3rd Tinnitus Research Initiative Meeting

From Clinical Practice to Basic Neuroscience and back

An International Conference on Tinnitus

June 24 - 26, 2009, Stresa, Italy

Program and Abstract Book

Program
and
Abstract Book

3rd Tinnitus Research Initiative Meeting

From Clinical Practice to Basic Neuroscience and back
An International Conference on Tinnitus

June 24-26, 2009, Stresa Italy

Organizing Office

Fondazione Ascolta e Vivi
Via V. Foppa, 15
20144 Milan, Italy
Phone 0039 0 2 72001824
E-Mail info@faev.org

Scientific Office

Tinnitus Research Initiative
University of Regensburg
Bezirksklinikum
Universitaetsstrasse 84
93053 Regensburg, Germany
Phone 0049 941 941 2096
Fax 0049 941 2025
E-Mail info@tinnitusresearch.org
www.tinnitusresearch.org

The organizers wish to express their thanks to all the persons helping in the organization of the 3rd TRI Meeting, especially Chiara Merlano, Cristina Mambretti, Sylvia Dorner-Mitschke and Susanne Staudinger.

TABLE OF CONTENTS

OVERVIEW SCIENTIFIC PROGRAM

	June 23rd	June 24th			June 25th			June 26th	
08:30 - 09:15		KEYNOTE: **Pain & Tinnitus: Similarities and Differences** Herta Flor			KEYNOTE: **Central Auditory System Correlates of Tinnitus and Hyperacusis** Jos Eggermont			KEYNOTE**: Tinnitus and Nonauditory Brain Areas** Pawel Jastreboff	
09:15 - 10:00		KEYNOTE: **Pharmacologic Targets for the Treatment of Pain and Tinnitus** Theo Meert			KEYNOTE: **The Medial Olivocochlear System & Protection from Acoustic Trauma** Ana Belén Elgoyhen			KEYNOTE: **A Heuristic Pathophysiological Model of Tinnitus** Dirk De Ridder	
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------									
10:30 - 12:15		**Hearing Aids & Tinnitus Devices for passive auditory stimulation** L. Del Bo	**Genetics of Tinnitus** A. Martini	**Neuroimaging / MRI** J. Melcher / M. Landgrebe	**Auditory Stimulation** A. Norena / L. Roberts	**Targets for Pharmaco-logic Interventions** A.B. Elgoyhen / M. Mulheran	**Tinnitus Assessment** R. Tyler	**Audiological Assessment** G. Searchfield	**Tinnitus: A Network Approach** W. Schlee / N. Weisz
-------Poster Session----------LUNCH (1h30)----------Poster Session----------LUNCH (1h30)---------- Poster Session-------									
13:45 - 15:30		**Hyperacusis** C. Herraiz / L. Del Bo	**Animal Models** R. Salvi	**Neuro-imaging EEG/MEG** N. Weisz	**Specific Forms of Tinnitus** A. Londero / T. Kleinjung	**Neuroplasticity Cellular mechanisms of Tinnitus** T. Tzounopoulos	**Pharmaco-logic Treatment of Tinnitus** J.M. Lainez / B. Langguth	**Tinnitus and Tinnitus Related Disorders** P. Jastreboff / G. Hajak	**Clinical Practice and Basic Neuroscience of Somato-sensory Tinnitus** T. Sanchez
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------									
16:00 - 18:00		**Auditory Training** G. Searchfield / L. Roberts	**Auditory System Neuro-physiology** A. Norena	**Neuro-stimulation** D. De Ridder / B. Langguth	**Non Conventional Approach** M. Mazzoli / E. Biesinger	**Strategies for Tinnitus Research** A. Møller	**Cochlear Stimulation** P. van de Heyning / R. Tyler	PLENUM: **Flowchart for the Clinical Management of Tinnitus**	
18:00 - 19:00					**TRI : An international Research Organisation** Open Meeting				
19:00 - 20:00	OPENING LECTURE: **Tinnitus: Present & Future** Aage Møller								
20:30	*Welcome Cocktail*				*GALA DINNER*				

DETAILED SCIENTIFIC PROGRAM

Wednesday, June 24th

08:30 - 09:15	**KEYNOTE: Herta Flor : Pain & Tinnitus: Similarities and Differences**		
09:15 - 10:00	**KEYNOTE: Theo Meert: Pharmacologic Targets for the Treatment of Pain and Tinnitus**		
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------			
10:30 - 12:15	**Hearing Aids & Tinnitus Devices for passive auditory stimulation** L. Del Bo **E. Biesinger** The Vibrant Sound Bridge - Amplification of the high frequencies and its effects on tinnitus **O. Dyrlund:** Acoustic environment classification technology for optimizing tinnitus sound therapy **E. Viirre:** The rationale of CST Stimulation **A. Norena:** The theory ot the auditory stimulation **R. Tyler:** A review of noise and music maskers **G. Searchfield:** High-fidelity amplification as a tinnitus management tool **A. Paglialonga:** The passive auditory stimulation workgroup presentation	**Genetics of Tinnitus** A. Martini **A. Martini:** Genetics of Tinnitus: What we know about **M. Pawelczyk:** Genetic factors for tinnitus and noise-induced hearing loss: are they different? **D. Stephens:** Psychosocial aspects of hereditary tinnitus **M. Knipper:** Trauma-induced alteration of activity-dependent genes in the auditory system: implications for tinnitus perception and auditory plasticity	**Neuroimaging/MRI** J. Melcher / M. Landgrebe **S. Kovacs:** Tonotopic changes in the auditory cortex in unilateral tinnitus patients: a fMRI study **M. Landgrebe:** Structural brain changes in tinnitus: Grey matter decrease in auditory and non-auditory brain areas **C. Lanting:** Somatosensory input to the auditory pathway in humans, an fMRI Study **J. Gu:** Auditory evoked potentials and FMRI in people with tinnitus and reduced tolerance of high-level sound
-------Poster Session----------LUNCH (1h30)----------Poster Session----------LUNCH (1h30)---------- Poster Session-------			
13:45 - 15:30	**Hyperacusis** C. Herraiz / L. Del Bo **C. Herraiz:** Hyperacusis: An overview **O. Wagenaar:** A cognitive model of tinnitus and hyperacusis **V. Ghulyan-Bedikian:** Hearing aids for hyperacusis sufferers with normal hearing **A. Berthold:** The significance of self asessment instruments in the diagnosos of hyperacusis: comparison of the german hyperacusis-questionnaire (GÜF) and the french hyperacusis-questionnaire (HQ)	**Animal Models** R. Salvi **R. Salvi:** Animal models-Insights and speculations relevant to human tinnitus **E. Lobarinas:** Update on the Gap Prepulse Inhibition of the Acoustic Startle Animal Model of Tinnitus and Treatment **M. Ralli:** Comparison of salicylate and quinine-induced tinnitus in rats using the acoustic startle reflex **L. Chen:** Impaired functions of gabaergic neurons in salycilate-induced tinnitus **A. Norena:** Auditory cortex changes in awake guinea pig after salicylate administration and noise trauma	**Neuroimaging EEG/MEG** N. Weisz **N. Weisz:** The Good and the Bad Vibrations - Tinnitus and Neuronal Oscillations **D. Reato:** Modulation of carbachol-evoked gamma activity in vitro with low-amplitude AC electric fields **M. Plazier:** The neural correlates of acute and chronic tinnitus **E. van der Loo:** Neural correlates related to the autonomous nervous system (ANS) in tinnitus distress **S. Vanneste:** Neural correlates of distress in tinnitus
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------			
16:00 - 18:00	**Auditory Training** G. Searchfield / L. Roberts **D. Hall:** Assessing the potential benefits from auditory perceptual training: deriving appropriate and testable hypotheses from physiological models of tinnitus **G. Searchfield:** Perceptual training for tinnitus management **L. Roberts**: Induction of neural plasticity by auditory training **D. Bosnyak:** Electrophysiological assessment of training outcomes using simultaneously evoked transient and steady-state responses **I. Viaud-Delmon:** Virtual reality for tinnitus rehabilitation **C. Herraiz:** Auditory discrimination training (ADT) for tinnitus treatment	**Auditory System Neurophysiology** A. Norena **A. Norena:** The long road to the neuroscience of tinnitus **M. Mulheran:** Characterisation of anomalous temporal discharge patterns in normal guinea pig cochlear nerve fibres **D. Robertson:** Changes in neural activity and gene expression in central nuclei after restricted unilateral cochlear lesions **J. Melcher:** A model for tinnitus generation based in the ventral, not dorsal, cochlear nucleus **H. Okamoto**: Attentional Effects on excitatory and inhibitory neural activity in the human auditory cortex	**Neurostimulation** D. De Ridder / B. Langguth **T. Sanchez:** Clinical and neuroimaging outcomes of the efficiacy of transcranial magnetic stimulation in patients with tinnitus and normal hearing **A. Londero:** Navigated rTMS for the treatment of tinnitus: assessment by AEPs and fMRI **A. Cacace:** Potential artifacts introduced in tinnitus studies using repetitive transcranial magnetic stimulation (rTMS) **A.S. Giani:** Treating tinnitus with TMS: theta burst stimulation and the relief of auditory phantom perceptions **G. Frank:** Which tinnitus patients benefit from rTMS? **E. Khedr:** One-year follow up of patients with chronic tinnitus treated with left temporoparietal rTMS

Thursday, June 25th

08:30 - 09:15	**KEYNOTE: Jos Eggermont: Central Auditory System Correlates of Tinnitus and Hyperacusis**		
09:15 - 10:00	**KEYNOTE: Ana Belén Elgoyhen: The Medial Olivocochlear System & Protection from Acoustic Trauma**		
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------			
10:30 - 12:15	**Auditory Stimulation** A. Norena/ L. Roberts **H. Stracke:** New music therapy for tinnitus patients based on lateral inhibition **P.A. Tass:** Long-lasting tinnitus relief achieved by acoustic coordinated reset stimulation **H. Nagashino:** Inhibition of oscillation in a computational model for tinnitus and its management by sound therapy **K.M. Heijneman:** A double-blind cross-over study to evaluate the effect of phase-shift sound therapy on tonal tinnitus **A. Norena:** Recovery after a noise trauma	**Targets for Pharmacologic Interventions** A.B. Elgoyhen / M. Mulheran **A. Fryatt:** Voltage-gated sodium channel expression in rat spiral ganglion neurons **T. Nakagawa:** Relief from peripheral tinnitus: sustained delivery of lidocaine into cochlea using PLGA microparticles **G. Parsons:** Effects of neramexane on inotropic a9a10 nicotinic receptors and human NMDA (NR1A/2A) - relevance for tinnitus	**Tinnitus Assessment** R. Tyler **R. Cima:** The tinnitus disability index: a novel measure for tinnitus-related disability **R. Figueiredo:** Analysis of the correlation between audiometirc thresholds, psycho-acoustic measures and validated questionnaires in tinnitus patients **R. Görtelmeyer:** Measuring tinnitus: a re-evaluation fo the dimensionality and congruent validity of the 12 items Tinnitus Handicap Inventory **A.V. Oliveira:** Tinnitus handicap inventory's relationship with sociodemographic aspects **G. Attanasio:** Sleep disturbance in chronic tinnitus patients **S. Vanneste:** Non-linear relationship for tinnitus between the intensity and the distress
-------Poster Session----------LUNCH (1h30)----------Poster Session----------LUNCH (1h30)---------- Poster Session-------			
13:45 - 15:30	**Specific Forms of Tinnitus** A. Londero / T. Kleinjung **S. Barozzi**: Paroxysmal positional vertigo and tinnitus **A. Londero**: Pulsatile tinnitus caused by dural arteriovenous shunts: effect of embolization on patient's quality of life **T. Sanchez**: Multidisciplinary evaluation of patients with tinnitus and complex auditory hallucinosis **R. Levine**: The somatosensory pulsatile tinnitus syndrome provides further support for the dorsal cochlear nucleus tinnitus hypothesis **T. Kleinjung:** The effect of middle ear surgery on tinnitus patients with conductive hearing loss **M. Ohki:** Idiopathic bilateral tinnitus concomitant to eye closure	**Neuroplasticity, Cellular Mechanisms of Tinnitus** T. Tzounopoulos **T. Tzounopoulos:** Mechanisms of synaptic plasticity in the auditory brainstem: plasticity-induced changes that could underlie tinnitus **D. Depireux:** Targeting and reducing noise trauma-induced tinnnitus in a rat model **M. Wehr:** Disruption of balanced cortical excitation and inhibition by acoustic trauma **W.H.A.M. Mulders:** Modulation hyperactivity in guinea pig inferior colliculus after acoustic trauma	**Pharmacologic Treatment of Tinnitus** J.M. Lainez / B. Langguth **M. Althaus:** Clinical development of new drugs for the treatment of tinnitus using the example of Neramexane **R. Figueiredo:** Effects of caffeine in tinnitus: preliminary data **I. Sziklai:** Tinnitus control by dopamine agonist pramipexole in presbycusis patients. A randomized, placebo-controlles, double-blind study **P. Enrico:** Antioxidants, minerals, vitamins, and herbal remedies in tinnitus therapy. An update. **C. Hoekstra:** Anticonvulsants for chronic tinnitus, a systematic review **T. Sakamoto:** Treatment of noise induced hearing loss by stealth-type nanoparticles encapsulating betamethasone phosphate
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------			
16:00 - 18:00	**Non Conventional Approach** M. Mazzoli / E. Biesinger **G. Attanasio:** Mindfulness based Tinnitus Treatment **E. Biesinger:** The effect of Qi Gong on somatosensoric tinnitus (**SST)** **M. Lopez-Gonzalez:** New diet for tinnitus: adenosine diet **M. Mazzoli:** Mindfulness based stress reduction (MBSR) intervention in tinnitus therapy **M. Savastano:** Low level laser therapy: tinnitus subjective characteristics and mesurements. Preliminary report **Z. Shemesh:** The non responder patients before they receive the accelerators	**Strategies for Tinnitus Research** A. Møller **S. Mitchell:** American Tinnitus Association - Roadmap for a Cure **P. Ciccarese:** Tinnitusbook: a proposal for an advanced scientific web community for tinnitus research **R. Goodey:** Learning from the literature **F. Zeman:** Tinnitus-Subtyping by establishing the TRI data base **B. Langguth:** TRI - together for a cure **D. Passali:** Survey study on tinnitus in the world **D. Goldman:** RNID - working towards a cure	**Cochlear Stimulation** P. van de Heyning / R. Tyler **R. Tyler:** Electrical stimulation of the cochlea to reduce tinnitus **Y. Cazals**: Cortical plasticity after unilateral deafness and electrical cochlear stmulation: a study in guinea pigs **R. Levine:** Continuous auricular electronical stimulation for tinnitus: an update **B. Frachet:** Cochlear implant and tinnitus Tinnelec device for tinnitus reduction **P. van de Heyning:** Electrical promontory stimulation and cochlear implantation for the treatment of tinnitus in single sided deafness
18:00 - 19:00	**TRI: An international Research Organisation - Open Meeting**		
20:30	*Gala Dinner*		

Friday, June 26th		
8:30 - 9:15	**KEYNOTE: Pawel Jastreboff: Tinnitus and Nonauditory Brain Areas**	
09:15 - 10:00	**KEYNOTE: Dirk De Ridder: A Heuristic Pathophysiological Model of Tinnitus**	
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------		
10:30 - 12:15	**Audiological Assessment** G. Searchfield **P. Gander:** The 40-hz auditory steady-state response in tinnitus and residual inhibition: effect of centre frequency of masking and probe sounds **E. de Kleine:** Wavelet analysis of contralateral suppression of otoacoustic emissions in tinnitus patients **L. Parra:** Spectral profil of tinnitus can be predicted from high-resolution audiogram and dpoae for a subset of subjects **I.M. Knudson:** Auditory peripheral dysfunction in tinnitus subjects with normal audiograms	**Tinnitus: A Network Approach** W. Schlee / N. Weisz **N. Weisz:** The relevance of short range and long range synchrony in the formation of the tinnitus network **W. Schlee:** Neuromagnetic Evidence for a Global Network of Tinnitus Perception **E. Diesch:** Interaction among steady-stat response components: enhancement in tinnitus patients, suppression in controls **M. Congedo:** Connectivity of group independent components; **D. Langers:** Functional interactions between auditory and limbic brain centers during sound perception and rest **V. Mattei:** Cortical functional connectivity at rest in tinnitus patients
-------Poster Session----------LUNCH (1h30)----------Poster Session----------LUNCH (1h30)---------- Poster Session------		
13:45 - 15:30	**Tinnitus and Tinnitus Related Disorders** P. Jastreboff / G. Hajak **P. Jastreboff:** Tinnitus and Hyperacusis **M. Landgrebe:** Tinnitus and somatoform disorders **B. Langguth:** Tinnitus and affective disorders **G. Hajak:** Tinnitus and sleep **J.M. Lainez:** Tinnitus and headache	**Clinical Practice and Basic Neuroscience of Somatosensory Tinnitus** T. Sanchez **C. Herraiz:** The Clinical Profile of the Patient with Somatosensory Tinnitus **S. Shore:** What the animal research has clarified in SS tinnitus **R. Salvi:** What the neuroimaging has demonstrated in somatosensoric tinnitus **T. Sanchez:** The present and future options for treating somatosensory tinnitus
----------Coffee Break (30 min)----------Coffee Break (30 min)----------Coffee Break (30 min)----------		
16:00 - 18:00	**Flowchart for the Clinical Management of Tinnitus** PLENUM	

Poster Presentations

June 24, 2009

Audiology (G. Searchfield)	
G. Baracca	Customized sound therapy for tinnitus: clinical testing
S. Bertet	Definition of a procedure for creating a synthetic tinnitus auditory image
A.C. Binetti	Tinnitus: residual inhibition in comparison with subjective evaluation and hyperacusis
S. Djokovic	Importance of the TEOAE in total diagnostics noise in ear
L. Parra (X. Zhou)	Perception thresholds of pure tone in notched noise correlate with generator component of distortion product oto-acoustic emissions
J. Smurzynski	Extended high frequency audiometry and distortion product otoacoustic emission in normal-hearing patients with unilateral tinnitus
K. Wise	Auditory attention, hearing and tinnitus
Neurobiology (A. Norena)	
S. Carmona	Median and long latency auditory evoked potentials in auditory processing disorder
M. Chrostowski	Oscillatory activity and tinnitus: a computational model
Z. Kapoula	Abnormalities of saccades, vergence, pursuit, optokinetic nystagmus and fixation in five subjects with tinnitus
Z. Kapoula	Postural instability in patients with highly modulated tinnitus: evidence for abnormal sensorimotor interaction
A. Norena	Neuronal correlate of a transient phantom auditory perception in the auditory cortex of the awake guinea pig
Epidemiology (C. Coelho)	
A.C. Binetti	Statistical study of a group of 174 patients suffering tinnitus in Buenos Aires city
S. Djokovic	Impact of etiological factors on the appearance of certain types of tinnitus
S. Forti	Does tinnitus exist in normal hearing patients?
G. Goebel	Profile of the German Tinnitus League (DTL): characteristics of the members compared with epidemiological dates
M. Landgrebe	Association of tinnitus and electromagnetic hypersensitivity: hints for a shared pathophysiology?
O. Meeus	The use of transcranial magnetic stimulation (TMS) in modulation of pure tone and narrow band noise tinnitus
O. Meeus	Correlation between hyperacusis measurements in tinnitus patients
V. Vielsmeier	Tinnitus and temporomandibular disorders - assessment of tinnitus in 600 consecutive patients presenting with TMJ complaints in a specialized university department

June 25, 2009

Treatment 1 (A. Londero)	
A. Crocetti	Neurofeedback training for tinnitus: An update
E. Frank	Pharmacological enhancement of low-frequency rTMS in tinnitus treatment by dopaminergic drugs
R. Guerrero	Electrical stimulation and silence therapy for chronic bilateral tinnitus - case study
E. Khedr	A comparative study: Contralateral versus ipsilateral rTMS of temproparietal cortex for the treatment of chronic tinnitus
I. Lorenz	The short-term impact of different rTMS parameters on tinnitus
M.S. Park	Transcutaneous electrical stimulation on pinna and mysofascial trigger points for relief of tinnitus
Audiological Treatment (C. Herraiz)	
P. Davis	Effects of severe unilateral hearing loss on tinnitus rehabilitation
L. Del Bo	Is the sound generator volume control needed for sound therapy with hearing instrument combination device?
H. Stracke	Notched-music training for chronic tonal tinnitus
M.-W. Suh	Specific Effects and Prognostic Factors of Hearing Aids on Tinnitus
D. Tavora-Vieira	Acoustic stimulation in tinnitus treatment for patients with significant level of hearing loss
P. van de Heyning	QEEG changes of the auditory cortex following cochlear implantation tinnitus in single sided deafness (SSD)
O. Meeus	Phase out treatment in pure tone and narrow band noise tinnitus patients

Others (E. Biesinger)	
S. Carmona	Audiologic and vestibular symptons in fabry disease, clinical presentation and possible site of the lesions
P. Giannini	Sleep complaints in suffereres tinnitus small patients
G. Goebel	Website of the European Federation of Tinnitus Associations (EUTI): Characteristics of the tinnitus related distress in 15 different languages of the Tinnitus-Questionnaire (MINI-TQ12)
B. Langguth	Consensus for tinnitus patient assessment and treatment outcome measurement
V. Vielsmeier	Treatment of tinnitus in a multidisciplinary clinic
P. Winkler	Early patient experience with the TIPA tinnitus device

June 26, 2009

Treatment 2 (A.B. Elgoyhen)	
R. Horie	Hydrogen protects auditory hair cells from free radicals in vivo
J. Kaltenbach	Effects of neramexane on tinnitus-related hyperactivity in the dorsal cochlear nucleus
K. Kobayashi	Application of PDA to tinnitus treatment
L. Lagemann	Preventing chronic tinnitus - music therapy for patients suffering from idiopathic sudden sensorineural hearing loss
R. Vergara	Tinnitus treatment with amitriptiline: special modality and timetable
Imaging (N. Weisz)	
L. Geven	Pet imaging for cortical hyperactivity in Tinnitus patients: interim analysis
S. Kovacs	Tonotopic changes in the auditory cortex in unilateral tinnitus patients: a fMRI study
M. Plazier	Neural differences between pure tone and noise-like tinnitus
M. Plazier	Unilateral perception of tinnitus and bilateral perception of tinnitus: preliminary results on the neural correlates
M. Plazier	Visual analogue scale (VAS) for tinnitus intensity and its repercussions on the neural network
S. Vanneste	Left-sided tinnitus compared to right-sided tinnitus: Is there a difference?
Somatosensory Tinnitus (T.G. Sanchez)	
C. Herraiz	Evaluation of Botulinum Toxin in the treatment of somatosensory tinnitus
C. Rocha	Efficacy of deactivation of myofascial trigger points in patients with both tinnitus and myofascial pain
T. Sanchez	Tender points can also evoke somatosensory modulation of tinnitus
T. Sanchez	Somatosensory modulation of tinnitus: a three-phase study from prevalence to treatment
M. Westcott	Somatosensory tinnitus and tonic tensor tympani syndrome (TTTS)

Posters of Oral Presentations

M. Althaus	Clinical development of new drugs for the treatment of tinnitus using the example of Neramexane
G. Attanasio	Tinnitusbook: a proposal for an advanced scientific web community for tinnitus research
R. Cima	The tinnitus disability index: a novel measure for tinnitus-related disability
R. Figueiredo	Analysis of the correlation between audiometirc thresholds, psycho-acoustic measures and validated questionnaires in tinnitus patients
R. Figueiredo	Effects of caffeine in tinnitus: preliminary data
R. Görtelmeyer	Measuring tinnitus: a re-evaluation of the dimensionality and congruent validity of the 12 items Tinnitus Handicap Inventory
D. Goldman	RNID - working towards a cure
M. Lopez-Gonzalez	New diet for tinnitus: adenosine diet
H. Okamoto	Attentional effects on excitatory and inhibitory neural activity in the human auditory cortex
L. Parra	Spectral profil of tinnitus can be predicted from high-resolution audiogram and DPOAE for a subset of subjects
G. Parsons	Effects of neramexane on inotropic a9a10 nicotinic receptors and human NMDA (NR1A/2A) - relevance for tinnitus
O. Wagenaar	A cognitive model of tinnitus and hyperacusis

Abstracts of Oral Presentations

TUESDAY
JUNE 23, 2009

19:00 - 20:00
Opening Lecture

TINNITUS: PRESENCE AND FUTURE

Aage R. Møller, Ph.D., D.Med.Sci.
University of Texas at Dallas, School of Behavioral and Brain Sciences, Richardson, Texas

Presently we are achieving great progress in understanding some of the pathologies that cause tinnitus. The focus on the nervous system in research and treatment has produced better treatment and opened up new areas of research in tinnitus. Morphological and physiological research regarding the interrelation between the somatosensory and auditory systems has already provided a better understanding of some forms of tinnitus. Exploring the role of plastic changes in tinnitus has been beneficial. Reversing “bad” plastic changes by electrical stimulation of specific structures of the brain has been used for treating several disorders for some time and it is now being explored for treatment of some forms of tinnitus. Recent years’ progress in understanding the role of the non-classical auditory pathways and the subcortical auditory route to the amygdala has helped explain some of the affective symptoms that are related to tinnitus.

In the future we can expect further benefit from the multidisciplinary approaches to research and treatment that has been in progress for some years to continue. Learning from other disorders will result in better understanding of what causes tinnitus. Considerable progress in understanding the pathology of many forms of tinnitus can be expected in the future from continuation of ongoing and new basic research projects. We should continue the search for new ways for reversing the ”bad” plastic changes that are involved in many forms of tinnitus. The use of sound treatment, electrical stimulation of the ear through cochlear implants, electrical stimulation of specific parts of the brain and the vagus nerve is already being explored and that should continue and be expanded with the goal of developing practical methods for treatment of patients. It is an obstacle, however, that so little is known about which parts of the CNS is pathologic and which parts display abnormal neural activity only because it receives abnormal input. Treatment of tinnitus patients and research on tinnitus in general are hampered by inability to distinguish between different forms of tinnitus. We need names for the different forms of tinnitus, some of which may be regarded as different diseases but with a common symptom: tinnitus.

The way a person perceives his/her tinnitus is important to consider in management of tinnitus. It is known that escapable and inescapable pain activates different parts of the pain pathways. Perhaps tinnitus that is perceived as being severe activates other parts of the CNS than less severe tinnitus. In the future, progress can be expected in understanding tinnitus from closed head injuries (including concussions) such as from falls, and other forms of accidents and from blast injuries caused by explosions. Will we finally get some reliable epidemiology?

Search for medications that can ameliorate tinnitus should continue in the path already of the past. The basis for all forms of treatment is naturally a better understanding of the pathophysiology of tinnitus, but serendipitous discoveries should not be ignored.

Understanding the role of neural plasticity in tinnitus will be important also in the future for development of effective treatments. Exploring the auditory system’s connections to other parts of the brain may reveal some unexplained features of tinnitus. So far little attention has been directed to the involvement of the autonomic system in tinnitus.

Thinking outside the box is still essential for success in research on tinnitus.

Better understanding of the pathology that causes symptoms such as hyperacusis that often accompany tinnitus may offer benefit in treatment and in research on disorders other than tinnitus. Search for an understanding of the pathologies such as misophonia and perhaps autism may benefit from knowledge and experience gained from studies of tinnitus.

While the goal for treatment of tinnitus should be eliminating the tinnitus, the value of reducing the tinnitus to a level where it is less burdensome should not be ignored. This does not mean that we should not give the patients hope for success in the treatment but unfulfilled goals will result in disappointment and search for other health professionals who may promise full relief.

WEDNESDAY
JUNE 24, 2009

8:30 - 10:00
Keynotes

8:30 - 9:15
PAIN AND TINNITUS: SIMILARITIES AND DIFFERENCES

Herta Flor
Department of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, Mannheim, Germany and University of Heidelberg, Germany

Tinnitus has often been viewed as a type of phantom sound and has been linked to the phenomenon of phantom limb pain. In this presentation pain and tinnitus will be contrasted on the neuroanatomical, neurophysiological and biobehavioral level.

Although there are similarities, there are also clear differences between pain and tinnitus, specifically on the behavioral level. We will discuss the implications of this comparison for the assessment and treatment of tinnitus.

9:15 - 10:00
PHARMACOLOGICAL TOOLS FOR THE TREATMENT OF PAIN AND TINNITUS: ANYTHING TO BE LEARNED FROM NEUROPATHIC PAIN RESEARCH?

Prof. Theo Meert, PhD, PhD
J&J PRD Neurosciences, B 2340 Beerse, Belgium

The aim of the presentation is to evaluate whether lessons can be learned from chronic and especially neuropathic pain research offering alternative treatment tools for tinnitus.

In general, damage of peripheral nerves by toxic agents (cytostatics, alcohol, viral infections, diabetis,..) or by insults / disruptions can lead to either a complete lost of function (as in some cases of complete neuropathy) or to symptoms of hyperalgesia and allodynia for different sensory modalities. These neuropathic pain syndromes are often explained in terms of ecthopic firing of the nerve endings, winding up based on NMDA mechanisms and peripheral and central sensitization; elements also observed to occur in tinnitus.

To study the basic mechanisms of neuropathic pain and to allow screening for novel treatment alternatives, multiple animal models have been developed. Some of these models will be discussed with special attention to variability in outcome measures and urgent need for standardization. Comparisons will be made to the tinnitus field.Also the use of non-neuropathic pain models (e.g. second phase formalin test) as a screening tool to predict activity against sensitization and possibly neuropathic pain syndromes is addressed.

With regard to drug treatment, current existing treatments for chronic pain, like tricyclic antidepressants, anticonvulsants and anti-epileptics but also opioids, are reviewed and discussed for their benefits in both neuropathic pain and tinnitus.

Additionally, the use of NMDA antagonists, channel blockers (NaV, Kv7, ...) and other treatment options to affect glutamatergic and GABA-ergic transmission are demonstrated in preclinical and clinical trials. Finally, some examples are given on growth factor (NGF, enovin, VEGF) interactions.

10:30 - 12:15
SYMPOSIUM
Hearing Aids and Tinnitus Devices for Passive Auditory Stimulation
Luca Del Bo

IS THE SOUND GENERATOR VOLUME CONTROL NEEDED FOR SOUND THERAPY WITH HEARING INSTRUMENT COMBINATION DEVICE?

Del Bo L. (1), Forti S. (2), Ambrosetti U. (2), Dyrlund O. (3)
(1) Fondazione Ascolta e Vivi, Milan, Italy; (2) Audiology Unit, Department of Scienze Chirurgiche Specialistiche, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e regina Elena, University of Milan, Italy; (3) GN Resound, Copenhagen, Denmark

Our previous studies demonstrated that new open ear combination prototype hearing instrument, was very useful in the tinnitus treatment. This instrument consists of an amplification part with advanced signal processing such as multi band wid e dynamic rage compression, digital feedback suppression and noise reduction, and an advanced sound generator part.

This combination has been chosen to obtain optimal compensation for the subjects hearing loss and provide the most effective sound enrichment for use in TRT. This prototype was been modified: the receiver was moved to the ear (RITE) and the volume control for noise generator was removed.

Aim of this study is to evaluate if the new prototype can deliver better results than the previous one.

20 tinnitus patients were randomly divided in two groups: the first group is using the original prototype, the second using the new modified one without volume control and with RITE. THI and VAS were administered at the beginning, and they will be administered after 3 and 6 months.

Our hypothesis is that the missing of volume control doesn't affect the sound treatment efficacy while the RITE can improve the outcomes.

THE VIBRANT SOUND BRIDGE® AMPLIFICATION OF THE HIGH FREQUENCIES AND ITS EFFECTS ON TINNITUS

E. Biesinger
ENT-Clinic 83278 Traunstein, Germany

There is an increasing evidence that enhancement of auditory input by the use of hearing aids can reduce tinnitus complaints. However due to technical reasons, sound amplification by hearing aids is limited by the high frequency range. Implantable devices such as the vibrant sound bridge allow amplification also for the high frequency range (10 000 Hz) and are therefore increasingly used for the treatment of hearing loss. In this study, since February 2007, 8 patients have got an

implantation of the Vibrant Soundbridge® (MED-EL), one patient bilateral, 7 patients unilateral.

All patients have high a frequency hearing loss and severe tinnitus and were fitted before with normal hearing aids. The results are investigated prospectively with a follow-up period of 2 years, using audiologic tests and for the tinnitus the Goebel-Hiller-Score, TBF-12 and VAS.

The results show a significant improvement of hearing concerning sound quality, hearing in background noise and tinnitus. In those patients who have shown residual inhibition, the tinnitus disappeared completely, after the device was activated. No complications due to the surgery have been observed.

High pitch tinnitus in combination with hearing loss in the high frequencies and residual inhibition is the perfect situation and indication for this partial implantable hearing aid.

TRI Grant EB 06 17, Sponsored by MED-EL

ACOUSTIC ENVIROMENT CLASSIFICATION TECHNOLOGY FOR OPTIMIZING TINNITUS SOUND THERAPHY

[1]Ole Dyrlund, [2]Luca Del Bo
[1]GNResound, Lautrupbjerg 9, DK2750 Ballerup Denmark, [2]Fondazione Ascolta e Vivi, Milan, Italy

Aims: 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 specifically to describe and evaluate the efficacy of the acoustic environment classification system controlling the sound generator level aiming to optimize the effect of the tinnitus sound therapy.

Methods and Results: The instrument consists of an amplification part with advanced signal processing such as multi band wide dynamic rage compression, digital feedback suppression and noise reduction, and an advanced sound generator part.

The 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 environmental steering is based on an environmental classification system which consider a number of acoustic factors 1) is there sound above an ambient level?, 2) is speech present?, 3) are other background noises present?, and 4) what are the levels of the sounds present?

The environmental steering feature utilizes the information from the classifier and ensured that the noise generator signal only applied in situations which are considered important for the effect of tinnitus sound therapy. The function of the environmental steering system will be described in detail and evaluation results of the from a multi center study with 40-45 tinnitus patients will be reported.

Conclusion: Based on comprehensive evaluation results, environmental classification technology seem to be valuable to optimize the effect of the tinnitus sound therapy.

THE RATIONALE OF CST STIMULATION

Erik Viirre M.D. Ph.D.
University of California, San Diego, Department of Neurosciences, Tinnitus Otosound Products, San Diego CA

Customized Sound Therapy (CST) is an FDA approved system of therapy for tinnitus using sound. The concept for CST arose from the observation that most chronic tinnitus (> 6 months) is a single sound. Patient directed sound matches for tinnitus sensations rarely are pure tones. Most patients suggest there is a “buzz” or a “hiss”, and yet the sound sensations have distinct center frequencies. Most center frequencies are in the range of 4 to 8 KHz. The most common sound sensation match is a center frequency with a narrow band noise (0.1% bandwidth). Perceptual threshold studies suggest that the bandwidth of a particular tonotopic pathway is on the order of 0.3% (Moore, 1997). Our approach to modeling and treating tinnitus has been that higher order auditory pathways involved in sound perception are over-active. Automatic gain control functions based on neural feedback occur in each tonotopic path all the way to thalamus and primary auditory cortex. Increased gain in a given tonotopic path would result in the percepts described above. Thus a potential approach to habituating activity related to tinnitus would be to affect the specific overactive path. Work with pure tones has shown them to be poor adaptation stimuli. Our insistence has been to produce a high fidelity replica of the tinnitus stimulus. This is then used as a habituation stimulus, not as a masking stimulus. The typical match with a narrow band of sound around the matched center frequency ensures that the particular overactive tonotopic pathway is encompassed in the envelope of the therapeutic stimulus. Note that many sounds, including white noise, amplified sounds and sounds with increased amplitude in the upper ranges will randomly provide some of the same stimulus, provided that the tinnitus frequency is in the sound envelope. However, the CST approach of creating a specific replica ensures that when the habituation stimulus is played, the offending tonotopic path is activated all the time. The CST workstation has been devised to enable audiologists to readily build a tinnitus replica, test it and provide it in a high-fidelity player to patients. Further, the sound player can include other sound stimuli, such as calming sounds to facilitate acceptance of the sound player by patients.

