIT stress reaction. This seems to be true in only about 15% of our patients.

Our results strongly support the concept that the target of tinnitus treatment should be the stress reaction of the patient, not the tinnitus sensation itself. There is new evidence showing that stress decreases the expression of some key neurotrophic factors in limbic structures that control mood and neuronal plasticity in general and that antidepressant treatment reverses or blocks the effects of stress (Duman and Monteggia, 2006, Castren et al 2007). Neurotrophic factors themselves do not control mood, but they act as necessary tools in the activity-dependent modulation of networks (Castren et al 2007). Therefore, in order to prevent more serious mood disorders such as depression, tinnitus induced stress treatment should be initiated at an early stage.

Basing on the data of the present study and recent stress/mood disorder research we have developed tinnitus management strategies aiming firstly, to relieve stress reaction of the patient and thus to prevent more serious mood disorders and secondly, to correct failed function of critical neuronal network through induction of activity-dependent neuronal plasticity. Preliminary results of our new tinnitus management strategies are presented and discussed.

THE SENSITIZATION MODEL FOR ACQUIRED CENTRALIZED TINNITUS

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Acquired centralized tinnitus (ACT) is the most frequent form of chronic tinnitus. The proposed ACTS (acquired centralized tinnitus sensitization) – assumes a peripheral initiation of tinnitus whereby sensitizing signals from the auditory system establish new neuronal connections in the brain. As a consequence, permanent neurophysiological malfunction within the information processing modules results. Successful treatment has to target these malfunctioning information processing. We present here neuro- and psychophysiological aspects of a recently suggested neurophysiological model which may explain the symptoms caused by central cognitive tinnitus sensitization: while conditioned reflexes as a causal agent of chronic tinnitus respond to extinction procedures, sensitization may initiate a vicious circle of overexcitation of the auditory system resisting extinction and habituation.

CHANGES IN THE CORTICAL SPECTRO-TEMPORAL RECEPTIVE FIELDS INDUCED BY NOTCHED STIMULI

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It is well-known that tinnitus is accompanied by hearing loss in the majority, if not all, subjects. Hearing loss has been shown to reduce sensory inputs sent towards the

auditory centers, resulting in dramatic central changes which may ultimately cause tinnitus. An auditory illusion, called Zwicker tone (ZT), shares some properties with tinnitus and as such has been considered as a transient tinnitus. The ZT can be induced after the presentation of a notched noise, and interestingly, the ZT presents a pitch corresponding to the notch of the noise (as tinnitus pitch corresponds to the frequency band of hearing loss). The notched noise, which induces a contrast of neural activity over frequencies (similar to what cochlear insults do), may induce comparable central changes than those causing tinnitus. In this context, studying the central changes induced by a notched stimulus can give some insights into the mechanisms of tinnitus. In the present study, we recorded neural activity (multi-unit activity and local field potentials) obtained in the auditory cortex of anesthetized guinea pigs evoked by control and notched stimuli. All stimuli used in the study served two purposes simultaneously; they provided a given sensory environment to the animal (simulating a hearing loss for instance), and at the same time, they allowed the characterization of the spectro-temporal receptive fields (STRFs) of cortical neurons. We will present preliminary results showing changes in STRFs induced by notched stimuli (vs control stimuli).

FREQUENCY TUNING IN CHRONIC TINNITUS PATIENTS

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Theories of tinnitus generation involve the assumption of altered inhibitory neural networks in the auditory cortex. If this were the case, it would be plausible to assume that those alterations would be reflected in auditory fields evoked in these networks.

To investigate the influence of loss of inhibition in the human auditory cortex we measured population-level frequency tuning in two groups (tinnitus patients vs. non-tinnitus subjects) by means of magnetoencephalography (MEG). The groups were matched in age, gender, and hearing level. During the presentation of auditory stimuli the subjects' attention was directed to the visual modality by showing an unknown silent movie and involving subjects into a memory task. The stimulation paradigm used was based on an experimental setup previously shown to be suitable for the investigation of neuromagnetic correlates of auditory tuning [1, 2]. The stimuli were tones of 2 different frequencies: one, the test stimulus (TS), was in the frequency range of the individual tinnitus percept, which was carefully determined. The other stimulus (CS= control stimulus) was in a frequency range distant from the tinnitus frequency. TS and CS were embedded in band eliminated noises (BENs) with notches of different width, the width being either 1/4, 1/2 or 1 critical band centered at the particular frequencies of the stimuli.

We hypothesized that for the tinnitus frequency the tuning would be duller in tinnitus patients compared to the control group. Moreover, in the tinnitus patients the tuning would be duller for the tinnitus frequency than for the control frequency, whereas this intra-individual difference in tuning sharpness would not be found in the control subjects.

1. Okamoto H, Stracke H, Wolters CH, Schmael F, Pantev C: Attention improves populationlevel frequency tuning in human auditory cortex. *J Neurosci* 2007, 27(39):10383-10390.

2. Sams M, Salmelin R: Evidence of sharp frequency tuning in the human auditory cortex. *Hear Res* 1994, 75(1-2):67-74.

POSTER PRESENTATION

JUNE 09, 2010, 02:30-03:30 P.M.

Case Reports

UNILATERAL TINNITUS – THE ONLY SYMPTOM OF A LARGE VESTIBULAR SCHWANNOMA

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Introduction: Vestibular schwannoma are relatively rare tumors also referred to as acoustic neuroma. Symptoms are based on its location and as the tumor grows, usually the symptoms advance.

Case outline: An eighteen year old patient had been presented to an otolaryngologist with buzzing in her right ear that had lasted for about 1 month. Her pure-tone audiometry findings showed slight asymmetry; in the right ear, slight ascendant type sensorineural hearing loss was found (25 dB HL at 125 Hz, 20 dB HL at 250 Hz, and 10 dB HL at other frequencies), while the threshold in the left ear was 15 dBHL at 125 Hz and 10 dB HL at other frequencies. After electronystagmography, otoacoustic emissions and auditory brain-stem responses we suspected on retrocochlear etiology of tinnitus.

MRI examination showed a large right cerebellopontine angle tumor, measuring 5x3 cm, which has shifted brain stem laterally.

Conclusion: Every case of unilateral tinnitus, asymmetric sensorineural hearing loss, or hypotonia of labyrinth not strictly accompanied by vertigo, needs to be further evaluate using a battery of audiologic tests whose findings may be normal. Audiologic tests should be repeated in cases of persistant symptoms and accompanied by cranial MRI, which is today considered a gold standard for diagnosis of vestibular schwannoma.

Key words: unilateral tinnitus, normal hearing, vestibular schwannoma

RECORDING AND ANALYSIS OF PULSATILE TINNITUS IN DURAL SINUS DIVERTICULUM

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Pulsatile tinnitus was recorded in a 57-year-old woman. It was pulse-synchronous and was audible by the examiner via Toynbee tube. Radiologic evaluation including CT angiography revealed dural sinus diverticulum on the lateral border of right middle cranial base above tegmen tympani and mastoid. Sound was digitally recorded in an audio booth using an insert phone-type recorder before and after surgery. Loudness of the peak and the trough of pulsations were measured. The frequency spectrum of the recorded tinnitus was generated using fast Fourier transformation analysis (FFT). Recording and analysis were also performed to evaluate if cervical compression

and neck rotation influence on the characteristics of tinnitus.

In the neutral position, the loudness of the peak was averaged as 68 dB SPL. It was decreased when she rotated her head to the right side (60 dB) or compressed her right neck (56 dB). Primary frequency in neutral position was around 800 Hz on spectral analysis. To expose the origin of turbulent venous flow, the middle fossa dura was exposed and skeletonized by drilling out temporal squama, and then further mastoidectomy was performed. The exposed dural sinus and the stalk was compressed and resurfaced with bone plates, bone pate and temporalis muscle fascia. After surgery, the loudness of the peak in neutral position decreased by 14 dB (peak 54 dB). Subjective symptom was reported to decrease over 50% compared to preoperative status, while pulsatile sound was no longer audible by the examiner. On audiogram, interestingly, low frequency sensorineural hearing loss was also improved with a threshold of 15-20 dB from 40 dB at 250 and 500 Hz.

Recording and analysis of pulsatile tinnitus may be a useful method of functional demonstration of annoying tinnitus in conjunction with radiologic diagnosis.

EARLY INTERVENTION IN SUDDEN ONSET TINNITUS

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Introduction: Sudden onset of severe spontaneous tinnitus in a previously asymptomatic patient is a catastrophic experience. Current treatment methods are generally directed to chronic cases. However the production of prolonged residual inhibition using low frequency non sinusoidal sound stimulation provides a method suitable for early intervention in the acute onset case. Two patients treated in this way have had successful outcomes.

Neurological models of tinnitus such as Jastrebof's which are the basis of current treatments for tinnitus attribute the persistence of tinnitus to the enhancement of non-auditory brain pathways such as the limbic system and thus treatment is aimed at modifying these pathways once they have developed. It is proposed in these treatment methods that the brain learns to suppress the new tinnitus pathways by plasticity.

The neurologic models imply that a proactive approach in recent onset severe tinnitus to prevent the development of these pathways before they become established may be more effective. This concept is similar to the management of sudden sensorineural hearing loss with intratympanic corticosteroids.

The models also imply that induced absence of tinnitus or significant reduction of tinnitus loudness (which constitutes residual inhibition) even if it is temporary, may be useful in preventing the establishment of chronic tinnitus pathways.