THE THEORY OF THE AUDITORY STIMULATION

A. Norena
**Université de Provence, CNRS UMR 6149, Marseille, France*

Tinnitus is associated, in the vast majority of cases, to a hearing loss. In this context, it has been hypothesized that hearing loss induces some changes in the auditory system which ultimately cause tinnitus. Two types of hypothesis have been proposed. 1) The peripheral damages, induced by a noise trauma for instance, cause the emergence of an aberrant neural activity at the auditory nerve level. This neural activity is then sent to the auditory centers where it will give rise to an auditory perception. This mechanism is somewhat similar to what happens when the auditory system is stimulated, i.e. peripheral excitation and processing by the centers of this increase in activity. 2) On the other hand, another view emphasizes that a hearing loss is associated to a decrease in neural activity at the auditory nerve level, which makes unlikely that the peripheral activity could be (directly) at the origin of tinnitus. This view is further corroborated by the fact that a section of the auditory nerve does not always abolish tinnitus. Nevertheless, the peripheral decrease of activity due to hearing loss has been shown to cause dramatic

central changes, which could be at the origin of tinnitus. While in the first model the peripheral aberrant neural activity should be blocked at the periphery, the second model suggests that the decrease in activity related to the hearing loss should be adequately compensated. Considering the second model more likely than the first one, we then have proposed to compensate for the decrease in sensory inputs related to the hearing loss. Several strategies can be used, depending on the level of hearing loss of the tinnitus subjects: acoustic stimulation and/or hearing aid, electric stimulation (extra-cochlear stimulation, cochlear implant).

A REVIEW OF NOISE AND MUSIC MASKERS

R. Tyler
Department of Otolaryngology, The University of Iowa, Iowa City, Iowa

Aims/Objectives: The aim is to review the literature on the different approaches and efficacy of different strategies of acoustic tinnitus masking.

Methods: The evolution of the use of noise, music and other acoustic stimuli to partially mask and totally mask tinnitus is reviewed. Studies attempting to quantify the effectiveness of maskers, particularly as an adjunct to counseling, will be reviewed.

Results: Several studies have suggested that maskers do not provide additional benefit to counseling alone. However, these studies are based on group data, and fail to consider that in some patients, tinnitus is made worse by noise. In addition, many of these studies utilize a noise with a focus on the 'mixing point', which is likely too intense for many patients. Other studies do show an added benefit of masking to counseling alone.

Conclusion: Many studies on the effectiveness of maskers have ignored individual differences among tinnitus patients. Clinical experience, supported by some studies, suggest that many individuals benefit from the use of maskers.

HI-FIDELITY AMPLIFICATION AS A TINNITUS MANAGEMENT TOOL

Grant D Searchfield PhD and Kei Kobayashi PhD
Audiology, School of Population Health, The University of Auckland

Modelling of the auditory system suggests that altered peripheral input to the central auditory system can lead to tinnitus perception.

Clinical evidence supports the use of hearing aids as part of a tinnitus management program. Although the underlying mechanism for hearing aid effects on tinnitus perception are unclear it appears that advances in hearing aid design have increased the success of hearing aids in the tinnitus role.

One key amplification parameter in reducing tinnitus may be bandwidth.

There are both technical and physiological limitations to provide "Hi-Fi" sound quality to hearing aid users with tinnitus.

The benefits, limitations and methods of high frequency amplification as a tinnitus management tool will be presented.

THE PASSIVE AUDITORY STIMULATION WORK GROUP

Alessia Paglialonga
Istituto di Ingegneria Biomedica, Consiglio Nazionale delle Ricerche, Politecnico di Milano, Piazza Leonardo da Vinci, 32, I-20133 Milano, Italy

Based on both theory and evidence that high-pitch auditory stimulation could induce neuroplasticity and reverse the neural correlates of tinnitus, the Passive Auditory Stimulation Work Group has launched, at the beginning of 2008, an International Project "Innovative auditory stimulation as enhancer of brain plasticity in tinnitus therapy", aimed at designing and evaluating, based on clinical trials, an innovative high-pitch passive auditory stimulation paradigm for tinnitus therapy.

A network of clinical sites is implementing a protocol that entails a three months auditory stimulation therapy treatment by means of an MP3-based ear level device. The test treatment includes a close-to-threshold high-pitch auditory stimulation therapy combined with an environmental relaxing sound. The control treatment is based on the sole environmental relaxing sound. An equal number of patients are recruited in the test and the control group.

An industrial partner, in close connection with the clinical participants, is developing an hearing aid that implements the high-pitch auditory stimulation.

Preliminary results will be presented and discussed.

10:30 - 12:15
SYMPOSIUM
Genetics of Tinnitus
Alessandro Martini

GENETICS OF TINNITUS: WHAT WE KNOW ABOUT

Alessandro Martini
Audiological Dept. Ferrara University, Italy

Tinnitus is a common condition but to date, few investigators have studied the influence of genetic factors on tinnitus. In a recent paper Hendrickx et al. (B-ENT. 2007) conducted a European multicentre study in which 198 families were recruited in seven European countries. The AA. reported a significant familial effect for tinnitus and concluded that this finding opens the door to specific studies that can determine whether this effect is due to a shared familial environment or the involvement of genetic factors. While several rare monogenic disorders have been described that are associated with tinnitus, the genetic underpinnings of the more common forms of the syndrome are still poorly understood. Hearing loss associated with tinnitus may help to differentiate different genetic causes (see Sadeghi et al., 2004 for Usher Syndrome and Matsunaga et al, 2004 for A1555G mitochondrial mutation). On the other hand a common genetic cause of tinnitus and depression was supposed and serotonin transporter gene SLC6A4 was reported as a potential candidate gene (Tyler RS, Coelho C, Noble W., 2006). We discuss here some data regarding the influence of gene mutations in tinnitus patients.

GENETIC FACTORS FOR TINNITUS AND NOISE-INDUCED HEARING LOSS: ARE THEY DIFFERENT?

Pawelczyk M.[1], Rajkowska E.[1], Dudarewicz A.[2], Van Laer L.[3], Fransen E.[3], Van Camp G.[3], Sliwinska-Kowalska M.[1,2]
[1]Department of Audiology and Phoniatrics, Institute of Occupational Medicine, Lodz, Poland, [2]Department of Physical Hazards, Institute of Occupational Medicine, Lodz, Poland, [3]Department of Medical Genetics, University of Antwerp, Antwerp, Belgium

Background: Tinnitus is a common condition marked by the auditory perception in the absence of an external source of sound. Several factors are known to influence tinnitus. The best documented are hearing loss, noise exposure, age, ototoxic drugs and hypertension. However, only certain individuals will develop tinnitus in the presence of the above mentioned risk factors. This individual susceptibility may be explained by genetic factors. Due to phenotypic heterogeneity and the variable penetrance of this condition genetic analysis are difficult to perform and received little attention up to now. One of the possible ways to assess individual susceptibility for the development of tinnitus is a candidate gene approach. Since tinnitus often occurs together with noise-induced hearing loss (NIHL), good candidate genes are previously described NIHL susceptibility genes.

Aim: To assess whether genetic variability in 10 potassium recycling pathway genes and in the Cadherin 23 gene are associated with tinnitus in subjects exposed to occupational noise.

Methods: The study group consisted of 626 noise exposed subjects (128 with tinnitus and 498 without). In total, 104 Single Nucleotide Polymorphisms (SNPs) were selected and genotyped. Subsequently statistical analysis (logistic regression with a correction for age and noise exposure level) was performed to investigate the genotype effects on tinnitus.

Results: We have found significant associations between tinnitus and some variants in KCNE1 and SLC12A2. These results hold promise as preliminary track to the identification of tinnitus susceptibility genes, but still need to be confirmed in other population, not exposed to noise.

PSYCHOSOCIAL ASPECTS OF HEREDITARY TINNITUS

Dafydd Stephens and Ilmari Pyykkö
Cardiff University, Wales & Tampere University, Finland

Aims: To investigate whether the psychosocial impact in people with tinnitus and a family history of tinnitus or hearing impairment differs from those without such a family history

Methods: Secondary analyses of two population studies; Direct approaches to patients with tinnitus; Secondary analysis of a survey of members of the Finnish Menière's Association.

Results: The results of the first two approaches have been published elsewhere1. The epidemiological studies showed that those with a family history were more likely to have tinnitus, to be more annoyed by it and to report that it had a greater impact on their lives. Direct questioning of patients, however, indicated fewer problems in those with role models, and a family history of tinnitus was more beneficial than one of hearing impairment. The identification of a clear role model is important.

Our latest study has involved 558 members of the Finnish Menière's Association. Tinnitus is a key symptom in the diagnosis of Menière's disorder. They were sent questionnaires about the symptoms, quality of life, activity limitations, participation restrictions and positive effects2. A family history of hearing or balance impairment in their siblings had no effect on either the presence or annoyance of the tinnitus, but a notable effect on its impact on their "Peace of Mind" resulting from the tinnitus. The family history group reported increased disturbance, particularly in those with more annoying tinnitus. Impacts on quality of life and positive experiences were more complicated and will be discussed.

Conclusions: The impact of a hereditary tinnitus is complicated and appears to be dependent on the population studied, in particular whether they have sought help for their symptom.

References: 1] Stephens D, Jones L. eds. The effects of genetic hearing impairment in the family. London, Whurr, 2006.

2] Stephens et al. Otol Neurotol 2007; 28: 982-987.

TRAUMA-INDUCED ALTERATION OF ACTIVITY-DEPENDENT GENES IN THE AUDITORY SYSTEM: IMPLICATIONS FOR TINNITUS PERCEPTION AND AUDITORY PLASTICITY

Singer W, Rüttiger L, Zuccotti A, Baur M, Reinbothe T, Panford-Walsh R, Köpschall I, Rohbock K, Zimmermann U, Knipper M
University of Tübingen, Department of Otorhinolaryngology, Hearing Research Center Tübingen, Molecular Neurobiology, Elfriede-Aulhorn-Straße 5 D-72076 Tübingen, German
Corresponding author: tel. +49 (0)7071-29 88244
fax +49 (0)7071-294950
e-mail Marlies.Knipper@uni-tuebingen.de

Aberrant neuronal activity, occurring during tinnitus, is known to lead to changes in neuronal plasticity. However, molecular changes following sensory trauma and the subsequent response of the central nervous system are only poorly understood. We focused on finding a molecular tool for monitoring the features of excitability, which occur in the auditory system following acoustic and ototoxic trauma. Of particular interest is the analysis of altered expression of activity-dependent genes in the peripheral and central auditory system, after various tinnitus-inducing paradigms. Activity-dependent genes are genes that alter their expression pattern during activity-induced changes in synaptic efficacy and plasticity.

In our rodent animal model, tinnitus was induced physiologically and pharmacologically by several traumata of different intensities, thereby allowing us to differentiate between animals which experience, and those, which do not experience, tinnitus. At different time points after trauma-induction, the expression of activity-dependent genes was analysed on mRNA and protein level in the cochlea, subcortical and cortical areas. We present here a summary of recent findings comparing and correlating expression of activity-dependent genes with tinnitus-behavior after different trauma paradigms. Moreover initial trials are done to pharmacologically reverse/influence changes in tinnitus behavior and in gene expression occurring after trauma, using local round window or systemic drug application. The data are discussed in the context of using activity-dependent genes to monitor trauma induced plasticity changes in the auditory system.

Supported by a grant from the Tinnitus Research Initiative, the Marie Curie Research Training Network CavNET MRTN-CT-2006-035367, Deutsche Forschungsgemeinschaft, grant DFG-En294/2-4 and the Hahn Stiftung (Index AG).

10:30 - 12:15
SYMPOSIUM
Neuroimaging/MRI
Jennifer Melcher / Michael Landgrebe

TONOTOPIC CHANGES IN THE AUDITORY CORTEX IN UNILATERAL TINNITUS PATIENTS: AN FMRI STUDY

S. Kovacs, D. De Ridder, R. Peeters, S. Sunaert
Department of Radiology, University Hospitals of the Catholic University Leuven, Herestraat 49, 3000 Leuven, Belgium

Previously, reduced fMRI activity was demonstrated in the auditory cortex (AC) of unilateral tinnitus patients. This was suggested to reflect plasticity effects within the AC (1). At present, our goal is to study the tonotopy of this plasticity effect in the AC by means of fMRI.

20 patients with unilateral tonal tinnitus (12 right- and 8 left-sided) and 20 healthy volunteers were scanned on a 3T MRI scanner. An EPI silent gap sequence was used during the stimulation paradigm. This paradigm consisted of a blocked design in which white noise filtered through either a narrow or a wide bandpass and tones were binaurally presented. The stimuli were either the tinnitus frequency experienced by the patients e.g. 800 0Hz (TF-session) or a different frequency e.g. 1000 Hz (OF-session). Healthy volunteers were stimulated with identical frequencies.

Significant fMRI activity was found bilaterally in the AC in both sessions for all subjects. In the AC, a higher fMRI activity for the OF-session than for the TF-session was shown. For the TF-session, a significant decrease of activity was found in the left AC for all patients. No such decrease was observed for the OF-session. The activity within either AC cannot be explained by sex, age, tinnitus side or tinnitus loudness. Moreover, the decreased fMRI activity in the TF session cannot be attributed to hearing loss, since no correlation was found between the decreased fMRI activity and dB loss on the TF. However, the fMRI activity in the left AC correlated significantly with the patient's total score on the TQ, intrusiveness and emotional plus cognitive distress subscores.

The decreased fMRI activity is a tonotopic effect in unilateral tinnitus patients, as we only find such a decrease for the TF-session. This study provides further support for the view of decreased fMRI activity as a reflection of plasticity effects within the AC of unilateral tinnitus patients.

1 Smits et al., Neuroradiology 2007;49(8):669-679

STRUCTURAL BRAIN CHANGES IN TINNITUS: GREY MATTER DECREASE IN AUDITORY AND NON-AUDITORY BRAIN AREAS

Michael Landgrebe*, Berthold Langguth, Katharina Rosengarth, Susanne Braun, Amelie Koch, Tobias Kleinjung[1], Arne May[2], Dirk De Ridder[3] and Goeran Hajak
Department of Psychiatry, Psychosomatic and Psychotherapy, University of Regensburg, Germany, [1]ENT Department, University of Regensburg, Germany, [2]Department of Systems Neuroscience, University of Hamburg, Germany, [3]Brain Research Center Antwerp for Innovative and Interdisciplinary Neuromodulation (BRAI[2]N), University of Antwerp

Tinnitus, the phantom perception of sound, is a frequent disorder that causes significant morbidity. The pathophysiological mechanisms involved in tinnitus gene ration are still under exploration. Electrophysiological and functional neuroimaging studies give increasing evidence for abnormal functioning both within the central auditory system and in non-auditory brain areas. However, observed changes show great variability, hence lacking a conclusive picture. Recently, structural alterations in the central nervous system have been detected in tinnitus patients by voxel-based morphometry (VBM).

Here we aimed to replicate these findings in an independent study sample. We performed structural MRI scans in 28 tinnitus patients with normal audiometry and used VBM to compare results with a control group, matched for age, sex and hearing status. As major results we found significant grey matter decreases in the tinnitus group in the right inferior colliculus and in the left hippocampus.

However, neither changes in the subcallosal area nor in the thalamus as described recently have been observed.

Our results underscore that (1.) VBM allows t o detect structural alterations in tinnitus patients, which seem to be related to tinnitus pathophysiology. (2.) Both, areas in the auditory and the limbic system are involved giving further evidence for the important role of the limbic system in the pathophysiology of tinnitus. (3.) Even groups with similar clinical characteristics might differ in the underlying neurobiological changes.

SOMATOSENSORY INPUT TO THE AUDITORY PATHWAY IN HUMANS, AN FMRI STUDY

Lanting C, de Kleine E, Eppinga E, van Dijk P
Department of Otorhinolaryngology / Head and Neck Surgery, University Medical Center Groningen, The Netherlands. Faculty of Medical Sciences, School of Behavioral and Cognitive Neurosciences, University of Groningen, The Netherlands

Aims: To identify the neural mechanisms that are responsible for somatic modulation of tinnitus, we measured the fMRI response to jaw protrusion, which in patients may lead to a perceptual change of their tinnitus.

Methods: 13 patients with tinnitus and 20 healthy controls were included in an fMRI experiment. All patients were able to modulate their tinnitus by performing jaw protrusion. Experiments were performed on a 3T Philips scanner, using sparse sampling (TR=10s). Experimental conditions consisted of bilateral broadband noise, jaw protrusion, the combination of both and a baseline condition. In addition to regression analysis, a region of interest analysis was performed to quantify responses to the experimental stimuli.

Results: The group analysis of the responses to sound showed activity in the auditory pathway, consisting of the

cochlear nucleus (CN), the inferior colliculus, the medial geniculate body, and the primary and secondary auditory cortex. Jaw protrusion involved the following structures: the cerebellum, the ventrolateral nucleus of the thalamus, the putamen, the motor cortex and the somatosensory cortex.

There were areas of overlapping activity between the auditory and somatic stimuli. The complete auditory pathway showed significant responses to jaw protrusion. In contrast, the somatosensory cortex only showed a response to jaw protrusion and not to sound stimuli. A difference between subject groups was found in the CN, where patients showed a larger response to protrusion than controls.

Conclusions: Somatosensory input to the auditory system can be measured throughout the auditory pathway in both tinnitus patients and healthy controls. Tinnitus patients show a larger response of the CN to jaw protrusion than controls indicating involvement of the CN in modulating their tinnitus. This suggests that the CN plays a key role in somatosensory modulation of tinnitus.

AUDITORY EVOKED POTENTIALS AND FMRI IN PEOPLE WITH TINNITUS AND REDUCED TOLERANCE OF HIGH-LEVEL SOUND

J. Gu, B. Hermann, R.A.Levine, J.R. Melcher
Massachusetts Eye and Ear Infirmary, Harvard-MIT Division of Health Sciences and Technology

Recently, we showed elevated fMRI activation in response to sound in the auditory pathway of people with tinnitus and the intolerance of high-level sound that often accompanies it [1]. We measured fMRI activation in tinnitus and non-tinnitus subjects with normal audiograms and quantified sound tolerance using loudness discomfort level and a questionnaire. Activation in midbrain and thalamus in creased with decreasing sound tolerance. Activation in primary auditory cortex (PAC) increased with diminished sound tolerance, with tinnitus, or both. fMRI identified specific, malfunctioning structures, but could not distinguish which of the many functionally distinct neurons within these structures operated abnormally. Auditory evoked potentials (AEPs) can help make this distinction since, unlike fMRI activation, AEPs specifically reflect activity in the subsets of neurons responding synchronously to the sound stimulus and with each other. We are measuring AEPs in the same subjects studied with fMRI to determine whether or not synchronously active neurons of the auditory pathway might contribute to the abnormally elevated responses to sound seen with fMRI.

To date, AEP testing has been performed in 3 tinnitus and 4 non-tinnitus subjects (binaural click stimulus, 3/s, 70 dB HL). The amplitude of wave V of the auditory brainstem response (vertex to left ear) and of cortically-generated P1/N1 (vertex, F3, F4 to left ear) was quantified.

Wave V amplitude increased with diminishing sound tolerance ($r = -0.8$, $p = 0.01$). While correlations between AEP amplitude and fMRI activation levels were not significant, P1/N1 amplitude tended to increase with increasing PAC activation ($r = 0.4 – 0.6$ depending on electrodes).

While preliminary, the results raise the possibility that neurons capable of conveying temporally synchronized activity play a role in tinnitus and intolerance of high-level sound.

[1] Gu J, Halpin C, Nam EC, Levine R, Melcher J. 2008; ARO Abstr 31:117.

[not attending]

FMRI STUDY OF PATIENTS SUFFERING FROM TINNITUS DURING STIMULATION USING INDIVIDUALLY RECONSTRUCTED TINNITUS SOUNDS

W. Delb(1), D. Wiebelt (1), C. Krick (2), D. Hecker (1), A. Rheinschmitt (1), C Lux-Wellenhof (1), PJ Jastreboff (3)
(1) Department of Experimental Audiology, University Hospital of Saarland, Homburg/Saar, Germany (2) Department of Neuroradiology, University Hospital of Saarland, Homburg/Saar, Germany (3) Department of Otolaryngology, Emory University, Atlanta, USA

Background: According to the neurophysiological model of tinnitus the development of tinnitus-related distress can be seen as the result of a learn ed association of the tinnitus related neuronal activity (tinnitus signal) and negative emotions. As a consequence the tinnitus signal continues to evoke negative reactions. As this effect should be specific to the patient's tinnitus, it is possible to expect that the brain regions activated by a sound similar to the patients individual tinnitus should differ from the brain regions activated by a different sound.

The aim of this study was to identify the brain structures involved in the development of tinnitus related distress.

Methods: 47 subjects were enrolled in the study. The patient's individual tinnitus was reconstructed using the technique of Norena et al. Functional MRI images were then obtained. Four stimulation conditions were applied in each patient; 1) the sound of individually reconstructed tinnitus (RTS), 2) the sound of tinnitus shifted towards lower frequencies by 1 1/2 octave, 3) a birds song 4) silence.

Results: Comparing the brain activation in response to RTS versus sound 2 a significant activation was found predominantly in the anterior cingulate cortex. A correlation analysis showed a highly significant correlation ($p<<0.001$) between brain activation (contrast between RTS and sound 2) in the anterior cingulate gyrus and tinnitus related distress.

Conclusion: Our study shows that the brain activation, as measured using fMRI, differs significantly when comparing RTS and sound 2. The difference in activation is most prominent in the anterior cingulate gyrus which is a part of the limbic system that seems to be involved in the processing of salient and unpleasant stimuli, and which is connected to other parts of the limbic system. Our results suggest that the anterior cingulate cortex might be a key structure in the processing of the tinnitus related signal and in the development of tinnitus distress.

13:45 - 15:30
SYMPOSIUM
Hyperacusis
Carlos Herraiz / Luca Del Bo

HYPERACUSIS: AN OVERVIEW

Carlos, Herraiz
MC PhD, Fundacion Hospital Alcorcon, Tinnitus Clinic. Department of Otorhinolaringology, Madrid, Spain

---

A COGNITIVE MODEL OF TINNITUS AND HYPERACUSIS

O. Wagenaar, M. Wieringa, J. Verschuure
Erasmus MC- University Medical Center Rotterdam, Netherlands

Aims: Presentation of a comprehensive neuro-psychological theory outlining a cognitive mechanism of tinnitus and hyperacusis.

Methods: We constructed a cognitive model of tinnitus and hyperacusis based on clinical data and scientific literature.

Results: A schematic model of functions and neuroanatomical localizations of Tinnitus and Hyperacusis in relation to central auditory processing (Bregman, 1990)will be shown. Literature, relevant to the model, will be discussed (i.e. Mühlau et al., 2006). New of this model is that we integrate these anatomical findings into a functional and cognitive mechanism.

Auditory perception is described in neuropsychological and cognitive terms with a strong focus on memory and attention and their role in Auditory Scene Analysis. Based on this model the mechanisms of tinnitus and hyperacusis can be explained as to have an adaptive function (plasticity) in patients with hearing loss. In contrast, in people with normal hearing tinnitus indicates a signalling function for treatable neuropsychological problems. As a consequence, tinnitus should be interpreted as a consequence of prior auditory or neuropsychological problems on which the focus of treatment should be placed, apart from the emotional/nervous reactions which causes only the chronicity of the phenomenon.

Conclusions: The model explains most forms of subjective tinnitus and hyperacusis and contributes to a better understanding of the pathogenesis of tinnitus. It also provides approaches for direct and indirect treatments on multidisciplinary levels.

References: 1. Bregman A.S. (1990). Auditory Scene Analysis: The perceptual organization of sound. Cambridge: MIT Press.

2. Mühlau M, Rauschecker JP, Oestreicher E, Gaser C, Röttinger M, Wohlschläger AM, Simon F, Etgen T, Conrad B, Sander. Structural brain changes in tinnitus. D.Cereb Cortex. 2006 Sep;16(9):1283-8.

HEARING AIDS FOR HYPERACUSIS SUFFERERS WITH NORMAL HEARING

V Ghulyan-Bedikian, S Pontet, P Coignac, F Paolino, M Paolino
IMERTA, Marseille, France

Aim: Our objective was to develop a structured auditory rehabilitation program allowing the hyperacusis patients with normal hearing to tolerate their sound environment while avoiding the permanent use of auditory protections. In this preliminary study we tested to see if our method could decrease the patients' auditory hypersensitivity.

Method: The "Velocity 24" hearing aid (SONIC) with a high compression level was used in association with a closed earmold. Two rehabilitation programs were created: the "principal program" (P1) was to be used throughout the study and the "maximum protection program" for an occasional use when the P1 would be insufficient to tolerate the sound environment. Six males (28-37 years old) with normal hearing who had consulted our Tinnitus Centre for a hyperacusis as their primary complaint participated in this study. At the start of the study, the hearing aid and the earmold were adapted for each patient. The patients were instructed to carry the device as often as possible. The sound compression was decreased progressively during the patient's weekly visits. So the minimal exit level was increased by 1-3dB at each visit. Two audiometries were performed (with headphones and free-field) to evaluate auditory thresholds and LDLs. A Hyperacusis Questionnaire (HQ) and a Sound Perception Scale (SPS) were also given to the patients before and after the 2 month experimentation period.

Results: At the start all the patients had low LDLs ranging from 35dB to 70dB. After 2 months therapy the Wilcoxon test showed a significant improvement of LDLs increasing up to 25 dB ($p<0.05$), especially for acute frequencies and in patients with moderate hyperacusis. The SPS was close to the normal although the HQ changes were not significant.

Conclusion: Our preliminary results show that this auditory rehabilitation program is promising for LDL improvement. Accompanied by counselling it could be helpful for hyperacusis sufferers.

THE SIGNIFICANCE OF SELF ASSESSMENT INSTRUMENTS IN THE DIAGNOSIS OF HYPERACUSIS: COMPARISON OF THE GERMAN HYPERACUSIS-QUESTIONNAIRE (GÜF) AND THE FRENCH HYPERACUSIS-QUESTIONNAIRE (HQ)

A. Berthold[(1)], G. Goebel[(2)], U. Floetzinger[(2)]
[(1)]Medical-Psychosomatic-Clinic Bad Arolsen, Germany, [(2)]Medical-Psychosomatic-Clinic Roseneck, Prien, Germany

Background: Hyperacusis is a condition that has not been sufficiently researched in terms of its symptomatology, diagnosis and therapy. The present study is designed to contribute to an improvement in the diagnosis of noise hypersensitivity by means of self assessment instruments, as well as improving concomitant research into hyperacusis therapy. Previous publications on the condition of hyperacusis have demonstrated that the Noise Hypersensitivity Questionnaire (GÜF; Nelting et al.) is, amongst other things, lacking in sensitivity and specificity (Goebel & Floetzinger 2008).

Methods: Study participants are about 120 inpatients with chronic tinnitus treated consecutively in a center for behavioral medicine. Besides the intake diagnostic on symptoms and tinnitus impairment (Structured Tinnitus-Interview; Goebel & Hiller 2001; Tinnitus- Questionnaire; Goebel & Hiller 1998), psychoacoustic parameters and Sensitivity to sounds (GÜF; HQ, Khalfa et al.) are tested.

Results: Hyperacusis is more common among women. In most cases the hyperacusis could be also found in the ear without tinnitus or hearing loss. Due to the conceptional similarities we expect a high degree of correlation between GÜF and HQ),a medium correlation between GÜF/HQ and psychological scales of the symptom checklist (SCL-R-90) and a low correlation between GÜF/HQ with psychoacoustic parameters.

Conclusion: Following the elimination of items an improvement in the test's psychometric properties is expected. Further studies should show if affective and cognitive aspects are stimuli for the development of hyperacusis.

Goebel & Floetzinger: Pilot- study to evaluate psychiatric-co-morbidity in tinnitus patients with and without hyperacusis (Audiological Medicine, 2008; 6: 78- 84).

Address for correspondence: A. Berthold (aberthold@schoen-kliniken.de), Medical-Psychosomatic-Clinic Bad Arolsen, Germany

13:45 - 15:30
SYMPOSIUM
Animal Models
Richard Salvi

ANIMAL MODELS - INSIGHTS AND SPECULATION RELEVANT TO HUMAN TINNITUS

R. Salvi, S. Kraus, D. Ding, E. Lobarinas, S. Manohar
Center of Hearing and Deafness, University at Buffalo, Buffalo, NY 14214

The neural generators that give rise to tinnitus are poorly understood, but there is growing evidence from human imaging studies that cochlear damage leads to aberrant neural activity in the central auditory system that is correlated with perception of tinnitus. Tinnitus persists in acoustic neuroma patients who undergo transection of the auditory nerve; such cases clearly rule out the cochlea as the site of tinnitus generation. In earlier PET imaging studies with patients who could modulate the loudness of their tinnitus with an oral-facial maneuver, we found that changes in tinnitus loudness were strongly correlated with altered neural activity in the left auditory cortex and surprisingly the left hippocampus and limbic system are intimately involved with memory and emotion and were postulated by Jastreboff to interact and reinforce the aberrant neural activity underlying tinnitus Although the hippocampus lies outside the classical auditory pathway, animal studies indicate that it responds to sounds. The hippocampus is a unique brain area where large numbers of stem cells are born throughout life; many of these newborn cells are destined to become neurons replenishing the pool that have died. It has long been known that tinnitus is associated with stress and depression and both of these conditions down regulate the production of hippocampal stem cells. The prevalence of tinnitus also increases with age; at the same time that stem cell production is declining. To elucidate the potential role of the hippocampus in tinnitus, we present data from animal models that show a link between stem cell production and conditions that induce tinnitus. It is unclear whether the link between stem cells production and tinnitus is causal or correlational; but answers to this question can be fruitfully explored using animal models and potential drugs to treat tinnitus (supported by TRI and NIH R01DC009091, R01DC009219).

UPDATE ON THE GAP PREPULSE INHIBITION OF THE ACOUSTIC STARTLE ANIMAL MODEL OF TINNITUS AND TREATMENT

Edward Lobarinas Ph.D. CCC-A
State University of New York at Buffalo, Center for Hearing and Deafness, Buffalo NY USA

Aims and objectives: Effective, reliable pharmacological treatment of tinnitus remains elusive. However, we have started a series of pre-clinical experiments to evaluate drugs of different classes that are potential candidates for tinnitus treatment using animals. One of the biggest challenges that remain is developing a reliable noise trauma model by which to induce tinnitus. This model should maximize the number of animals that develop chronic tinnitus and restrict hearing loss to that analogous with hearing loss associated with what is observed in the clinical setting. We have continued to further develop the gap prepulse inhibition of the acoustic startle (GPIAS) paradigm to expand its usefulness, enrich the quality and accuracy of the data, and explore additional co-variates of tinnitus including hyperacusis. The goal of the current project is to evaluate innovative pharmacological strategies, pre-clinically, using our tinnitus animal model. Here we discuss up to date results on pharmacological treatment that target GABAergic function as well as other sites. We will present updates on new procedures and our newly developed protocol to further enhance and expedite our preclinical drug trials.

Methods: We have used the GPIAS to determine the onset, pitch, and persistence of tinnitus and to evaluate potential pharmacological treatments using a new high-frequency noise exposure (16 kHz, 120 dB SPL). In addition, we are evaluating and confirming the effects of noise trauma using distortion product otoacoustic emissions and evaluating changes in post trauma abnormal loudness growth by evaluating the growth of the startle function in relation to startle intensity.

Conclusions: GPIAS can yield frequency specific and time dependent assays of the presence of tinnitus in animals. We have developed new procedures to ensure integrity of the response and report updated results on the effects of drug treatments on persistent tinnitus.

COMPARISON OF SALICYLATE AND QUININE-INDUCED TINNITUS IN RATS USING THE ACOUSTIC STARTLE REFLEX

M. Ralli, A.R. Fetoni, S.L.M. Eramo, E. Lobarinas, D. Troiani, R. Salvi, G. Paludetti
Institute of Otolaryngology and Human Physiology, Università Cattolica del Sacro Cuore, Largo A. Gemelli 8, Rome Italy; Center for Hearing and Deafness, Department of Communicative Disorders and Sciences, University at Buffalo, Buffalo NY United States

Sodium salicylate and quinine have been shown to reliably induce short-term dose-dependent tinnitus when administered at high doses. The present study compared salicylate to quinine induced tinnitus-like behavior in rats using the gap pre-pulse inhibition of acoustic startle (GPIAS). Thirty-six rats were divided into 3 groups and were treated daily for four consecutive days; one group (n=12) was injected intraperitoneally with salicylate (300 mg/kg), the second (n=12) was treated with quinine by gavage at a dose of 200 mg/kg, the third group (n=12) was used as control (saline IP 300 ml/kg). All rats were subsequently tested for tinnitus and hearing loss at 6, 12, 16 and 20 kHz at 2, 24, 48, 72 and 96 hours after the first drug administration; tinnitus was assessed using GPIAS, hearing function was measured with DPOAE, ABR and noise-burst pre-pulse inhibition of acoustic startle (NBPIAS). The results revealed transient tinnitus-like behavior with a pitch near 16 kHz in all rats following salicylate or quinine treatment, starting 2 h after treatment, lasting for the entire length of treatment (4 days) and resolving spontaneously 24 h after the last day of treatment. GPIAS alterations were more evident and consistent across animals in the salicylate group. No changes in G PIAS were observed in animals in the control group. Hearing function was tested in all animals. Both salicylate and quinine caused an average temporary threshold shift of less than 10 dB and essentially no permanent shift. DPOAEs were tested in all animals at 4, 8, 12, 16 and 20 kHz daily for five consecutive days. In the salicylate group, high level DPOAEs were slightly affected; most changes could only be seen 2 h after injection. Low-level DPOAEs were affected at all frequencies, with an evident, progressive dose-dependent effect at 8, 12 and 16 kHz. A complete reversibility was observed 1 day after the end of treatment. (Supported in part by NIH grants R01DC009091, R01DC009219 and TRI)

IMPAIRED FUNCTIONS OF GABAERGIC NEURONS IN SALICYLATE-INDUCED TINNITUS

Su Y-Y, Luo B, Wang H-T, Chen L
Auditory Research Laboratory, School of Life Sciences, University of Science and Technology of China, Hefei 230027, China

Aims/Objectives: Sodium salicylate (NaSal) can penetrate the blood-brain barrier to directly target neurons in the central auditory system. The purpose of the present study was to examine how NaSal changes functional behaviors of GABAergic neurons of the central auditory system in salicylate-induced tinnitus.

Methods: Brain slice preparation and whole-cell patch-clamp techniques were deployed to record the serotonin-induced activity and the current-evoked firing from GABAergic neurons in the central auditory pathways in the presence and absence of NaSal (1.4 mM).

Results: In inferior colliculus slices, NaSal suppressed the serotonin-induced enhancement of GABAergic spontaneous inhibitory postsynaptic currents. In auditory cortex slices, NaSal significantly depressed the current-evoked firing in fast-spiking interneurons (GABAergic neurons), but not in pyramidal neurons (glutamatergic neurons).

Conclusions: NaSal preferentially impairs functions of GABAergic neurons in the central auditory pathways. Our study raises a possibility that NaSal alters the balance between excitation and inhibition to produce tinnitus in the central auditory system through targeting the GABAergic system.

This work was supported by the National Natural Science Foundation of China (Grants 30470560 and 30730041), the National Basic Research Program of China (Grant 2007CB512306) and the CAS Knowledge Innovation Project (Grant KSCX1-YW-R-36).

AUDITORY CORTEX CHANGES IN AWAKE GUINEA PIG AFTER SALICYLATE ADMINISTRATION AND NOISE TRAUMA.

[1]Arnaud Norena, [1]Graeme Moffat and [2]Yves Cazals
[1]Université de Provence, CNRS UMR 6149, Marseille, France, [2]Université Paul Cézanne, CNRS UMR 6153-1147 INRA, Marseille, France

It is well known that both high doses of salicylate and noise trauma are followed by tinnitus in humans and animals. However, the mechanisms by which salicylate and noise trauma induce tinnitus are unclear. Noise trauma, for instance, has been suggested to induce tinnitus through quick central changes, i.e. release from central inhibition due to the immediate noise-induced hearing loss. On the other hand, salicylate has been shown to have a central effect, while salicylate-induced tinnitus has been suggested to have a peripheral origin. Indeed, the application of NMDA-antagonist into the perilymphatic fluids of the cochlea suppresses tinnitus. In this context, the present study is aimed at studying and comparing the central effects of salicylate and noise trauma in awake guinea pigs. Neural activity (local field potentials) were recorded from microelectrodes (75 µ) chronically implanted in the auditory cortex before and after salicylate administration (300 mg/kg). On the same animals that received a dose of salicylate, neural activity was recorded before (3 days after salicylate injection) and, few minutes, 1, 3, 7 and 15 days after a noise trauma (8 kHz, 1/3 oct wide, 120 dB SPL, 2 h). Our study corroborates with earlier results showing a dramatic increase of evoked responses few hours after salicylate administration. Interestingly, the neural responses were increased over a large frequency band at moderate-to-high intensity levels (60-80 dB SPL), and over a narrow frequency band (around 10 kHz) at low intensity levels (20 dB SPL). This result is intriguing since salicylate-induced tinnitus has been shown to present a dominant pitch at around 10 kHz. Furthermore, we observed that noise trauma could increase the evoked cortical responses at moderate-to-high intensity levels, which is consistent with the literature. However, the effects were highly variable across animals; for instance, the maximum increase in responses was seen immediately or 1 day after the trauma. Finally, preliminary analyses do not show a large effect of salicylate and noise trauma on spontaneous activity. However, the magnitude spectrum shows a tendency to decrease after salicylate injection and noise trauma over a broad frequency band (10-30 Hz)

13:45 - 15:30
SYMPOSIUM
Neuroimaging EEG / MEG
Nathan Weisz

THE GOOD AND THE BAD VIBRATIONS - TINNITUS AND NEURONAL OSCILLATIONS

Nathan Weisz; Thomas Hartmann; Isabel Lorenz; Winfried Schlee
Dept. of Psychology; University of Konstanz

Oscillatory neuronal activity is ubiquitous throughout the brain, which - if generated macroscopically - can even be recorded via non-invasive techniques such as EEG and MEG. An increasing amount of evidence supports the view that brain oscillations are crucially involved in diverse cognitive operations such as attention and working memory. Recent notions state that the importance of oscillations - particularly in the alpha (~10 Hz) and gamma (>30 Hz) range - could lie in coordinating timing of neuronal activity. This means that oscillations either directly or indirectly reflect mechanisms regulating excitability within these assemblies. In the context of cognitive tasks, this reflects the "healthy" or "good" aspect of brain oscillations. Yet, even when "doing nothing" (resting), prominent brain oscillations can be recorded, particularly in the alpha range, seemingly not serving any function. Based on research from our group, we argue that the spontaneous activity rhythm recorded at rest, reflects the basic excitatory-inhibitory balance in such a manner that spontaneous or "spurious" synchronization between excitatory neurons is suppressed. This is partly shown also by our group that modulations of ongoing oscillatory activity is associated with altered perception / performance once a pertubation by stimulation takes place. In tinnitus ongoing spontaneous activity is altered in circumscribed brain regions in such a manner that "spontaneous" synchronization of neuronal activity takes place. Furthermore we argue that this activity does not remain restricted to auditory brain regions but enters higher-order brain regions to become a conscious percept. This aspect reflects the "unhealthy" or "bad" aspect of brain oscillations, i.e. once the mechanism underlying their generation become disturbed pathological conditions can arise. In this talk I will present arguments and evidence for the "good" and "bad" side of neuronal oscillations.

LOW AMPLITUDE ELECTRICAL STIMULATION MODULATES INDUCED GAMMA ACTIVITY IN VITRO

Davide Reato, Marom Bikson, Lucas C. Parra
Department of Biomedical Engineering, The City College of New York of the City, University of New York, New York, New York, U.S.A.

Recent studies shown that tinnitus correlates with an alteration of rhythmic activity in the electro-encephalogram. In particular, elevated gamma and a reduced alpha band power were observed when comparing tinnitus to non-tinnitus subjects. If these changes are causally related to tinnitus, then a potential treatment should aim at reducing the strength of the gamma frequency rhythm. Various forms of electrical stimulation have been proposed as treatment for tinnitus. However, the potential mechanisms of action remain uncertain. In the present study we analyzed the effect of weak electrical stimulation (<10mV/mm) on persistent gamma activity in vitro. We find that gamma power can indeed be reduced or modulated depending on the applied wave forms. In this study gamma activity was pharmacologically induced in a hippocampal preparation using carbachol. While the relevance of this preparation for cortical gamma activity is unclear, its simplicity allows for a detailed analysis of network mechanisms. In the present study we applied DC and AC spatially uniform electric fields oriented orthogonally across the CA3 pyramidal layer. DC and low frequency electrical stimulation modulated the gamma oscillations with suppression observed for hyperpolarizing electric fields. AC electric fields in the gamma band frequencies also suppressed the endogenous gamma rhythm while inducing an oscillation at half of the frequency of the stimulation (subharmonics). We reproduced the experimental results using a computational network model. The goal of this is to explain how the small effect on the single neuron (<1mV) can lead to drastic changes in network dynamics. The model explained the effect of DC and low frequency (<10Hz) stimulation in term of a modulation of the firing rate of neurons. The effect of fast AC stimulation (20Hz-40Hz) results from an increase in spiking precision of pyramidal neurons. These results suggest that it is possible to change the dynamics of an active neuronal network with low-amplitude electric fields. Combining this study with specific models of elevated gamma activity in tinnitus could be useful to predict the effects of electrotherapeutical approaches to tinnitus.

THE NEURAL CORRELATES OF ACUTE AND CHRONIC TINNITUS

Sven Vanneste, Mark Plazier, Jan Ost, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning, Marco Congedo, Dirk De Ridder
Brai^{2}n, University Antwerp, Wilrijkstraat 10, 2650 Edegem

The perception of tinnitus knows a high prevalence in the population and 1-2% suffers from a high amount of distress. rTMS studies of the auditory cortex for tinnitus suppression clearly state that the amount of tinnitus suppression by auditory cortex TMS decrease in time. A possible explanation of these results might be that the neural generator of tinnitus changes over time.

Aims: The neural generators of tinnitus related to the duration of tinnitus are analyzed, separating acute and chronic group with a cut-off of 4 years.

Methods: EEG recordings were acquired with 19 electrodes and one bipolar electrode to track eye movements.

sLORETA transformations were made and Current Density measurements were compared for different frequency bands. Significant results were formulated with a p <<.05.br> 12 patients were selected all suffering from unilateral left-sided narrow band noise tinnitus with an average VAS score for intensity of 6.00 vs. 6.86 respectively. The group was divided in 6 patients with acute tinnitus (<4 years) and 6 patients with chronic tinnitus> 4 years).

Results: In chronic tinnitus compared to acute tinnitus we found a significant decrease of gamma band activity in the left auditory cortex and increased theta activity in the bilateral auditory cortex. In the dorsal anterior cingulated cortex we found an increase in gamma-band activity and increased high beta-band activity in the left parahippocampal cortex.

Conclusion: According to our results the neural network changes for chronic in comparison to acute tinnitus. A surprising finding is the shift in gamma band activity between the left and right auditory cortex in acute and chronic tinnitus patients respectively. These results have to be placed in the scope of the other variables influencing the neural generators of tinnitus to get to a more general insight.

NEURAL CORRELATES RELATED TO THE AUTONOMOUS NERVOUS SYSTEM (AND) IN TINNITUS DISTRESS

E van der Loo, S Vanneste, M Congedo, M Plazier, J Ost, T Menovsky, P van de Heyning, D De Ridder
BRAI^{2}N, University Hospital Antwerp, Antwerp, Belgium

Background: 1-2% of tinnitus sufferers are severely disabled by their tinnitus. It has been suggested that a fighting attitude towards tinnitus in a maladaptive coping group suggests a sympathetic (OS) hyperactivity, whereas effective coping reflects a parasympathetic (PS) dominance. Heart Rate Variability (HRV) is a marker of autonomic functions. In HRV frequency domain, normalized units (nu) of low and high frequency (LF, HF) components reflect OS and PS influences respectively.

Aims: The aim of this study is to find out if areas known to be involved in the ANS show changes in activity related to tinnitus distress. For this HRV markers are correlated to TQ scores. Neural activity in predefined areas is related to these scores.

Methods: 10 patients with right-sided unilateral tinnitus were analyzed. EEG and ECG signals are recorded over 5' in supine position using a 32 channel digital EEG (sr=500Hz). EEG artefacts are rejected offline after visual inspection.

OS (LF nu) and PS (HF nu) markers of HRV are correlated to TQ scores.

Current density trend analyses are performed with E-LORETA beam forming at regions of interest (left and right anterior insula) related to TQ score. Significant trends are formulated with a p<<.05.br>

Results: TQ scores correlate positively with OS marker (r=0.579, p<<<.05), and negatively with PS marker (r=-0.581, p.05). Increasing TQ scores show increase in the left anterior insula the alpha band and decreasing activity at 4Hz and high gamma.

In the right anterior insula increasing TQscores show increased activity in the delta and gamma band.

Conclusion: Our results show a positive relation between OS load and tinnitus distress. Previous fMRI studies demonstrate right insula activation is related to the OS system, whereas left insula activity is related to the PS system. Our results confirm this in that increasing tinnitus distress, and thus increasing sympathetic load, is related

to increased gamma band activity in the right anterior insula.

THE NEURAL CORELLATES OF DISTRESS IN TINNITUS

Sven Vanneste, Mark Plazier, Jan Ost, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning, Marco Congedo, Dirk De Ridder
Brai²n, University Antwerp, Wilrijkstraat 10, 2650 Edegem

Background: The perception of tinnitus knows a high prevalence in the population and 1-2% suffers from a high amount of distress. One way to score the distress caused by the tinnitus is using the 4 grades of the tinnitus questionnaire of Goebel and Hiller. Grade 4 represents psychological decompensated tinnitus patients.

Aims: The neural network of tinnitus distress is analyzed.

Methods: EEG recordings were acquired with 19 electrodes. Acquisition was preformed with MITSAR amplifiers at a sampling rate of 500 Hz in an eyes closed situation.

Loretta transformations were made and Current Density measurements were compared for different frequency bands. A between-subjects t-test comparison was preformed between the acute and the chronic group for each frequency band. Significant results were formulated with a p <<.05.br> 13 patients were selected all suffering from tinnitus and divided in two groups of distress. Low distress was defined as a grade 1 on the Tinnitus Questionnaire (Goebel Hiller), High distress was defined as a grade 4 on the TQ.

Results: In the high distress group compared to the low distress group a higher current density was found in alpha-frequency band in the amygdale, subgenual anterior cingulated cortex and parahippocampal cortex, bilaterally, but predominantly on the right. In the right insula similar findings are noted.

In the posterior cingulated gyrus we found a decrease in alpha-band activity in the high distress group compared to the low distress group.

Conclusion: Distress mainly seems to have an effect on other structures than the auditory cortex. These structures involve the amygdala-insula and parahippocampal area as well as the anterior and posterior cingulated gyrus.

In the treatment of tinnitus the reduction of distress might be as important as the decrease in tinnitus intensity, in order to get satisfying therapeutic results.

16:00 - 18:00
SYMPOSIUM
Auditory Training
Grant Searchfield / Larry Roberts

Reduction in tinnitus may occur with perceptual training which aids in the development of appropriate neural networks and or activity - a process of learning-related plasticity. Perceptual training consists of auditory, or other sensory, tasks which generally involve the participant attending to and responding to sound. In this symposium the physiological basis of auditory training will be examined, along with how these changes can be measured. The clinical effectiveness of auditory discrimination therapy will be introduced. A panel of researchers involved in the study of perceptual training will discuss how the information provided in the preceding talks and their own research may influence future developments of effective sound-based tinnitus treatments.

ASSESSING THE POTENTIAL BENEFITS FROM AUDITORY PERCEPTUAL TRAINING: DERIVING APPROPRIATE AND TESTABLE HYPOTHESES FROM PHYSIOLOGICAL MODELS OF TINNITUS

DA Hall
National Biomedical Research Unit in Hearing, Nottingham

In 2008, a National Biomedical Research Unit in Hearing (NBRUH) was created in Nottingham, UK. We are pursuing an agenda of evidence-based translational research with the common scientific theme of examining the potential for auditory perceptual training to deliver broad patient benefits.

My group will push forward ideas for reducing tinnitus via a simple listening test.

If successful, the test can be packaged in such a way that it can be practiced at home, thus reducing the burden on health care delivery.

The basic premise is that repeated listening to a sound will in time “correct” the abnormal patterns of activity in the central auditory system that are thought to underlie the sensation of tinnitus, thus altering its subjective qualities.

The scientific model on which this treatment is based concerns cortical reorganisation after hearing loss.

Animal studies have shown that a maladaptive response to a loss of input can in some cases cause an expansion of the tonotopic map so that this affected portion now becomes responsive to the adjacent frequency at which hearing threshold is normal - the lesion-edge frequency.

A physiological model of tinnitus proposes that the phantom auditory sensation is a direct consequence of such cortical reorganisation.

The method of treatment is currently based on evidence from normally hearing listeners that frequency discrimination training alters the tonotopic representation of the trained sound frequencies. If the training sound is carefully chosen to stimulate specific tinnitus-generating regions of the central auditory system, frequency discrimination training using such sounds may rebalance the impaired cortical representation of that frequency, and hence reduce tinnitus.

As a prelude to the rest of this symposium, I will discuss the physiological mechanisms that motivate this approach and predictions that arise from it. I will also report on preliminary work already published and highlight key issues for future research.

PERCEPTUAL TRAINING FOR TINNITUS MANAGEMENT

Searchfield G, Jepsen K, Coad G, Kobayashi K, Sanders M
Audiology, School of Population Health, The University of Auckland

Aims: New methods of treating tinnitus using auditory perceptual training are proposed. Perceptual training can be considered to consist of two broad approaches, a bottom-up focus and a top-down focus. In the bottom-up approach tasks involve discrimination of basic elements comprising sound (e.g. frequency and intensity discrimination) in the top-down approach the stimuli are more complex and the tasks more representative of “normal perceptual activities” (e.g. speech recognition).

The research described in this study considers the application of both approaches with particular emphasis on whether frequency categorisation (FCT) or discrimination training (FDT) can force the rejection of the aberrant activity that underlie tinnitus and whether this can be objectively demonstrated in changes in AEP recordings. FDT teaches participants to differentiate between similar sounds. Categorization training teaches participants to identify stimuli within a particular frequency range as members of the same category, leading to a decrease in sensitivity to stimuli in that category. Categorisation training has been shown to reduce cortical activation in normal hearing listeners (1). It is hypothesized that FCT could be used to reverse changes in cortical plasticity that may be contributing to the tinnitus sensation, thus reducing tinnitus severity.

Methods: Twenty-four participants underwent assessment and training. Assessment of Tinnitus Pitch Match (TPM), tinnitus handicap, Just Noticeable Difference (JND) at pitch match, and P1N1P2 AEP complex (64 channel BioSemi EEG system; at pitch match, one octave below pitch match and at 750 Hz) were undertaken before and after participants completed FCT or FDT for 21 training sessions over 3 weeks. Auditory training was carried out daily in the participants own home using a Palm Tungsten E2 PDA. Training stimuli were samples of narrowband noise (1/18 octave, 500ms in duration and separated by 750ms) with different centre frequencies created by filtering white noise with a fourth order chebyshev bandpass filter. For FCT participants were trained to identify sounds belonging to a training region which extended 2 JNDs above and below the pitch match frequency. For FDT participants were trained to discriminate between sounds in a training region which extended 2 JNDs above and below the pitch match frequency.

Results: Our preliminary evidence suggests that FCT is more successful in altering tinnitus perception than FDT. It appears that frequent exposure to a stimulus leads to a larger cortical representation, and that larger cortical representations lead to better discrimination. When participants are required to categorise sounds in groups discrimination of more frequently encountered stimuli is worse than discrimination of less frequently encountered stimuli and cortical representation is reduced.

Conclusions: The results of this study suggest that short-duration perceptual training can contribute to a reduction in tinnitus perception and that these perceptual changes can be observed as changes in auditory evoked potentials.

References: 1. Guenther F, Nieto-Castanon A, Ghosh S, Tourville J. J Sp Lang Hear Res. 2004; 47:46-57.

INDUCTION OF NEURAL PLASTICITY BY AUDITORY TRAINING

Larry E. Roberts
Department of Psychology, Neuroscience, and Behaviour, McMaster University, Hamilton, Ontario, Canada L8S 4K1

Applications of acoustic training to tinnitus necessarily entail assumptions about the mechanism of tinnitus as well as about how acoustic training modifies neural representations for sound in the human auditory system.

At present, our understanding of both domains is incomplete. In ongoing research, we have begun to identify using the stimulus-driven 40-Hz auditory steady-state response (SSR) some principles that guide remodeling of the auditory cortex in normal hearing subjects and in tinnitus subjects.

By employing 1-sec bursts of 40-Hz amplitude modulated stimulation, we are able to simultaneously image neural changes taking place in the auditory core region (where the cortical sources of the SSR are found) and in secondary auditory belt regions (where familiar N1 and P2 transient responses localize, these extracted from the same data set).

Results from these experiments give a picture of neuroplastic reorganization that differs in several respects from expectations based on animal studies. We discuss possible mechanisms underlying the effects and their application to segregating synchronous neural activity in deafferented auditory cortex which may underlie the tinnitus sensation.

A successful application to tinnitus may inform us about mechanisms not only of tinnitus but also of neural plasticity in the human auditory system.

ELECTROPHYSIOLOGICAL ASSESSMENT OF TRAINING OUTCOMES USING SIMULTANEOUSLY EVOKED TRANSIENT AND STEADY-STATE RESPONSES

Bosnyak D, Gander P, & Roberts L
Department of Psychology, Neuroscience, and Behaviour McMaster University, Hamilton, Ontario, Canada L8S 4K1

Tinnitus is often accompanied by mild sensorineural hearing loss at the frequencies of the tinnitus sensation. This deafferentation is known to lead to imbalances in levels of excitation and inhibition delivered to primary auditory cortex (PAC). Synapses mediating intracortical inputs may be strengthened at the expense of synapses mediating thalamocortical inputs, generating abnormal synchronous activity in the frequency regions of PAC affected by the hearing loss.

Acoustic training using auditory stimuli within the tinnitus spectrum could be expected to remodel cortical representations for these stimuli by strengthening thalamocortical drive and diminishing the involvement of the affected neurons in hypersynchrony thus diminishing tinnitus.

In ongoing research, we have begun to identify using the 40-Hz auditory steady state response (SSR) the principles that guide remodelling in the auditory core region in normal hearing and tinnitus subjects. By using 1-sec bursts of 40-Hz amplitude modulated stimulation, we are able to simultaneously elicit a SSR, localizing to PAC, and familiar N1 and P2 auditory evoked responses whose sources localize to secondary auditory belt regions.

Completed experiments have found that the amplitude of the SSR is modulated by attention, but its phase is modified by experience. The phase effect (a phase advance) could reflect coding of the steady-state stimulus by subpopulations of neurons that are recruited by competitive mechanisms for their short latencies. We can also induce an enhancement of SSR amplitude, but only if a single carrier frequency is trained (competitive interactions consequent on training multiple frequencies appear to preserve a normalized tonotopic representation). These results in normal hearing subjects appear to hold when the trained carrier frequency is at 2 or 5 kHz (the latter frequency within the typical tinnitus spectrum). Assessment of training effects on tinnitus are in progress and will be reported.

VIRTUAL REALITY FOR TINNITUS REHABILITATION

A Baskind, S Bertet, P Bonfils, A Londero, I Viaud-Delmon, O Warusfel
CNRS UMR 9912 and IRCAM; CNRS UMR 7060 and Hopital Europoen Georges Pompidou; Paris, France

We developed a visual and auditory 3D Virtual Environment (VE) dedicated to the rehabilitation of tinnitus. Our aim is to investigate whether immersive Virtual Reality (VR) can contribute to tinnitus treatment by promoting plasticity, through the active manipulation of a 3D auditory object linked to a visual representation. Although VR techniques are very attractive for health care, their adaptations are mandatory in order to allow their practical clinical use. In the case of tinnitus patients, a special effort has to be dedicated to the work on the monitoring of 3D audio features.

Our rehabilitation protocol is composed of two main steps. In a first test, an acoustic modelisation of the perceived tinnitus is established. The acoustic model is then used as a tinnitus avatar in the second step, involving three auditory and visual VE designed in Virtools, a VR development application.

The three VEs were chosen as representative of realistic situations (countryside, urban and indoor scenes) and are inhabited with a collection of auditory sources (e.g.: animals, cars, domestic noises). These auditory sources are spatialized according to the location and orientation of the patient in the VE.

Immersion is provided through the use of a stereoscopic Head Mounted Display equipped with a head sensor and headphones. An additional sensor attached to the tip of a rod allows the patient to control the virtual position of the tinnitus avatar through the displacement of the rod. The position and orientation of the two sensors are tracked with infra-red cameras.

A randomised clinical trial will compare VR rehabilitation to cognitive-behavioral therapy and delayed treatment. The efficacy will be evaluated by standardised questionnaires.

This research is supported by a TRI Grant (PB 07 01) and Amplifon

---

AUDITORY DISCRIMINATION TRAINING (ADT) FOR TINNITUS TREATMENT

Carlos Herraiz
MC PhD, Fundacion Hospital Alcorcon, Tinnitus Clinic. Department of Otorhinolaringology, Madrid, Spain

The tonotopic representation in the auditory cortex changes after peripheral deafferentantion or acoustic overstimulation. Tinnitus mechanisms have been associated with cortical reorganization. Some authors have demonstrated that tinnitus could be secondary to the increase of representation of the lesion-edge cortical areas. Other recent studies have demonstrated opposite arguments to that theory: increased spontaneous firing rates and burst-firing activity in the areas of primary auditory cortex corresponding to the most damage cochlear areas. Reorganisation process related to tinnitus persistence would be more enhanced in the hearing loss areas instead of lesion-edge frequencies.

Auditory rehabilitation has proved to be effective in functional changes of cortical tonotopy. Published studies on Auditory Discrimination Training (ADT) suggest a positive effect on tinnitus management. ADT have shown a tinnitus improvement in 45.5% of the patients treated and a significant relief in VAS and THI scores. Our presentation will describe the possible mechanisms of action and the effect on tinnitus of different tested ADT paradigms. Indications, method, dose, and sound strategy need to be standardised.

16:00 - 18:00
SYMPOSIUM
Auditory System Neurophysiology
Arnaud Norena

THE LONG ROAD TO THE NEUROSCIENCES OF TINNITUS

Arnaud Norena
Université de Provence, CNRS UMR 6149, Marseille, France

Over the past ten years, researchers and clinicians have witnessed a change in the neurophysiological origins of the tinnitus paradigm. In the eighties, many models (discordant damages between inner and outer hair cells, efferent system control release, ephaptic connections between auditory nerve fibers …) suggested that the aberrant neural activity causing tinnitus originated from the periphery. According to this model, the centers role was limited to the interpretation of aberrant neural signal as a sound and to emotional evaluation of the perception. As a consequence, treatments aimed at reducing tinnitus should focus on the interpretation/evaluation level of the symptom. However, this model has been weakened by several results. Mainly, hearing loss (often present with tinnitus) is associated to a decrease in neural activity at the auditory nerve level, and the auditory nerve section does not abolish tinnitus. On the other hand, more recent studies have shown that hearing loss induced a decrease in central inhibition, alteration in the tonotopic map and, importantly, changes in the pattern of spontaneous firing potentially related to tinnitus. These central changes are meant to be caused by a decrease in sensory inputs (due to hearing loss), since enriching the acoustic environment with high frequencies after a noise trauma prevents the emergence of the central changes listed above. This central model has inspired two lines of clinical treatment. First, compensating the reduced sensory inputs by providing subjects with an enriched acoustic environment should prevent the emergence of the aberrant neural activity underlying tinnitus. Second, cortical stimulation should interfere (suppression, modulation?) with the neural activity underlying tinnitus. While animal studies should continue investigating the potential neural correlates of tinnitus and provide an improved model that could account for tinnitus, we believe that the neurosciences of tinnitus can also benefit from clinical studies. For instance, extra-cochlear stimulation with positive currents has been shown to efficiently reduce tinnitus. This result challenges the “central” model developed here since positive current tends to hyperpolarize auditory nerve fibers. Finally, there is much to know about the cortical stimulation parameters which consistently decrease tinnitus. Namely, it would be of great interest to assess the effects of these stimulations on neural activity and compared them to those induced by stimulations which are not efficient for reducing tinnitus.

CHARACTERISATION OF ANOMALOUS TEMPORAL DISCHARGE PATTERNS IN NORMAL GUINEA PIG COCHLEAR NERVE FIBRES

Mulheran M
Department of Cell Physiology and Pharmacology, University of Leicester, UK LE1 9HN

Background: Anomalous neuronal temporal discharge patterns have been considered as a neurophysiological

correlate for certain types of tinnitus following ototrauma. One class of discharge anomaly manifests as an increased proportion of spikes pairs with interspike interval between 1-2ms. However, there have been reports of this anomaly in non-traumatised cochlear nerve fibres. This study aimed to further characterise this anomaly in a population of normal cochlear nerve fibres.

Methods: Single unit (n=180) microelectrode recordings were made in anaesthetised guinea pigs monitored for normal systemic function. Experimental details are given elsewhere(1). Quantification of anomalous spiking pattern was based on early (e) spike interval counts from the first 10 consecutive positive bin counts for a fibre's Interspike Interval Histogram (ISIH). ISIHs were constructed from;10 000 spike counts; 100us binwidth; 256 bins. This count was termed the %eISI.

Results: Anomalous spiking behaviour was based on the presence of an early (1-2ms)ISIH mode which was seen in 35% (63/180) of fibres. Based on the %eISI distribution histogram, these divided into 3 groups with significantly different mean %eISIs of: 4.2%;9.2%;22% ($p<<0.001$), cf. 3% for normal unimodal (4-7ms) ISIHs. No relationship was apparent with other measures of fibre function including: CF; threshold; Q'10'dB; spontaneous rate; absolute refractory period.

Conclusion: Whilst anomalous discharge activity may well correlate with certain types of tinnitus, in this guinea pig model, it was observed in about a third of cochlear fibres exhibiting otherwise normal activity. These anomalies may form part of a spectrum of normal discharge behaviour, or alternatively reflect some acute generalised tinnitiform activity arising from experimental procedure. At a minimum, it suggests care needs to be taken in choice of animal model used in electrophysiological studies of tinnitus.

1. Mulheran M. Hear Res, 1999; 134:145-52

CHANGES IN NEURAL ACTIVITY AND GENE EXPRESSION IN CENTRAL NUCLEI AFTER RESTRICTED UNILATERAL COCHLEAR LESIONS

D Robertson, S Dong, WHAM Mulders, J Rodger
School of Biomedical Biomolecular and Chemical Sciences and School of Animal Biology, The University of Western Australia, 6009 Australia

School of Biomedical Biomolecular and Chemical Sciences and School of Animal Biology, The University of Western Australia, 6009 Australia

Aims: Changes in auditory input as a result of cochlear damage trigger a range of changes in central nuclei of the auditory system, including spontaneous hyperactivity and map plasticity. Changes in gene expression accompanying altered auditory input have most often been investigated using total cochlear ablation. We therefore evaluated, in the same animals, the effect of limited cochlear lesions on spontaneous firing rates of midbrain neurons and expression of genes related to synaptic function and neuronal excitability.

Methods: Anaesthetized guinea pigs (n=5) received a mechanical lesion to the left organ of Corti (Robertson et al. J.Acoust.Soc.Am.(1980)67,1295-1303). 1 week after, extracellular single neuron recordings were made from the contralateral inferior colliculus. qRT-PCR quantified mRNA levels of 10 genes in inferior colliculus and cochlear nucleus.

Results: after 1 week, all animals had elevated cochlear neural thesholds between 10 and 20kHz.Spontaneous activity was significantly higher in contralateral inferior colliculus compared to unlesioned animals. Expression of TASK5 (potassium leakage channel) and genes related to GABAergic neurotransmission were reduced in inferior colliculus and cochlear nucleus ($P<0.05$). Glycine receptor expression was depressed in cochlear nucleus.There was no change in gene expression related to serotoninergic or glutamatergic transmission. Changes in expression in inferior colliculus were bilateral but those in cochlear nucleus were ipsilateral to the lesioned cochlea.

Conclusions: altered input from a restricted region of the cochlea results in increased excitability in auditory midbrain. This is accompanied by reduced expression of genes related to inhibitory neurotransmission and intrinsic electrical stability of neuronal membrane potential. The distribution of ipsilateral and bilateral changes in cochlear nucleus and inferior colliculus respectively is consistent with the anatomical organization of the ascending pathways.

A MODEL FOR TINNITUS GENERATION BASED IN THE VENTRAL, NOT DORSAL, COCHLEAR NUCLEUS

Jennifer R. Melcher
Mass. Eye and Ear Infirmary, Boston MA USA

Many neural representations have been proposed to underlie the tinnitus percept including elevated neural firing rate, abnormal temporal patterns of neural discharge, reorganized tonotopic maps, and increased correlation between neurons. By "increased correlation" we specifically mean that the spontaneous firing patterns of two or more neurons are correlated with one another to an abnormally high degree. Recently, Eggermont and co-workers reported enhanced inter-neuronal correlations within the auditory cortex of animals having a pattern of peripheral damage often associated with tinnitus. But cortex may not be special in showing such enhanced correlations. We suggest that cochlear nucleus neurons directly innervated by the cochlear nerve could show enhanced inter-neuronal correlation following peripheral deafferentation and that the spherical bushy cells of the ventral cochlear nucleus are particularly likely candidates for exhibiting this phenomenon. We will explain how several structural and functional aspects of cochlear-nerve fibers and spherical bushy cells may conspire to increase the degree to which spherical bushy cells are correlated with one another following cochlear hair cell or spiral ganglion loss. We will also discuss how these correlations might help account for various aspects of tinnitus phenomenology including, differences between people in the quality of the tinnitus percept, onset of tinnitus immediately following acoustic over-exposure, and the occurrence of tinnitus in some ears, but not others with seemingly identical damage.

Supported by the Tinnitus Research Initiative.

ATTENTIONAL EFFECTS ON EXCITATORY AND INHIBITORY NEURAL ACTIVITY IN THE HUMAN AUDITORY CORTEX

Okamoto H, Stracke H, Pantev C
Institute for Biomagnetism and Biosignalanalysis, Westfalian Wilhelms-University Münster, Münster 48149, Germany

In daily life, auditory focused attention plays an important role in extracting relevant auditory signals from simultaneously present, irrelevant noises. The enhancement of excitatory and inhibitory neural activity by attention seems to improve the auditory performance during picking up relevant auditory signals in noisy environments. In the present studies, we investigated auditory magnetic fields in humans that were evoked by pure tones embedded in band-eliminated noises during

two different stimulus sequencing conditions (constant vs. random) and under two different auditory focused attentional states (focused vs. distracted) by means of magnetoencephalography (MEG). In total, we used identical auditory stimuli between conditions, but the attentional states and the stimulus sequencing differed. During the focused attention condition, subjects performed an auditory task, whereas they watched a silent movie during the distracted attention condition. Constant stimulus sequencing blocks were characterized by the simultaneous presentation of pure tones of identical frequency with band-eliminated noises, whereas random sequencing blocks were characterized by the simultaneous presentation of pure tones of random frequencies and band-eliminated noises. We demonstrated that auditory evoked neural responses were larger in the focused auditory attention and in the constant sequencing conditions compared to the distracted auditory attention and the random sequencing conditions, particularly when the simultaneously presented noises contained narrow stop-bands. The present studies confirmed that population-level frequency tuning in human auditory cortex can be sharpened by focused auditory attention in a frequency-specific manner. Attention does not only amplify the excitatory neural activity corresponding to the task relevant auditory signal, but also enhances the inhibitory neural activity to suppress the task irrelevant neural activity.

[not attending]

THALAMIC GATING OF AUDITORY ACTIVITY VIA NUCLEUS ACCUMBENS IN THE RAT

J. P. Rauschecker, X. Zhan, P. Kusmierek
Georgetown University Medical Center, Washington, DC, USA

In a previous imaging study Muehlau et al. [1] demonstrated structural changes in the auditory thalamus and nucleus accumbens (NAc) of a large group of human tinnitus patients. Specifically, voxel-based morphometry (VBM) based on high-resolution MRI showed a reduced volume of the NAc and an increased grey-matter density in the auditory thalamus. A three-pronged model of tinnitus has been based on these results: (i) The tinnitus sensation initially results from lesion-induced reorganization and hyperactivity in central auditory pathways [2]. (ii) Long-term habituation via the NAc normally leads to a disappearance of the tinnitus sensation. (iii) Chronic tinnitus results from a compromised function of the NAc and concomitant lack of habituation and inhibition in the auditory thalamus.

We are currently undertaking neuroanatomical pathway tracing and electrophysiological studies of the auditory thalamic and NAc pathway in the rat with the aim of establishing a new animal model of tinnitus.

At this initial stage we are seeking to test the following functional-anatomical hypothesis: The dorsal part of the medial geniculate nucleus (MGd) projects to the NAc via the amygdala, and the NAc projects back to the auditory portion of the thalamic reticular nucleus (TRN). The TRN exerts an inhibitory influence on the specific (lemniscal) auditory pathway from the inferior colliculus to the ventral part of the medial geniculate (MGv) and auditory cortex (AC). Electrical stimulation of the NAc will be used to demonstrate the inhibitory influence of the NAc on MGv and AC neurons via the TRN. Inactivation of the NAc by reversible lesion should lead to hyperactivity in MGv and AC due to lack of this inhibitory influence.

1. Muehlau M, Rauschecker JP, Oestreicher E, Gaser C, Roettinger M, Simon F, Etgen T, Conrad B, Sander D. Cerebral Cortex, 2006; 16(9):1283-1288

2. Leaver AM, Renier L, Purcell J, Costanzo M, Fieger A, Morgan S, Kim HJ, Rauschecker JP. Soc Neurosci, 2006; 32:800.2

16:00 - 18:00
SYMPOSIUM
Neurostimulation
Dirk De Ridder / Berthold Langguth

Neuroimaging and electrophysiology findings within the last decade have clearly demonstrated that chronic tinnitus is the consequence of alteration of neural activity in the central nervous system. In more detail, it is assumed, that hearing loss, which is frequently occurring in tinnitus patients, results in a dysbalance between inhibitory and facilitatory mechanisms in the central auditory system, which in turn gives rise to increased neural activity throughout the central auditory pathways. The activity in the auditory pathways is additionally modulated by other brain areas, such as the limbic system. So it is assumed that tinnitus is perceived, when increased activity in the auditory pathways is not sufficiently reduced due to impaired function of the limbic system.