Methods: It has recently been demonstrated that prolonged periods of partial or complete inhibition can be induced by a series of very low frequency non sinusoidal sounds (TIPA). The patient listens to this sound sequence for twelve minutes using high definition headphones once or twice a day.

CASE #1

A tertiary referred 48 year old female school teacher had been woken from her sleep with unilateral roaring tinnitus. She had no illnesses, no vertigo and normal hearing. She was treated six weeks after onset and experienced twelve hours of complete absence of tinnitus following exposure to the low frequency sound twice a day. After four days her tinnitus returned and could not be inhibited. She stopped treatment and was given Amitriptyline to allay her anxiety. Six days later her tinnitus reduced to a minimal level and has remained insignificant subsequently.

CASE #2

A twenty five year old female developed moderate unilateral tinnitus with normal hearing after an upper respiratory infection. When the tinnitus failed to subside over eight weeks she was given a single trial exposure to the low frequency sound and experienced complete residual inhibition for twelve hours. Continuing treatment was recommended but she reported one week later that she no longer had any tinnitus and has remained in remission.

Discussion: It is arguable whether the low frequency sound signal played a significant role in the recovery of these two patients. However the same conundrum applies when patients treated with corticosteroids recover from sudden sensorineural hearing loss. Nevertheless the TIPA sound signal is a low risk treatment option with potentially significant therapeutic effect and experience with this treatment in chronic tinnitus cases suggests that it is playing a role.

Others

AMERICAN TINNITUS ASSOCIATION : OUR MISSION TO CURE TINNITUS

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This will be presented by the chair of the ATA Board of Directors, Dr. Gary Reul Ed.D. and ATA's Executive Director, Michael Malusevic. It will cover ATA policies that have created their programs focused on finding a cure for tinnitus and will also detail components of these programs that both directly and indirectly provide research funding opportunities to tinnitus investigators.

The American Tinnitus Association (ATA) exists to cure tinnitus through the development of resources that advance tinnitus research. To accomplish this mission ATA directly funds cutting-edge research and advocates for increased federal research budgets for tinnitus. ATA's research grant program has awarded over \$5 million in pilot grants to tinnitus researchers, some of whom have gone on to receive larger grants from the U.S. National Institutes of Health (NIH) and more recently, the U.S. Department of Defense (DoD).

ATA's Scientific Advisory Committee (SAC), comprised of accomplished researchers who take a multi-disciplinary approach to tinnitus research, advises ATA on our research program. SAC includes neurologists, audiologists, psychologists and otolaryngologists. In 2005, five members of ATA's Scientific Advisory Committee created a document called the Roadmap to a Cure. The Roadmap breaks tinnitus research into four paths of study. It prioritizes these areas and highlights opportunities for further investigation. The ultimate intent of the Roadmap is finding a cure(s) for tinnitus. Two of the paths are dedicated to studying the basic underlying mechanisms of where and how tinnitus starts and two are devoted to clinical applications to mitigate and ultimately cure tinnitus.

ATA's Scientific Advisory Committee and Board of Directors adopted this document and use it as a guide when reviewing research grant proposals submitted to ATA.

ATA's robust Advocacy program targets U.S. government agencies with the capacity to fund tinnitus research and seeks to establish or increase those budgets. Our efforts are targeted at the NIH, the DoD and the Department of Veterans Affairs. These legislative efforts have increased tinnitus research funding by these three agencies by approximately \$8 million collectively over the past three years. ATA also has membership programs targeted at tinnitus health professionals and researchers that offer increased visibility to the tinnitus patient community.

Somatosensory Tinnitus

QIGONG FOR THE TREATMENT OF TINNITUS: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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Tinnitus is a frequent disorder which is very difficult to treat. Qigong is a mind-full exercise and an important constituent of traditional Chinese medicine practice. Here we performed a randomized controlled trial to evaluate the effect of a Qigong intervention on patients with tinnitus. We hypothesized, that especially tinnitus patients with somatosensory components may benefit from the mind-body technique Qigong.

Eighty patients with tinnitus of at least 3 months duration were randomly assigned to an intervention group (N= 40) consisting of ten Qigong training sessions in 5 weeks or a waiting-list control group (N=40). Tinnitus severity was assessed with a visual analogue scale (VAS) and with a tinnitus questionnaire (TBF-12) before treatment, immediately after treatment, and one and three months after treatment.

Qigong did not cause any side effects and was completed by 80 % of the assigned patients. Compared with the control group, Qigong participants experienced improvement in tinnitus severity, as reflected by a significant reduction in both the VAS scale and the TBF-12. In the subgroup of patients with somatosensory tinnitus Qigong effects were more pronounced resulting in a highly significant improvement in both scales compared to the waiting list group.

These findings suggest that Qigong interventions could be a useful complement to the therapeutic management of patients with tinnitus and especially for those with somatosensory components. Contentment with the intervention, a high degree of completion and stability of the effects for at least 3 months after the intervention further underscores the potential of Qigong in the treatment of tinnitus.

MUSCULAR TENSION AND TINNITUS. AN EXPERIMENTAL TRIAL OF TRIGGER POINT INJECTIONS ON TINNITUS

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The connection of tinnitus and muscular tension was investigated. The study was planned to search a possibility to relieve tinnitus by treating muscular tension. The coincidence of these two was found during muscle tension treatments.

178 tinnitus patients were treated during 1991-1993 in Imatra Honkaharju hospital for tinnitus. They were asked to take part in an open treatment study. 39 patients served as controls. Hearing was measured with audiometer and tinnitus was homed-in with audiometer after patient description of the tinnitus type. Tinnitus was classified by sound/ ear, not by the patients with tinnitus. Thus a patient with bilateral tinnitus was classified as 2 tinnitus cases, one tinnitus in the right ear, another in the left ear. Thus more tinnitus measurements, than patients with tinnitus, were achieved. Tinnitus was treated with cold spray, stretching and trigger point injection with lidocain 1% local anesthetic. The number of tinnitus treatment settings varied from 1 to 56, the time between treatments was from 4 to 40 days. A high pitched ringing sound was most common: 51 cases of ringing in the right ear and 58 cases in the left ear in the treatment group and 10 cases in the right and 11 cases in the left ear in the control group.

Results: Tinnitus changed statistically during the treatments. Before the first treatment the medium tinnitus in the right ear was 47.2 dB, and 30 minutes after the treatment, it was 42dB, $p < 0.01$. The medium left ear tinnitus, changed likewise from 47.5 dB to 43.4 dB, $p < 0.001$. The same phenomenon occurred in every treatment. Part of the tinnitus changes took place during the post-treatment days and part of the effect came after a week from the treatment. After the first treatment a temporary relief of tinnitus occurred in 51% of the right ear tinnitus and 44% of the left ear tinnitus. Because a part of patients had bilateral relief of tinnitus and others had no effect, could be estimated, that one third of the patients had benefit from the treatment. Women had different tinnitus than men; male patients reported more ringing tinnitus and female had a broader spectrum of tinnitus sounds. Women had more benefit from the treatment.

Conclusion: Muscular tension affects tinnitus sounds and tinnitus can be generated from tense muscles from the area around ear and neck. Tinnitus can be treated by relieving muscular tension in trigger points in these areas. Autonomic nerves may play a part in this phenomenon.

CONTINUOUS AURICULAR ELECTRICAL STIMULATION QUIETS THE TINNITUS OF THE SOMATOSENSORY PULSATILE TINNITUS SYNDROME

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Our clinical experience and review of reports of treatment modalities directed toward the somatosensory system, such as periauricular electrical stimulation and auriculotherapy (acupuncture applied to the auricle), support the hypothesis that these modalities can benefit individuals with somatic tinnitus. We began a trial of P-Stim for subjects with such tinnitus, because P-Stim incorporates both periauricular electrical stimulation and auriculotherapy. P-Stim is a battery powered disposable

device designed to provide 1/sec electrical pulses to 3 needles for 4 successive days. The 2 mm long, 0.4 mm diameter needles are placed on the auricle at low electrical impedance points nearby blood vessels. From our initial study of 22 subjects with a variety of tinnitus characteristics, 2 subjects with somatosensory pulsatile tinnitus syndrome appeared to respond favorably to P-Stim. We now report our results from treating another 10 subjects with somatosensory pulsatile tinnitus syndrome.

Methods: Subjects ranged in age between 48 and 66. 2 M, 8 F. Pulsatile tinnitus was AU in 3, AD in 5, and AS in 2. Six could abolish their tinnitus completely with strong muscle contractions of their jaw or neck. Four could suppress the pulsations but not the tinnitus altogether with such muscle contractions. P-Stim was placed on the auricle weekly where it remained for 4 days. The subject then disposed of it. P-Stim was replaced weekly by the investigator. Subjects maintained a daily VAS log of their tinnitus loudness, annoyance, awareness and location. Subjects were to receive P-Stim weekly until their response plateaued.

Results: 5 of the 10 subjects completed the trial as planned. 3 subjects who have now treated 6, 7, and 14 weeks respectively have had major sustained reduction (>50%) in all 3 VAS measures of tinnitus. Another 2 subjects completed the study after 29 and 11 P-Stim treatments respectively with only minor reductions in their pulsatile tinnitus and no intervals without tinnitus.