The involvement of specific brain regions in the pathophysiology of tinnitus, as identified by neuroimaging, present targets for therapy by means of neurostimulation. Pilot studies have demonstrated efficacy for both transcranial magnetic stimulation and epidural electrical stimulation of the auditory cortex. Within this symposium papers are presented which aim to further elucidate the involved neurobiological mechanisms (Sanchez, Londero, Lorenz), focus on study methodology (Cacace) try to identify predictors for successful treatment outcome (Frank) and aim to improve efficacy by investigating innovative stimulation protocols (Giani).

CLINICAL AND NEUROIMAGING OUTCOMES OF THE EFFICACY OF TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH TINNITUS AND NORMAL HEARING

Marcondes RA, Sanchez TG, Kii MA, Ono CR, Buschpiguel C, Marcolin MA, Langguth B.
Tinnitus Research Group, Otolaryngology Department, University of São Paulo School of Medicine

Objectives: The targeted modulation of tinnitus-related cortical activity through repetitive transcranial magnetic stimulation (rTMS) has been recently proposed as a promising new treatment approach. However, its efficacy in patients without hearing loss - which might represent a potential bias for the neuroplasticity of auditory cortex - has never been studied. The objective of this study was to investigate both immediate and long-term effects of low frequency (1 Hz) rTMS in patients with tinnitus and normal hearing sensititvity.

Methods: Using a randomized double-blind and parallel clinical trial, 20 patients with chronic tinnitus and normal pure-tone audiometry were divided to receive either active or placebo transcranial magnetic stimulation over the left temporoparietal cortex for 5 consecutive days. A thorough medical and audiological evaluation was conducted in all patients, including the clinical evaluation through the Tinnitus Handicap Inventory before and after one and 6 months of the rTMS. Moreover, a functional neuroimage evaluation included and ECD-SPECT imaging, which was performed before and 14 days after rTMS.

Results: From the clinical point of view, the group submitted to active rTMS presented significant improvement of the tinnitus by the THI score, which was sustained up to six months, when compared to the group that received the sham rTMS. SPECT measurements demonstrated a reduction of metabolic activity in the left temporal lobe after active rTMS when compared to the one before rTMS.

Conclusion: These results support the potential of rTMS as a therapeutic tool for the treatment of chronic tinnitus, by demonstrating a significant reduction of tinnitus complaints over a period of at least six months and a significant reduction of neural activity in the temporal cortex.

NAVIGATED RTMS FOR THE TREATMENT OF TINNITUS: ASSESSMENT BY AEPS AND FMRI

Londero A.[1], Guimont F.[2], Brugières P.[3], Iglesias S.[4], Franco Rodrigues A.[4], Liégeois-Chauvel C.[2], Lefaucheur J.P.[4]
[1]Service ORL HEG Pompidou, CNRS 7060, Paris, France. [2]INSERM U751, Faculté de Médecine, Aix-Marseille Université, France. [3]Service de Neuroradiologie, Hôpital H. Mondor, Créteil, France. [4]Service Explorations Fonctionnelles, Hôpital H. Mondor, Créteil, France

Background/aims: Tinnitus could be relieved by sessions of repetitive transcranial magnetic stimulation (rTMS). However, the involved mechanisms remain largely unknown. We compared clinical efficacy of low frequency rTMS to changes occurring in auditory evoked potentials (AEPs) and functional magnetic resonance imaging (fMRI).

Methods: In six patients with chronic refractory unilateral or predominantly lateralized tinnitus, MRI-guided navigated rTMS was applied to the auditory cortex contralateral to tinnitus side at low-frequency (1Hz) for 20 min per day during 5 days. Short-term (1-5 days) effects of rTMS were assessed on clinical scores, 64-electrode AEP recordings to tone burst stimulation, and intensity and volume of fMRI activation to broad frequency auditory stimulation.

Results: Baseline fMRI activation of the auditory cortices was low in 3 patients and elevated in 3 patients. These last patients also presented high tinnitus-related distress scores. In addition, asymmetric fMRI activation was found in 4 patients, predominant controlaterally to tinnitus side whereas AEPs displayed more symmetric patterns. After rTMS, 5 patients clinically improved and one was unchanged. In responders, AEPs showed asymmetric N1/P2 amplitude changes likely due to a better synchronization in auditory cortex activity. In patients with low baseline fMRI activation, it increased bilaterally after rTMS, whereas it decreased in patients with elevated baseline values. The best rTMS effects were clinically observed in the two patients with asymmetric baseline hyperactivity. The 3 patients who had low baseline fMRI activation improved at various clinical levels.

Conclusions: The variety of AEP and fMRI changes produced by 1Hz-rTMS likely reflect various types of tinnitus-related cortical dysfunctions, possibly related to various profiles of clinical responses to rTMS. Further research is warranted to evaluate the validity of these data on larger populations.

POTENTIAL ARTIFACTS INTRODUCED IN TINNITUS STUDIES USING REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS)

A. Cacace[1], V. Ramachandran[1], R. Burkard[2], R. Tyler[3]
[1]Wayne State University, Detroit, MI, [2]University at Buffalo, Buffalo, NY, [3]University of Iowa, Iowa City, IA

Aims: Because audible switching transients are produced during rTMS, concerns exist that these acoustic events can influence tinnitus and confound changes observed in these experiments. We quantified the acoustic output of a sham and actual figure-of-eight coil of a commercial TMS device in the sound field and with a probe microphone placed in the ear canal and determined the effectiveness of commonly used acoustic attenuation devices under different experimental conditions.

Methods: rTMS outputs were generated by a commercial system (MAGSTIM; sham coil: 1684; actual coil: 1640); acoustic measurements from the ear canal were made using a probe-microphone (Etymotic ER-7C) routed to a computer controlled digital oscilloscope/spectrum analyzer (PICO electronics, 2203; Dell, 1530); sound-field measures were made using a sound-level meter (Brüel & Kjaer, 2231). Probe-microphone measurements were made at two levels (50% and 25% re: maximum output) and under three experimental conditions: open ear, with a commercial earplug and with a commercial earplug + circumaural earmuffs. After obtaining informed consent, data were collected from eight adults in a single-walled test booth.

Results: The acoustic output of the actual coil was ~25 dB lower than the sham coil and these data were included in our calculation of sound levels reaching the ear drum. Real-ear peak SPLs were larger in females vs. males (when combined, 50% output condition = 129 dB pSPL; 25% output condition = 120 dB pSPL, unattenuated condition). Attenuation values between open ear vs. earplug conditions were ~20 dB; the combined earplug + earmuff condition provided an additional 14 dB of attenuation.

Conclusion: Assuming earplugs provide ~20 dB of attenuation, then use of this device will reduce but not eliminate acoustic stimulation during rTMS. Therefore, acoustic output of individual coils can be a confounding factor because the sound it produces could increase or decrease the magnitude of tinnitus.

TREATING TINNITUS WITH TMS: THETA BURST STIMULATION AND THE RELIEF OF AUDITORY PHANTOM PERCEPTIONS

A.S. Giani, W. Harnisch, R. Hagen, C.G. Varallay, L. Solymosi, T. Polak, M. Plichta, A.T. Sack, A.J. Fallgatter
Dept. of Psychiatry, University of Wuerzburg, Germany

Objective: People suffering from chronic tinnitus continuously experience auditory noise in the absence of any auditory stimulation. This phantom perception has been related to an enhanced activation of the auditory cortex. Theta burst stimulation (TBS) represents a convenient tool that effectively inhibits this hyperactivity. Hence, TBS might release patients from their distressing auditory perceptions.

Methods: In a placebo controlled design the effect of two weeks of TBS on chronic tinnitus was evaluated for 12 tinnitus patients. During each session two trains of each 200 theta bursts (one burst = 3 pulses, 50Hz) were applied, resulting in a total of 1200 pulses. By means of a neuronavigation device the TMS coil could be located exactly above the auditory cortex. For evaluation of the cortical activation we depicted the hemodynamic response

using near infrared spectroscopy (NIRS). Lastly, the excitability of the motor cortex was assessed using a double pulse TMS paradigm.

Results: Preliminary results reveal that TBS can effectively improve tinnitus severity. In some patients the score on the tinnitus questionnaire and on the tinnitus handicap inventory declined by maximally 50%.

Discussion: The effectiveness of TBS will be evaluated. Moreover the effect of TBS on the hemodynamic (NIRS) response and on cortical excitability (double pulse TMS) will be discussed and related to changes in tinnitus severity.

WHICH TINNITUS PATIENTS BENEFIT FROM RTMS?

G Frank, T Kleinjung, M Landgrebe, G Hajak, B Langguth
Tinnituscenter Regensburg and Department of Psychiatry, Psychosomatics and Psychotherapy, University of Regensburg, Germany

Aims/Objectives: Currently, several studies suggest that repetitive transcranial magnetic stimulation (rTMS) represents a clinically useful contribution to the treatment of chronic tinnitus. However results are characterized by a high variability. Therefore the identification of predictors for treatment response is of utmost importance.

Methods: Clinical data of 104 tinnitus patients were evaluated retrospectively. All patients were treated with a standardized rTMS procedure (1 Hz, 10 days, 2000 stimuli / day, over the left temporal cortex). We investigated if parameters like age, lateralisation and duration of tinnitus und the extent of hearing loss had a significant effect on the outcome, being measured with a standardized tinnitus questionnaire by Goebel and Hiller (1998). Statistical data analysis was performed using SPSS. Study parameters were analysed with correlation und regression analyses.

Results: The following significant predictors were found: unilateral tinnitus was associated with a better outcome than bilateral tinnitus 12 and 90 days after the rTMS treatment. The extent of hearing loss and tinnitus duration influenced the outcome significantly, too. Tinnitus patients with no or only slight hearing loss and short disease duration benefited significantly better from rTMS than patients with marked hearing loss and longer disease duration.

Conclusion: By demonstrating an important role for tinnitus duration and hearing loss our results confirm previous data from smaller samples. Furthermore this study suggests for the first time that unilateral tinnitus responds better to rTMS than bilateral tinnitus.

These results will enable to better select patients for rTMS treatment. Furthermore the results suggest that different forms of tinnitus with specific clinical characteristics differ in their underlying pathophysiology.

ONE-YEAR FOLLOW UP OF PATIENTS WITH CHRONIC TINNITUS TREATED WITH LEFT TEMPOROPARIETAL RTMS

Eman M. Khedr, John C. Rothwell and Amal El-Atar
Department of Neurology,Assiut University Hospital Assiut, Egypt

Background and purpose: Although there are a number of positive reports on the therapeutic effects of repetitive transcranial magnetic stimulation (rTMS) for treatment of tinnitus, there are few details about the duration of treatment effects or the relative efficiency of different rTMS protocols.

Material and Methods: Sixty six patients with chronic tinnitus were divided into four groups, receiving sham rTMS, 1, 10 and 25 Hz rTMS applied each day for 10 days over left temporoparietal cortex.

They were followed up at 4 months and 1 year using the tinnitus questionnaire [Tinnitus Handicap Inventory (THI)] and self ratings of annoyance as well as measures of residual inhibition.

Results: A two factor ANOVA revealed a significant "rTMS x time" interaction indicating that real and sham rTMS had different effects on the THI scale and annoyance of tinnitus (P = 0.026 and 0.046 respectively). After 1 year, the tinnitus was absent in one or both ears of 10 patients who had received real rTMS: one of these was in the 1 Hz group, four patients were in the 10 Hz group and five patients were in the 25 Hz group.

Conclusion: Some patients show a lasting benefit at 1 year after 10 days of rTMS treatment. It appears that treatment at 10 or 25 Hz may be more beneficial than at 1 Hz, although more work is necessary to validate this conclusion.

THURSDAY
JUNE 25, 2009

8:30 - 10:00
Keynotes

8:30 - 9:15

CENTRAL AUDITORY SYSTEM CORRELATES OF TINNITUS AND HYPERACUSIS

J. Eggermont
Department of Physiology and Pharmacology, Department of Psychology, University of Calgary, Calgary, Alberta, Canada

In humans with tinnitus, functional imaging and EEG recording suggest potential tonotopic map changes in primary auditory cortex (AI); changes in the EEG spectrum, increased auditory evoked potentials (AEP) and increased spontaneous activity in areas close to secondary auditory cortex (AII) and association cortex. Increased dipole moments, BOLD responses and AEPs may indicate hyperacusis and increased synchrony. In the cat, chronic noise trauma results in increased spontaneous firing rates (SFR), increased neural synchrony and changed tonotopic maps in AI. These changes are prevented by balancing the output of the auditory nerve fibers across frequency starting immediately after the noise exposure. This can be done by presenting an enriched acoustic environment (EAE) that is enhanced in the hearing loss frequencies, or in humans by providing a hearing aid with sufficient output in the hearing loss range. Salicylates do not appear to change SFR in AI, but do so in AII, however, neural synchrony changes were not

observed. The dorsal cochlear nucleus (DCN) has been extensively studied and comparisons with behavior suggest an important role in tinnitus. However, whereas in AI SFR is significantly increased within 1-2 hours after the trauma, in DCN it takes 2-5 days. Corticofugal effects may be partly responsible for this. Delayed effects of somatosensory inputs to the DCN are also important to increase SFR after hearing loss. In turn this increased activity will likely affect SFR increases down stream in the central nervous system. One of the problematic issues is tinnitus and hyperacusis without audiometric hearing loss. Our results applying and EAE in normal hearing cats indicate a potential biological substrate. We found no effects on hearing thresholds, but the response of AI neurons to the EAE frequency range was severely depressed, that the SFR was significantly increased for frequency regions above and below the EAE frequency range, potentially signaling tinnitus. In addition we found strongly increased stimulus driven firing rates in these frequency regions, potentially indicating hyperacusis. This suggests that one has to be careful to interpret increased responsiveness to sound in functional imaging or AEP measurements as indicating tinnitus; it is more likely to represent hyperacusis or even recruitment.

9:15 - 10:00

THE MEDIAL OLIVOCOCHLEAR SYSTEM AND PROTECTION FROM ACOUSTIC TRAUMA

Ana Belén Elgoyhen
Institute for Research in Genetic Engineering and Molecular Biology, Buenos Aires, Argentina, elgoyhen@dna.uba.ar

Sound-induced acoustic injury is one of the most common causes of hearing loss and tinnitus. Although prevention from exposure to intense sound would be the obvious way to keep our inner ear healthy, finding alternatives to increase resistance to damage is a research field of great interest. The medial olivocochlear (MOC) pathway provides inhibitory feedback, through the release of acetylcholine (ACh) from brainstem neurons onto outer hair cells (OHCs) of the cochlea, reducing their ability to amplify sounds, and thus reducing cochlear sensitivity. Although many possible roles for this pathway have been proposed, understanding remains incomplete. We have explored the MOC pathway's function by generating a strain of genetically modified mice carrying a mutation in the nicotinic acetylcholine receptor (nAChR) subunit expressed by OHCs. We tested the effect of the mutation by recording signals from hair cells in cochlear preparations in vitro. Mutant hair cells exhibited greater sensitivity to exogenous ACh and the synaptic currents were prolonged in comparison to wild type preparations, indicating that the mutation enhanced nAChR function. To determine the consequences of this enhanced receptor function for cochlear responses, we measured auditory brainstem responses and distortion product otoacoustic emissions. The threshold levels of sound required to evoke these responses were elevated in the mutant mice, suggesting that the baseline inhibitory effect of the MOC pathway was enhanced. Furthermore, suppression of OHC-mediated amplification produced by stimulating the MOC pathway electrically was enhanced and dramatically prolonged in mutant mice. Surprisingly, mutant mice had a greater resistance to permanent acoustic injury resulting from exposure to 100 dB sounds, indicating that activation of the MOC feedback can protect the inner ear from noise-induced damage. Thus, the efferent pathway provides a promising target for pharmacological prevention of inner ear pathologies derived from acoustic injury, such as hearing loss and tinnitus. Finding drugs that mimic the effect of the mutation would be the developmental path to follow.

10:30 - 12:15
SYMPOSIUM
Auditory Stimulation
Arnaud Norena / Larry Roberts

NEW MUSIC THERAPY FOR TINNITUS PATIENTS BASED ON LATERAL INHIBITION

Stracke H, Okamoto H Pantev C
Malmedyweg 15, 48149, Muenster Germany/ Institute for Biomagnetism and Biosignalanalysis

Recent neuroscientific research revealed that tinnitus is presumably caused by maladaptive reorganization in the auditory cortex. However, widely used treatment approaches (e.g. tinnitus retraining therapy) focus mainly on the limbic and autonomic nervous systems, but not on the auditory cortex itself. Here, we propose a novel tinnitus treatment strategy based on the lateral inhibitory system in the auditory pathway in conjunction with cortical reorganization. Our recent study [1] demonstrated that the neural activities in the auditory cortex can be strongly reduced by the inhibitory neural networks from the surrounding neurons. Here we show decrements of tinnitus symptoms by enhancing the lateral inhibitory process in the auditory cortex. We found that patients, who had listened daily (over the course of one year) to music, which we have manipulated in the way that it could stimulate the lateral inhibition from the surrounding neurons to the cortical areas corresponding to the individual tinnitus frequency ("target" group), experienced significantly reduced subjective tinnitus loudness and exhibited reduced evoked activity in the primary and the non-primary auditory cortical areas contributing to the tinnitus when compared to patients who either received an analogous placebo treatment ("placebo" group) or no treatment ("control" group). These findings substantiate that the sensation of chronic tinnitus can be significantly diminished by targeted modification of brain activity. Further, compared to the indirect cognitive and behavioural symptom reducing approaches, our results reflect the invention of an effective strategy to treat tinnitus, suggesting an enjoyable way for the causal treatment originating from maladaptive reorganization in the auditory cortex.

1. Pantev C, Okamoto H, Ross B, Stoll W, Ciurlia-Guy E, Kakigi R, Kubo T: Lateral inhibition and habituation of the human auditory cortex. Eur J Neurosci 2004, 19:2337-2344.

LONG-LASTING TINNITUS RELIEF ACHIEVED BY ACOUSTIC COORDINATED RESET STIMULATION

Tass PA, Wenzel G, Hauptmann C, Mojallal H, Janssen D, Maron L, Freund H-J, Lenarz T
Institute for Neuroscience and Medicine, Neuromodulation, (INM-7), Research Center Juelich

Aims: To develop an acoustic stimulation therapy for patients with chronic tonal tinnitus that causes long-lasting therapeutic effects.

Methods: Coordinated reset (CR) stimulation effectively desynchronizes neuronal populations [1]. CR is based on the theory of statistical physics and nonlinear dynamics [1, 2]. The goal of CR stimulation is not only to specifically counteract synchrony, but also to unlearn pathological synchrony by reshaping network connectivity (anti-kindling) [2]. Acoustic CR stimulation, a periodically administered randomized sequence of tones (appropriately grouped around the patient specific tinnitus frequency), was delivered via patient adapted sound generator for in

total 4 hours per day in 13 patients with chronic tonal tinnitus as exclusive therapy. Subjective loudness was daily monitored with follow ups after 1, 2, 6, 8, and 12 weeks (still ongoing).

Results: After 3 months in 9 patients (69 %) we observed long-lasting therapeutic effects which outlasted cessation of CR stimulation, i.e. the daily CR dose significantly decreased the whole day tinnitus loudness. In 2 patients (12.5 %) CR therapy had a tinnitus masking effect. In 1 patient (7.7 %) CR was not effective. 1 patient (7.7 %) discontinued CR therapy.

Conclusion: Our results suggest that acoustic CR stimulation provides an effective tinnitus therapy. According to its theoretical foundation CR might counteract tinnitus, a phantom phenomenon, by therapeutic reshaping of abnormal connectivity in the auditory cortex.

1. Tass PA. Biol Cybern, 2003; 94: 58-66

2. Tass PA, Majtanik M. Biol Cybern, 2006; 94: 58-66

INHIBITION OF OSCILLATION IN A COMPUTATIONAL MODEL FOR TINNITUS AND ITS MANAGEMENT BY SOUND THERAPY

H. Nagashino*, Y. Kinouchi*, A. A. Danesh and A. S. Pandya****
**The University of Tokushima, Tokushima, Japan, **Florida Atlantic University, Boca Raton, Florida, USA*

Background/Aims: Sound therapy is one of the treatment options for tinnitus. The mechanisms of tinnitus and its management by sound therapy are not clear. The goal of the present study is to construct a model for tinnitus generation and sound therapy from the viewpoint of neural engineering. Previously we proposed a neural oscillator model and demonstrated the inhibition of oscillation that corresponds to tinnitus. In the present study we propose a more biologically plausible model using a neuron model of a simplified version of Hodgkin-Huxley equation.

Methods: The model is composed of two excitatory neurons and one inhibitory neuron. The two excitatory neurons, E1 and E2, are mutually coupled forming a positive feedback loop. The excitatory neuron E1 and the inhibitory neuron I are also mutually coupled forming a negative feedback loop. The neuron E1 receives external stimuli similar to the acoustic stimuli that are employed in sound therapy. We express the dynamics of the model by ordinary nonlinear differential equations. It is assumed that the coupling strength (C12) from the neuron E1 to the neuron E2 has plasticity.

Results: Computer simulations revealed that similar to the previous model, the present model also has two stable solutions, a non-firing state and a firing state. The former corresponds to the state in which tinnitus is not perceived, and the latter, which is oscillation, is related to the state in which tinnitus is perceived. The weaker the coupling is, the smaller is the basin of the state space corresponding to the firing state. By adding constant or pulse train input to the neuron E1, we are able to reduce the coupling strength C12 so that the oscillation is inhibited.

Conclusions: Our team constructed a computational model with plasticity to explain the mechanisms of tinnitus and its management by sound therapy. Through analysis of this model, it was found out that we can inhibit the oscillation by supplying external stimuli to the model.

A DOUBLE-BLIND CROSS-OVER STUDY TO EVALUATE THE EFFECT OF PHASE-SHIFT SOUND THERAPY ON TONAL TINNITUS

K.M. Heijneman, E. de Kleine, P. van Dijk
Department of Otorhinolaryngology, University Medical Centre Groningen

Background/aims: 10-15 % of the general population complains about tinnitus, with in most of the cases only remedies based upon the psychological coping mechanism. Tinnitus may be temporary reduced after the presentation of sound. This phenomenon is termed residual inhibition. A new therapy based on residual inhibition, is the PhaseOut Treatment. Typically, sounds can give residual inhibition that lasts seconds to a few minutes. In contrast, the PhaseOut stimulus, which is a tone that is repeatedly shifted in phase, has been described to result in residual inhibition that lasts longer (1).

Aim: To evaluate the effect of the PhaseOut treatment.

Methods: 26 patients with tone-tinnitus and normal hearing to mild hearing loss participated in this randomized double blind cross-over study. A treatment consists of a week with a 30 minutes phase shift sound therapy on Monday, Wednesday and Friday. The placebo was identical, except that a pure tone was used for sound stimulation. The second treatment was 5 weeks after the first. The evaluation was performed by measuring the tinnitus loudness match, VAS and questionnaires (THI, TRQ, HADS, VE and SF-36). The evaluation moments were before treatment and a 1 week after both the treatments. In addition, subjects completed a diary.

Preliminary results: The matched tinnitus loudness shows a significant decrease immediately after treatment A ($p<<0.05$). The questionnaires and other measurements show no further significant changes between both treatments and in comparison with the baseline values. br> Conclusion: The preliminary analysis showed an immediate positive effect on tinnitus loudness. Further evaluation of our data may identify other treatment effects.

1. Lipman RI, Lipman SP. Otolaryngol Head Neck Surg 2007;136(5);763-768.

RECOVERY OF HEARING AFTER A NOISE TRAUMA

Tomasi M., Etchelecou MC., Coulet O, Derkenne R, Norena A.
Université de Provence, CNRS UMR 6149, Marseille, France

Severe noise trauma in humans is usually followed by hearing loss and tinnitus. However, hearing can spontaneously recover within one week after the trauma. Usually, when hearing comes back to normal, tinnitus disappears. In humans, the mechanisms accounting for this spontaneous recovery, as well as whether this process can be further enhanced by a given treatment, remain unclear. Importantly, it is assumed that the severity of tinnitus will be inversely proportional to the auditory recovery. In this context, it was recently shown that cats exposed to noise trauma and placed immediately thereafter in an enriched acoustic environment had reduced hearing loss in the high frequencies. Furthermore, the neural activity in the auditory cortex did not present the pattern changes of neural firing observed after a noise trauma potentially related to tinnitus. This suggests that an enriched acoustic environment provided immediately after a noise trauma could reduce the noise-induced hearing loss and prevent the central changes potentially causing tinnitus. In the present study, we observed hearing recovery, in a population of military staff exposed to a noise trauma, under two conditions. Subjects were either

provided with: 1) a “standard” treatment (vasodilators and corticoids) or, 2) an enriched acoustic environment (in addition to the “standard” treatment). Our results suggest that the acoustic trauma results in the emergence of “dead regions” (no functioning hair cells and/or neurons in a circumscribed frequency range) in some subjects (shifted tip of the psychophysical tuning curves - PTCs). Interestingly, few days after the trauma and in parallel to the recovery of hearing as assessed from absolute thresholds, some PTCs do not show a shifted tip, suggesting a recovery of regions previously “dead” or non functional. Overall, our results show that the auditory recovery with the standard treatment is very large, and at this point of the study, it is unclear whether the enriched acoustic environment further increases the recovery of hearing.

10:30 - 12:15 SYMPOSIUM Target for Pharmacologic Interventions Ana Belén Elgoyhen / Mike Mulheran

VOLTAGE-GATED SODIUM CHANNEL EXPRESSION IN RAT SPIRAL GANGLION NEURONS

Fryatt A[1], Vial C[1], Mulheran M[1], Gunthorpe M[2], Grubb B[1]
[1]Department of Cell Physiology and Pharmacology, University of Leicester, UK LE1 9HN [2]GlaxoSmithKline Research & Development, Harlow, UK CM19 5AW

Aims: The aim of this study was to characterise expression and distribution pattern of the voltage-gated sodium channel family (VGSC or NaV) subtypes in rat spiral ganglion neurons. These channels have been identified as a potential target for a number of tinnitolytics and a fuller understanding of their expression and distribution would contribute to a more precise targeting of those channels involved in tinnitogenesis.

Methods: RT-PCR was performed with primers designed specifically for the NaV subtypes 1.1-1.3 and 1.6-1.9 using adult Wistar rat spiral ganglia neurons (SGN). Fluorescent and non- fluorescent immunohistochemistry was performed on sections of rat cochleae using antibodies specific for the above NaV subtypes. Additionally dual labelling was carried out using peripherin antibody to discriminate between Type I and II SGN. Sections were viewed using confocal and light microscopy. SGN cell body area and staining intensity were measured.

Results: PCR products were observed for NaV1.1, NaV1.6 and NaV1.7. Both NaV 1.7 and NaV1.6 showed positive labelling of the SGN in sections from rat using both fluorescent and non-fluorescent imaging methods. Faint staining of SGN cell bodies and processes was observed using NaV1.1 antibodies. Dual labelling experiments showed Type II SGN (peripherin positive) exhibited both significantly reduced fluorescence and smaller cell body area than VGSC subtypes in Type I SGN (peripherin negative).

Conclusion: These results provide novel evidence for differences in expression and distribution of the NaV1.7, NaV1.6 and NaV1.1 in the rodent SGN. This expression pattern was unexpected as it appears that it overlaps with classically held patterns for the peripheral and central nervous system. This may have considerable relevance for the targeting of tinnitolytics in the auditory periphery.

RELIEF FROM PERIPHERAL TINNITUS: SUSTAINED DELIVERY OF LIDOCAINE INTO THE COCHLEA USING PLGA MICROPARTICLES

Nakagawa T, Horie RT, Sakamoto T, Tabata Y, Okamura N, Tomiyama N, Ito J
Department of Otolaryngology, Head and Neck Surgery, Graduate School of Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Objectives: Our ultimate goal is to establish a novel strategy for long term-attenuation of peripheral tinnitus by local, sustained delivery of lidocaine. The aim of this study was to examine the efficacy of poly lactic/glycolic acid (PLGA) microparticles encapsulated lidocaine for sustained delivery of lidocaine into the cochlear fluid.

Methods: We made lidocaine-loaded PLGA microparticles, and examined their in vitro release profile. To evaluate in vivo release profile, we measured lidocaine concentrations in the perilymph at different time points following placing lidocaine-loaded PLGA microparticles on the round window membrane of guinea pigs. We also examined effects of local application of lidocaine-loaded PLGA microparticles on auditory and vestibular functions, and on inflammation in the middle ear.

Results: In vitro analyses revealed that PLGA microparticles released over 70% of lidocaine for the first 7 days, and gradually released residual lidocaine contents for consecutive 50 days. In vivo analyses demonstrated that high concentrations of lidocaine in the perilymph were maintained for 3 days, and that lidocaine in the perilymph was still detectable 14 days after application. Local application of lidocaine-loaded PLGA microparticles caused temporal shifts of auditory brain stem responses, no nystagmus or no significant inflammation in the middle ear mucosa.

Conclusions: These findings demonstrate the safety and the potential of PLGA microparticles for sustained delivery of lidocaine into the cochlea, suggesting potential use of lidocaine-loaded PLGA microparticles for attenuation of peripheral tinnitus.

EFFECTS OF NERAMEXANE ON IONOTROPIC A9A10 NICOTINIC RECEPTORS AND HUMAN NMDA (NR1A/2A) - RELEVANCE FOR TINNITUS

C.G. Parsons [1], K.E. Gilling [1], G. Rammes [2], B. Elgoyhen [3], P.V. Plazas [3]
[1]Merz Pharmaceuticals, Frankfurt, D-60318 Germany; [2]Clinical Neuropharmacology, Max Planck Institute of Psychiatry, Munich, D-80804 Germany; [3]Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular, Buenos Aires, Argentina.

Aims/Objectives: Potential mechanisms underlying tinnitus include cochlear and central auditory neurotransmission involving NMDA receptors - important for synaptic plasticity - which might be involved in the chronification / centralization of tinnitus. Tinnitus has also been proposed to cause activation of efferents to OHCs which inhibits their activity via transient a9/a10 nicotinic receptor-mediated EPSCs, coupled via Ca2+ influx to prolonged SK2 channel-mediated IPSPs. However, this could result in reduced afferent activity with enhanced tinnitus due to central "edge" effects.

Results: Neramexane blocked a9/a10 nicotinic receptors expressed in Xenopus oocytes with an IC50 of 0.39uM. Antagonism was agonist concentration independent but essentially voltage-independent. [3H]methyllycaconitine binding experiments confirmed non-competitive inhibition. Neramexane also blocked native a9/a10-containing receptors of rat IHCs with an IC50 of 0.30uM.

Neramexane blocked human NR1a/2A receptors in a concentration (IC50 = 0.24uM) and strongly voltage-dependent (d=0.9) manner. These patch clamp experiments revealed that neramexane had particularly rapid onset blocking kinetics (kon=1.39*106M-1s-1), whilst the offset kinetics were of a similar magnitude to those seen with open channel blockers of moderate potency (koff = 0.42s-1). This fully accounted for the improved potency at NMDA receptors without a slowing in offset kinetics. The Kd calculated as Koff/Kon (0.30uM) was similar to that determined at equilibrium.

Conclusion: Potentially synergistic effects of neramexane at both a9/a10 nicotinic and NMDA receptors could be relevant for the treatment of tinnitus. a9/a10 nicotinic receptor antagonism could help restore physiological patterns of neuronal activity by preventing edge effects in central pathways. NMDA receptor antagonism might ameliorate the chronification / centralization of tinnitus. Such possibilities require verification with further experiments.

10:30 - 12:15
SYMPOSIUM
Tinnitus Assessment
Richard Tyler

THE TINNITUS DISABILITY INDEX: A NOVEL MEASURE FOR TINNITUS-RELATED DISABILITY

Cima RFF, Joore MA, Anteunis LJC, Maes IH, Vlaeyen JWS
Otorhinolaryngology & Head and Neck Surgery, University *Hospital* Maastricht*,* Maastricht*, The Netherlands.*

Aims: To date, a sound measure for assessing level of disability associated with tinnitus does not exist. The Tinnitus Disability Inventory (TDI), based on the Pain Disability Inventory (PDI) (1), is presented as a novel measure for tinnitus-related disability. The TDI consists of 7 items scored on a 10 point Likert scale, corresponding to 7 major aspects of daily life. Subjects judge the extent to which tinnitus affects their functioning in each of these 7 life domains. In this study, reliability and validity of the TDI were investigated.

Methods: In a cross-sectional study (N=436) the TDI, the Short Form 36 (SF36: General health), and the Tinnitus Questionnaire (TQ: tinnitus-related distress), were completed online. Cronbach's alphas were calculated to assess reliability. A principal component analysis of the TDI was carried out to assess factor structure. Finally, a stepwise regression analysis was performed to investigate construct validity.

Results: Internal consistencies were considered excellent (TDI, α= .89; SF36, α= .94; TQ, α= .94). The principal component analysis yielded a 1 factor structure accounting for > 61% of total variance. The multiple regression analysis showed that disability due to Tinnitus was predicted by general health status (R^2Change=.20, P<.001) and tinnitus distress (R^2Change=.35, P<.001), controlled for age, gender, education, and time since onset (Total model: R^2=.57, F=78, P<.001).

Conclusion: Results provide firm support that the TDI is a reliable and valid measure for assessing tinnitus-related disability. A principal component analysis revealed a single factor. A multiple regression analysis provided evidence for construct validity; TDI scores were significantly associated with general health status, and ratings of tinnitus distress. The TDI appears to be valid, reliable, with the advantage that it is not confounded by tinnitus severity and tinnitus distress.

References: 1. Tait RC, Chibnall JT, Krause S. Pain, 1990; 40: 171-182.

ANALYSIS OF THE CORRELATION BETWEEN AUDIOMETRIC THRESHOLDS, PSYCHO-ACOUSTIC MEASURES AND VALIDATED QUESTIONNAIRES IN TINNITUS PATIENTS

Figueiredo RR, Rates MA, Azevedo AA, Oliveira PM,Navarro P
OTOSUL,Otorrinolaringologia Sul-Fluminense, Volta Redonda,RJ, Brazil; Clinica de Tratamento e Pesquisa em Zumbido, Belo Horizonte,MG,Brazil

Introduction: One of the most difficult topics of tinnitus treatment is the lack of general consensus concerning measurement methods. The most commonly used methods are tinnitus questionnaires, psycho-acoustic methods and tinnitus scales, which have been poorly correlated in many studies. Psycho-acoustic measures depend on patients' concentration and ability to distinguish different sounds and also on examiner training. These facts may account for poor correlation to the questionnaires.

Aim: To evaluate the correlation between the audiometric thresholds (including the cut-off frequencies on slope hearing losses), pitch masking (PM), minimum masking level (MML), Tinnitus Handicap Inventory (THI) and the Beck Depression Inventory (BDI) in tinnitus patients.

Material and method: 49 patients with tinnitus as the main complaint underwent tonal audiometry with PM and MML. They also fulfilled the THI and BDI questionnaires, in their Brazilian Portuguese validated versions.