Unfortunately 5 subjects withdrew prematurely despite all of them having episodes of no tinnitus for tens of minutes. 2 withdrew after 2 weeks and another 2 after 5 weeks. Another subject had multiple 20 minute episodes with no tinnitus but had no sustained diminishing of her tinnitus; she withdrew after 9 sessions.

When the first 2 subjects of our original trial are combined with the current 3 responders, we find that 5 of 7 subjects (70%) who completed the full P-Stim trial had >50% sustained reductions in their tinnitus VAS scores.

Conclusion: Continuous auricular electrical stimulation can cause sustained quieting of the tinnitus of 70% of subjects with the somatosensory pulsatile tinnitus syndrome.

CLINICAL CHARACTERISTICS AND THERAPEUTIC RESPONSES OF MUSCLE ORIGIN TINNITUS

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Objectives: Proper diagnosis of the muscle origin tinnitus and its differentiation from sensorineural tinnitus could be important in managing the patients with tinnitus. We performed this study to further understand the clinical characteristics of muscle origin tinnitus, to evaluate the therapeutic response of each modality and to suggest the diagnostic and therapeutic guideline for muscle origin tinnitus.

Materials and Methods: Twenty two patients who were diagnosed as muscle origin tinnitus at tertiary referral center of tinnitus clinic from October 2003 to August 2009 have been included in this study. Their clinical characteristics, audiologic findings, psychological status and the responses of medical treatment, tinnitus retraining therapy and surgical therapy have been analyzed retrospectively.

Results: All of the patients with palatal myoclonus (PM) tinnitus showed clicking tinnitus, whereas those with middle ear myoclonus (MEM) tinnitus had different types of sound including crackling, buzzing, tapping, etc. Predisposing factors of PM and MEM seemed to be stressful event and loud sound exposure, respectively. Inspection of palatal motion using nasal endoscope was the most valuable diagnostic method in PM. Observation of the tympanic membrane movement with ear endoscope or documentation of perturbation in impedance audiogram was valuable in MEM. More than half of the patients showed improvement in their tinnitus with the medical therapy and/or tinnitus retraining therapy. Botox injection (PM tinnitus) or middle ear tendon sectioning (MEM tinnitus) seemed to be prompt and promising treatment modality.

Conclusion: Understanding clinical, audiologic characteristics of the muscle origin tinnitus will be helpful for early diagnosis and treatment of the patients with muscle origin tinnitus. Further studies investigating possible pathomechanism of muscle origin tinnitus will be necessary.

KEY WORDS: Tinnitus, Muscle, Myoclonus, Palatal, Middle ear

EFFICACY OF MYOFASCIAL TRIGGER POINT DEACTIVATION FOR TINNITUS TREATMENT

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Introduction: The relationship between tinnitus and myofascial trigger points has been subject to debate but few therapeutic guidelines have been proposed. This study aims at analyzing (1) efficacy of myofascial trigger point deactivation for the relief of tinnitus in patients with myofascial pain syndrome; (2) correlation of laterality between tinnitus and pain – and the relief of both of them – as well as (3) whether the presence of tinnitus modulation upon trigger point palpation is a good predictor for the treatment.

Methods: A double-blind randomized placebo controlled clinical trial was developed in order to ascertain efficacy of 10 sessions of myofascial trigger point deactivation in a population suffering from both tinnitus and myofascial pain syndrome. Inclusion criteria were: presence of tinnitus and at least one active trigger point in eight possible muscles of the head, neck or shoulder girdle, excluding patients with generalized pain or undergoing recent treatment for both symptoms. After having been selected by an otologist and evaluated by a “blind researcher” in the beginning and after the fifth and tenth session, subjects were directed to a physiotherapist, who randomized them in two groups and treated both. The experimental group was subject to myofascial trigger point deactivation by means of digital pressure and guidance related to procedures to be followed at home, whereas the control group was subject to weekly light pressure in spots adjacent to the existing trigger points.

Results: Treatment of the experimental group was more effective in relation to tinnitus loudness, number of sounds, total value of the Tinnitus Handicap Inventory as well as modulation intensity ($p < 0,001$). There was an association between pain relief and tinnitus relief ($p = 0,013$; Spearman correlation = 0,426) and treatment was effective in all pain-related variables ($p < 0,001$) such as: pain intensity, algometer value and amount of active and latent trigger points. Laterality correlation was also observed between the side with the worst tinnitus and the side with pain in 54.4% of the cases (Kappa = 0,32; $p < 0,001$). Tinnitus modulation was frequent in both experimental and control

groups (75.7% e 83.3% respectively), even though such phenomenon does not influence the prognosis of the treatment. Nevertheless, diminishing tinnitus intensity was a good predictor for tinnitus relief ($p = 0,002$).

Conclusions: The experimental group was more effective in all variables subject to evaluation after treatment with myofascial trigger point deactivation. Laterality correlation of both symptoms was also observed as well as the existence of a direct link between pain relief and tinnitus relief. Modulation of tinnitus during trigger point evaluation does not influence the treatment prognosis, even though diminishing intensity during modulation allows more tinnitus relief than raising intensity or modifying the type of sound.

TINNITUS AND TEMPOROMANDIBULAR JOINT DISORDERS – A SPECIAL SUBGROUP OF TINNITUS PATIENTS?

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A correlation between disorders of the temporomandibular joint and tinnitus is frequently discussed. Treatment of TMJ dysfunction can also improve the symptoms of chronic tinnitus. Therefore, we started a study in 2008 at the University of Regensburg to investigate this potential relationship.

All patients (about 1000 patients) presenting at the Department of Dentistry with complaints of temporomandibular joint dysfunctions were assessed for concomitant tinnitus complaints. A subgroup of 30 patients was identified suffering from both TMJ disorder and tinnitus. The subgroup was further investigated in this study. Standard treatment for TMJ disorders (splint, manual or drug therapy) was performed and potential changes of tinnitus were assessed during a follow-up period of three to five months with a tinnitus questionnaire (Tinnitus Handicap Inventory, THI). Additionally, all patients of the subgroup received audiologic assessment including a pure tone audiogram, tinnitus pitch and loudness matching and minimal masking level. The clinical and audiologic characteristics of the subgroup were compared to data from patients attending the special Tinnitus Clinic at the same institution.

As a first result, about 44% of the 30 patients reported an improvement of their tinnitus distress after the TMJ treatment. Furthermore, this population of patients differs significantly from patients attending the multidisciplinary tinnitus clinic. Differences concerned the parameters gender, age and hearing loss. First, the subgroup consisted of mainly young female persons (about 60%). Secondly, their average hearing threshold in the pure tone audiogram was better than the one of a population usually presented at the tinnitus clinic.

In conclusion, treatment of TMJ dysfunction can improve tinnitus distress. Furthermore, patients with TMJ disorders and tinnitus represent a distinct subgroup of tinnitus patients with special clinical and audiologic characteristics. In many cases they are young female nearly normal hearing persons in contrast to the “ordinary” tinnitus patient.

Special Forms of Tinnitus

BOTULINUM TOXIN TREATMENT FOR OBJECTIVE TINNITUS CAUSED BY PALATAL MYOCLONUS

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Objective tinnitus is defined as the perception of sound, potentially audible by the others, generated within the body by vibratory rather than neural activity. One of the cause of the emergence of objective non pulsatile tinnitus is the palatal tremor (formerly palatal myoclonus), that is thought to be secondary to rhythmic involuntary contractions of the soft palate. The palatal myoclonus can be classified as essential, in absence of other neurological symptoms, or symptomatic, when it is part of a more widespread neurological condition. The prevalence of essential palatal myoclonus, that usually emerges as an isolated symptom, is low, however it may be a distressing problem for the patients who experience it. The aetiology of this symptom is not well understood and still today it does not exist an election therapy for it. Several medications have been tried, as anticonvulsivants and sedatives, but without a significant improvement. Also surgical treatment was not resolutive. In the past decades local injection of botulinum toxin seemed to produce good results in treated patients, even if there are few cases reported in literature.

In this study 4 patients with objective tinnitus caused by palatal myoclonus underwent selective botulinum toxin treatment under videoendoscopic guidance. The toxin has been injected into the levator and tensor palatine muscles. All treated patients showed an important reduction of the tinnitus perception and the palatal myoclonus disappeared or was markedly reduced, as documented by the fibroendoscopy examination. No relevant side effects have been shown by the four patients. The benefits lasted 2 to 4 months. These results confirm that selective botulinum toxin treatment can be efficient and safe in reducing objective tinnitus related to palatal myoclonus.

TINNITUS IN VESTIBULAR MIGRAINE

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Vestibular Migraine, defined using the criteria proposed by Neuhauser et al, 2001, conforms the third most common etiology of vertigo and dizziness in our Clinics. Usually, while referring to this pathology, the description of the clinical situation includes tinnitus. However many publications lack a particular description of special characteristics of this symptom. Particular characteristics of tinnitus could be used while defining clinical differences between vestibular migraine and Meniere's Disease in early stages. We have studied the tinnitus characteristics in a population of 50 patients, randomly selected, suffering of vestibular migraine. Patients with basilar migraine were excluded. Criteria evaluated were presence of tinnitus and its loudness, frequency being most affected, residual inhibition effect, relationship with vertigo crisis, other risk factors for tinnitus, presence or not of associated hypoacusys and fullness during crisis, age of the patient, sex and age of presence of first clinical symptoms. Most of this group of patients suffered from tinnitus, in total 29 patients. Only nine of them had variations during crisis, not all of them could relate the tinnitus to the onset of

migraine, so that the relationship between vestibular migraine and tinnitus could not be documented in the whole group of tinnitus sufferers. The symptom characteristics were different to those described in the literature in patients with Meniere's Disease, being in all cases matched with frequencies between 2000 and 8000 Hz. None of the patients had tinnitus affecting lowest frequencies.