Results: There was no statistically significant correlation between the THI and MML (p>0,05), both in patients with BDI scores under and above 14 points. A slight statistically significant tendency correlation was found between age and MML (p=0,074) in unilateral hearing losses, the elder patients perceiving tinnitus louder. There was no statistically significant correlation (p>0,05) between the worst threshold frequency and PM, as well as between the cut-off frequency and the PM in patients with slope hearing losses (n=18, p>0,05).

Conclusions: There is no statistically significant correlation between psycho-acoustic measures (PM and MML), audiometric thresholds and validated questionnaires, with a slight tendency for louder tinnitus in elder patients. Our results are with other studies and these findings may reflect multiple aspects of different subtypes of tinnitus patients, as well as influence of non-auditory aspects of tinnitus and inconstant responses at the psycho-acoustic measures.

MEASURING TINNITUS: A RE-EVALUATION OF THE DIMENSIONALITY AND CONGRUENT VALIDITY OF THE 12 ITEMS TINNITUS HANDICAP INVENTORY

Goertelmeyer R[1], Suckfuell, M[2], Wittmann, W[3]
[1] Merz Pharmaceuticals Frankfurt, [2] Ludwig-Maximilians-Universitaet Muenchen, [3] Universitaet Mannheim

Objectives: Subjective tinnitus is defined by the patient's report of an unpleasant and disturbing noise in the absence of a physical stimulus. Subjective tinnitus is therefore quantifiable only by validated self-assessment tools. Correlations between annoyance and tinnitus sensation are weak. Among the widely used tinnitus rating scales, the THI [1] and the THI-12 [2] are regarded as validated and reliable tools. The dimensionality of the THI and the THI-12 is still under discussion. The objective of the present study is to re-evaluate the dimensionality and

validity of the THI-12 considering the correlations to interview assessments of tinnitus sensation.

Methods: Screening and baseline data of n=612 screened and n=433 randomized patients of a randomized, placebo-controlled trial, were used for factor analyses (PCA orthogonal rotation). Internal consistency was estimated using Cronbach alpha index, test-retest reliability, rtt, was estimated by correlating the scales from screening and baseline. Correlations of the TBF-12 scales with interview items were performed to evaluate congruent validity.

Results: Three factors were extracted. Factor 1 emotional, factor 2 social impairment, and factor 3 impairment in attention. Internal consistency of the three factors from the screening and baseline data is Alpha < 0.70. The test-retest reliability, is moderately high, rtt ≥ 0.59. The correlation with interview items is moderate for factors 1 and 2 and low r < 0.32 for factor 3.

Conclusion: The factor analyses revealed a three factor solution in contrast to [2]. The subscales could be of importance for the differential evaluation, the total score may be used for a global assessment of treatment effects in tinnitus. The correlations of the THI-12 total and subscales with sensation of tinnitus are in accordance with literature.

1.Newman, C W et al.(1996). Archives of otolaryngology--head & neck surgery, 122 (2), 143-148.

2.Greimel, K et al. (2000). THI-12 Manual.

TINNITUS HANDICAP INVENTORY'S RELATIONSHIP WITH SOCIODEMOGRAPHIC ASPECTS

Oliveira A. V. & Meneses R. F.
ENT Department Militar Hospital - Porto - Portugal & Faculdade de Ciencias Humanas e Sociais - Universidade Fernando Pessoa - Porto - Portugal

AIMS/OBJECTIVES: Subjective tinnitus are difficult to measure and associate with problems in daily life. Questionnaires can identify which individual aspects are more affected. They are important in intervention, allowing for a standardized pre-post intervention comparison. The Tinnitus Handicap Inventory (THI)1, focuses on behavioural difficulties and emotional aspects related to tinnitus. Since tinnitus is very distressing for some patients, identifying patients profile is clinically relevant.

The aim of the study was explore the relations between the THI scores and sociodemographic aspects.

METHODS: 74 patients(34 males; M=55,6 years(SD=13,6;18-79) with tinnitus were evaluated (tonal and speech audiometry, impedancimetry and tinnitus measurements), and, they answered to a sociodemographic questionnaire and the European Portuguese THI2.

RESULTS: THI scores were: Total: M=47,6(SD=22,8;8-100), Functional: M=20,6(SD=10,0;2-44), Emotional: M=17,2(SD=9,2;2-36), Catastrophic: M=9,8(SD=5,1;0-20). After confirming the normal distribution, t test and Pearson r were performed.

Women had worse THI scores:

THI Total - t(72)=2,336; p=0,022; Mfemale=53,62; Mmale=41,62

THI Functional - -t(72)=2,213; p=0,030; Mfemale=23,08; Mmale=18,05

THI Emotional - t(72)=-2,682; p=0,009; Mfemale=20,00; Mmale= 14,49

No relation was found between THI scores and: age, civil status, professional activity or schooling.

CONCLUSION: The results suggest that: a) women have intervention needs that differ from those of men; b) individuals with different civil status, professional activity and schooling do not necessarily differ on their intervention needs.

1-Newman CW, Jacobson GP, Spitzer JB.Development of the Tinnitus Handicap Inventory.Arch Otolaryngol Head Neck Surg,1996;122:143-148.

2-Oliveira V, Meneses R.Versao Portuguesa do Tinnitus Handicap Inventory (THI).In: Leal I, Ribeiro JLP, Jesus SN(eds.).Actas 6º Congresso Nacional Psicologia da Saude. Lisboa: Instituto Superior de Psicologia Aplicada,2006:819-823.

SLEEP DISTURBANCE IN CHRONIC TINNITUS PATIENTS

G. Attanasio [(a)], R. Roukos [(a)], S. Ventura [(b)] and M. Saponara [(a)]
[(a)]Dept. of Neurology and Otolaryngology, Univ. La Sapienza, Rome, IT; [(b)]ACSE - Association of Social-Educational Counseling, Rome, IT

The purpose of the study is to examine sleep records and polysomnographic data for assessing the reported prevalence and severity of sleep disturbance in chronic tinnitus patients.

Recent studies (1,2) have shown a decreased tolerance and increased discomfort with tinnitus, when associated with insomnia and depression. In our experience, majority of patients refers changes in tinnitus perception at awakening, with a significant increasing of severity of the symptom after 1 or 2 hours of sleep.

Patients were selected from waiting lists of the Dept. of Neurology and Otolaryngology Ambulatory of the University of Rome "La Sapienza" and underwent an ENT visit with following tests: audiometry, tympanometry with tubaric functionality manoeuvres, nasal fibroscopy, daytime sleepiness questionnaire. Tinnitus perception and tolerability were measured using Newman Questionnaire (THI) before and after the sleep time, while BDI, STAI X-2, and DISS #330 were used for evaluate respectively depression, anxiety and stress perception. Polysomnography was recorded using 22 channels (12 referential, 2 bipolar, 7 unipolar, 1 SpO2). Sleep-waked states were based on electroencephalogram, electrooculogram, legs position, electrocardiogram, body position, nasal and oral flow, thoracic and abdominal movements, snoring noise and pulse oximetry. Polysomnograms were analyzed following the Rechtschaffen and Kales International Criteria for sleep-wake scoring and the American Accademy for Sleep Medicine recommendation for the scoring and breathing events.

(1) Bartels H, Middel BL, van der Laan BF, Staal MJ, Albers FW, The additive effect of co-occurring anxiety and depression on health status, quality of life and coping strategies in help-seeking tinnitus sufferers. Ear Hear. 2008 Dec;29(6):947-56.

(2) Crönlein T, Langguth B, Geisler P, Hajak G. Tinnitus and insomnia. Prog Brain Res. 2007;166:227-33.

NON-LINEAR RELATIONSHIP FOR TINNITUS BETWEEN THE INTENSITY AND THE DISTRESS

Sven Vanneste, Dirk De Ridder, Mark Plazier, Jan Ost, Berthold Langguth, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning
Brai²n, University Antwerp, Wilrijkstraat 10, 2650 Edegem

Background: In a population, up to 5 -15% experience tinnitus continuously. About 6 to 25 % of the affected people report interference with their life as tinnitus causes a considerable amount of distress. Although researchers agree that the intensity of the phantom sound and the distress related to tinnitus are both important aspects of tinnitus, it is not clear how these concepts are related.

Aims: Is there a kind of relationship between the intensity of tinnitus and the distress it causes?

Methods: In three studies the relationship was verified using curve estimation based on regression analysis using different models (namely linear, quadratic, exponential and cubic). Intensity was measured using the visual analogue scale (from 0 - 10) and distress was measured using the Tinnitus Questionnaire (Goebel and Hiller) or other distress related items.

Results: The results clearly show that the cubic model explains most of the variance (r^2 was .29, .35 and .41, respectively for the different populations).

The relationship indicates that there is a VAS intensity drop off, which is around 4 on a scale from 0 to 10. On the VAS higher than 4 the scores on distress are high and the upper and lower ends of the distress scores are almost equal. On the other hand: on scores lower than 4 on the VAS intensity a steep decrease in distress takes place.

Conclusion: These results have implications for research and clinical practice. The key to achieve satisfying therapeutic results (distress decrease) is to decrease the VAS intensity score below the drop off (4). By researching new therapeutic modalities the change to achieve a high success rate depends on the baseline average VAS. The further the baseline is removed from the drop off score: the bigger the reduction in VAS is needed to reduce distress. This latter remark might explain why some studies found satisfying results in tinnitus treatment, where other similar studies did not obtain satisfying results.

13:45 - 15:30
SYMPOSIUM
Specific Forms of Tinnitus
Alain Londero / Tobias Kleinjung

PAROXYSMAL POSITIONAL VERTIGO AND TINNITUS

S. Barozzi, D. Soi, M. Socci, A. Cesarani
Audiology Unit, I.R.C.C.S. Fondazione Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena.

Department of Otolaryngology, University of Milan, via Pace 9, Milan, Italy.

While dealing with patients suffering from paroxysmal positional vertigo (PPV) we noticed in some cases that together with the appearance of vertigo or shortly before that, a new tinnitus began or a pre-existent one mutated, and it disappeared immediately after the liberatory manoeuvres. Rarely the tinnitus appeared right after the manoeuvres. Other Authors [1] detected the disappearance of tinnitus in some patients after Semont's and Epley's manoeuvres for rehabilitation of PPV and attributed it to a reduction in autonomic activity.

Aim of this study was to describe the prevalence and the clinic patterns of tinnitus in PPV patients and to suggest a new interpretative hypothesis.

We examined a group of patients affected by PPV and tinnitus. We administered questionnaires, audiometric and immitance tests and a clinic vestibular evaluation to the patients before and after repositioning manoeuvres.

The tinnitus was mostly monolateral, intermittent, positional and ipsilateral to the semicircular canal interested by the PPV.

This clinic observation suggests a possible vestibular origin of tinnitus determined by the otoliths that slipped into the cochlear duct through the ductus reuniens, the joining channel between the cochlea and sacculus of the membranous labyrinth of the inner ear.

1. Gavalas GJ, Passou EM, Vathilakis JM. Tinnitus of vestibular origin. Scand Audiol Suppl. 2001;(52):185-6.

Corresponding Author: Stefania Barozzi, M.D., Audiology Unit, I.R.C.C.S. Fondazione Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena. Department of Otolaryngology, University of Milan, via Pace 9, 20122, Milan, Italy.

E-mail: stefania.barozzi@unimi.it

PULSATILE TINNITUS CAUSED BY DURAL ARTERIOVENOUS SHUNTS: EFFECT OF EMBOLIZATION ON PATIENTS' QUALITY OF LIFE

Londero A, Guedin P, Rodesch G
HEGP CNRS UMR 7060 Paris, France; Hôpital FOCH Suresnes, France

Aim/objectives: Pulsatile tinnitus (PT) are pulse-synchronous bruits that may be related to benign dural arterio-venous shunts with sinus venous drainage (DAVS with SVD) and may be poorly tolerated. DAVS treatment is debatable because of the procedure risks and the favourable spontaneous evolution often reported.

Methods: We describe therapeutic management of PT due to DAVS. The clinical files of 23 consecutive patients suffering from DAVSs with SVD have been retrospectively reviewed. DAVS angio-architecture and localisation, clinical presentation, therapeutic protocol and follow up have been analyzed with special interest to quality of life impairment before and after treatment.

Results: Five patients were not treated because they eventually tolerated their bruit. Eighteen patients with disabling PT were treated by endovascular methods (78%). Transarterial embolization with glue through the main dural feeders of the DAVS was achieved in 13 patients. Because of local conditions, five patients were treated by transvenous approach with occlusion of the pathological sinus with coils. Cure of the DAVS was obtained in 12 cases of lateral sinus shunts (67%). Partial anatomical results were obtained in the remaining 6 patients (33%), all treated transarterially (evaluated morphological gain > 66 % (4 cases), of 50% (1 case), of 33% (1 case)). The venous drainage of the brain was preserved in all patients. Clinically, in the 12 cured patients PT totally disappeared immediately after procedure. In the six partially treated patients tinnitus was no longer intrusive (Level 0 or 1 on a 0 to 5 scale). No permanent morbidity or mortality occurred. Patients were clinically and/or radiologically followed up (mean follow-up 78 mo). No recurrence of the symptoms or of the treated lesion occurred in patients considered cured. Partially treated patients remained stable.

Conclusion: DAVS with SVD can be safely managed by embolization, with proper improvement of the PT.

Therapeutic strategy has to be adapted to the patient's tolerance of the bruit.

MULTIDISCIPLINARY EVALUATION OF PATIENTS WITH TINNITUS AND COMPLEX AUDITORY HALLUCINOSIS

Rocha SCM, Sanchez TG, Kii MA, Pereira C, Borelli D, Forlenza O.
Tinnitus Research Group, Otolaryngology Department, University of São Paulo School of Medicine

Objectives: Complex auditory hallucinations/hallucinosis relate to the auditory perception of music or voices without an external stimulus. The hallucination is often considered as a major symptom of psychiatric disorders, but may also have organic causes. The hallucinosis involves the concept of preserved contact with reality, being aware that no one else hears such sounds. We aimed to characterize the complex auditory hallucinations/hallucinosis in patients with tinnitus by a multidisciplinary team.

Methods: All patients from our Tinnitus Research Group who complained of complex auditory hallucination/hallucinosis were enrolled. They underwent a thorough evaluation by the same multidisciplinary team (otologist, audiologist, neurologist and psychiatrist) and the following data was selected for analisys: pure-tone audiometry, EEG, Tinnitus Handicap Inventory, Hoffman Auditory Hallucinations Rating Scale and Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders.

Results: We enrolled 18 patients, with predominance of women (88,8%; mean age 59.7±15.6y). All had a preserved contact with reality (hallucinosis) and 12 (66.6%) heard musical sounds, 16.7% verbal sounds and 16.7% musical plus verbal sounds. The context of musical hallucinosis was often reported as pleasant, but its repetition disturbed all subjects. Concomitant tinnitus was reported by 88.8% subjects, and hearing loss was present in 100% of the audiometries (bilateral in 88.8% and profound in 61.1%). The THI score varied from 22 to 96 (mean 51), and functional and emotional domains were equally represented. The time of onset of hearing loss and tinnitus was similar (mean 15.4±13.7 and 15.8±19.0, respectively), but the hallucinosis started 10.8±11.6 years later than the hearing loss. Among 15 patients evaluated by the neurologist, one had temporal epilepsy. Among 16 cases seen by the psychiatrist, 68.7% had some degree of depression and 25% didn't have a psychiatric diagnosis.

Conclusion: Complex auditory hallucinosis is probably more common in otologic patients than realized, mainly in females. It can be associated to tinnitus and hearing loss, not necessarily in profound or long term deafness, and usually starts much later than the otologic symptoms, suggesting the influence of neuroplasticity.

THE SOMATOSENSORY PULSATILE TINNITUS SYNDROME PROVIDES FURTHER SUPPORT FOR THE DORSAL COCHLEAR NUCLEUS TINNITUS HYPOTHESIS

Levine R, Melcher J, Nam E
Massachusetts Eye & Ear Infirmary, Boston

Kaltenbach provided evidence for the dorsal cochlear nucleus (DCN) hypothesis: tinnitus related to hearing loss was due to increased DCN activity. Subsequently, we extended this hypothesis to include tinnitus related to a somatic disorder. We proposed that, via CNS somatosensory pathways, somatic dysfunction of the head or upper lateral neck causes increased DCN activity and thereby tinnitus. Likewise somatic modulation of tinnitus, which occurs in about 80% of tinnitus subjects, is similarly mediated.

Because (a) the DCN is architectonically similar to the electrosensory nucleus of fish, and (b) the fish electrosensory nucleus performs a sensory subtraction, it has been hypothesized that the DCN also performs a sensory subtraction. Just as the electrosensory nucleus subtracts from its total signal its self-generated electrical signals to obtain the environmental electrical signals, so too the DCN subtracts from its total signal its self-generated acoustical signals to obtain the environmental acoustical signals. For the DCN the self-generated acoustical signals are the somatosounds generated by respirations, chewing, self-vocalizations, and heart beats.

We have recently described the somatosensory pulsatile tinnitus syndrome (SPTS), whose features are cardiac synchronous tinnitus that is high-pitched and suppressed by activation of the somatosensory system of the jaw or upper lateral neck. All objective testing is negative.

Because objective testing is negative, the SPTS must be on a neural, not acoustic basis. We hypothesize that SPTS is due to failure of the DCN to suppress self-generated cardiac somatosounds. Hence the SPTS may provide support for the DCN tinnitus hypothesis.

1. Levine, R, et al. Somatosensory pulsatile tinnitus syndrome: Trends Amplif, 2008; 12: 242-253

THE EFFECT OF MIDDLE EAR SURGERY ON TINNITUS IN PATIENTS WITH CONDUCTIVE HEARING LOSS

T. Kleinjung
Department of Otorhinolaryngology, University of Regensburg. Germany, and Interdisciplinary Tinnitus Treatment and Research Center, University of Regensburg, Germany

Hearing loss causes deprivation of input which can lead to the development of tinnitus through expression of maladaptive neural plasticity. Therefore patients with conductive hearing loss due to otosclerosis or chronic otitis media often suffer from tinnitus. Main reasons for middle ear surgery are the eradication of inflammatory pathology from middle ear structures, the closure of the tympanic membrane and the improvement of hearing.

The restoration of hearing plays an important role in tinnitus treatment. Especially the benefit of hearing aids on tinnitus is well documented in multiple studies. This presentation focuses on the value of middle ear surgery in terms of tinnitus improvement.

A review of available data in literature is provided. This should help surgeons to answer the patients' questions with regard to the change of a pre-existing tinnitus after surgery. In conclusion stapedotomy and tympanoplasty can result in a good tinnitus control in approximately two thirds of patients. Both procedures are very unlikely to make the symptom tinnitus worse if surgery results in hearing improvement.

IDIOPATHIC BILATERAL TINNITUS CONCOMITANT TO EYE CLOSURE

M Ohki, H Ichinose, H Mouri
Department of Otolaryngology, Red Cross Hospital, Tokyo, Japan

Methods: We examined in a 13-year-old girl who had complained of left sided intermittent low-pitched tinnitus

synchronously during eye closing or blinking. Otoscopic examination, pure tone audiometry, tympanogram, impedance audiometry, electroneuronography and blink reflex were examined. CT scan and MR imaging were also perfomed.

Results: She never has past history including facial palsy, facial spasm or neurolog ical disorders. The tympanic membranes were normal on both sides. The pharynx and larynx did not reveal abnormal muscular movements. The both tympanic membranes retracted concomitant to eye blinking or onset of eye closure during otoscopic examination. The posterior superior quadrant of the tympanic membrane was most moved inward. She recognized low-pitched tinnitus coincident with these movements of tympanic membrane. While she kept her eyes open, she never felt the tinnitus. Pure tone audiometry showed normal auditory threshold on both sides. Tympanogram was bilaterally type A. Impedance audiometry demonstrated normal acoustic reflex. However, when compliance was examined during eye blinking and eye closure in impedance audiometry, it rapidly decreased concomitant to eye blinking and during eye closure. After ceasing eye blinking or eye closure, compliance returned to normal revel. Electroneuronography revealed normal function of facial nerve. Electromyography using surface electrodes on m. orbicularis oculi and m. orbicularis oris never present synkinesis. Blink reflex demonstrated normal responses. CT scan and MR imaging denied central lesions.

Conclusion: We report a rare case of tinnitus due to stapedial muscle contraction coincident to eye closing or blinking.

13:45 - 15:30
SYMPOSIUM
Neuroplasticity, Cellular Mechanisms of Tinnitus
Thanos Tzounopoulos

MECHANISMS OF SYNAPTIC PLASTICITY IN THE AUDITORY BRAINSTEM: PLASTICITY-INDUCED CHANGES THAT COULD UNDERLIE TINNITUS

Thanos Tzounopoulos
3500 Terrace Street BST W1457, Pittsburg, 15261/ Univ. of Pittsburgh

Tinnitus is the persistent perception of a subjective sound. Tinnitus is almost universally experienced in some forms. In most cases recovery may occur in seconds, hours or days.

How does tinnitus shift from a transient condition to a life-long disorder? Several lines of evidence, including clinical studies and animal models, indicate that the brain, rather than the inner ear, may in some cases be the site of maintenance of tinnitus.

One hypothesis is that normal electrical activity in the auditory system becomes pathologically persistent due to plasticity-like mechanism that can lead to long-term changes in the communication between neurons.

A candidate site for the expression of this so-called synaptic plasticity is a region of the brainstem called the Dorsal Cochlear Nucleus (DCN), a site of integration of acoustic and multimodal, sensory inputs.

Here we present recent findings on cellular mechanisms observed in the DCN that can lead to long-term changes on the synaptic strength between different neurons in the DCN.

These cellular mechanisms could provide candidate signaling pathways underlying the induction (ignition) and/or the expression (maintenance) of tinnitus.

TARGETING AND REDUCING NOISE TRAUMA-INDUCED TINNITUS IN A RAT MODEL

Depireux D
U of Md Medical School, Baltimore

Converging evidence points to the central involvement of the inferior colliculus of the auditory midbrain in the development and maintenance of tinnitus. Therefore, in rats equipped with chronic multi-electrode arrays implanted in auditory midbrain, we quantify changes in neural spontaneous activity, excitability and sound coding before and after noise trauma-induced tinnitus, while verifying the presence of tinnitus through a behavioral assay and the auditory brainstem response. We also examine lateralized immunocytochemical changes in midbrain following one-sided trauma. With a better understanding of the mechanism involved in the generation of tinnitus, we use this model to understand the mechanism of action of Lidocaine, the only drug known to consistently, albeit temporarily, provide relief from tinnitus.

DISRUPTION OF BALANCED CORTICAL EXCITATION AND INHIBITION BY ACOUSTIC TRAUMA.

Scholl, B. and Wehr, M.
Institute of Neuroscience and Department of Psychology, 1254 University of Oregon, Eugene, Oregon, USA 97403

Objectives: Hearing loss can produce rapid shifts in the receptive fields of cortical neurons, but the synaptic mechanisms underlying these changes, and their significance with respect to tinnitus, remain unknown. Here we tested the hypothesis that these receptive field shifts are caused by the unmasking of subthreshold inputs by a selective loss of synaptic inhibition, and that this loss of inhibition can lead to hyperexcitability and tinnitus.

Methods: We used in vivo whole cell recordings to directly measure tone-evoked excitatory and inhibitory synaptic inputs in auditory cortical neurons in anesthetized rats before and after acoustic trauma. We also used a behavioral measure of tinnitus, based on gap-detection, in a separate group of rats exposed to similar acoustic trauma.

Results: Acute acoustic trauma disrupted the balance of excitation and inhibition by selectively increasing and reducing the strength of inhibition at different positions within the receptive field. Inhibition was abolished for low frequency stimuli, but was markedly enhanced for high frequency stimuli. These changes led to hyperexcitability and an expansion of receptive fields towards low frequencies. Similar acoustic trauma induced behavioral gap-detection deficits that were consistent with a tinnitus percept within the same range of low frequencies.

Conclusions: These results demonstrate that the rapid receptive field shifts caused by acoustic trauma are due to distinct mechanisms at different positions within the receptive field, which depend on differential disruption of excitation and inhibition. These receptive field changes are consistent with a model in which loss of synaptic inhibition leads to cortical hyperexcitability and tinnitus.

MODULATING HYPERACTIVITY IN GUINEA PIG INFERIOR COLLICULUS AFTER ACOUSTIC TRAUMA

Mulders, W.H.A.M., Robertson, D.
University of Western Australia, Crawley, Australia

Aims/Objectives: Tinnitus is often associated with a mild hearing loss. It has been reported that tinnitus is accompanied by hyperactivity in central auditory pathways, and the current view is that this is a centrally generated plastic response to altered input. We have developed a guinea pig model using acoustic trauma to induce mild hearing loss and spontaneous hyperactivity in inferior colliculus. We investigated whether this central hyperactivity can be modulated by treatments affecting cochlear output.

Methods: Anaesthetized guinea pigs were exposed to a loud tone (1 hr, 10 kHz, 124 dB). Two to four weeks after recovery, single neuron recordings in inferior colliculus were made to establish increased levels of spontaneous activity. Several methods were then used to alter cochlear neural output and the effects on highly spontaneous neurons were assessed. Methods included cochlear ablation, cochlear perfusion with kainic acid and electrical stimulation of the olivocochlear efferent system.

Results: Firstly, we found that the spontaneous hyperactivity in inferior colliculus disappeared after cochlear silencing. Secondly, stimulation of the efferent system also suppressed the spontaneous hyperactivity in inferior colliculus. Interestingly, in some instances the central suppression was much longer lasting than reported previously for primary afferents.

Conclusion: Our findings seem to be conflict with the present view that hyperactivity is centrally generated. However, this dependency on the cochlea does not necessarily indicate that the central hyperactivity is a direct result of increased cochlear spontaneous activity. We hypothesize that central hyperexcitability could result in greater neuronal firing to normal levels of cochlear spontaneous activity. Finally, more research is needed to investigate whether the increased central effects of olivocochlear stimulation are due to central intrinsic circuitry or to co-activation of central olivocochlear collaterals.

13:45 - 15:30
SYMPOSIUM
Pharmacologic Treatment of Tinnitus
José Miguel Lainez / Berthold Langguth

PHARMACOLOGIC TREATMENT OF TINNITUS

Jose-Miguel Lainez [1], Berthold Langguth [2]
[1]University of Valencia, Department of Neurology, Otorhinolaryngology and Radiology, Valencia, Spain, [2]Department of Psychiatry, Psychosomatics and Psychotherapy, University Regensburg

Whereas tinnitus research traditionally focussed on the ear, where tinnitus is perceived, neuroimaging and electrophysiology findings within the last decade have clearly demonstrated that chronic tinnitus is the consequence of alteration of neural activity in the central nervous system. In more detail, it is assumed, that hearing loss, which is frequently occurring in tinnitus patients, results in a dysbalance between inhibitory and facilitatory mechanisms in the central auditory system, which in turn gives rise to increased neural activity throughout the central auditory pathways. The activity in the auditory pathways is additionally modulated by other brain areas, such as the limbic system. So it is assumed that tinnitus is perceived, when increased activity in the auditory pathways is not sufficiently reduced due to impaired function of the limbic system.

This implies that both, the cochlea and he central nervous system might represent potential targets for pharmacologic treatment. Even if currently no drug is approved for tinnitus and no drug has shown efficacy as evidenced by replicated positive findings in at least two well conducted trials, there is no reason to believe that tinnitus can not efficiently reduced by pharmacologic treatment. After a short introduction the presentations will give an overview about drugs, which are frequently used in clinical practice (Enrico, Hoekstra), present data from recent clinical studies (Sziklai, Sakamoto) and focus on strategies for drug development (Figureido, Althaus).

CLINICAL DEVELOPMENT OF NEW DRUGS FOR THE TREATMENT OF TINNITUS USING THE EXAMPLE OF NERAMEXANE

Althaus M* for the NERAMEXANE TINNITUS STUDY GROUP
**Merz Pharmaceuticals, Frankfurt, D-60318 Germany*

Aims/Objectives: Clinical development of new drugs for the treatment of tinnitus has to comply with continuously growing requirements for a later marketing authorization in an international regulatory framework.

Methods: Neramexane is a novel drug with a dual mode of action that is currently in Phase 3 of clinical development for the treatment of tinnitus. The first Phase 2 study was a combined proof of concept and 4-arm dose-selection study that enrolled more than 400 patients with subjective tinnitus. The primary efficacy variable, the Tinnitus Handicap Inventory (THI-12), showed a clear trend towards improvement of tinnitus suffering in the medium and high dose group. This finding was in line with consistent beneficial effects observed in secondary parameters and allowed a proper dose selection for the Phase 3 program.

Results: The Phase 3 program was developed in close consultation with the European and US Competent Authorities and will enrol another 1,200 patients in 3 international clinical studies. All studies are following a randomized, placebo-controlled multi-centre design and will use the validated THI-12 as main outcome parameter. Since the scales used in the studies are not readily available in validated versions for all languages, a comprehensive validation program has been launched. The study designs match to a large extent and differ only in single aspects. This allows to address specific questions on e.g. duration of the treatment effect or potential side effects after withdrawal of the study drug, while the consistency in the design facilitates meta-analyses across all studies.

Conclusion: The example of neramexane shows that development of pharmacological treatments for tinnitus can only be achieved by international networking, in co-operation with study centres, and in close consultancy with the Competent Authorities. Linguistic and psychometrical validation of the outcome measures is essential just as a proper dose-selection.

EFFECTS OF CAFFEINE IN TINNITUS: PRELIMINARY DATA

Figueiredo RR, Azevedo AA, Rates MA, Moreira RKP, Oliveira PM, Navarro P
OTOSUL,Otorrinolaringologia Sul-Fluminense,Volta Redonda,RJ,Brazil;Clínica de Tratamento e Pesquisa em Zumbido, Belo Horizonte,MG, Brazil; Serviço de Otorrinolaringologia da Santa Casa de Misericórdia,Belo Horizonte,MG,Brazil.

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.

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: 13 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 somatosensory tinnitus were excluded. A Brazilian Portuguese version of THI and a VAS scale 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 10 points or mores were considered as improvement or worsening.

Results: 1 patient dropped out. Of the remaining 12, 5 (41.6 %) had their tinnitus improvement and 1 (8.33 %) had a slight worsening (12 points). 2 patients had a strong effect on THI scores (56 and 50 points). Overall average results were a reduction of 9 points in THI and 1 point in VAS.

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.

TINNITUS CONTROL BY DOPAMINE AGONIST PRAMIPEXOLE IN PRESBYCUSIS PATIENTS. A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND STUDY

I.Sziklai, J. Szilvassy
University of Debrecen, Dept of Otolaryngology & HNS

Background: The concept of the study derives from the observations that tinnitus perception is in prefrontal, primary temporal and temporo-parietal associative areas, as well as the limbic system that overlaps cerebral dopaminergic projections. Dopaminergic pathways can be modulated by various agonists and antagonists and some of these drugs can reduce the perception of tinnitus.

Methods: Our randomized, placebo-controlled double-blind clinical study was concerned with the possibility that pramipexole, a dopamine receptor agonist, used for treatment of Parkinsonism, can be beneficial for prespycusis patients with tinnitus. The study included 40 patients with subjective tinnitus with age over 50 yr for each. They were randomized to two groups of 20. A group took prapimexole applied over a period of 4 weeks according to treatment schedule as follows: 3X0.088, 3X0.18, 3X0.7 and from 3X0.18 to 3X0.088 mg on 1st, 2nd, 3rd and 4th week , respectively. Patients in the 2nd group were given placebo. Determination of subjective grading of tinnitus perception (including frequency and intensity assessments) completed with the use of Tinnitus Handicap Inventory (THI) questionary served as primary end point. Results from objective and subjective audiometric evaluations served as secondary end point. The anticipated study-period is 1 year.

Results: 21 patients finished the treatment by now. Due to the double blinde nature of the study, it is non known who were treated with drug or placebo. Tinnitus decreased in 13 of 21 patients shown by tinnitus matching audiometry and THI score in correlation with the ECOG N1 amplitude. Those, who exhibited improvement, produced greater post-treatment SP/AP ratio.

Conclusion: The result expected will shed light on new possibilites in treatment of tinnitus with dopaminergic receptor agonists. Moreover, in case of positive outcome, the study may provide evidence for a second indication for an antiparkinson drug running in the market.

ANTIOXIDANTS, MINERALS, VITAMINS, AND HERBAL REMEDIES IN TINNITUS THERAPY. AN UPDATE.

Paolo Enrico, Donatella Sirca and Maddalena Mereu
Department of Biomedical Sciences, University of Sassari, V.le S. Pietro 43/B, 07100 Sassari, Italy

Complementary and alternative medicine (CAM) products are very popular in western countries and are often used by patients with tinnitus. We have recently reviewed this phenomenon showing that, although the peculiar nature of tinnitus makes it difficult to draw clear-cut conclusions, CAM pharmacological approach to tinnitus lacks scientific support and is probably not clinically effective either (1). Despite the scarce scientific evidence in favor of the role of vitamins, minerals, antioxidant and herbal products in tinnitus therapy, these products are getting increasingly popular among patients and (being wrongly perceived as harmless), are habitually used without medical guidance.

In the recent literature, several randomized placebo-controlled trials have further confirmed the lack of protective and therapeutic effect of vitamins, antioxidants and some herbal products against many diseases including tinnitus. At the same time a large evidence is accumulating on the potential dangers hidden in the use of “natural” and “biological” products. Indeed, CAM products may augment or antagonize the actions of prescription and nonprescription drugs, with chemical and biological pollution of these products being also a growing concern.

We update here the review published in 2007 “Antioxidants, minerals, vitamins, and herbal remedies in tinnitus therapy”, with the latest available evidence published on the use of CAM products in tinnitus therapy, with a particular emphasis on direct toxicity and possibilities of interaction with prescription drugs.

References: 1) Enrico P et al. Prog Brain Res. 2007;166:323-330. Review.

ANTICONVULSANTS FOR CHRONIC TINNITUS, A SYSTEMATIC REVIEW

Hoekstra CEL, Rynja SP, van Zanten GA, Rovers MM
University Medical Center Utrecht, the Netherlands

Background: Chronic tinnitus originates from increased spontaneous firing and enhanced synchronization of neurons in the auditory system caused by reduced inhibition, elicited by decreased cochlear output. Curative therapies are difficult to develop. The role of pharmacotherapy is unclear. Anticonvulsants may diminish this neuronal hyperactivity in two ways: 1) enhancing inhibition through γ-aminobutyric acid, the main inhibitory neurotransmitter of the auditory system, and 2) lessening

the glutamate transmission, the main excitatory neurotransmitter.

Methods: Systematic searches were conducted in PubMed and EMBASE for randomized placebo controlled trials on patients with chronic tinnitus treated with oral anticonvulsants. Studies on patients with somatosounds/pulsatile tinnitus or auditory hallucinations were excluded. As primary outcome the improvement in tinnitus was taken, measured with validated tinnitus questionnaires. Secondary outcomes analyzed were improvement measured with self-assessment scores and improvement in global well-being or accompanying symptoms.

Results: The combined searches resulted in 323 studies. After detailed screening for eligibility 9 articles remained. These trials investigated 4 anticonvulsants; gabapentin was analyzed 4 times, carbamazepine 3 times and lamotrigine and flunarizine once. All studies were evaluated on methodological quality. Eight studies were of insufficient or questionable quality. Major methodological problems were the randomization and blinding process and large drop out rates. The one study with sufficient quality looked at the effect of 8 weeks of 3600mg gabapentin per day. After treatment the Tinnitus Handicap Inventory in the intervention group was 0.3 points lower than in the control group (95% CI -5.5 -- 6.2), indicating that gabapentin is not effective.

Conclusions: There is no evidence for a positive effect of anticonvulsants on tinnitus. Studies performed until now are of low methodological quality.

TREATMENT OF NOISE INDUCED HEARING LOSS BY STEALTH-TYPE NANOPARTICLES ENCAPSULATING BETAMETHASONE PHOSPHATE

Sakamoto T, Horie R, Nakagawa T, Higaki M, Ishihara M. Ito J
(1)Department of Otolaryngology-Head and Neck Surgery, Kyoto University, Kawaharacho 54, Shogoin, Sakyo-ku, Kyoto, 606-8507, Japan

Background: Hearing impairment is a major cause of tinnitus. Systemic application of large amount of steroid is the standard therapy for the acute sensori-neural hearing loss, however, it has considerable risks such as hyperglycemia, gastric ulcer, electrolyte abnormality, and so on. Reasons for the use of large amount of steroid include the limited blood flow of the cochlea and the existence of the barrier called blood-cochlear barrier. Drug delivery system may provide good modification of this therapy. We previously showed that conventional poly (lactic-co-glycolic acid) (PLGA) nanoparticles seldom arrive in the cochlea and accumulate in the liver suggesting active uptake in the reticuloendothelial system (RES). In this study, we used stealth-type poly lactic acid (PLA) nanoparticles, which have poly (ethylene glycol) (PEG) coating on their surface. Stealth nanoparticles are thought to have longer circulation time in the blood due to reduced RES uptake.

Objectives: To examine the therapeutic potential of betamethasone phosphate (BP) encapsulated in stealth-type nanoparticles.

Methods: PLA nanoparticles encapsulating Rhodamine B (Stealth Nano-Rhodamine) and betamethasone phosphate (Stealth Nano-Steroid) are prepared by an oil-in-water solvent diffusion method. CBA/N mice (male, 4-6 weeks) are exposed to loud noise (8 KHz band noise, 120 dB 2h) to induced noise trauma, followed by the intravenous injection of Stealth Nano-Rhodamine, Stealth Nano-Steroid or betamethasone phosphate. Quantifications of tissue betamethasone concentrations, repeated ABR measurements and histological analyses were performed.

Results: In the Stealth Nano-Steroid group, tissue concentrations of betamethasone were higher, hearing recovery was better, and the more inner/outer hair cells were preserved.

Conclusion: Stealth nano-steroid would provide better option for the treatment of noise induced hearing loss.

16:00 - 18:00
SYMPOSIUM
Non Conventional Approach
Manuela Mazzoli / Eberhard Biesinger

MINDFULNESS BASED TINNITUS TREATMENT

G. Attanasio [(a)], L.Vistarini [(b)], S.Ventura [(c)]
[a]Dept. of Neurology and Otolaryngology, Univ. La Sapienza, Rome, IT; [b]IPRA - Institute Post Rationalist, Rome, IT; [c]ACSE - Association Counseling Social-Educational, Rome, IT.

Different clinical approaches have been proposed for the emotional distress associated with chronic tinnitus: hypnosis, relaxation training, biofeedback, as well as cognitive behavioural therapy (CBT) combining relaxation techniques and coping strategies. Mindfulness based treatments for chronic diseases have progressively gained interest in the last years (1): the aim of the study is to verify whether a structured mindfulness based stress reduction programme, is able to improve tinnitus tolerability. And decrease its intrusiveness.

Non-lateralized tinnitus patients, since at least one year, were selected from waiting lists of the Dept. of Neurology and Otolaryngology Ambulatory of the University of Rome “La Sapienza” and divided in two groups: 13 patients (test group) received the mindfulness intervention consisting of eight weekly sessions of 2 hours and homework exercises of 1 hour a day; 15 remaining patients (control group) waited two months without any therapy. Both groups received the same set of questionnaires at the beginning and at the end of the study. Tinnitus perception and tolerability were measured using Newman Questionnaire, while Back Depression Inventory, State Trait Anxiety Inventory X-2, and Disability Scale DISS #330 were respectively used for evaluate depression, anxiety and stress perception. Results showed statistically significant reduction of depressive symptoms, an improvement of tinnitus tolerability and lower level of its intrusiveness. Interestingly, it was observed a no n significant reduction of anxiety and a relevant impact of a subjective stress.

1. Kabat-Zinn, J., Lipworth, L. and Burney, R. The clinical use of mindfulness meditation for the self-regulation of chronic pain. J. Behav. Med, 1985 8:163-190.

THE EFFECT OF QI GONG ON SOMATOSENSORIC TINNITUS (SST)

E. Biesinger
ENT-Clinic 83278 Traunstein, Germany

The focus of this study was to determine the therapeutical effects of Qi Gong on tinnitus, specifically in somatosensory tinnitus.

This research is based on a former study conducted by the German Tinnitus league (1996).

It showed that from all used therapies, Qi Gong and Thai Chi provided the best results.

It is postulated, that Qi Gong as a positive influence on the somatoric system, is relaxing and also has a distraction effect.

The task of this study was to determine, if patients with somatosensoric tinnitus have more profit from Qi Gong therapy, than the ones with other causes of tinnitus.

Patients with tinnitus and duration of less than 3 months were included after a wash-out-phase of a medicamentous acute therapy of minimum 2 weeks.

All kinds of tinnitus are included, e.g. after sudden hearing loss, noise trauma etc.

4 groups were examined:

1. patients with obviously SST, treated with Qi Gong

2. patients with obviously SST, non treated

3. patients without SST, treated with Qi Gong

4. Untreated Control group

The assessment of the results were performed with Visual analogue scale (VAS), TBF-12 (Greimel et al) and a specific test battery for functional testing for somatosensory tinnitus.

When publishing this abstract, the evaluation of the results was not yet finished.

TRI Grant 2007, Somatosensory work group.

NEW DIET FOR TINNITUS: ADENOSINE DIET

M.A. Lopez-Gonzalez, F. Esteban
Hospital Universitario Virgen del Rocio, Sevilla, Spain

Background: Nucleic acids contain purines and pyrimidines. Two bases of nucleic acids, adenine and guanine, are derived of a purine. When purines are catabolized, uric acid is formed. Allopurinol is a structural isomer of hypoxanthine (a naturally occurring purine in the body) and is an enzyme inhibitor, inhibiting xanthine oxidase. Xanthine oxidase is responsible for the successive oxidation of hypoxanthine and xanthine resulting in the production of uric acid, the product of human purine metabolism. In addition to blocking uric acid production, inhibition of xanthine oxidase causes an increase in hypoxanthine and xanthine, which are converted to adenosine. Allopurinol has been used in the treatment of epilepsy, schyzophrenia, autism, aggressive behavior, and depression. Adenosine is a neuromodulator of the central nervous system, through A1a and A2a receptors, acting on the neural hyperexcitability and stress, inhibiting glutaminergic and dopaminergic neutrotransmission. It is anxiolitic and neuroprotective.

Method: Proposal of a rich diet in nucleic acids plus allopurinol to obtain high levels of adenosine in the central nervous system. The diet enriched in nucleic acids would be obtained of foods like: Seafood, shellfish. Beef, veal, pork, lamb, sheep, rabbit, poultry, venison. Anchovies, sardines, herring, mackerel, carp, cod, perch, salmon, trout, tuna. Asparagus, lentils, kidney beans, mushrooms, green peas, dried peas, spinach, cauliflower. Oatmeal, wheat bran, wheat germ. Soup, gravy, consomme, bouillon, meat extracts. Fructose (processed foods and soda beverages).

Allopurinol at dose of 300 mg twice a day.

This diet should be symptomatic, only when tinnitus causes discomfort.

Side effects: Adenosine diet would increase uric acid, but allopurinol transforms uric acid in adenosine. Allopurinol can produce rash in sensibilized people. Interactions of allopurinol in: azathioprine, cyclosporine, mercaptopurine, dicoumarol, warfarin, chlorpropamide.

MINDFULNESS BASED STRESS REDUCTION (MBSR) INTERVENTION IN TINNITUS THERAPY

M. Mazzoli[(1,2)], T. Sintoni[(2)], K. Stellato[(3)], A. Crocetti[(4)], M. Da Col [(5)], F. Covizzi[(1)], A. Magnano San Lio[(1)], A. Roccato[(5)].
[(1)]Az. Ospedaliera-Università di Padova, ORL-Otochirurgia, via Giustiniani 2, 35128 Padova, Italy
[(2)]Istituto per l'evoluzione armonica dell'Uomo,(www.ieau.it), Cremona, Italy
[(3)]Mente e benessere, (www.menteebenessere.org), Belluno, Italy
[(4)]Fondazione Ascolta e Vivi Onlus, (www.aevo.org), Milano, Italy
[(5)]Divisione ORL dell'ospedale S. Maria del Prato – Feltre (BL), Italy
contact: manuela.mazzoli@gmail.com

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 increased after treatment in most subjects.

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

LOW LEVEL LASER THERAPY: TINNITUS SUBJECTIVE CHARACTERISTICS AND MEASUREMENTS. PRELIMINARY REPORT

M.Savastano, MD*, L. Termine,Tech*, Vlatko Prosenikliev, MD**
Department of Medical-Surgical Specialities, Section of Otorhinolaryngology, University of Padua Via Giustiniani 2 35128 PADOVA e-mail: marina.savastano@unipd.it

Low-level-laser-therapy (LLLT) has been recently discussed as a therapeutic procedure for chronic tinnitus. The present study refers to the results obtained from the application of LLT to a tinnitus population. This study considered 49 consecutive tinnitus sufferers, observed by the ENT Section of the Department of Medical-Surgical Specialities of Padua University. All patients(G1) underwent the application of a Soft Laser system, applied 1 x per day, 20 minutes, for three months. As control group(G2) were considered 10 subjects treated with a Laser placebo. The data have been collected before the first LLT application(T0)and after three months(T3). The following parameters were considered. The subjective discomfort caused by tinnitus, tested using a Visual Analogue Scale(VAS), tinnitus annoyance studied using the Tinnitus Handicap Inventory(THI), the audiometric evaluation using liminar audiometry, Tinnitus

measurements: tinnitus loudness, spectral composition, masking effectiveness and residual inhibition. For the statistical analysis the Wilkoxon test for paired data has been applied. As for G1 is concerned the following results has been observed.VAS and THI:difference To-T3 not significant(p= 0.059, p=0.057). The difference of the intensity T0-T3 is statistically significant (p= 0.0032). The difference of the residual inhibition T0-T3 is not relevant(p= 0.54). As for G2 is concerned, the difference To-T3 for VAS and THI is statistically relevant (p= 0.01, p=0.017). The difference T0-T3 of tinnitus intensity and residual inhibition is not relevant (p= 0.093, p=0.47). In our study the most relevant effect of the LLT is the reduction of tinnitus intensity in the group treatmented with active laser. As for VAS, THI and residual inhibition, no relevant modifications have been observed in the sample group. In the control group a variation for VAS and THI was observed. The present follow-up is 3 months, but the study is still going on until a follow-up of 6.

THE NON RESPONDER PATIENTS BEFORE THEY RECEIVE THE ACCELERATORS

Shemesh Zecharya, M.D.
Hadassah Hospital, Jerusalem, Israel

In any therapeutic approach to tinnitus patients it is possible to find favorable responders, non responders and the patients who are in between. The Partially Treated Tinnitus Patients (PTTP) include many problematic matching between patients and treatment programs, such as: non compliant patients, aggravants, patients with factitious disorders, patients who are involved in litigation, secondary gain, primary gain, unrecognized organic factors, inability to tolerate the treatment program (disgusting diet, side effects of the treatment, ineffective social support system), doubts about the treatment plan or the skills of the therapist and inability to cover the expenses of the treatment. The aim of this study is to isolate a sub-group of tinnitus patients who do not have good response to the metabolic approach, or who show poor response. These patients will have the option to try food supplements as accelerators of their treatment.

A sub-group of 18 partially treated patients, with undetermined cause of being poor responders, received financial coverage of 90% of their expenses for special medications. Analysis of the results showed that 12 of them had slight improvement on the TQ (Tinnitus Questionnaire) score during 5 months of treatment and 6 had slight deterioration on the TQ. More detailed statistical analysis would be presented in the presentation.

16:00 - 18:00
SYMPOSIUM
Strategies for Tinnitus Research
Aage Møller

AMERICAN TINNITUS ASSOCIATION – ROADMAP TO A CURE

Mitchell, S.

American Tinnitus Association, PO Box 5, Portland, Oregon 97207-0005 USA

This presentation will discuss the components of the American Tinnitus Association's *Roadmap to a Cure*, where it has taken the tinnitus research community, the current status of tinnitus research, and where we are headed next.

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. In addition, we actively encourage the United States (U.S.) federal government to increase their appropriated budget for tinnitus research through various agencies. ATA's research grant program has awarded nearly $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[1] 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.

Path A includes identifying where tinnitus starts and is specific to the areas of the auditory system that show tinnitus-related abnormalities. Investigations that fall under Path A can also include measuring changes in the activity of the auditory system and related tinnitus perception. Path B includes areas of study that investigate how tinnitus starts. Projects under Path B seek to identify which nerves or cells cause tinnitus-generating signals in the auditory system and determine the difference between tinnitus-causing cells and "normal" cells.

Studies in Path C, are dedicated to developing therapies that can test tinnitus suppression and use their results to target cells that generate tinnitus. Path D focuses on the optimization of therapies developed in Path C, refining and improving treatment delivery in order to reduce any potential side-effects of a particular treatment.

The Roadmap's four-pronged approach is what guides SAC and our Board of Directors as they evaluate the increasing number of excellent tinnitus research proposals received by ATA. The ATA anticipates that this Roadmap will be expanded and updated as continuing research discovers new paths to a cure. ATA encourages all tinnitus investigators, world-wide, to continually submit proposals and encourage others in the field of tinnitus research to submit to ATA.

For more information on ATA's research grant program that awards up to $100,000 per year over 3 years for a potential maximum of $300,000 please contact ATA's Director of Research & Special Projects, Daniel Born at daniel@ata.org or (800) 634-8978 x 211 or visit the research section of ATA's Web site: www.ata.org/research.

---

[1] Kaltenbach, J., Salvi, R., Cacace, A., Seidman, M., Rubenstein, J.

TINNITUSBOOK: A PROPOSAL FOR AN ADVANCED SCIENTIFIC WEB COMMUNITY FOR TINNITUS RESEARCH

G. Attanasio[a,f], P. Ciccarese[b,c], E. Wu[e], T. Clark[b,c,d], E. Pecis[f], R. Filipo[a]
[a]Dept. Neurol and Otolaryngol, Univ La Sapienza, Rome,IT; [b]Massachusetts Gen. Hosp., Boston,MA; [c]Harvard Med. School, Boston,MA; [d]Harvard Initiative in Innovative Computing, Cambridge,MA; [e]Alzheimer Res. Forum Found., Boston, MA; [f]Acufeni.net web por

Aims/Objectives: Based on the positive results following the publishing of the portal Acufeni.net, we propose to work with the Dept of Neurology and Otolaryngology of the University of Rome "La Sapienza", the Initiative in Innovative Computing at Harvard University and the Department of Neurology of the Massachusetts General Hospital to create a new interdisciplinary online resource connecting researchers with researchers, TinnitusBook, to facilitate rapid progress in Tinnitus research. The goal of TinnitusBook will be to bring together the best thinking and resources in the Tinnitus research community; to enable dynamic online discussions, facilitate collaborative work, surface new ideas, share resources, and bring forward new opportunities for translational research; and above all, to speed the development of a cure for Tinnitus.

Methods: TinnitusBook will be a collaborative scientific web community and knowledgebase in the field of Tinnitus, based on Web 3.0 (social web plus semantic web) technologies pioneered by the successful SWAN project in Alzheimer Disease research, PDOnline in Parkinson Disease research and Stembook in Stem Cells research. TinnitusBook will utilize the Science Collaboration Framework Web 3.0 toolkit as foundational technology. It will publish news, scientific articles, reviews and discussions, and it will provide users with access to a growing semantically-structured knowledgebase of scientific findings, evidence and resources.

Preliminary Results: We have developed acufeni.net a successful web portal whose goal is connecting Tinnitus patients with clinicians online to facilitate informed decision-making on Tinnitus healthcare. We now propose, for the Tinnitus research community, the adoption of the Science Collaboration Framework that has successfully served as technological and methodological infrastructure for PDOnline for Parkinson Disease research and Stembook for Stem Cells research.

LEARNING FROM THE LITERATURE

Ron Goodey
Otologist, Auckland New Zealand

In April 2006, with encouragement of Dr de Nora, the Tinnitus Research Initiative commissioned the accumulation of tinnitus citations into an EndNote library. The aim was to provide research workers with a quickly accessible, comprehensive database of all journal articles plus a wide range of other references which include "tinnitus" in the title and/or abstract.

By January 2009, the database included 7635 references of which 5893 were from peer reviewed journals. 576 of the references had been published or presented during 2008 and of these 369 were from peer reviewed journals. The figures for 2008 will be a little larger by the time of the 3rd TRI conference in June 2009. Comparison with earlier years shows a steady increase in the number of tinnitus articles appearing in journals each year from 63 in 1980, to 219 in 1990, 229 in 2000, and 426 in 2007.

As a clinician, my main interest is in improving my treatments of patients with tinnitus. I therefore search for and monitor journal articles which have "therapy", "therapeutic", &/or "treatment" in the title or keywords. The number of such articles has increased from 26 in 1980 to 43 in 1990, 100 in 2000, and 137 in 2007 (but so far only 82 for 2008).

In managing patients with tinnitus, I like to think about the influences of sensory inputs, centrally acting chemical agents, direct stimulation of the central nervous system and "psychological" influences. I expect at least two of these approaches will be involved if a patient's chronic tinnitus is to be ameliorated or cured.

1. Sensory inputs. In the Tinnitus database, all journal citations on therapeutic influences of sensory inputs, focus either on stimulating the auditory or the somatosensory pathways (including electrical stimulation of either). I cannot find any articles, which report effects on tinnitus of olfaction, vestibular stimulation, vision or other sensory inputs. Drugs may influence peripheral auditory function and, in doing so, facilitate treatment of tinnitus. There are exciting new developments to protect, repair or replace inner ear hair cells. I find this work in the auditory neuroscience literature rather than in the tinnitus database.

2. Drugs, hormones and dietary factors can influence central neural activity and the changes we describe as neural plasticity. They may have an important role to play in tinnitus treatment, especially when used in conjunction with the more targeted influences of peripheral and/or direct stimulation.

When I search "drug" in the database I find a marked decrease in the number of references over the last three years. At first, I assumed that the word "drug" had fallen out of favour as a keyword. However, further analysis shows that the number of references reporting drug trials for tinnitus really has dropped. This drop may reflect disillusionment from previous disappointing trials and/or the reduction in the number of new drugs becoming available because of bureaucratic obstacles and reduced cost effectiveness of bringing new drugs to market. We need to remember that one drug, intravenous lidocaine, consistently though temporarily relieves tinnitus.

TINNITUS-SUBTYPING BY ESTABLISHING THE TRI DATA BASE

F. Zeman*, M. Koller*, Y. Eberl*, M. Mohr [1], B. Langguth [2], M. Landgrebe [2]
**Center for Clinical Studies, University Hospital Regensburg, [1]ManaThea GmbH, Regensburg, [2]Department of Psychiatry, Psychosomatics and Psychotherapy, University Regensburg*

Tinnitus, i.e. the perception of sound in the absence of corresponding external sounds, represents a wide-spread affliction within the population (about 5% suffer from severe tinnitus). Patients with tinnitus present with a variety of symptoms, and a wide range of therapies are available for tinnitus treatment. Although many of these therapies take effect in individual patients, no study has yet been able to confirm one particular therapy as a standard one of tinnitus treatment. Thus, to find such a treatment option for patients with tinnitus, the primary objectives of the TRI database are: 1) to collect data (both prospective and retrospective) on patient characteristics, treatments, and outcomes for over 1000 patients with different tinnitus symptoms, and 2) to establish a data repository - maintained on a secure platform - that will help identifying promising treatment options and will serve as a basis for future research. The TRI Data Base (TRIDB) was designed and structured in such a way that all data collected according to GCP-guidelines and the TRI-consensus can be fed into the base. The data base contains physical, audiological, and psychophysical examinations as well as the questionnaires TSCHQ, THI,

TBF-12, BDI, WHOQOL-BREF, and TQ. All participating centers, 14 up so far, have direct access to the server via the internet through a virtual private network (VPN), which means safe data entries and queries are possible at any time. The data base is coded in SQL and the servers are located in Regensburg. Data will be analyzed by the Center for Clinical Studies in Regensburg with the software SPSS 15.0 and SAS 9.1.

TRI - TOGETHER FOR A CURE

Berthold Langguth
Tinnituscenter and Department of Psychiatry, Psychosomatics and Psychotherapy, University of Regensburg, Germany

The Tinnitus Research Initiative (TRI) is a privately-funded organisation dedicated to the development of effective treatments for all types of tinnitus so that relief can be obtained by everyone who suffers from it.

The activities of TRI are based on the belief that collaboration across disciplines is essential. In this context TRI promotes and supports multidisciplinary biomedical research which will lead to a better understanding of tinnitus and to novel, effective therapies for its treatment. Special emphasis is placed on collaboration and knowledge-sharing among the institutions supported by TRI.

In order to achieve its goals, TRI implemented seven workgroups, each one dedicated to a specific topic and to gathering worldwide expertise in the domain. Workgroups execute a research plan, which is constantly adapted and challenged by new input. Moreover TRI has an open call for proposals through the grant and exploratory grant program. Finally, a yearly meeting with conferences and workshops stimulates cooperation between funded researchers, clinicians and new participants. TRI is interested in new collaborations and is always available to discuss new opportunities.

SURVEY STUDY ON TINNITUS IN THE WORLD

Desiderio Passali and the International Tinnitus Study Group

On behalf of IFOS (International Federation of Otorhinolaryngological Societies) we carried out a cognitive study in order to better know some data about tinnitus all over the world.

For this purpose we sent a questionnaire with several questions to opinion leaders Chairmen and Directors of ENT Departments.

We selected more than 200 Colleagues experts and involved in this topic from all the four continents (20 from Africa, 50 from Europe, 50 from Asia/Oceania, 80 from America and more) asking data about epidemiology, classification, diagnosis, natural history and treatment.

In this short report we will present and comment the interesting data obtained from the analysis of all the answers we received back, trying to find an explanation for several, sometime original approaches, as well as common ideas, in different Countries.

Our goal is to try to propose a common “language” for this important topic.

This work was supported by the National Natural Science Foundation of China (Grants 30470560 and 30730041), the National Basic Research Program of China (Grant 2007CB512306) and the CAS Knowledge Innovation Project (Grant KSCX1-YW-R-36).

RNID – WORKING TOWARDS A CURE

D Goldman, J Robinson and R Holme
RNID, London, UK

The Royal National Institute for Deaf People (RNID) is the largest charity representing deaf and hard of hearing people in the UK. Our vision is a world where deafness, hearing loss and tinnitus do not limit opportunity, and where people value their hearing. A key part of achieving this vision is to provide support to people with tinnitus and to drive research forward, so that effective treatments and ultimately a cure for tinnitus are found. We have approached this in the following ways:

1. Research Funding: We fund scientific projects around the world aiming to understand the causes of tinnitus, to develop treatments and to, ultimately, find a cure for tinnitus.

2. Involving industry: We have published a tinnitus market report to highlight the need for tinnitus treatments and the commercial opportunities this holds for industry. We also offer consultancy services to help companies to become involved in tinnitus research.

3. Supporting people with tinnitus: We provide information about tinnitus via a free helpline and fact sheets as well as recommending and selling products to alleviate tinnitus.

4. Helping professionals: Our biannual Tinnitus Focus magazine communicates the latest scientific advances to healthcare professionals to ensure the newest research knowledge reaches those who treat patients.

At this meeting, we will give an overview over these different approaches and the impact made. To read more about how we support tinnitus research, visit our website www.rnid.org.uk/research.

16:00 - 18:00
SYMPOSIUM
Cochlear Stimulation
Paul van de Heyning / Richard Tyler

ELECTRICAL STIMULATION OF THE COCHLEA TO REDUCE TINNITUS

Richard S. Tyler, Claudia Coelho, Anne K. Gehringer, Stephanie A. Gogel, Shelley Witt, Tao Pan
University of Iowa, Department of Otolaryngology Head and Neck Surgery and Speech Pathology and Audiology, Iowa City, IA, USA

The possible mechanisms of cochlear tinnitus include a variety of patterns of neural activity, which can be modified by the presentation of electrical current. It is likely that central tinnitus can also be modified by peripheral stimulation. We review early studies of extracochlear and intracochlear stimulation of tinnitus showing that tinnitus can be totally or partially suppressed in some patients. Those who receive cochlear implants (CIs) often report tinnitus reduction with implant use, although some recipients without tinnitus acquire it postimplantation. We present new data from 153 CI patients who were administered the Tinnitus Handicap Questionnaire preoperatively and postoperatively. Additionally, we attempt to determine the characteristics of those patients who acquired tinnitus after receiving a CI. We then compare data from a single patient who was implanted with a CI to reduce tinnitus, and finally show a field trial of a patient who compare the effectiveness of two different stimulation algorithms to suppress tinnitus.

CORTICAL PLASTICITY AFTER UNILATERAL DEAFNESS AND ELECTRICAL COCHLEAR STIMULATION: A STUDY IN GUINEA PIGS

Yves Cazals
Centre de Recherche en NeuroBiologie et NeuroPhysiologie de Marseille Cnrs 6231

Tinnitus often arises after deafness, possibly as an outcome of lack of input from the deaf cochlea and in association with cortical remodeling. Re-supplying an input from a deaf ear may be one way to diminish or suppress tinnitus. This is feasible on cophotic human ears and is the object of a conjunct study under the same grant (Frachet et al. abstract). The present study produced total deafness on one ear of guinea pigs and expose d some of these ears to electrical stimulation eight hours a day for three weeks starting two days after deafness. Functional assessment of auditory cortex was performed on awake animals with chronically implanted electrodes over several months before and after induced unilateral deafness, using various acoustic and electric stimuli. Auditory cortical responses underwent considerable modifications after deafness which were only minimally influenced by electrical stimulation of the deaf ear. These results illustrate the limited effects of electrical stimulation of a deaf cochlea in unilateral deafness and emphasize the need to better understand and improve its efficacy.

(Supported by ANR-TECSAN Stesu grant)

CONTINUOUS AURICULAR ELECTRICAL STIMULATION FOR TINNITUS: AN UPDATE

Levine R, Cardarelli F, Melcher J, Szeles J
Massachusetts Eye & Ear Infirmary, Boston

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 symmetric hearing thresholds but asymmetric widely fluctuating tinnitus. We began a P-Stim (PS) trial, because it incorporates both modalities. PS 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.

METHODS: PS was initially offered to 24 patients. The plan was to apply the device weekly for 3 consecutive weeks. If any improvement occurred during that time then treatments would continue weekly until improvement plateaued.

RESULTS: Of the 24 subjects 9 completed the 3 weeks. Four had tinnitus quieting, so they continued with weekly PS applications. By about 8 PS applications all had plateaued. Three had sustained improvement in their tinnitus. For 2 improvement persisted without additional treatments for over a year. One had a tinnitus recrudescence after 5 months; a second set of 10 applications regained his improvement. Another 2 had sustained improvement with less than 3 treatments. While seven subjects had their continuous tinnitus abolished between 3 to 48 hours, none was permanently abolished. In one other subject ear pain and sudden brief unilateral tapering tinnitus were permanently abolished.

The best responders had either ear pain with tinnitus in the ipsilateral ear or had the “somatic pulsatile tinnitus syndrome”. The pain was more responsive than the tinnitus in these subjects. All responders had fluctuating tinnitus.

CONCLUSION: Continuous auricular electrical stimulation can quiet some fluctuating tinnitus particularly if associated with deep ear pain.

COCHLEAR IMPLANT AND TINNITUS - A RETROSPECTIVE STUDY

B. FRACHET, V. PEAN
Hôpital Avicenne, Bobigny, France. Neurelec, Vallauris, France.

Suppression of tinnitus by electrical stimulation via a cochlear implant has been reported for many years. Some individuals who undergo cochlear implant surgery report total or partial relief of the symptoms even in the controlateral ear. The mechanisms involved in this suppression are not clear. Our aim was to study tinnitus in individuals before surgery and after cochlear implant activation and to observe modifications in the perception of tinnitus,

We conducted a retrospective study of 128 postlingual adults who had profound sensorineural hearing loss and underwent cochlear implant surgery at the cochlear implant sector of the Otorhinolaryngology Department, Hospital Avicenne, Bobigny, France, since 1997.

The effects of cochlear implant on loudness, annoyance, daily duration, location, and residual inhibition of tinnitus were evaluated by a closed-ended, quantifiable questionnaire. Questions include monolateral/bilateral tinnitus, results after implantation, tinnitus evolution in time, total suppression, partial relief, results CI on/off, etc.

Different time will be considered : (1) before Cochlear implantation (CI) ; (2) after surgery and before activation ; (3) after activation ; (4) today.

The device employed in this procedure was the Digisonic multichannel device (Neurelec, Vallauris, France)

TINNELEC DEVICE FOR TINNITUS REDUCTION

B. Frachet, B. Meyer, B. Fraysse, V. Pean
Hôpital Avicenne, Bobigny, France. Hôpital Beaujon, Paris, France. CHU Toulouse, France. Neurelec, Vallauris, France.

Suppression of tinnitus by electrical stimulation has been reported for many years. The Tinnelec device of Neurelec Company (Vallauris, France) has been developed for extracochlear electrical stimulation. Description of the device will be done.

New patients with cophosis on one ear and ipsilateral tinnitus have been implanted and results will be analysed.

Moreover, results on psychoacoustical tests to measure (1) the tonality of the tinnitus; (2) the tonality generated by the electrical stimulation; (3) the difference of feeling - tonality according to the frequency of stimulation will be presented.

ELECTRICAL PROMONTORY STIMULATION AND COCHLEAR IMPLANTATION FOR THE TREATMENT OF TINNITUS IN SINGLE SIDED DEAFNESS

Paul van de Heyning*, Olivier Meeus, Andrea Kleine Punte, Katrien Vermeire and Dirk De Ridder*
*Dept of Otorhinolaryngology, *BRAI²N, Antwerp University Hospital, University of Antwerp, Belgium, C. Doppler Laboratory for Active Implantable Systems, University of Innsbruck, Austria*
Email adress corresponding author: paul.van.de.Heyning@uza.be

Objectives: To assess the effectiveness of cochlear implantation and promontory stimulation to reduce tinnitusloudness and tinnitussuffering of patients in whom single sided deafness (SSD) provoked incapacitating tinnitus.

Methods: 22 patients were selected for cochlear implantation in the deaf ear in which the tinnitus was perceived. Selection criteria are 1 unilateral tinnitus due to profound unilateral sensorineural hearing loss 2 incapacitating tinnitus refractive to conservative treatment modalities (e.g. tinnitus retraining therapie) 3 in the contralateral ear no or moderate hearing loss 4 adult and consenting with the study according to the IRB.

Tinnitus was assessed using a comprehensive tinnitus assessment schedule comprising tinnitus characterization, pitch sensation, sensation level, visual analogue scale (VAS) for loudness, and the tinnitus questionnaire (TQ) following Goebel, which is a tinnitus specific quality of life questionnaire.

Hearing evaluation was performed using headphones and free field speech in noise, the disability hearing scale and the SSQ questionnaire.

Evalution was performed preoperatively, 1, 3, 6, 12 ,and every 12 months postfitting.

All patients were implanted with a Med-el cochlea implant with the electrode being full inserted in the scala tympani and fitted with a CIS strategy.

Results: All 22 patients used their cochlear implant every day, the whole day throughout the full evaluation period. A significant tinnitus reduction was realized in all 22 patients. Mean VAS score decreased from 8.5 (sd 1.3) to 2.5 (sd1.9) ($p<0.01$) at 24 months while wearing the CI. The TQ decreased from 58.4 to 39.9 ($p<0.01$) in that period. The degree of improvement of the hearing did not correlate with the degree of tinnitus control.

Conclusions: The preliminary results of these 22 cochlear implantations suggest that CI is an adequate treatment for incapacitating tinnitus can significantly decrease or even abolisch unilateral continuous tinnitus in a deaf ear. There was no conflict between the hearing with CI and the hearing in the opposite ear. These results support the hypothesis that tinnitus is a deafferentiation type sensation in these patients and that the physiopathological mechanism is reversible or at least partially.

References: Van de Heyning,P.; Vermeire,K.; Diebl,M.; Nopp,P.; Anderson,I.; De Ridder,D Ann Otol Rhinol Laryngol 2008;177: 645-652

Disclosure: MED-EL GmbH, Innsbruck, Austria provided the implants.

18:00 - 19:00
Open Meeting
TRI: An International Research Organisation

FRIDAY
JUNE 26, 2009

8:30 - 10:00
Keynotes

8:30 - 9:15
TINNITUS AND NONAUDITORY BRAIN AREAS

Pawel J. Jastreboff
Tinnitus and Hyperacusis Center, Emory University Atlanta, Georgia

The crucial postulate of the neurophysiological model of tinnitus (Jastreboff, P.J. Phantom auditory perception (Tinnitus): mechanisms of generation and perception. Neuroscience Research, 8:221-254, 1990) was that the auditory system plays a secondary role in clinically-significant tinnitus and that the other systems of the brain are dominant. The limbic and autonomic nervous systems were pointed out as main players, while involvement of other systems (e.g., prefrontal cortex, cerebellum) was postulated as well. In case of the auditory system the stress was placed on extralemniscal pathways. The plasticity of the brain and creation of new functional connections between the auditory and the limbic and autonomic nervous systems were inherent features.

During subsequent years it became clear that the functional connections are governed by the principles of conditioned reflexes, and that the subconscious level of the brain plays the substantial (even dominant) role. The model was based on general knowledge of neuroscience and clinical observations of tinnitus-evoked problems, but lacked an experimental support. Nevertheless, on the base of this model a new method of treatment (Tinnitus Retraining Therapy - TRT) was proposed which was strictly based on the model and which aims at retraining both conscious and subconscious conceptions between the auditory and nonauditory parts of the brain to achieve habituation of tinnitus-evoked reactions and subsequently tinnitus perception. One of the novel features of TRT was that it did not attempt to affect generation of tinnitus signal or to simplistically suppress negative reactions evoked by tinnitus, but it crucial mechanisms of action was to eliminate (by retraining and extinction of conditioned reflexes) the connections of the auditory with nonauditory parts of the brain.

Since the model was proposed extensive research confirmed involvement of nonauditory parts of the brain in tinnitus and delineated specific areas and subsystems which are involved in processing tinnitus-related neuronal activity (tinnitus signal). So far, the research fully confirmed significant activation of the limbic system and pointed out a number of specific brain structures which are involved in tinnitus. Interestingly, it turned out that somatosensory system plays substantial role in modulation of the tinnitus signal and may be potentially useful clinically. At this stage it is possible only to speculate on the role of specific structures and their relative importance, but innovative experiments combined with new techniques in imaging and recording the neuronal activity should provide better insight into mechanisms of tinnitus, and through this provide basis for creation of more effective methods of tinnitus treatment.