NEW PATHOGEN AND THERAPY IN 17 CASES OF CHRONIC CONDUCTIVE TINNITUS

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In this clinical study, 17 chronic tinnitus patients are treated by modern acupuncture (MAC), a new treatment based on neuroanatomy for nerves' disturbances. Patients suffer from 1-10 years of tinnitus with some sleeping, depression and headache concomitant symptoms. After many pharmaceuticals and even traditional acupuncture therapies, their tinnitus has not any improvement. With 5-10 times' MAC cure, 15 of them are recovered, two non result. The most difficult on diagnosis of tinnitus is the principal obstacle for its treatment, which reflecting on the long period of confusion in its pathogen. This study has tried to probe into these pathogenic and therapeutic problems. The traditional clinical surgical (mechanic) and pharmaceuticals (chemic) treatment for tinnitus is not satisfied by its poor results, because of their practice and theoretic limitation. The breaking through of cure for tinnitus should dependent on the new theory and new practice.

The result of this clinical research has demonstrated that:

I. Major tinnitus is possibly formed by Cervicobasilar Part (CBP) biological structure injury, blocked and changed the information conducted by cranial nerves roots VIII.

II. Most of tinnitus should be considered as a disturbance of nerves system. The wrong biological information conducted by the cranial nerve VIII. involves the auditory center signal analysis disorder.

III. This kind of nervous block may happen in patients with road accident, long time's low head position work and study, CBP getting cold or wind, and CBP arthritis etc.

IV. It can be named conductive tinnitus, belonging to Nerve-Block-Involved-Symptoms (NBIS). The MAC helpful specialty is that it is the only directly nerves-touching clinical treatment today.

V. Some correlative factors and concomitant symptoms in tinnitus have been found in this study. It shows that tinnitus is not a disease, only one of the Cervicobasilar Syndromes (CBS).

VI. The new concept, criterion and treatment of tinnitus are suggested.

RECORDING AND ANALYSIS OF PULSATILE TINNITUS IN DURAL SINUS DIVERTICULUM

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Pulsatile tinnitus was recorded in a 57-year-old woman. It was pulse-synchronous and was audible by the examiner via Toynbee tube. Radiologic evaluation including CT angiography revealed dural sinus diverticulum on the lateral border of right middle cranial base above tegmen tympani and mastoid. Sound was digitally recorded in an audio booth using an insert phone-type recorder before and after surgery. Loudness of the peak and the trough of pulsations were measured. The frequency spectrum of the recorded tinnitus was generated using fast Fourier transformation analysis (FFT). Recording and analysis were also performed to evaluate if cervical compression and neck rotation influence on the characteristics of tinnitus.

In the neutral position, the loudness of the peak was averaged as 68 dB SPL. It was decreased when she rotated her head to the right side (60 dB) or compressed her right neck (56 dB). Primary frequency in neutral position was around 800 Hz on spectral analysis. To expose the origin of turbulent venous flow, the middle fossa dura was exposed and skeletonized by drilling out temporal squama, and then further mastoidectomy was performed. The exposed dural sinus and the stalk was compressed and resurfaced with bone plates, bone pate and temporalis muscle fascia. After surgery, the loudness of the peak in neutral position decreased by 14 dB (peak 54 dB). Subjective symptom was reported to decrease over 50% compared to preoperative status, while pulsatile sound was no longer audible by the examiner. On audiogram, interestingly, low frequency sensorineural hearing loss was also improved with a threshold of 15-20 dB from 40 dB at 250 and 500 Hz.

Recording and analysis of pulsatile tinnitus may be a useful method of functional demonstration of annoying tinnitus in conjunction with radiologic diagnosis.

EVALUATION OF TINNITUS IN THE PATIENTS WITH MENIERE'S DISEASE

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Introduction: Tinnitus is one of the main problems in Meniere's disease. The objective of this study is to analyze

the pattern and characteristic of tinnitus in Meniere's disease.

Materials and Methods: Retrospective review of medical records was performed for the patients diagnosed as Meniere's disease in Seoul National University Hospital between January 2005 and December 2009. Correlation of tinnitus with symptoms of Meniere's disease such as vertigo, earfullness and hearing level was analyzed. Mean hearing level was the average of 3 air conduction threshold: 0.5, 1 and 2 KHz. Patients were divided into 4 groups according to mean hearing level.

Results: A total of 169 patients were enrolled in this study and was composed of 64 men and 105 women, with a mean age of 48.2 (range, 13 -79 years). Among them, 148 patients (87.6%) had a tinnitus as a symptom but there was no statistically significant difference between male and female. Tinnitus incidence was evaluated according to hearing level and showed a statistically significant increase as mean hearing level increased ($p=0.041$). There was not significant correlation between incidence of tinnitus and earfullness.

Conclusion: Our data shows that tinnitus could be related with hearing level. Further study about the response to treatment, quality of life is needed.

A CASE OF PALATAL MYOCLONUS ASSOCIATED WITH OROFACIAL BUCCAL DYSTONIA

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Palatal myoclonus is a rare condition in which there are rhythmic jerky movements of the soft palate and sometimes other brainstem innervated muscles. A particularly annoying symptom is rhythmic clicking sound in the ear due to the opening and closing of the Eustachian tube. Orofacial buccal dystonia is a focal dystonia with sustained spasms of the masticatory, facial, or lingual muscles. Frequent symptoms of this disease are mainly reported as involuntary and possibly painful jaw opening, closing, deflecting, retruding, or a combination of the above. However, subtle and unnoticeable involuntary movement of the multiple facial muscles, which might be an infrequent symptom of orofacial buccal dystonia, makes this disease hard to diagnose. Understanding of the functional orofacial anatomy responsible for the clinical symptoms and signs is necessary for proper diagnosis. Here we report a rare case of palatal myoclonus associated with orofacial buccal dystonia which has never been reported yet. Diagnostic approach and treatment result after dysport injection with proper directive counseling will be described.

KEY WORDS: Palatal myoclonus, Tinnitus, Dystonia, Orofacial

POSTER PRESENTATION

JUNE 10, 2010, 02:30-03:30 P.M.

Auditory Stimulation

CUSTOMIZED SOUND THERAPY FOR TINNITUS

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Recent experimentations in the field of neuroscience have indicated that reduction of the sensory inputs due to injury of hearing peripheral system (cochlea, inner hair cells and/or acoustic nerve fibers) leads to a reduction of the central inhibition and to changes of the pattern of spontaneous neural discharges in the auditory centers. Such an aberrant activity could be at the basis of tinnitus. According to this new model, a new type of sound therapy, customized sound therapy (CST), has been developed. It is aimed to reduce overactive auditory network, experiencing a sound that reproduce the characteristics of subjective tinnitus. The objective of this study was to test CST for efficacy in a group of patients affected by light to moderate tinnitus, in a case-control study. We also compared the results of CST and TRT after three months of treatment.

Methods: 38 subjects were selected from the clinical population presenting with chronic tinnitus and enrolled in the clinical testing project. We administered CST in a group of 19 subjects and a simple white noise in a group of 9 subjects. Tinnitus Handicap Inventory (THI) and VAS scores were obtained pre and post-therapy and at follow-up at 3 months. We compared the results with a group of 10 subjects that underwent TRT for three months. IRB approved consent was obtained.

Results: the results in the 16 subjects completing CST treatment (3 patients dropped out before the end of the therapy) showed significant improvements in THI scores and in VAS score for the tinnitus life effect after 8 weeks of CST therapy. This results have been maintained at the follow-up at 3 months. In the control group only the VAS score for the annoyance of tinnitus showed a significant decrease. TRT group showed a significant decrease of both THI and VAS for annoyance.

Conclusions: results of this study suggest CST can improve THI scores and thus may be an effective means of managing tinnitus. Considering that CST is a short-term and comfortable administration therapy, if compared with TRT, it should be suitable especially for patients affected by light to moderate tinnitus.

SEQUENTIAL PHASE SHIFT SOUND CANCELLATION RX PREDOMINANT TONE TINNITUS

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Objective: To report clinical data from six centers in the US, Western Europe and Asia which have used phase-shift sound wave cancellation for treatment of predominant tone tinnitus, from the first treatment in 2004 to 2009.

Method: Clinical data were obtained from New York City, London, Erie (Pennsylvania, USA), Antwerp, Grottamare (Italy) and Kuala Lumpur, and summarized.

Results: A total of 525 patients were treated. A reduction in tinnitus volume (defined as more than 6 dB) was seen in 301 or 57 % of patients.

A STUDY OF MUSIC THERAPY USING "1/F- FLUCTUATION SOUNDS" FOR TINNITUS PATIENTS

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It is well known that lack of auditory stimulations act to make hyperactive disorders that involve a tinnitus and hyperacusis. These uncomfortable symptoms are induced by an expression of neural plasticity. The sufficient stimulation such as noise, music, and environment sound will decrease these phantom sensations up to a point. Clinician prefers to use the sound generator (SG) for a tinnitus treatment. The advantageous effect of SG based tinnitus therapy is exactly supported with the clinical studies. But the patient must receive the medical prescription because it is medical act in Japan. The music and the environment sound based therapies are still in question in spite of its usefulness and effectiveness. In fact, few clinical reports are there.

It is difficult to select the suitable music or environment sound from the huge number of CD in market without the idea of what kind of sound elements is appropriate for tinnitus therapy.

In this study, we are focused on the rhythm element that is called 1/f-fluctuation, which has been argued regarding its healing effect. The "f" means the instantaneous frequency that consisted with zero cross points. The commercially available music CD "Mimi Supplement (SRJ inc.)" is designed for the 1/f-fluctuation (from 1/1000Hz to 10Hz) with the Digital Signal Processing technology. We used this CD for the tinnitus music therapy.

34 tinnitus patients were participated in the study. All patients who had accepted to attend the therapy before SG based therapy. Tinnitus patient with the ear diseases like a sudden deafness, a conductive deafness and other type of organic disorders was excluded. Patients underwent the 1/f-fluctuation based musical therapy at least 3 months. Tinnitus patients were evaluated with the satisfaction survey, Tinnitus Handicap Inventory (THI) and Visual Analogue Scale (VAS) and compared to the previous reports of SG based therapy.

94% of the patients reported the therapy as "significant improvement" or "reasonable improvement". Only 6%

complained of "invalid". The improvement of the score of THI and VAS was statistically confirmed by a Wilcoxon signed-ranks test (a one-sided test).

ur study suggested that the 1/f-fluctuation based musical therapy is predictably effective for tinnitus. And no patients switched to TRT using SG after this therapy. It is concluded that the 1/f fluctuation musical therapy must have equivalent treatment values like SG.

BENEFIT FROM AND ECONOMIC VALUE ASSOCIATED WITH TWO ALTERNATIVE SOUND THERAPY TINNITUS MANAGEMENT OPTIONS

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Introduction and Aims: Ear-level sound generators (SG) and the Neuromonics Tinnitus Treatment (NTT) are two sound therapy options used to provide tinnitus relief. SG employ a broadband noise used for tinnitus masking or habituation. NTT employs music stimuli customized by spectral modification based on the patient's hearing loss. The aims of this study were to: (1) evaluate changes in perceived tinnitus activity limitation/participation up to one year following initiation of treatment for each device option; and (2) compare the economic value of each treatment using cost-effectiveness (CEA) and cost-utility analyses (CUA).

Methods: Ninety patients drawn from the Head & Neck Institute at the Cleveland Clinic participated. Forty-five were fitted with SG and 45 were fitted with NTT. Patient characteristics including age, gender, hearing loss, duration of tinnitus, and tinnitus dimensions (quality, location, pitch rating, and loudness rating) will be presented. The Tinnitus Handicap Inventory (THI) was administered to evaluate activity limitation/participation restriction associated with the consequences of tinnitus. Magnitude estimations scales (0 – 10) were used to determine subjects' rating of pitch and loudness. All subjects participated in a 1.5-2 hour group education session prior to an individual tinnitus evaluation and sound therapy device selection. Based on individual preference, subjects were fitted with either SG or the Neuromonics device. The THI was administered prior to device fitting and at approximately 6 and 12 months after the initiation of treatment.

Results: Mean performance on the THI demonstrated a significant reduction in perceived handicap between baseline measures and 6 months postfitting for both SG (65 points at baseline and 41 points at 6 months) and NTT (58 points at baseline and 36 points at 6 months); there were no statistically significant differences in mean THI performance between 6 months and 12 months postfitting for either treatment option. Moreover, there were no significant difference in THI scores between SG and NTT treatments at any of the time intervals evaluated. The CEA consists of three separate incremental comparisons: cost (i.e., retail cost to patient for device/treatment); effectiveness (i.e., benefit derived from changes in THI scores); and cost-effectiveness ratio between treatment alternatives (i.e., SG and NTT). CUA for each option will be calculated to determine quality adjusted life years.

Conclusions: Both sound therapy options provide a significant reduction in tinnitus handicap following 6 months of treatment and remained stable out to 1 year; however, differences between treatment options at each time interval were equivalent. The CEA and CUA provide exploratory techniques for examining the economic value associated with device alternatives.

CLINICAL APPLICATION OF A NEW TINNITUS SOUND GENERATOR (TSG) DEVICE

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Tinnitus is a concern for many people, and affects approximately 10% of the population. As hearing loss is increasingly identified and diagnosed, this trend is most likely to continue and grow. Many tinnitus sufferers, and clinicians, have struggled finding flexible tinnitus treatment devices that are suitable components of a tinnitus treatment and counseling support program. ReSound LiveTMTTS is an advanced combination hearing instrument and Tinnitus Sound Generator (TSG) device that provides fitting flexibility for clinicians, and an innovative TSG solution for their patients. This session will review general tinnitus knowledge, and clinical application on how to maximize the TSG features with ReSound LiveTMTTS. In addition, data from multiple trials, that have shown that ReSound LiveTMTTS, in combination with a sound tinnitus counseling program, is an effective tool in helping to provide tinnitus sufferers improvement and relief from their tinnitus, will be discussed.

TINNITUS SUPPRESSION BY LOW-RATE MODULATED SOUNDS

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Objective: Numerous treatments have been attempted to remedy tinnitus, but a definitive treatment does not exist. Acoustic stimulation has been used to mask tinnitus, but this is usually effective only when the tinnitus is relatively soft. In our study, we aimed to find an effective means of suppressing tinnitus via modified acoustic stimulation. Suppression differs from masking in that effective tinnitus suppressors are often lower in level and with different temporal and spectral properties than the perceived tinnitus, whereas maskers are often presented at an equal or louder level and share similar temporal and spectral properties as the perceived tinnitus.

Methodology: A prospective study design was undertaken to identify customized and patterned acoustic stimuli in a group of patients whose tinnitus could not be controlled by current conventional methods. We focused on low-rate amplitude-modulated (AM) or frequency-modulated (FM) sounds because they have been shown to produce sustained and highly synchronized cortical responses in the brain. In addition to AM and FM tones, we investigated pure tones, and band-pass noise. External stimuli were delivered acoustically via headphones to 20 subjects with chronic (>6 months) tinnitus. The external sound therapy was presented for three minutes and the tinnitus loudness rank recorded every 30 seconds. Suppression was defined as a percent reduction in baseline tinnitus rankings greater than or equal to 30%. Stimulus type and frequency range were modeled alone and in combination with other subject factors to predict suppression and determine which combination of parameters was the most likely to result in suppression.

Results: On average, tinnitus was pitch matched to a 7092 Hz tone and had a loudness ranking of 5.2 on a visual-analog scale from 1 and 10. Twelve of the 20 subjects experienced suppression to some degree.

Subjects with suppression had louder tinnitus at baseline. The best conditions that elicited suppression were amplitude-modulated pure-tones with carrier frequencies between 6000 and 9000 Hz. In subjects with at least some suppression, amplitude- and frequency- modulated pure-tones were significantly more likely to result in total suppression compared to un-modulated pure-tones. No subject experienced total suppression with white noise, the traditional sound therapy approach.

Conclusions: The present result suggests that suppression sound therapy is an underexplored but promising area of research for tinnitus treatment. Further work is needed to elucidate the individual differences in the success of tinnitus suppressor tones in order to improve the lives of patients with tinnitus.

Acknowledgements: Work support by the American Tinnitus Association.

FIRST YEAR FINDINGS OF THREE-YEAR STUDY OF LONG-TERM BENEFITS OF NEUROMONICS TREATMENT

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Introduction and Aims: Sound generators and HA/s have been the primary tools used by audiologists to provide tinnitus relief. The Neuromonics Tinnitus Treatment (NTT) is one option for treating tinnitus. It uses four different tracks of music that are spectrally-modified based on the patient's hearing loss. The purpose of this study was to investigate the long-term clinical efficacy of the NTT for reducing perceived tinnitus, the associated distress and handicap, and the user acceptability of the device. The current data set represents preliminary findings related to changes in performance during the first year of the three-year longitudinal study.

Subjects: To date, 40 subjects from 6 medical centers/private practices have been enrolled. Inclusion criteria are: > 17 points on the Tinnitus Reaction Question (TRQ); four-frequency PTA (0.5, 1, 2, 4 kHz) < 50 dB HL, bilaterally; normal cognition, comprehension, and manual dexterity; no significant depressive or anxiety (score of < 11 points on the Hospital Anxiety and Depression Scale [HADS]); no pulsatile tinnitus; and no complicating medical/otologic conditions (e.g., unstable Meniere's disease). Enrollment occurs after the patient chooses the NTT as the treatment option. Patients receive a small fee for completion of the questionnaires.

Methods: A series of questionnaires were administered at various times during the initial year. The TRQ and Tinnitus Handicap Inventory (THI) were administered at pretreatment, 2, 4, 6, and 12 months. The Neuromonics Treatment Completion Questionnaire was administered at the conclusion of the treatment – typically around 6 months postfitting. In addition, minimum masking levels and loudness discomfort levels psychoacoustic measures were assessed at baseline and 6-months after initiation of treatment. The HADS was also readministered at 6 months to evaluate changes in anxiety, depression, and stress.