9:15 - 10:00
A HEURISTIC PATHOPHYSIOLOGICAL MODEL OF TINNITUS

Dirk De Ridder
TRI Tinnitus Clinic, BRAI^{2}N & Dept of Neurosurgery, University Hospital Antwerp, Belgium

Background: Tinnitus and tinnitus distress have a high prevalence. A pathophysiological working model of tinnitus and tinnitus distress is needed to better understand tinnitus, to stimulate research and to develop better treatments

Methods: Based on anatomical, physiological and pathophysiological research in the auditory, somatosensory, visual and olfactory system and based on consciousness research a heuristic model of how tinnitus and tinnitus distress is generated in the brain can be proposed

Results: Tinnitus intensity has been suggested to relate to gamma band activity in the auditory system. This gamma band activity seems to be a requirement but is not sufficient for tinnitus to develop. It could be considered a carrier wave on which the tinnitus related information is communicated, which can be retrieved by AM analysis or ICA. The isolated auditory thalamocortical activity should also be connected to a global workspace activation, in order be consciously perceived. The percept itself might be generated in the dorsolateral prefrontal cortex, the intensity in the auditory cortex.

Tinnitus distress seems to be generated in a separate rightsided anterior cingulate-anterior insula-parietal network.

In time the neural generators of tinnitus change and seem to frontalize to the anterior cingulate, BA10, and parahippocampus. Therefore it can be hypothesized that in time these separate tinnitus intensity and tinnitus distress networks become fused, resulting in intractability. The dorsal anterior cingulate as hub connecting the tinnitus intensity and tinnitus distress network might link this fused network to an allostatic reward system, and indirectly to the parahippocampal memory system, keeping the tinnitus constantly in focus of conscious attention.

Conclusion: A heuristic model can be proposed that may serve as a working model to be criticized, adapted, and improved with new scientific discoveries

10:30 - 12:15
SYMPOSIUM
Audiological Assessment
Grant Searchfield

THE 40-HZ AUDITORY STEADY-STATE RESPONSE IN TINNITUS AND RESIDUAL INHIBITION: EFFECT OF CENTRE FREQUENCY OF MASKING AND PROBE SOUNDS

Gander P, Bosnyak D, & Roberts L
Department of Psychology, Neuroscience, and Behaviour McMaster University, Hamilton, Ontario, Canada L8S 4K1

Background: We have reported that the 40-Hz auditory “steady state response” (aSSR, recorded by EEG and

localizing to primary auditory cortex, A1) is reduced in tinnitus but is augmented from baseline during residual inhibition (RI) compared to age matched controls1. Here we ask whether these effects depend on the centre frequency (CF) of the masking and probe sounds used to image A1.

Methods: We compared aSSR amplitudes evoked by brief tone probes (5 kHz, 500 ms, 40-Hz AM) between young subjects without tinnitus (G1), older subjects without tinnitus (G2), and age-matched older subjects with tinnitus (G3). Within each group, comparisons were made between a condition in which a band-pass masking noise (CF 5.0 kHz, 30 sec) preceded the probe stimuli (masking condition) and when it did not (no-masking condition). In two further groups of older subjects with (G4) and without (G5) tinnitus, the CF of the masking and probe stimuli was 500 Hz (below the tinnitus frequency range).

Results: In the no-masking condition aSSR amplitude was larger in older (G2) than younger (G1) controls, but was reduced in tinnitus (G3 versus G2). In tinnitus subjects only (G3), aSSR amplitude was larger after masking where tinnitus was partially suppressed (RI), compared to the no-masking condition (tinnitus present). Groups G4 and G5 are in progress and will be reported.

Conclusions: Increased aSSR amplitude with age (G2 versus G1, no-masking) may reflect changes in intracortical inhibition related to aging2. Masking in the tinnitus frequency range (CF 5 kHz) may briefly disrupt synchronous neural activity underlying tinnitus (G3 versus G2), returning the auditory cortex to a more normal state. If so, no effects of tinnitus or masking are expected when the CF of masking and probe sounds is below the tinnitus frequency region (G4 and G5).

1. Bosnyak DJ, Gander PE, Roberts LE. Society for Neuroscience 2008: 850.13.

2. Ling LL, Hughes LF, Caspary DM. Neuroscience, 2005; 1103-13.

WAVELET ANALYSIS OF CONTRALATERAL SUPPRESSION OF OTOACOUSTIC EMISSIONS IN TINNITUS PATIENTS

E. de Kleine, L.I. Geven, H.P. Wit and P. van Dijk
University Medical Center Groningen, The Netherlands

Objective: The efferent auditory system has been hypothesised as a factor in the pathophysiology of tinnitus. The efferent system in humans can only be partly tested in a non-invasive manner by suppression of otoacoustic emissions with contralateral acoustic stimulation. Contralateral suppression represents the function of the medial olivocochlear efferent system. With standard analysing techniques, information is lost from the emissions signal. Wavelet-analysis is a technique which conserves both time and frequency information, present in both the emissions signal as well as the suppression. This makes wavelet analysis a sophisticated and useful method for analysing otoacoustic emissions (1).

Methods: Otoacoustic emissions were measured in tinnitus patients and control subjects with and without contralateral acoustic stimulation. Wavelet analysis was performed on the otoacoustic emission signal for all the included ears. Suppression was calculated by subtracting the suppressed emission from the unsuppressed emission. Also the amount of suppression was analysed with the wavelet analysis technique.

Results: Wavelet analysis of the otoacoustic emission signal showed no difference between tinnitus patients and healthy control subjects in the time-frequency domain of the emission. Maximum amplitude was between 1 and 2 kHz. The amount of suppression was equal for tinnitus patients and control subjects.

Conclusion: With conservation of the time-frequency information in the emission, no difference could be detected between tinnitus patients and control subjects. Both the amplitude and the suppression of the otoacoustic emission were comparable. So, the function of the medial olivocochlear efferent system is comparable between both groups.

1. Wit HP, Van Dijk P, Avan P. Hear Res, 1994;73:141-147

SPECTRAL PROFILE OF TINNITUS CAN BE PREDICTED FROM HIGH-RESOLUTION AUDIOGRAM AND DPOAE FOR A SUBSET OF SUBJECTS

Xiang Zhou, Simon Henin, Glenis Long, Lucas C. Parra
City University of New York

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 predicted that the tinnitus percept can be determined for individual subjects from measures of their peripheral processing when obtained with sufficient frequency resolution. The aim of this ongoing study is therefore to find a correlation between the tinnitus percept with measures of peripheral processing on an individual subject basis. To asses peripheral processing, we measured Distortion Products Oto-Acoustic Emission (DPOAE) with high frequency resolution (160 points per octave) as well as band-noise audiograms (6 points per octave). The tinnitus percept was assessed using the well-established tinnitus-likeness test. This test asks subjects to rate how much their tinnitus resembles a pure tone or tonal noise at various frequencies thus providing a 'tinnitus spectrum'. All measures were obtained in the frequency range of 1kHz to 8kHz. Preliminary results show that for a subset of subjects the tinnitus spectrum can indeed be predicted purely from these physiological measures (with $p<0.05$). The observed correlation ($c=0.81+0.09$) of the estimated tinnitus spectrum with the observed likeness ratings is as good as can be expected given the subject's repeat-variability ($c=0.82+0.15$). The remaining subjects contrasted this group in that they had uniform audiograms and tended to give inconsistent likeness ratings ($c=0.1+0.2$). We conclude that for a subset of individuals, the subjective tinnitus percept can be traced back to objectively measurable hearing deficits. This suggests that for these subjects correcting the peripheral hearing deficit captured by these objective measures may alleviate their tinnitus percept, consistent with current attempts to treat tinnitus using custom-fit auditory stimulation.

AUDITORY PERIPHERAL DYSFUNCTION IN TINNITUS SUBJECTS WITH NORMAL AUDIOGRAMS

I. M. Knudson, C. Shera, J. Gu, R.A. Levine, J.R. Melcher
Mass. Eye and Ear Infirmary, Boston USA

A fundamental but unanswered question is whether peripheral auditory damage is a prerequisite for developing tinnitus. We are addressing this question by comprehensively comparing the auditory periphery of tinnitus and non-tinnitus subjects with normal audiograms. 5 tinnitus (8 ears) and 5 non-tinnitus subjects (8 ears) have each been tested in 3 - 4 3-hr sessions. Measurements include: pure tone audiometry to 16 kHz, distortion product otoacoustic emissions (DPOAEs) (L1, L2 = 55, 40 dB SPL,

f2/f1 = 1.2; f2 = 1 - 8 kHz, 28 pts/oct) with and without contralateral noise, auditory brainstem responses (ABRs)(clicks, 30 - 80 dB HL). There were no systematic differences between the tinnitus and non-tinnitus subjects in either threshold from 125 to 16000 Hz or the growth of ABR amplitude with level (wave V; microvolts/dB). However, tinnitus subjects showed a more pronounced "dip" in DPOAE magnitude near f2 = 2 - 4 kHz compared to non-tinnitus subjects, in agreement with [1] and suggesting outer hair cell dysfunction in the tinnitus subjects. A dip index that ranged from 0 (no dip) to 1 was 0.5 - 1 for tinnitus and 0 - 0.6 for non-tinnitus subjects. In a pair-wise comparison of DPOAE measurements made with and without contralateral noise, there was a systematic change (consistent suppression or enhancement across measurements) in DPOAE magnitude for approx. 20% of f2 values in both tinnitus and non-tinnitus subjects. This result suggests that medial efferent feedback to the cochlea was operative in the tinnitus subjects in contrast to [2]. The present results and [1] suggest that many tinnitus subjects with normal audiograms have an abnormal auditory periphery. The precise abnormalities and their prevalence among tinnitus patients with normal thresholds should become clear as this study progresses.

[1] Acker L, Shera C, Melcher JR Assoc. Res. Otolaryngol. Abstracts. 2008; 31: 687.

[2] Riga M, Papadas, T, Werner JA, Dalchow CV Otol & Neurotol. 2007; 28: 185-190.

10:30 - 12:15
SYMPOSIUM
Tinnitus: A Network Approach
Winfried Schlee / Nathan Weisz

THE RELEVANCE OF SHORT-RANGE AND LONG-RANGE SYNCHRONY IN THE FORMATION OF THE TINNITUS NETWORK

Schlee Winfried, Weisz Nathan
University of Konstanz, Konstanz, Germany

Synchronous firing of neurons is a well-established phenomenon of the central nervous system. It is proposed that neuronal synchronization serves as a mechanism for communication between groups of neurons. This may be established over short distances - between cortical columns that are separated by only a few millimeters - or over long distances between spatially distributed brain regions. Neuronal synchronization over the short and the long-range might be an important mechanism for the brain that binds information from different specialized brain areas to form a consistent perception.

The perception of tinnitus is typically characterized by auditory qualities, classification and associations of the tone as well as emotional aspects. Thus, we assume the existence of a tinnitus network that binds together all these characteristics. To gain an understanding of this tinnitus network we need to combine measures of short-range synchronization between different auditory sources in the temporal plane with measures of long-range synchronization between auditory and extra-auditory brain areas.

The presentations within this symposium will explore the short and long-range properties of the tinnitus network in patients with chronic tinnitus. Aim of the discussion is 1) to integrate this knowledge for a deeper understanding of the tinnitus network and 2) learn about the robustness of this network. How does the network change with ongoing tinnitus duration? What are possible ways to disturb the tinnitus network ?

NEUROMAGNETIC EVIDENCE FOR A GLOBAL NETWORK OF TINNITUS PERCEPTION

Schlee W., Müller N., Lorenz I., Hartmann T., Keil J., Weisz N.
University of Konstanz, Germany

Subjective tinnitus is defined as an auditory phantom perception in the absence of any physical source. Consequently, in the resting state, tinnitus patients distinguish themselves from control subjects by having a conscious perception of a sound. Several studies have suggested that conscious perception is associated with a transient synchronization of widely distributed neural assemblies. While unconscious processing is characterized by locally restricted coordination of neuronal activity, conscious processing requires long-range synchronization of neuronal activity in a global network. Since tinnitus is an ongoing conscious perception of a phantom sound, we hypothesized to find an ongoing synchronization between distant brain regions.

Using magnetoencephalographic recordings we conducted several studies to investigate the neuromagnetic activity in auditory areas together with the long-range communication across spatially distributed brain regions. Five minutes of resting-state recordings revealed significant alterations of the inter-areal synchronization in tinnitus compared to a control group. The results suggest the existence of a global tinnitus network that is localized in frontal, parietal and cingular regions of the cortex. Top-down influence of the global network on the auditory cortex correlated positively with the strength of tinnitus distress. Furthermore, we found that the manifestation of tinnitus symptoms is correlated with changes in the architecture of the global tinnitus network.

CONNECTIVITY OF GROUP INDEPENDENT COMPONENTS; FROM LOCAL AND DISTRIBUTED SYNCHRONIZATION TO BRAIN NETWORK

Marco Congedo [a], Roy E. John [b], Dirk De Ridder[c], Leslie Prichep [b], Robert Isenhart [b]
[a]Gipsa-lab, National Center for Scientific Research (cnrs), University Joseph Fourier, University, Stendhal, Grenoble Institute of Technology, Grenoble, France., [b]Brain Research Laboratory, New York University Medical School, Department of Psychiatry, [c]Brain Research Center Antwerp for Innovative and Interdisciplinary Neuromodulation (BRAI²N) & Dept of Neurosurgery, University and Hospital of Antwerp, Belgium

The aim of this work is to study the dependence of robust eyes-closed resting EEG sources isolated by group blind source separation (gBSS). We employ a test-retest strategy using two large sample normative databases (N=57 and N=84). Using a BSS method in the complex Fourier domain, we show that we can rigorously study the out-of-phase dependence of the extracted components, albeit they are extracted so as to be in-phase independent (by BSS definition). Our focus on lagged communication between components effectively yields dependence measures unbiased by volume conduction effects, which is a major concern about the validity of any dependence measures issued by EEG measurements. We are able to show the organization of the extracted components in two networks. Within each network components oscillate coherently with multiple-frequency dynamics, whereas between networks they exchange information at non-random multiple time-lag rates.

FUNCTIONAL INTERACTIONS BETWEEN AUDITORY AND LIMBIC BRAIN CENTERS DURING SOUND PERCEPTION AND REST

Langers D. & van Dijk P.
Dept. of Otorhinolaryngology, University Medical Center Groningen, Groningen, The Netherlands

Aims: Previous fMRI experiments revealed sound-evoked responses in the limbic lobe [1]. The present study investigates how the reported activity and associated functional connectivity patterns depend on the acoustic environment. In particular, limbic involvement in sound processing was assessed during rest.

Methods: 12 healthy subjects were included in an fMRI study that comprised two paradigms: in half of all runs, a variety of sound fragments was presented for subjects to memorize; in the other runs, subjects were not presented with any stimuli. In addition to conventional activation analyses, we carried out independent component analyses (ICA) to identify the involved brain systems and functional connectivity analyses (FCA) to assess functional interactions between selected brain regions.

Results: Sound-evoked activation was observed throughout the classical auditory pathway, as well as in the frontal lobe and cerebellum. For both paradigms, ICA succeeded in identifying the auditory system in a comparable fashion. In addition, ICA consistently extracted other 'non-auditory' brain systems, including the mediotemporal and cingulate limbic lobes. FCA revealed functional interactions within the sub-cortical classical auditory pathway as well as within the auditory cortex. Surprisingly, irrespective of the employed paradigm, functional connectivity from the MGB was found to be much stronger towards the mediotemporal limbic lobe than towards the auditory cortex.

Conclusion: Our findings confirm that strong functional relationships exist between auditory and non-auditory processing centers. Furthermore, these relationships can be identified in sound-evoked and resting-state conditions. This opens the road to measure interactions between the auditory and limbic systems in tinnitus patients during natural resting conditions.

References: 1. Langers DRM, Melcher JR. In: Abstracts of the 14th Annual Meeting of the Organization for Human Brain Mapping. NeuroImage, 2008, 41(S1):e1. (500 words)

CORTICAL FUNCTIONAL CONNECTIVITY AT REST IN TINNITUS PATIENTS

D. Alpini, V. Mattei, M. Garegnani, L. Pugnetti
Scientific Institute S. Maria Nascente, Don C. Gnocchi Foundation, Via Capecelatro 66, Milan, ITALY

Background/aims: changes in EEG spectrum at rest fitting a pathophysiological model based on auditory cortical deafferentation and abnormal thalamo-cortical interplay have been shown in patients with tinnitus. The functional connectivity of widespread networks is also affected if probed during auditory stimulation (1). Our aim was to ascertain if cortical connectivity at rest also shows some deviant pattern in patients with persistent tinnitus.

Methods: using 32 channel EEG recordings at rest with eyes closed we compared the spectral power and connectivity in 8 frequency bands of 12 patients and age-matched healthy controls. One minute of artifact free, vigilance controlled EEG was analyzed for each subject. Tinnitus was reported as bilateral in 6 and monolateral in the remaining 6 patients. Five cortical ROIs were defined based on areas known to process auditory input in the temporal, dorsal and medial frontal, lymbic and parietal lobes, using e-LORETA software (2). Lagged linear connectivity (corrected standardized covariance) was measured between all pairs of ROIs, for each frequency band, for each subject, and the 2 groups compared by means of t-tests with non parametric randomization.

Results: patients showed a greater connectivity between left and right temporal cortices in the delta band, right temporal and left frontal cortices in the theta band, and a reduced connectivity between left temporal, left parietal and right lymbic areas in the fast beta band.

Conclusion: these findings are consistent with the notion of abnormal delta and beta power over temporal areas in resting conditions, and further suggest an involvement of distant cortical areas critical for selective attention to auditory input and emotional responses.

1. Schlee W., Weisz N., Bertrand O., Hartmann T., Elbert T. PLoS ONE, 2008;3:e3720.

2. Pasqual-Marqui RD., Esslen M., Kochi K., Lehmann D. Meth Find Exp Clin Pharmacol, 2002; 24: 91-95

13:45 - 15:30
SYMPOSIUM
Tinnitus and Tinnitus Related Disorders
Pawel Jastreboff / Goeran Hajak

TINNITUS AND HYPERACUSIS

P. Jastreboff
Tinnitus and Hyperacusis Center, Emory University Atlanta, Georgia

---

TINNITUS AND SOMATOFORM DISORDERS

Michael Landgrebe, Tobias Kleinjung, Göran Hajak, Berthold Langguth
Tinnituscenter and Department of Psychiatry, Psychosomatics and Psychotherapy, University of Regensburg, Germany

Tinnitus is a severe, chronic disease with high morbidity and not yet fully understood pathophysiology. From a clinical point of view, tinnitus does show some similarities with other chronic disease states like somatoform disorders or chronic pain syndromes. For example, somatic findings (e.g. amount of hearing loss) cannot explain the amount of subjective suffering. Hence, higher cognitive and emotional factors seem to play a pivotal role by determining the amount of suffering from the tinnitus percept. In accordance with this, recent neuroimaging studies have shown that the same cortical areas known to be crucially involved in the perception of pain seem also to play a role in the pathophysiology of somatoform disorders as well as tinnitus. A better understanding of these higher cognitive processes in the pathophysiology of tinnitus may help to improve therapeutic strategies and may lead to new approaches focusing at a normalization of this altered cortical activity.

TINNITUS AND AFFECTIVE DISORDERS

Berthold Langguth, Michael Landgrebe, Tobias Kleinjung, Göran Hajak
Tinnituscenter and Department of Psychiatry, Psychosomatics and Psychotherapy, University of Regensburg, Germany

Tinnitus is frequently associated with mood alterations, anxiety, loss of energy, anhedonia, sleep disturbance and sometimes also with suicidality. Tinnitus severity as measured with Tinnitus Questionnaires correlates highly with the amount of depressive symptoms. While the clinical relation between tinnitus and depression is obvious, the nature of this relationship is still a matter of discussion. Possible explanations include depression as a reaction to tinnitus, tinnitus as a symptom of depression or a direct interaction on the neuronal level.

Also the knowledge about the underlying neurobiological mechanisms is still developing. Recent neuroimaging studies indicate, that the pathophysiology of tinnitus involves alterations in the central auditory system, but also in brain areas involved in emotion regulation.

Awareness of a high rate of affective comorbidity is important for the management of tinnitus patients, adequate treatment has to consider possible interactions and cover specific pharmacological and behavioral concepts.

TINNITUS AND SLEEP

Goeran Hajak and Berthold Langguth
Department of Psychiatry, Psychosomatics and Psychotherapy, University of Regensburg

“I could deal with tinnitus alone but not with the disturbed sleep”.

This statement made by a tinnitus patient highlights the particular problem of individuals with tinnitus and sleep problems, namely that coping with tinnitus is impaired by disturbed sleep. Sleep problems are a frequent complaint in patients with tinnitus with a prevalence ranging from up to 77%. The importance to assure undisturbed sleep in tinnitus patients is supported by findings that insomnia is associated with greater perceived loudness of tinnitus and tinnitus is perceived to be more severe in combination with disturbed sleep.

While the clinical correlation between tinnitus and disturbed sleep is obvious, knowledge about pathophysiological interactions of the auditory system and related brain areas with sleep regulation is still developing. Most promising models to explain comorbidity of tinnitus and insomnia are direct neuronal interaction, signal-related arousal disturbance, stress-related alteration of homeostatic sleep processes and negative feed back by tinnitus induced mental disorder.

Adequate treatment has to consider these interactions and cover specific medical and behavioral concepts, all of them being currently rather experimental than evidenced based.

13:45 - 15:30
SYMPOSIUM
Clinical Practice and Basic Neuroscience of Somatosensory Tinnitus
Tanit Ganz Sanchez

THE CLINICAL PROFILE OF THE PATIENT WITH SOMATOSENSORY TINNITUS

Carlos Herraiz
MC PhD, Fundacion Hospital Alcorcon, Tinnitus Clinic. Department of Otorhinolaringology, Madrid, Spain

The objective of this presentation is to describe the clinical characteristics of the patients presenting a somatosensory tinnitus (SST). The SST syndrome describes the tinnitus generated after a somatosensory injure. Somatosensory modulation of the tinnitus is related to those patients who can change the loudness or pitch of their tinnitus with muscle or cutaneous stimulation. The clinical report with special attention to the somatosensory injury as a possible etiology of the tinnitus is one of the main criteria for SST diagnosis. The SST test, based on Levine 2004 and Biesinger 2008, evaluates tinnitus characteristics according to orofacial, neck and arm movements or changes after stimulation of different head and neck trigger points. In this presentation, we will discuss about clinical characteristics, concomitant bone and muscle disorders in SST patients, acoustic features of SST and the evaluation protocol that we follow in our clinic.

WHAT THE ANIMAL RESEARCH HAS CLARIFIED IN SOMATOSENSORY TINNITUS

Susan Shore
Hearing Research Institute, University of Michigan

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.

We will 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 which correlated increased spontaneous rates with the behavioral verification of tinnitus, we extend these findings to suggest that the neurons responsible for this increased SR are primarily those that receive excitatory somatosensory inputs (S. E. Shore et al., 2008). These findings support the contention 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 somatosenosry system that occurs to balance the loss of excitatory input from the auditory nerve.

References: Shore SE, Koehler S, Oldakowski M, Hughes LF, Syed S (2008) Dorsal cochlear nucleus responses to somatosensory stimulation are enhanced after noise-induced hearing loss. Eur J Neurosci 27:155-168.

Zeng C, Nannapaneni N, Zhou J, Hughes L, Shore S (2009) Cochlear damage changes the distribution of vesicular glutamate transporters associated with auditory and non-auditory inputs to the cochlear nucleus Journal of Neuroscience In Press.

WHAT THE NEUROIMAGING HAS DEMONSTRATED IN SOMATOSENSORY TINNITUS

Richard Salvi
Center for Hearing & Deafness, University of Buffalo; Department of Communicative Disorders & Sciences

Some patients are able to modulate the loudness and pitch of their tinnitus typically by moving their head, neck, shoulder, jaw or eyes, a phenomenon often referred to as somatic tinnitus. Somatic tinnitus was once considered to be a rare phenomenon, but recent surveys indicate that is far more common than anticipated. The ability of subjects to voluntarily modulate their tinnitus provides brain imaging researchers with a unique and powerful subject pool that can be used to identifying regions of the brain that undergo a change in activity when the tinnitus percept is voluntarily altered. We use positron emission tomography (PET) and radiolabeled water to map the changes in brain activity in two groups of patients with somatic tinnitus. One group could modulate the loudness of their tinnitus with an oral facial movement (OFM) consisting of a jaw clench. The second group involved patients who had undergone acoustic neuroma surgery and could modulate the loudness and pitch of their tinnitus by lateral eye gaze (gaze-evoked tinnitus, GET). Using PET imaging and Statistical Parametric Mapping (SPM) to contrast loud versus quiet tinnitus states, we showed that OFM produced a significant increase in activity in the auditory cortex contralateral to the ear in which the tinnitus was perceived. Since unilateral activation of auditory cortex in OFM tinnitus is fundamentally different from the bilateral cortical activation produced by a real sound, we concluded that the tinnitus generator was in the central auditory pathway. OFM also caused unilateral activation in the medial geniculate and limbic regions including the hippocampus, the later regions being important because of their involvement in memory and emotion. In GET patients, who experience tinnitus in their denervated (dead) ear, lateral eye gaze evoked activity in the auditory brainstem or in regions adjacent to auditory cortex. Subjective tinnitus was once considered a difficult if not impossible phenomenon to investigate; however, rapid advances in brain imaging combined with patients who can modulate their tinnitus have allowed researchers to pinpoint regions of the brain involved in the perception and modulation of tinnitus. (Research supported in part by grants from ATA and NIH)

THE PRESENT AND FUTURE OPTIONS FOR TREATING SOMATOSENSORY TINNITUS

Tanit Ganz Sanchez, MD, PhD
Discipline of Otolaryngology at University of São Paulo School of Medicine

Treating subjective complaints is never an easy task, and this surely applies to tinnitus. While professionals and public still search for a single, effective, quick and easy “miraculous” method to treat most tinnitus patients, we are sure that this is not the right way. There is a strong need to determine different clinical subgroups and their targeted strategies. Such strategy should start with the specific procedures that have some potential to cure the subgroup. If they fail, we would then choose the procedures able to manage the patient. Of course you have to consider some variables, such as the cause(s) behind each tinnitus, the time of onset, the degree of hearing loss and other concomitant symptoms, the patient’s profile and his previous non-successful attempts.

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.

We will present our experience with treatment of the somatosensory tinnitus (which start after jaw and neck injuries) and with the somatosensory modulation of tinnitus (which starts after regular auditory injury, but has temporary changes during muscular, visual or tactile stimulation). We will also comment ongoing results obtained from deactivation of myofascial trigger points, repetitive muscular training based on the pattern of modulation, acupuncture, medication, and electric stimulation.

1. Sanchez TG, Guerra GCY, Lorenzi MC, Brandão AL, Bento, RF. The influence of voluntary muscle contractions upon the onset and modulation of tinnitus. Audiol NeuroOtol, 7(6): 370-5, 2002.

2. Sanchez TG, Pio MRB. Abolição de zumbido evocado pela movimentação ocular por meio da repetição do deslocamento do olhar: um método inovador. 2007, 11(3):jul/set. (500 words)

16:00 - 18:00
PLENUM
Flowchart for the Clinical Management of Tinnitus

Abstracts of Poster Presentations

POSTER PRESENTATION
JUNE 24, 2009, 12:55

Audiology
(G. Searchfield)

CUSTOMIZED SOUND THERAPY FOR TINNITUS: CLINICAL TESTING

Baracca G*, Del Bo L, Inguanta A, Viirre E
Fondazione Ascolta e Vivi, via Foppa 15 20144 Milano; Università degli Studi di Milano, UO Audiologia, Via Pace 9, Milano

Objectives: Customized Sound Therapy (CST) is a sound therapy for tinnitus developed by Tinnitus Otosound Products. CST is based on the concept that hearing loss in a specific tonotopic circuit is the origin of mild, constant, chronic tinnitus (greater than 6 months). With the workstation that has been developed for CST, sounds can be rapidly designed and presented to patients. Most often, such a replica is not a pure tone, but typically is a sound with a center frequency with a superimposed narrow band (on the order of 0.1%) noise. Finalizing sound selection is done in a test-retest reliability format using a two-alternative forced choice mode. Tinnitus therapy is then delivered by having the patient listen to the sound stimulus with a specially designed sound player 2 to 3 hours daily for 6 to 8 weeks. The objective of this study was to test CST for efficacy in a conventional clinical setting in an open label, non blinded format.

Methods: 20 Subjects were selected from the clinical population presenting with chronic tinnitus. They were screened for medical/audiologic disorders and enrolled in the clinical testing project. IRB approved consent was obtained. Tinnitus Handicap Inventory (THI) scores were obtained pre-therapy and at follow-up at 1 and 3 months.

Results: At the time of this report, 14 subjects had sound replicas. The matched center frequencies ranged from 500 to 14000 Hz with a mean of 6800 Hz. Preliminary results in subjects completing treatment show improvements in THI scores after 3 months of CST therapy. At the conference, results from all subjects completing three months of CST will be reported.

Conclusions: CST is a therapy for tinnitus that uses sounds designed to match the frequency and qualitative aspects of tinnitus sensation. Use of narrow band sound improves the matching of the replica to the tinnitus sensation. Preliminary results suggest CST can improve THI scores and thus may be an effective means of managing tinnitus.

DEFINITION OF A PROCEDURE FOR CREATING A SYNTHETIC TINNITUS AUDITORY IMAGE

Bertet S, Baskind A, Londero A, Warusfel O, Viaud-Delmon I, Bonfils P
CNRS UMR 9912, IRCAM; CNRS UMR 7060 and Hôpital Européen Georges Pompidou; Paris, France

Aims: The spectral characterization of tinnitus is not a straightforward process. With this goal in mind, a listening experiment has been carried out on unilateral tinnitus patients aiming at creating a credible tinnitus auditory image (tinnitus avatar). The method used in this test was chosen considering the results of a previous experiment, which investigated several methods for creating such avatar. This study is part of a larger project based on visual and auditory 3D Virtual Reality.

Method: The goal is to recreate a realistic tinnitus image perceived in the middle of the head by using a synthetic signal (pure tone frequency and narrow band noise) played in the contra lateral ear. To do so, the signal has to match the spectrum and intensity of the tinnitus percept. After performing a 1/3 octave pure tone audiogram, two one-hour test sessions were done at one week intervals. A training procedure taught the patients frequency and loudness matching. Then, by means of a graphical interface, patients were asked to adjust a sound played into their contra lateral ear so that it matched their tinnitus in frequency and loudness. Finally, the avatars created in each session were evaluated and compared against their tinnitus on a visual analog scale (VAS).

Results: 12 patients were tested (6 right, 6 left tinnitus). 8 patients created a convincing avatar giving them a percept of fusion (i.e. tinnitus perceived in the head and in the contra lateral ear) and a high VAS score. Avatars were reproducible throughout the two sessions (6 patients creating very similar sounds and 2 making an octave error). 4 patients were not able to create an avatar because of tinnitus complexity and/or because of little computer skills.

Conclusion: Though it is a difficult task, the creation of a synthetic sound comparable to the tinnitus percept seems to be possible. Then, the clinical use of these tinnitus avatars in 3D Virtual Reality environments can be explored by further research.

TINNITUS: RESIDUAL INHIBITION IN COMPARISON WITH SUBJECTIVE EVALUATION AND HYPERACUSIS

C. Binetti, A. Wendel
Buenos Aires British Hospital, "Jose de San Martin" Clinicas Hospital, Buenos Aires, Argentina

Argentina is a large country, Buenos Aires being one of the main urban cities. However, many patients that leave far away from Buenos Aires, have tinnitus. The tests for residual inhibition are made only in Buenos Aires. Then, it would be very useful to know if this therapy would be a good choice for each patient before they have to travel. In this case, tests sent through internet would be the first choice.

Aims: The aim of this work was to evaluate if there is a valid correlation between residual inhibition tests and subjective tinnitus parameters measured by the tinnitus handicap inventory (THI), the visual-analogical scale for tinnitus and the hyperacusis questionnaire.

Methods: It is a prospective observational study for statistical correlation. One hundred patients were included. 18 to 78 years old (mean age 52.5). 44% were females. The most common cause of tinnitus was presbyacusis.

Results: Results show that the majority of patients with positive tests for residual inhibition have moderate results in visual-analogical scale for tinnitus, no or low incapacity in THI, and low hyperacusis results in respective questionnaire.

This study shows that in this situation, more patients are needed in order to extent the validity of our results.

IMPORTANCE OF THE TEOAE IN TOTAL DIAGNOSTICS NOISE IN EAR

N. Buncic, S. Djokovic, P. Janic, Lj. Ignjatovic, A. Bukumirovic
Railway Health Care Institute Serbia, Faculty for Special Education and Rehabilitation, University of Belgrade, School of Medicine, University of Belgrade

TEOAE as a diagnostic method is usually practised for examination of the functions of outer hair cells or for testing the functions of sound reception that allows easy and quick diagnostics of cochlear damage. In recent years more and more is examined the application of the method OAE in diagnostic and evaluation of hearing disorders due to different etiological factors. Tinnitus is one of the most frequent disorders of the auditory system, and it draws great attention in the field of diagnostics, treatment and cure.

The aim of the work was to show the frequency of various types of noise and their mutual relationship with etiological factors, with special emphasis on the importance of TEOAE in diagnosing noise.

The study group consisted of a total of 2600 patients treated in the period of 2007 to 2009 in Railway Health Care Institute Serbia. Instruments included the following: ORL exam., detailed history, audiometry, tympanometry, TEOAE, AEP, HR, doppler scan MAV, X-ray mastoid by Schuler, RTG pyramid by STENWERSU, MR heads, TCD, multislice scanner .

The results were analyzed and show that the overall sample diagnosed and treated 623 patients with tinnitus. The largest number, 492 patients or 79% had tinnitus as rustle. Therefore it is this type of tinnitus especially compared and analyzed in relation to etiological factors.

The results indicate that the maximum number of noise vascular genesis Eustachian tube disfunction, with acute illnesses and chronical middle ear inflammation. Based on the analyzed results can be concluded that TEOAE should become a standard method of testing tinnitus. It is worth stressing that TEOAE not only can objectively show the noise in the ear but in most cases points to the etiological factor that caused it. Diagnosed patients are adequately treated by etiological factors by the ORL specialist. The overall diagnosis and treatment of patients with tinnitus is particularly important to highlight teamwork: ORL specialist and surdo-audiologist.

EXTENDED HIGH-FREQUENCY AUDIOMETRY AND DISTORTION PRODUCT OTOACOUSTIC EMISSIONS IN NORMAL-HEARING PATIENTS WITH UNILATERAL TINNITUS

Smurzynski J[1], Fabijanska A[2], Kochanek K[2], Skarzynski H[2]
[1]Department of Communicative Disorders, East Tennessee State University, Johnson City TN, USA; [2]Institute of Physiology and Pathology of Hearing, Warsaw, Poland

Some tinnitus patients have normal hearing on the conventional audiogram. It has been suggested that the presence of a limited area of damaged outer hair cells (OHCs) with intact inner hair cells, which is not detected on the audiogram, results in unbalanced neural activity between Type I and Type II fibers leading to tinnitus. Distortion product otoacoustic emissions (DPOAEs) provided ambiguous data of OHC function in normal-hearing tinnitus patients when compared to non-tinnitus controls. It is known that hearing loss in the extended high-frequency (EHF) region may decrease DPOAEs evoked at lower frequencies. Results of EHF audiometry in tinnitus patients are limited. The aim of the study was to evaluate DPOAEs and EHF thresholds in normal-hearing patients reporting unilateral tinnitus in left ear. Thus, each subject acted as their own control.

Data were obtained for 25 subjects with bilateral hearing thresholds <25 dB HL from 0.25 to 8 kHz and <70 dB HL at 10, 12.5, 14, and 16 kHz. The DP-grams were measured in the 0.5-8 kHz range using 65/55-dB SPL primaries and f2/f1=1.2. The data analyses included DPOAEs with S/N>3dB.