Results and Conclusions: To date, a significant reduction in the scores of the TRQ and THI has been seen at 6 months with similar findings at 12 months. The greatest reductions for both measures occurred by 2 months. Similarly, a reduction in mean performance on the HADS between baseline and 6 months was observed for both the anxiety and depression scales. Results over the course of the first year of a three-year benefit study suggest that the NTT is an effective tool for tinnitus relief.

SPECIFIC EFFECTS AND PROGNOSTIC FACTORS OF HEARING AIDS ON TINNITUS

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Introduction: It is known that hearing aids can be effective in treating patients with both tinnitus and hearing loss. However, there is not enough information on the actual treatment result of hearing aids on tinnitus.

The aim of this study was to disclose the specific effects of hearing aids in relieving tinnitus and to find out relevant prognostic factors.

Materials and method: Prospective study was done on 10 patients who had both tinnitus and hearing loss. All the patients underwent tinnitus evaluation, such as pitch matching, loudness matching, minimum masking level (MML) and residual inhibition (RI). Also self-reported outcome measures of tinnitus and hearing handicap such as Visual Analog Scale (VAS), Tinnitus Handicap Inventory (THI) and Hearing Handicap Inventory for the Elderly (HHIE) and Tinnitus intake/outcome Interview (TI) was investigated.

The results were analyzed before treatment, 3week and 3 month after treatment. Result: After 3 months, the success rate of tinnitus control was 90% by VAS and 70% by THI. The alleviation rate was 52.3% by VAS, 48.0% by THI and 50 % by TI. The characteristics of the tinnitus such as MML and RI had also changed to be more favorably. The pretreatment VAS, THI, HHIE, TI had a significant correlation with the 3 months change in total THI score. Duration of the tinnitus had a significant correlation with the change in RI.

Conclusion: After using a hearing aid for 3 months, subjective discomfort due to tinnitus significantly improved in 70~90% of the patients. The mean alleviation rate was about 35-55% of the pretreatment discomfort level. Not only did the patient's perception of discomfort decrease but also the nature of the tinnitus changed more favorably. The most important prognostic factor was the degree of pretreatment discomfort. In the patients whose pretreatment discomfort level was greater, a more substantial improvement could be expected.

Brain Stimulation

RTMS FOR THE TREATMENT OF TINNITUS: ARE THERE CLINICAL PARAMETERS WHICH PREDICT THE THERAPEUTIC RESPONSE AND WHAT HAPPENS WITH RESPONDERS OVER LONGER FOLLOW-UP PERIODS?

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Tinnitus is a severe problem for many patients in the developed nations. Since a few years, rTMS has been investigated for the treatment of tinnitus based on the hypothesis that it can reduce cortical hyperexcitability in stimulated cortical areas. In several studies it has been shown that rTMS can reduce tinnitus. However the effect size is only moderate and interindividualvariability in treatment effects is high. In this context it is of high interest which group of patients benefits and if there are some clinical parameters that help to predict the therapeutic outcome. To investigate this question we analysed results from 235 patients, who were treated with rTMS because of chronic tinnitus. Patients received either a standard protocol of low-frequency rTMS (110% motor threshold, 1 Hz, 2000 stimuli/day, left primary auditory cortex) (188

patients) or combined frontal and temporal rTMS (110% motor threshold, 2000 stimuli @ 20 Hz, left dorsolateral-prefrontal cortex + 2000 stimuli @ 1 Hz left temporal cortex) (47 patients). The coil position was determined by the 10/20 EEG system. The treatment outcome was assessed with a standardized tinnitus questionnaire (TQ, Tinnitusfragebogen). Response criterion was an improvement of at least 10 points in the TQ score between baseline and the follow-up assessment 90 days after treatment.

50 patients showed such a clinical improvement and were classified as responders. To define clinical characteristics between the responder and non-responder group we compared the two groups in their clinical and demographic characteristics.

Responders did differ from non-responders only in the baseline score of the TQ. There were no significant differences in all other assessed parameters (gender, age, tinnitus duration, tinnitus laterality, motor threshold, handedness, stimulation protocol). As expected the treatment effect in the responder group was much higher as compared to the non-responder group. A long term follow-up assessment of the responders (in average 2 years after treatment) revealed a lasting beneficial treatment effect, further supporting the clinical relevance of rTMS in the treatment of tinnitus.

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR TREATMENT OF CHRONIC TINNITUS.

-CLINICAL AND EXPERIMENTAL STUDY-

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There are several evidences suggesting that tinnitus is associated with functional alterations in the central nervous system. Repetitive transcranial magnetic stimulation (rTMS) has been used to modify the neural activity at the stimulated area and at a distance along functional anatomical connections. Depending on stimulation parameters, cortical networks can be functionally inhibited or modulated in their activities. Low frequency rTMS has been reported to decrease cortical excitability. Thus, this technique has been expected to alleviate tinnitus by modulating the excitability of the auditory cortex. In this study, we aimed to investigate the effects of low frequency rTMS on chronic tinnitus and determine the factors predicting beneficial outcomes with rTMS treatment. In addition, we also experimentally investigated the gene expressions such as c-Fos in the auditory cortex before and after rTMS.

CLINICAL IMPROVEMENT AFTER REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IS ACCOMPANIED BY CHANGES IN GRAY MATTER DETECTED BY Voxel-BASED MORPHOLOGY

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Tinnitus, the phantom perception of sound, is a frequent disorder that causes significant morbidity. Up to now,

effective treatment options are still missing. Repetitive transcranial magnetic stimulation (rTMS) has been introduced as a novel, non-invasive treatment option. Results of studies conducted so far have been shown moderate treatment effects. To further improve efficacy of stimulation protocols, a better understanding of the neurobiological mechanisms by which rTMS exerts its effects is needed. Therefore, we conducted a voxel-based morphology (VBM) study in tinnitus patients treated with a combined protocol of prefrontal and temporal rTMS-stimulation. 13 tinnitus patients (4 female; mean age 46.5 years \pm 9.2; average tinnitus duration 25.2 \pm 22.0 months) have been treated on 10 consecutive days with a combination of 20 Hz rTMS stimulation of the left dorsolateral prefrontal cortex followed by 1 Hz stimulation of the left temporal cortex. VBM was performed according to standardized protocols before and after treatment. At the end of treatment (day 12), mean change in tinnitus severity assessed by the tinnitus questionnaire of Goebel&Hiller was 5.4 points, which increased to 10 points at the end of follow-up (day 90; 50.2 \pm 19.4 vs. 40.2 \pm 21.2; $p < 0.0001$). This clinical improvement was accompanied by a significant decrease in gray matter in the left inferior frontal and medial frontal gyrus ($p < 0.05$; corrected); i.e. in areas being shown to be involved in higher order processing of acoustic stimuli. This study underscores that rTMS represents an effective treatment option for chronic tinnitus and demonstrates that clinical changes are accompanied by structural alterations in cortical areas related to auditory processing.

Cochlear Implant

TINNITUS AFTER COCHLEAR IMPLANTATION

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Introduction: Cochlear implantation for hearing rehabilitation in deaf patients is a well established therapy. In some cases the patients complains about tinnitus before or after implantation.

Materials, methods: 62 patients were implanted in our department in the last 7 years (2003- 2009), 5 postlingually deaf adults and the other 57 were children. In 4 cases the patients complains about tinnitus after implantation.

Results: In 2 cases the tinnitus was suppressed while using the device. In one case the patient reports a decrease in tinnitus intensity, by using the implants and in one case the tinnitus did not change after implantation.

Conclusions: Our results from this small group suggest that in majority of cases, the implanted devices due to electrical stimulation have influenced the evolution of tinnitus.

ELECTRIC ACOUSTIC STIMULATION AND TINNITUS**Andrea Kleine Punte**¹(andrea.kleinepunte@gmail.com), Dirk De Ridder²(dirk.de.ridder@uza.be), Paul Van de Heyning¹

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Background: Electric Acoustic Stimulation (EAS) is a treatment for patients with severe to profound high frequency sensorineural hearing loss and functional low frequency hearing. This type of hearing loss is often accompanied by subjective tinnitus, and can even be the main complaint of the patient. Research on cochlear implantation as tinnitus treatment (Van de Heyning et al., 2008) suggests that EAS may also be a viable tinnitus treatment in patients with severe high frequency hearing loss. The working mechanisms are explained and a case study is discussed.

Methods: A 22 year old male presented at the University Hospital Antwerp with a main complaint of severe subjective tinnitus and a secondary complaint of reduced speech recognition, especially in noise. This patient had bilateral profound high frequency hearing loss and tinnitus due to ototoxic medication. A MED-EL SonataT1100 FlexEAS electrode was implanted and combined with a DUET speech processor. Assessment of tinnitus consisted of a) tinnitus frequency determination, b) tinnitus loudness assessment, c) residual inhibition possibilities, d) subjective loudness on a Visual Analogue Scale (VAS), and e) Tinnitus Questionnaire (TQ). Hearing was assessed with unaided pure tone audiometry with insert earphones, speech recognition of monosyllables and sentences in quiet (at 70 dB SPL) and sentences in noise (10 dB SNR) in Free Field. The patient was tested preoperatively, 1, 3 and 12 months after first fitting.

Results: Pre-operatively this patient suffered from bilateral subjective tinnitus at 6000 Hz of 10 dB Sensation Level (SL) in the right ear and 20 dB SL in the left ear. Masking of tinnitus was possible, but residual inhibition was negative. The subjective tinnitus loudness on the VAS was 10/10 for both ears. Tinnitus was present for 6 years and remained intractable over time. The total score on the TQ was 69/72, which reflects a degree 4, decompensated tinnitus. With EAS tinnitus was reduced bilaterally to 3/10 after 3 months and to 0/10 after 12 months. Without EAS, tinnitus was 2/10 on the VAS.

Conclusions: Electric Acoustic Stimulation can significantly reduce tinnitus in patients suffering from tinnitus and profound high frequency hearing loss. Restored auditory input with EAS can reverse the deafferentation process causing tinnitus. Although EAS was implemented unilaterally, bilateral tinnitus suppression was obtained.

Neurofeedback**DEVELOPING A BRAIN COMPUTER INTERFACE (BCI) FOR NEUROMODULATION OF TINNITUS DISABILITY****Burke Richmond**¹ (Richmond@surgery.wisc.edu), **Leo Walton**² (leowalton@gmail.com) and **Justin Williams**² (jwilliams@engr.wisc.edu)¹Department of Surgery, Division of Otolaryngology, The University of Wisconsin Medical School, Madison, WI 53792²Department of Biomedical Engineering, The University of Wisconsin, Madison, WI 53706

Clinically, tinnitus remains an open frontier for the development of innovative and more effective treatment strategies. Brain Computer Interface (BCI) represents cutting edge technology that may be employed to reduce tinnitus disability. Our group developed a proof of concept BCI technology that uses imagined motor control signals to transform an audiovisual scene displayed on a monitor, with the aim to modulate or eliminate subjective tinnitus.

Tinnitus represents a spectrum of auditory percepts, with various pathophysiological mechanisms. Notably the degree of auditory system injury does not reliably predict tinnitus disability. The functional response is broad: some subjects with tinnitus quickly habituate and adapt, while others develop neuropsychiatric sequelae and psychosocial disruption.

The behavioral response to tinnitus is multifactorial; non-auditory cortical responses as much as disordered auditory pathways appear to govern disability. Converging evidence suggests that ST may emerge from threshold changes within distributed neural networks that underlie auditory processing, cognition and consciousness.

BCI acquires and processes electroencephalography (EEG) signals to trigger a computer modulated output and may also induce neuroplastic changes. The latter offers a therapeutic opportunity to bypass or shift behavioral responses to neural injury and maladaptive cortical mapping for the treatment of tinnitus and other neurological disorders.

Tinnitus has been characterized as a phantom auditory percept, associated with changes in cortical mapping and brain connectivity. As such, tinnitus may become disabling because it represents a "disembodied" and unintegrated perception and trigger a cascade of negative behavioral responses. We propose that the BCI provides a means to shift the behavioral response to tinnitus by integrating the phantom sound into a meaningful context. In our model, the BCI uses audiovisual feedback to engage the distributed cortical networks that underlie audiovisual integration for sound localization. The aim is to extinguish the negative behavioral response and possibly the tinnitus percept itself.

Future work will involve the development of a protocol to refine the BCI interface, assess alternate cortical signals, and pilot the technology with normal and tinnitus subjects.

Nutrition**MICRONUTRIENTS IN PREVENTION AND IMPROVEMENT OF STANDARD THERAPY IN TINNITUS****Kedar N. Prasad, Ph.D., William C. Cole, Ph.D. and Gerald M. Haase, M.D.**

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It has been estimated that about one-third of adult Americans experience tinnitus at some time in their lives. At present there is no preventive strategy to reduce the incidence of tinnitus. Noise and vibration are two of the major factors in inducing tinnitus. About 21 to 42 percent of tinnitus is induced by exposure to noise. Both vibrations and intense noise generate excessive amounts of free radicals and cause inflammation that damage hair cells leading to tinnitus. The levels of nitric oxide, peroxynitrite, oxidative stress, nuclear factor-kappa-beta (NF-kappaB), glutamate receptor (N-methyl-D-aspartate) and markers of

inflammation are elevated in tinnitus. When hair cells are damaged, glutamate, an excitatory neurotransmitter responsible for converting vibrational sound into electrical signals, is produced in excessive amounts. Excessive amounts of glutamate are very toxic to neurons. Damage to peripheral auditory and somatosensory systems causes imbalance between excitatory and inhibitory neurotransmitters in the mid brain auditory cortex and brain stem. This imbalance causes hyperactivity in the auditory cortex leading to the perception of phantom sounds (tinnitus). Antioxidants reduced noise-induced hearing loss in animal models, and blocked toxicity of glutamate in neurons. Therefore, supplementation with antioxidants appears to be one of the rational choices for prevention of tinnitus.

About 34 % of tinnitus patients had post traumatic stress disorder (PTSD), and most patients with severe disabling subjective idiopathic tinnitus (SIT) exhibited neurodegeneration in the brain some of which resemble Alzheimer's disease (AD), suggesting some linkage of neuronal mechanisms associated with these disorders. Indeed, increased oxidative stress and chronic inflammation have also been found in patients with AD and PTSD. There is no effective treatment of SIT. An oral supplementation with antioxidants reduced the subjective discomfort and tinnitus intensity in patients with idiopathic tinnitus. The rationale for combining a standardized optimal micronutrient formulation in combination with standard therapy such as glutamate antagonists, steroids, sulpiride (a D2 antagonist of dopamine receptors) that could be used in audiology practice to improve the management of tinnitus will be discussed.

Animal Pathophysiology

EFFECTS OF LOCAL SALICYLATE APPLICATION ON INFERIOR COLICULUS NEURONAL ACTIVITY IN VIVO

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Temporary tinnitus can be induced reliably in humans and animals by systemic salicylate application. Recent findings, however, suggest pronounced differences between tinnitus induced by cochlear trauma and salicylate-induced tinnitus. As salicylate potentially influences neuronal activity in the whole auditory pathway and has a strong effect on cochlear sound processing it is difficult to compare its effects to that of other tinnitus induction techniques. So far, research of local effects of salicylate on the auditory system was conducted in vitro only. This study therefore aims to describe salicylate's local effects on auditory processing in the central nucleus of the inferior colliculus (ICc) in the intact brain in vivo. Single unit recordings during local microiontophoretic salicylate application in the ICc of Mongolian gerbils revealed significant increases in both evoked and spontaneous activity, the latter being significantly stronger. Results of the application of gabazine, a specific GABA_A antagonist, were comparable to that of salicylate for spontaneous activity, but much stronger for evoked activity. None of the two substances changed neuronal tuning sharpness or the characteristic frequency sound pressure level (lowest SPL needed to evoke a response), but gabazine was able to transform closed, non-v-shaped into v-shaped frequency response areas. Another effect could be observed in neurons with high spontaneous background activity: While both salicylate and gabazine increased spontaneous and evoked activity in these neurons, inhibitory sidebands at the flanks of the neurons were uninfluenced.

The general increase in evoked activity suggests a role of the ICc in salicylate-evoked hyperacusis, while the rise of spontaneous activity is in accordance with the results from slice studies and could be a component of salicylate-induced central tinnitus. Nevertheless, depending on the tinnitus induction method, a decrease of ICc spontaneous activity can also be observed.

The lack of effects of salicylate and gabazine on the tuning sharpness and the inhibitory sidebands of ICc neurons gives evidence for further inhibitory mechanisms, on which local application of the two substances has little to no influence.

Pharmacology

ORAL GLYCINE INHIBITS CORTICAL ACTIVITY IN TINNITUS PATIENTS

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Introduction: Glycine is an inhibitory neurotransmitter involved in various neuronal layers of the cortex, brainstem auditory nuclei such as the cochlear nuclei, inferior colliculus, and the superior olivary complex. Glycine at high-dose inhibits the N1P2 slope of LDAEP (loudness dependence auditory evoked potential) in healthy adults (1). The current study administers oral glycine to tinnitus patients, recording LDAEP (N1P2).

Material and methods: Six patients with tinnitus (3 females and 3 males with mean age of 46.0 years old, range 32-71 years old) were treated with oral glycine (10g/8 hours for 30 days). N1P2 slopes were registered before and after the therapy with stimuli to 60, 70, 80, 90 and 100 dB. Glycine, as well as cortisol and prolactin (stress hormones) were determined in serum before and after therapy. THI and TRQ questionnaires were filled before and after treatment.

Results: N1P2 slope was attenuated a 41.1% in the range 60-80 dB with statistic significance. N1P2 slope in the range 60-100 dB can not be determined because the linearity only was reached in the range 60-80 dB. Mean values before and after treatment were to glycine of 167 micromol/L, and 202 micromol/L, to cortisol of 527.5 and 457.0, to prolactin of 310.7, and 283.0. Mean values before and after therapy to tinnitus questionnaires were to THI of 45.7, and 43.0; to TRQ of 22.0, and 21.5. All these values without significance statistics.

Discussion: More patients in the study, other doses of glycine, other times of treatment, as well as other inhibitory neurotransmitters (taurine), can be used, to get statistic significance in all measures.

Conclusion: Oral glycine attenuates cortical activity in tinnitus patients, decreases stress hormones, but not improves tinnitus questionnaires.

Reference:

1. O'Neill BV, Croft RJ, Leung S, Oliver Ch, Phan KL, Nathan PJ. High-dose glycine inhibits the loudness dependence of the auditory evoked potential (LDAEP) in healthy humans. *Psychopharmacol* 2007;195:85-93.

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WINE AND HISTAMINE IN TINNITUS

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Introduction: Histamine is a neurotransmitter related to tinnitus (1), and food intolerance (2). Wine can contain natural histamine. The current study put in relationship, the intake of white wine, without and with natural histamine, and tinnitus.

Material and methods: Fifteen patients with tinnitus (3 female and 12 males, mean age of 47.1 years old) took a dose of 2cc of white wine/kg of body weight. White wine (15° alcohol) without histamine (<0.05 mg/l, trade mark: fino tio mateo) and white wine (15° alcohol) with histamine (9 mg/l, trade mark: manzanilla la alegría). A questionnaire about food intolerance (3) was filled before the study and after the intake of each white wine, as well as a VAS - Visual Analogical Scale (0-10) about tinnitus annoyance.

Results: The values of the food intolerance questionnaire were: before study, 199.2 points; after white wine without histamine, 180.1 (improvement of 9.6%); and after white wine with histamine 182.0 (improvement of 8.6%). The values of VAS were: before study, 7.9; after white wine without histamine, 7.0 (improvement of 11.4%); and after white wine with histamine, 6.6 (improvement of 16.5%). All theses values without statistic significance.

Discussion: It could be interesting to increase the number of patients, to test other types of doses of wine, other sort of wines (red), and other doses of histamine in wines, to know if the inhibitory effect on tinnitus could be enhanced.

Conclusions:

1. Both white wines (15° alcohol) improved the punctuation of both, food intolerance questionnaire and VAS.
2. Natural histamine of white wine improved lightly VAS, comparing to white wine without histamine, but not improved the food intolerance questionnaire.

(This summary has been done with the results of ten patients, because the study has yet not finalized).

References:

1. Lopez-Gonzalez MA, Moliner-Peir F, Alfaro-Garcia J, Esteban F. Sulpiride plus hydroxyzine decrease tinnitus perception. *Auris Nasus Larynx* 2007;34:23-27.
2. Maintz L, Novak N. Histamine and histamine intolerance. *Am J Clin Nutr* 2007;85:1185-96.
3. Lopez-Gonzalez MA, Esteban F. Tinnitus as a signal of distress. Sevilla, Spain, 2010, ISBN-13: 978-84-692-3367-2.

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TREATMENT OF TINNITUS IN HYPERTENSIVE PATIENTS

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Tinnitus is a signalling symptom, a kind of a SOS message informing the organism about an ongoing pathological

process. Prevalence of tinnitus among population is quite significant, that yet shows a growing tendency. Cardiovascular diseases and atherosclerosis are specifically the ones that are under major scrutiny.

The purpose of our research lies in the investigation of preductal (trimetazidin) effect on the intensity of tinnitus in hypertensive patients.

The examined 40 hypertensive patients have been complaining of tinnitus, hearing loss. Moreover, some of them had even vertigo complaints. As for the nature of tinnitus, the examined 24 patients used to specify it being constant, the other 11 characterised it as being pulsing and another 4 -intermittent. The prevailing majority of patients would point out high frequency noise comparable with whistle. There were also some rarely down parallels between tinnitus and the car engine noise.

The examination of hearing function included otoscopy, tuning fork testing, pure tone audiometry, impedance testing, and speech discrimination. The implemented methods allowed us to diagnose first stage sensorinural hearing loss revealed in 3 patients, 2nd stage- in 22 and 3rd in 15 patients.

Apart from the subjective estimation of tinnitus, we have also implemented electroacoustic examination. The spectrogram of noise in the majority of cases corresponded to 4000Hz and 8000 HZ tones.

All the patients were divided into 2 groups; 20 patients in each. The patients of the control group were prescribed a traditional course of the conservative treatment of sensorinural hearing loss, including Tanakan, Betaserk, Gliatilin, and Levokarnitin. Patients of the main group, except the traditional treatment, Preduktal (trimetazidin) was prescribed, which is known as an antiischemic and antianginal drug, reinforcing the metabolism of glucose, increasing the formation of adenosintriphosphoric acid, improving reducibility of myocardium, and being the drug of choice for all patients with ischemic disease of heart.

Effectiveness of treatment was estimated on the grounds of both subjective and objective criteria on 10th, 20th and 30th day of the treatment. All those 20 patients, who had received preductal, were without exception noted to experience reduction of intensity of tinnitus on 10th day of the treatment, on 20th day 14 of them have shown hearing improvement, changing of frequency of tinnitus. On 30th day of treatment in 17 patients' tinnitus was completely interrupted. In 3 patients tinnitus significantly decreased. In those 3 patients the spectrogram of noise corresponded to 500Hz tone. All patients of main group have noted hearing improvement, speech understanding. However, thresholds of air conduction decreased in 20-25dB only in low frequency sounds.

The Patients of the control group also noted a positive change on 30-th day of the examination reflected in the reduction of intensity and improvement in hearing. However, the noise was noted to be completely ceased only in 4 patients.

The concluded results testify the efficiency pathogenetically substantiated therapy in the treatment of tinnitus in the hypertensive patients.

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Specialized neuro-/otologist

History

Self-performed questionnaires

- Tinnitus Handicap Inventory
- Tinnitus Questionnaire
- Case History Questionnaire
- Tinnitus Severity Grading (E.Biesinger)

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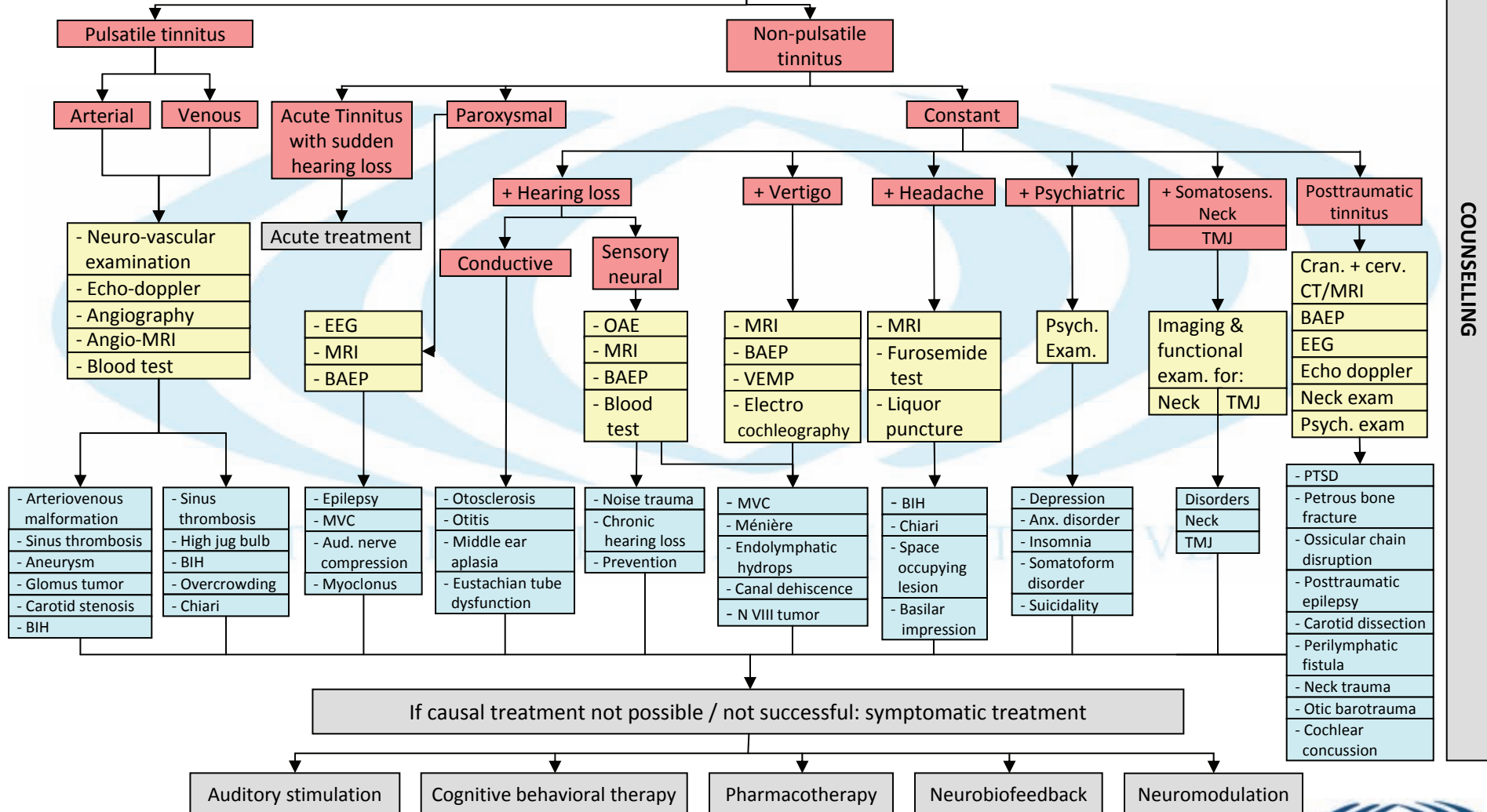
Clinical examination

- Otoscopy
- Cranio-mandibular & neck examination
- Auscultations

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Audiological measurements

- Audiometry
- Tinnitus matching
- Loudness Discomfort Level
- Tympanometry
- Tubal-impedance-manometry



COUNSELLING