Median audiometric data showed that thresholds in the left ears were significantly higher than those in the right ears at all four EHFs. Mean DPOAE levels of the left ears were lower than those of the right ears in the frequency range above 1 kHz. Additionally, a paired-comparison test of DPOAE levels of each patient's right and left ear revealed significant differences at 6, and 8 kHz.

The results indicate that: 1. OHC impairment in the most basal region reduces contribution to more apically generated DPOAEs; 2. OHC impairment in a limited area, which may be revealed by DPOAEs but not by conventional audiometry, can contribute to tinnitus generation; and 3. patients with unilateral tinnitus and normal hearing on the conventional audiogram are likely to demonstrate hearing loss in the EHF region.

AUDITORY ATTENTION, HEARING AND TINNITUS

Wise K., Singh D., Searchfield G. D., Magnusson J.
University of Auckland; Auckland, New Zealand

Aims: Tinnitus may be linked to aberrant, attention-related processes (1). Reducing tinnitus annoyance may involve decreasing tinnitus' attention-capturing properties. The effect of informational masking & attention tasks on tinnitus was investigated.

Methods: 1. Three groups of participants: Tinnitus sufferers, controls (no tinnitus, but matched for hearing loss) and otologically-normal participants, were compared for performance on the Comprehensive Attention Battery (CAB); investigating attention domain tasks.

2. Three groups of participants: Tinnitus sufferers and 2 groups of controls, were compared to see if tinnitus improvements could be due to administration of CAB and/or the Coordinate Response Measure (CRM)—an informational masking test—and to investigate potential learning effects.

Results: 1. Selective attention domain tests showed better control-group performance than the tinnitus-group for 2, focused attention tasks ($p = 0.06$ & $p = 0.02$). No significant difference was noted between tinnitus & control groups for divided attention tasks. Analysis of CAB and questionnaire scores revealed $R2 = 0.22$; showing evidence ($p = 0.06$) for greater tinnitus handicap hindering selective attention task execution.

2. Results examining the effect of CRM and CAB on tinnitus and control groups will be presented.

Conclusions: The hypothesis: Bothersome tinnitus & underlying, aberrant central processes contributing to its perception disrupt selective attention processes; is supported. Tinnitus questionnaire scores may be predicative, indicating less selective attention resources available to tinnitus sufferers, explaining poorer performance. 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.

PERCEPTION THRESHOLDS OF PURE TONE IN NOTCHED NOISE CORRELATE WITH GENERATOR COMPONENT OF DISTORTION PRODUCT OTO-ACOUSTIC EMISSIONS

Xiang Zhou, Suzanne Thompson, Glenis Long, Lucas C. Parra
City University of New York

We propose that tinnitus is the result of neuronal gain-adaptation. According to our computational model, the strength of tinnitus is a function of the degree of compression of the cochlear amplifier. Thus, the specific aim of this study was to find a link between the strength of gain-adaptation and cochlear compression. We hypothesized that gain adaptation may be assessed psychophysically by the sensitization that a priming signal can induce on the detection of pure tones. We measured perception thresholds of pure tones in notched-noise following various priming signals (band and notched noise, with silence and white-noise as control conditions). Cochlear compression was assessed by extracting the generator component of Distortion Product Oto-Acoustic Emission (DPOAE) across frequency using primaries sweeping continuously from 1kHz to 4kHz. The psychophysical experiment revealed sensitization larger than expected by conventional forward masking (p<<<<0.04, N=6). This highlights the uniqueness of the observed sensitization effect, which is counter to the more common increase in perceptual thresholds. We did not, however, find a link between sensitization and compression. Instead, stronger sensitization correlated with stronger DPOAE for low primer levels (c=0.27, p0.01, N=11). Together these data suggest that the short-term dynamic adaptation leading to sensitization is mediated by the amplification mechanism of outer hair-cells. Interestingly, compression correlated reliably across frequencies with the perception thresholds for individual subjects (c=0.67**??**0.13, p0.05, N=8 of 11 subjects). This reliable, within-subject correlation of a psychophysical perception threshold with the objective physiological measure of compression establishes our particular DPOAE paradigm as a strong candidate for the assessment of peripheral hearing. This is particularly relevant given the simplicity of the test making it attractive for use in a clinical setting.

Neurobiology (A. Norena)

MEDIAN AND LONG LATENCY AUDITORY EVOKED POTENTIALS IN AUDITORY PROCESSING DISORDER

Sergio Carmona, Diego Castagnino, Lic. Marisa Moreno, Lic. Susana Domínguez
Institution, contact data Instituto de Neurociencias de Buenos Aires (INEBA), Guardia Vieja 4435 – C1192AAW, scarmona@ineba.net

Introduction: Auditory processing disorder (APD) it is not and infrequent cause of difficulties in the acquisition of the language. Median and long latency (CERA) Evoked Potential (EP) can study the auditory pathway condition at the level of the thalamic radiation and primary auditory cortex.

Objectives: Demonstrate the utility of these EP techniques in patients with APD.

Design: Observational – Transversal

Patients and Methods: We studied two females of 8 years old.

Patient 1; suffered prenatal anoxia, she presented delay in language acquisition and later, at the school, difficulties reading and writing.

Patient 2; without relevant antecedent in her medical history with difficulties reading and writing from the beginning of the school.

Both patients received conventional speech language therapy without improvements of their symptoms.

We recorded the response to a click for median latency EP and to a pure tone of 2000 Hz. with duration of 50 ms. for long latency EP.

Results: Patient 1: Presented a large asymmetry with normal responses to the monaural stimulation in the right ear and no response to the monaural stimulation in the left ear. When bilateral stimulation was used the response disappears indicating interhemispheric interference

Patient 2: Large asymmetry with both types of EP

Conclusions: These finding are indicating interhemispheric interference. Median and long latency auditory Evoked Potentials could be useful techniques to check objectively and to follow-up patients with APD.

OSCILLATORY ACTIVITY AND TINNITUS: A COMPUTATIONAL MODEL

Michael Chrostowski[1], Suzanna Becker[1], Lucas C. Parra[2]
[1] McMaster University, [2] City College of New York

Tinnitus may persist because of lasting neural activity changes in the auditory cortex. Altered cortical synchrony and abnormal power in alpha (8-12 Hz), delta (1.5-4 Hz) and gamma (>30 Hz) -band activity have been linked to tinnitus in animal models and in tinnitus subjects. We aim to shed light on how these changes may occur after hearing loss using a biologically plausible computational model of the primary auditory cortex (AI).

We base our model on recent and established research on the auditory cortical circuit. The neural units are described by the Izhikevich (2003) spiking model, which can reproduce activity seen in a vast array of cortical neurons. Specifically, we set the parameters to produce a layer of excitatory regular-spiking neurons and inhibitory fast-spiking neurons. Afferent and lateral connections are based on in vivo characterizations of auditory receptive fields. We also include homeostatic plasticity rules that alter connections between neural units when spiking deviates from a set firing rate.

Simulation results from our model show reduced alpha-band activity, and elevated gamma-band and delta-band activity in regions that have higher firing rates. In our current simulations, such spike rates represent an acoustic stimulus, but the effect may be similar to the kind of elevated firing that has been induced by acoustic trauma in animal models. Elevated gamma-band activity seems to be driven by fast-spiking inhibitory neurons, while regular-spiking neurons appear to underlie elevated delta-band activity. Our model indicates that both types of neurons play a role in mediating alpha-band activity.

Presently, we have developed a biophysically detailed model that captures the key dynamics required to simulate oscillations and tinnitus. Next, we can simulate hearing

loss to observe its effects on oscillatory activity in relevant frequency bands. Our simulation results indicate that aberrant neural activity in excitatory and inhibitory cells in the auditory cortex may underlie the altered oscillatory activity seen in tinnitus subjects.

References

1. Izhikevich E.M. (2003). IEEE Transactions on Neural Networks, 14:1569-1572.

ABNORMALITIES OF SACCADES, VERGENCE, PURSUIT, OPTOKINETIC NYSTAGMUS AND FIXATION IN FIVE SUBJECTS WITH TINNITUS

Z. Kapoula [1], Q. Yang [1], M. Vernet[1], P. Bonfils[2], A. Londero[2]
[1]Laboratoire IRIS, CNRS, FRE 3154, Service d'Ophtalmologie-ORL-Stomatologie, Hôpital Européen Georges Pompidou, 20 rue Leblanc, Paris, France; [2]Service d'ORL et de Chirurgie cervico-faciale, Hôpital Européen Georges Pompidou, Faculté de médecine Paris-Descartes, Université Paris V et Laboratoire CNRS UMR 7060, 20 rue Leblanc, Paris, France

Objective: Recent studies (Jozefowicz-Korczynska & Pajor, 2002; Mezzalira et al. 2007) suggested abnormalities of eye movements (saccades, smooth pursuit and optokinetic nystagmus - OKN) in tinnitus. The goal of this study is to examine all types of eye movements (saccades, smooth pursuit, OKN, vergence and fixation) in five patients with tinnitus modulated by gaze, jaw and/or neck movements.

Methods: Eye movements were recorded with the Eyelink II video system.

Results: Saccades showed long latency, low mean velocity, low gain with high variability, particularly in the vertical direction; fixation was characterized by high frequency of saccade intrusions with large amplitude; vergence failed completely for 3 subjects, the other two showed abnormally long latency; smooth pursuit showed low gain particularly in the vertical direction (0.46±0.06), and it was characterised by high frequency of catch-up saccades with high amplitude, including predictive saccades; OKN also showed low gain particularly in the vertical direction (0.4±0.22). Each subject showed abnormalities for more than one type of eye movement, and for certain directions. Overall, the most pronounced and common deficits were on vergence, vertical smooth pursuit and OKN.

Conclusions: As abnormalities were present for several types of eye movements we suggest dysfunction of oculomotor areas involved in almost all types of eye movements such as posterior parietal cortex (PPC) and cerebellum. These areas are highly involved in control of vergence, vertical smooth pursuit and OKN that are most affected. Tinnitus and eye movement dysfunctioning can be both manifestations of mild cortical-brainstem-cerebellar syndrome. This is line in with the brain imaging studies (Lockwood et al. 2001) showing abnormal cross-modal interaction between gaze signals and activation of auditory cortex in modulated somatic tinnitus. Further comparative studies in tinnitus patients without modulation are needed.

POSTURAL INSTABILITY IN PATIENTS WITH HIGHLY MODULATED TINNITUS: EVIDENCE FOR ABNORMAL SENSORIMOTOR INTERACTION

Z. Kapoula[1], Q. Yang [1], M. Vernet [1], P. Bonfils [2], A. Londero [2]
[1]Laboratoire IRIS, CNRS, FRE 3154, Service d'Ophtalmologie-ORL-Stomatologie, Hôpital Européen Georges Pompidou, 20 rue Leblanc, Paris, France; [2]Service d'ORL et de Chirurgie cervico-faciale, Hôpital Européen Georges Pompidou, Faculté de médecine Paris-Descartes, Université Paris V et Laboratoire CNRS UMR 7060, 20 rue Leblanc, Paris, France

Objective: Many patients show modulation of tinnitus by gaze, jaw or neck movements. Such modulation could reflect abnormal sensorimotor integration and interaction between various inputs. Postural control is based on multi-sensory integration (visual, vestibular, somatosensory, oculomotor). This study examines the quality of postural performance in quiet stance in such patients.

Methods: 23 patients (50±12 years) were selected in the ENT service because of their highly modulating tinnitus. Twelve reported exclusively or predominately left tinnitus, eight right and three bilateral. Eighteen control subjects were also tested (51±12 years). Subjects were asked to fixate a target at 40cm for 51s; posturography was done with the platform (Technoconcept, 40Hz) in eyes open, and eyes closed condition.

Results: Tinnitus subjects showed abnormally high lateral body sway (SDx). This was corroborated by fast Fourrier Transformation (FFTx) and wavelet transform. The power spectrum was significantly higher for tinnitus than controls: FFTx significant difference for the frequency band 0-0.5Hz; wavelet analysis, Px significant for the bands 0-0.5Hz and 0-1.5Hz. Lateral sway for tinnitus was higher for both conditions (eyes open eyes closed). Like controls, tinnitus patients showed better postural stability with eyes open than eyes closed, i.e. normal Romberg quotient. Tinnitus patients showed less lateral sway when fixated straight ahead than lateral, while subjects with right tinnitus showed the opposite

Conclusions: Increased body sway in the lateral plane only and particularly for low and middle range of frequencies could be due to tinnitus itself. Body sway at low and middle frequencies is believed to be under the control of visual and vestibular system. Similarly to external sound stimulation tinnitus could influence lateral sway by activating attention shift, and vestibular potential response. Poor integration of sensorimotor signals is another possibility.

NEURAL CORRELATE OF A TRANSIENT PHANTOM AUDITORY PERCEPTION IN THE AUDITORY CORTEX OF THE AWAKE GUINEA PIG

Graeme Moffat*, Yves Cazals# and Arnaud Norena*
**Université de Provence, CNRS UMR 6149, Marseille, France*
#Université Paul Cézanne, CNRS UMR 6153-1147 INRA, Marseille, France

The transient phantom auditory percept of the Zwicker tone, in which the presentation of a notch-filtered noise can induce the perception of a narrow-band or tonal auditory after-image related to the stimulus, has been proposed as a valuable model in helping to decipher the central auditory mechanisms of tinnitus. Using stimuli known to induce this phantom percept in humans, we attempted to isolate the neural correlates of this phenomenon in the auditory cortex of awake guinea pigs. Of note, an increase in power in the delta (0-4 Hz) EEG band, possibly corresponding to the Zwicker tone percept,

suggest a target within auditory cortex for the detection of tinnitus.

Epidemiology (C. Coelho)

STATISTICAL STUDY OF A GROUP OF 174 PATIENTS WITH TINNITUS IN BUENOS AIRES CITY

C. Binetti, A. Wendel
Buenos Aires British Hospital, "Jose de San Martin" Clinicas Hospital, Buenos Aires, Argentina

It is a retrospective statistical study of 174 patients who came to consultation only for there tinnitus, between July to December 2008. A complete clinical history and otolaryngologic evaluation were done. All patients have done a tonal audiometry, logoaudiometry, acuphenometry, timpanometry, impedanciometry, otoacoustic emissions, PEAT, and MRI of inner ear with and without gadolinium.

As results, the majority of patients had presbyacusis and, in second place, tinnitus in association with vestibulocochlear pathology. Acoustic trauma or damage by noise were not common. Most affected people were women (70.7%). The ages of consultation ranged from 24 to 86 years old.

Results were different to expected. This may be because most of these patients were form the private and semiprivate systems, and have no exposition to working noise and also because they have more information than other people about noise exposition and prevention of damage.

IMPACT OF ETIOLOGICAL FACTORS ON THE APPEARANCE OF CERTAIN TYPES OF TINNITUS

N. Buncic, S. Djokovic, P. Janic, Lj. Ignjatovic, N. Dimic, A. Bukumirovic
Railway Health Care Institute Serbia, Faculty for Special Education and Rehabilitation, University of Belgrade, School of Medicine, University of Belgrade

Tinnitus is a sound sensation that a person records in the ears or in head. Its source is in the organism and may be temporary or permanent. Patients register it differently, as: water rustle, rustle of steam, wind, paper jam, birdie, birdie and a rustle, the sound of cricket etc. Given that tinnitus can be of different frequency and intensity, to some patients it seems to be intolerable and causes them nervousness, insomnia, fear, interference with communication, reduction of work capacity. It is assumed that in Serbia 30% of the population has some form of tinnitus.

The aim of the work is to present our approach in treating this pathology in in the " Railway Health Care Institute Serbia" over the population of adult patients diagnosed and treated in the institute. Patients in question were treated in the "Railway Health Care Institute Serbia" in the period 2007 to 2009. All patients were classified by gender and age, according to the dated and type of tinnitus, according to localization, etiology and lateralization of tinnitus.

Instruments that was used in this study imply: history, ORL examination, tonal audiometry, timpanometry, TEOAE, AEP, HR, COLOR DOPPLER SCAN MAV, X-ray pyramid by Stenwers-in, X-ray mastoid by Schueller, X-ray of the cervical spine, multislice scanner with contrast of ear and head. If necessary we had an additional index, such as neurological, hematologic cardiologic testing.

The results indicate that the Department of audiovestibulogy ORL service in the period from January 1st 2007 to February 1st 2009 processed a total of 2654 patients. From this number, 623 patients complained of the presence of some form of tinnitus. In the follow up of the patients with tinnitus 51% were female and 49% male. In relation to age tinnitus is the most present by persons over 50 years old. Based on the results there is a connection between the type of tinnitus and etiological factors.

DOES TINNITUS EXIST IN NORMAL HEARING PATIENTS?

Forti S.[1], Ambrosetti U.[1], Berto V.[2], Del Bo L.[2]
[1]Audiology Unit, Department of Scienze Chirurgiche Specialistiche, Fondazione IRCCS Ospedale Maggiore Policlinico Mangiagalli e Regina Elena, University of Milan, Italy ; [2]Fondazione Ascolta e Vivi, Milan, Italy

The correlation between tinnitus and hearing threshold was often evaluated. Many authors reported that a big percentage of tinnitus patients suffered from hearing loss. But the auditory evaluation in tinnitus patients with normal hearing threshold was often little accurate. In 2008 Ami and colleagues suggested that reduced outer hair cell activity, as detected by reduced DPOAE levels, may manifest as tinnitus even before there is a shift on hearing threshold. In order to investigate the correlations between tinnitus and hearing threshold and between tinnitus and outer hair cell activity, we analyzed 150 tinnitus patients. All subjects were submitted to audiometric evaluation, including pure tone audiometry (PTA; 250 - 16,000 Hz), immittance, high-definition distortion product otoacoustic emissions (DPOAE; 10 p./octave). In particular the focus was on normal hearing subjects: normal hearing was defined as PTA maximum threshold 20dB HL for frequencies between 250 and 16,000 Hz in both ears; type A tympanogram and counter-lateral stapedial reflex recordable at the threshold (90 dB). First analyzes showed that an important percentage of tinnitus patients has a PTA threshold at 15dB HL for frequencies between 250 and 8,000 Hz, further statistical analyses will be performed on DPOAE and on PTA between 8kHz and 16 k Hz.

PROFILE OF THE GERMAN TINNITUS LEAGUE (DTL): CHARACTERISTICS OF THE MEMBERS COMPAREND WITH EPIDEMIOLOGICAL DATES.

G. GOEBEL [1], H. KNOER [1], E. KNOER [1], W. HILLER [2]
[1]German Tinnitus League, Wuppertal, Germany, [2]University of Mainz, Germany

Background: The German Tinnitus League (DTL) was established 1986 (Hans Knör) and is Europe's largest self-help organization. Little is known about the characteristics of the members compared with the general population with chronic tinnitus.

Methods: In 1998/99 the DTL initiated a representative tinnitus-study of citizens in Germany. The basis of the investigation was a 45-item questionnaire, partly based on the Structured Tinnitus Interview (STI).

For comparing both profiles a large questionnaire survey was conducted using a newly designed, comprehensive instrument covering the major characteristics of tinnitus history, etiology and tinnitus severity. Items were taken both from the Mini-Tinnitus Questionnaire (MINI-TQ12; Hiller & Goebel 2004) and the Structured Tinnitus Interview (STI). The questionnaire was mailed in January 2004 to all members of the DTL.

Results: The prevalence of tinnitus shows a pronounced increase between the 50th and 80th year of age. The

mean age of the 5000 DTL-members is 56,4 years (SD 12,2 years, range 16 to 95 years).

In the general population 37% hear the tinnitus in their ears during silence (grade I), 44% with low level of ambient noise (grade II) and in 17% of cases, the ear noise is louder than all background noise (grade III). In contrast, the members of the DTL were shown to have grade I in 8%, grade II in 60% and grade III in 32%. 19% of the general population reported that the tinnitus increased continually in contrast to the DTL (13%). In both studies we find hyperacusis in 44% of the cases.

In the DTL-study tinnitus was associated with hearing problems in 80% in contrast to the general population in 53% of the cases.

Conclusion: As expected, the members of the DTL had higher tinnitus related distress when compared with the general population.

Hiller W. Goebel G. Rapid assessment of tinnitus-related psychological distress using the Mini-TQ

International Journal of Audiology, 2004; 43: 600-604

Address for correspondence: Gerhard Goebel (ggoebel@schoen-kliniken.de), Roseneck Center for Behavioral Medicine D-83209 Prien, Germany

---

ASSOCIATION OF TINNITUS AND ELECTROMAGNETIC HYPERSENSITIVITY: HINTS FOR A SHARED PATHOPHYSIOLOGY?

Michael Landgrebe*[1], Ulrich Frick [1,2], Simone Hauser [1], Goeran Hajak [1], and Berthold Langguth [1]
[1]Department of Psychiatry, Psychosomatics, and Psychotherapy, University of Regensburg, Germany, [2] Carinthia University of Applied Sciences, Feldkirchen, Austria

Background: Tinnitus is a frequent condition with high morbidity and impairment in quality of life. The pathophysiology is still incompletely understood. Electromagnetic fields are discussed to be involved in the multi-factorial pathogenesis of tinnitus, but data proofing this relationship are very limited. Potential health hazards of electromagnetic fields (EMF) have been under discussion for long. Especially, individuals claiming themselves to be electromagnetic hypersensitive suffer from a variety of unspecific symptoms, which they attribute to EMF-exposure. The aim of the study was to elucidate the relationship between EMF-exposure, electromagnetic hypersensitivity and tinnitus using a case-control design.

Methodology: Tinnitus occurrence and tinnitus severity were assessed by questionnaires in 89 electromagnetic hypersensitive patients and 107 controls matched for age-, gender and EMF-exposure. Using a logistic regression approach, potential risk factors for the development of tinnitus were evaluated.

Findings: Tinnitus was significantly more frequent in the electromagnetic hypersensitive group (50.72% vs. 17.5%) whereas tinnitus duration and severity did not differ between groups. Electromagnetic hypersensitivity and tinnitus were independent risk factors for sleep disturbances. However, measures of individual EMF-exposure like e.g. cell phone use did not show any association with tinnitus.

Conclusions: Our data indicate that tinnitus is associated with subjective electromagnetic hypersensitivity. An individual vulnerability probably due to an over activated cortical distress network seems to be responsible for, both, electromagnetic hypersensitivity and tinnitus. Hence, therapeutic efforts should focus on treatment strategies (e.g. cognitive behavioral therapy) aiming at normalizing this dysfunctional distress network.

CORRELATION BETWEEN HYPERACUSIS MEASUREMENTS IN TINNITUS PATIENTS

Meeus O., Spaepen M., De Ridder D., van de Heyning P.
University Department of Otorhinolaryngology and Head and Neck Surgery and Neurosurgery, Brain Research center Antwerp for Innovative & Interdisciplinary Neuromodulation (BRAI[2]N), Antwerp University Hospital (UZA), University of Antwerp, Wilrijkstraat 10

Introduction: Hyperacusis can be defined as an abnormal lowered tolerance to (any) noise and is reported in 30% up to 79% of tinnitus sufferers. This wide prevalence range can be explained by the subjectiveness of the complaints and the lack of uniform quantification procedures. To date, no study was found to compare results obtained with different hyperacusis measurement procedures.

Aim: To investigate the correlation between hyperacusis measurements in daily ENT practice.

Methods: Hyperacusis was assessed in 46 patients with primary complaints of tinnitus. All patients underwent thorough ENT clinical examination including otoscopy and audiometric evaluation. Patients complaining of recruitment or known with Ménière's disease were excluded from the study. Hyperacusis measurement included:

1. the Hyperacusis Questionnaire (HQ)

2. the Multiple-Activity Scale for Hyperacusis (MASH)

3. the Tinnitus Questionnaire

4. audiometric measurements including uncomfortable loudness level (ULL) and dynamic range (DR)

5. two additional questions: "Do you tolerate noise less?" and "Are you afraid of noise?"

Results: A correlation was found between scores on the HQ and the MASH (p=0.000, r=0.583). Significantly higher scores for both questionnaires were found in patients reporting decreased sound tolerance (p=0.000 and 0.002 respectively) or fear of noise (p=0.002 and 0.004 respectively).

In all patients, ULL values were significantly lower at 125Hz compared to all other frequencies, independently of their hyperacusis complaints (p=0.000).

Overall, no correlations were found between scores on the questionnaires and audiometric measurements including ULL and DR.

Conclusion: The HQ and MASH are valid measurement tools for hyperacusis. No correlations were found between audiometric measurements and hyperacusis complaints assessed with questionnaires.

THE USE OF TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN MODULATION OF PURE TONE AND NARROW BAND NOISE TINNITUS

Meeus O., De Ridder D., van de Heyning P.
University Department of Otorhinolaryngology and Head and Neck Surgery and Neurosurgery, Brain Research center Antwerp for Innovative & Interdisciplinary Neuromodulation (BRAI²N), Antwerp University Hospital (UZA), University of Antwerp, Belgium

Introduction: To date, studies have already demonstrated transient pure tone tinnitus reduction following tonic TMS and rTMS. rTMS was even proposed as a possible treatment for chronic tinnitus. In a study with 12 auditory cortex implantation patients, the absence of white noise suppression with tonic TMS was pointed out, while other studies could demonstrate the suppression of this white noise tinnitus using burst TMS in 14 patients.

Aim: The aim of this study is to investigate the different effects of tonic and burst TMS on tinnitus and to compare the results obtained in both pure tone and white noise tinnitus patients.

Material and methods: Fifty tinnitus patients were included in the study. 31 patients had pure tone tinnitus and 19 patients had noise like tinnitus.

Successive stimulation of the auditory cortex with tonic and burst TMS was administered in 200 pulses at 50% intensity to included patients. A possible tinnitus masking resulting from the sound of the TMS could be excluded as a result of an additional sham stimulation. Tinnitus intensity was assessed using a visual analogue scale.

Results: Mean tinnitus reduction in unilateral pure tone tinnitus patients was significantly higher after burst TMS compared to tonic TMS (p=0,041). No statistic significant difference in tinnitus reduction between pure tone or white noise tinnitus could be seen after either tonic or burst TMS. For unilateral pure tone tinnitus, higher tinnitus reduction could be achieved following high frequency stimulation (5, 10 and 20Hz) compared to low frequency stimulation (1Hz) (p=0,008). Higher tinnitus reduction was seen when stimulation intensity in function to the muscle threshold was higher (p=0,022).

Conclusion: This study was performed in order to investigate the effect of tonic and burst TMS in pure tone and narrow band noise tinnitus patients. Data suggest different reactions between both patient categories. Increased tinnitus reduction was seen with higher stimulation intensity.

TINNITUS AND TEMPOROMANDIBULAR JOINT DISORDERS – ASSESSMENT OF TINNITUS IN 600 CONSECUTIVE PATIENTS PRESENTING WITH TMJ COMPLAINTS IN A SPECIALIZED UNIVERSITY DEPARTMENT

V. Vielsmeier [1], B. Langguth [2], R. Bürgers [3], T. Kleinjung [1]
[1]Department of Otorhinolaryngology, University of Regensburg, [2]Department of Psychiatry and Psychotherapy, University of Regensburg; [3]Department of Dentistry, University of Regensburg

Aims: The aim of this study was to investigate the relationship between temporomandibular joint disorders (TMJ) and chronic tinnitus.

Methods: During a period of ten months all patients who presented at the Department of Dentistry with complaints of temporomandibular joint (TMJ) dysfunction were assessed for tinnitus. Standard treatment for TMJ disorders was performed and potential changes of tinnitus were assessed during a follow-up period of three months.

Results: From february 2008 till november 2008 608 patients were presented at the Department of Dentistry with TMJ complaints. TMJ dysfunctions were diagnosed in 61 patients, 19 suffered from tinnitus. All these patients were seen in the tinnitus clinic, completed a tinnitus questionnaire and received audiologic assessment including tinnitus pitch and loudness matching and minimal masking level. After three months of standard treatment by splint. Manual or drug therapy Tinnitus severity and TMJ complaints were reassessed. About 50% of patients reported substantial improvement of both TMJ dysfunction and tinnitus.

Conclusions: Disorders of the temporomandibular joint are frequently related to tinnitus. Treatment of TMJ dysfunction can also improve the symptoms of chronic tinnitus. It has to be considered that the presented data come from an observational study under naturalistic conditions and not from a controlled trial.

POSTER PRESENTATION
JUNE 25, 2009, 12:55

Treatment 1
(A. Londero)

NEUROFEEDBACK TRAINING FOR TINNITUS: AN UPDATE

Crocetti A., Del Bo L., Forti S.
Del Bo tecnologia per l'ascolto, Milano

Aims: It has been proved that patients with tinnitus show an altered electroencephalographic (EEG) pattern, with less alpha brain waves rhythm from temporal lobe and more delta rhythm from frontal lobe, if compared with people without tinnitus.

We have tried to modify the EEG, thanks to a neurofeedback training aimed to alpha/delta ratio increasing.

Here results at the end of the therapy and follow up at one, three and six months are presented.

Methods: The assessment is made by Tinnitus Handicap Inventory (THI), Visuo Analogical Scales (VAS) and ratio of alpha/delta brain waves rhythms.

We have selected a group of 15 patients with tinnitus of neurophysiologic aetiology, aged more than 18, and without psychiatric or neurologic diseases.

Treatment is composed of 12 sessions, 3 times per week.

Acting on cortical plasticity, neurofeedback training stimulates the reorganization of auditory cortex.

Results: Neurofeedback training shows its efficacy in tinnitus treating.

Objective data, such as alpha/delta ratio, has an increasing trend during the treatment. Also subjective measures reveal an enhancement: after the training,

significant decreasing at the THI score (p=0.014) and at VAS (intensity, annoyance, effect on life, level of problems due to tinnitus) has been found. This significant difference at THI score is maintained at follow up at one, three and six months, indicating a long lasting effect of the treatment. Similar results about follow up concerning VAS.

Conclusions: It seems that better results are achieved if there is no comorbidity with audiological diseases (endolymphatic hydrops, Menière disease) and if tinnitus has a recent origin.

Our experience suggests neurofeedback training as useful for lowering the tinnitus intensity. The method is worth of, and needs, deepening, considering also brief period asked to achieve the results described.

PHARMACOLOGICAL ENHANCEMENT OF LOW-FREQUENCY RTMS IN TINNITUS TREATMENT BY DOPAMINERGIC DRUGS

Frank E, Wilfurth S, Landgrebe M, Kleinjung T, Vielsmeier V, Hajak G, Langguth B.
Department of Psychiatry, University of Regensburg, Regensburg, Germany

OBJEKTIVE: Low-frequency repetitive transcranial magnetic stimulation (rTMS) is effective in the treatment of chronic tinnitus. Experimental data from motor cortex stimulation in healthy subjects indicate that the suppressing effect of low-frequency rTMS could be modulated by dopaminergic transmission. Here we investigated whether administration of an dopamine reuptake inhibitor before low-frequency rTMS enhances its efficacy in tinnitus treatment.

STUDY DESIGN: 16 patients with chronic tinnitus received 150 mg of buproprion 5 hours before each session of low-frequency rTMS. Results were compared with a matched control group of 16 patients who received the same treatment, but without buproprion. Treatment outcome was assessed with a standardized tinnitus questionnaire.

RESULT: In an earlier study we have demonstrated, that the administration of levodopa does not enhance the effect of low-frequency rTMS in the treatment of tinnitus. Similarly the inhibition of dopamine reuptake seems not to enhance rTMS effects.

CONCLUSION: Our pilot studies do not support the notion that clinical effects of low frequency rTMS in the treatment of tinnitus can be enhanced by dopaminergic drugs.

ELECTRICAL STIMULATION AND SILENCE THERAPY FOR CHRONIC BILATERAL TINNITUS – CASE STUDY

JC Guerrero R.
Asociacion Colombiana De Tinnitus, Carrera 55 No 8-04, Bogota, Colombia

Theoretical Basis: Tinnitus is a phantom sound generated by central or peripheral auditory structures, in a local or systemic way.

Through magnetic recordings (qEEG or MEG) has find coherence between the theta and gamma activity at cortical level in patients with tinnitus, also, a decrease of the alpha activity, accompanied by a shift to the left of their pick [1].

A way to increase the alpha activity is through the concentration and selective attention [2], therefore through exercises or concentration tasks the alpha activity is increased.

Case Study: Patient with bilateral tinnitus with 16 years of tinnitus duration, which has been suppressed in more than 95% (100% - correspond to absolute silence) through two procedures:

- Direct electrical stimulation at epidural level.

- Silence therapy.

Initially it has found that patient respond to repetitive transcranial magnetic stimulation (rTMS) at low frequency (1 Hz) [3]. Later is carried out electrical direct stimulation at epidural level [4], through the implant of an electrode in the right auditory cortex. A suppression of 80% of tinnitus in a permanent way is gotten.

Silence therapy has begun approximately for 1 year, which is a novel therapy that consists on forcing the tinnitus to diminish or to disappear through the meditation and concentration exercises with selective attention to the silence. To control the gamma activity, plugs are inserted in the patient's ears, eliminating the external noise completely. [5].

After several sessions the patient feels transitory tinnitus (duration of some seconds), which indicates a positive reorganization in the tonotopic map, because the patient experiences a decrease or suppression in some bands of the tinnitus spectrum. Through this therapy it has been possible obtain until 95% of suppression of the tinnitus in a permanent and bilateral way.

With the purpose of prove that a cortical change has begun, we take an electroencephalogram (qEEG), which is compared with another taken previously before beginning the silence therapy, there is an increase in the alpha frequency and a decrease in the theta and gamma frequency, also, an audiometry shows a decrease in the auditory loss hearing.

Conclusion: The silence therapy is a novel therapy that potentializes the effect of electrical and magnetical stimulation in patients that suffer chronic tinnitus.

Bibliography:

Worden MS, Foxe JJ, Wang N, Simpson GV (2000) Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. J Neurosci 20:RC63.

Llinas RR, Ribary U, Jeanmonod D, Kronberg E, Mitra PP. Thalamocortical dysrhythmia: a neurological and neuropschiatric syndrome characterized by magnetoencephalography. Proc Natl Acad Sci USA 1999,96: 15222-15227

Fierro M, Bobadilla H, et al. Revista Neurológica Española, 2006;12:758-759

De Ridder D, De Mulder G, Verstraeten E, et al. Primary and secondary auditory cortex stimulation for intractable tinnitus. ORL J Otorhinolaryngol Relat Spec 2006; 68: 48-54.

Guerrero JC. Theorical basis of silence therapy (in press.)

A COMPARATIVE STUDY : CONTRALATERAL VERSUS IPSILATERAL RTMS OF TEMPROPARIETAL CORTEX FOR THE TREATMENT OF CHRONIC TINNITUS

Khedr Eman, Rothwell JC, Ettar Amal and Ahmed Mohammed, Khalifa Hosam
Department of Neurology, Assiut University Hospital, Assiut/Egypt

Background: Based on our previous study both frequencies (1 and 25 Hz) had a long term therapeutic effect on chronic tinnitus. All previous studies were applied

the rTMS on the left temproparietal side whether the tinnitus from right or left or bilateral depending on the previous fMRI and PET that hyperactivity was pronounced in the left auditory cortex. However, in patients with lateralized tinnitus, fMRI activation was lateralized towards the side of perceived tinnitus in the primary auditory cortex and in patients with right-sided tinnitus. Supporting to this results, change in tinnitus after rTMS was typically greatest in the ear contralateral to stimulation.

Aim of the study: we will evaluate the impact of both frequencies (1 Hz and 25 Hz) and side (contralateral and ipsilateral to the side of tinnitus) of repetitive transcranial magnetic stimulation (rTMS) on patients with unilateral chronic intractable tinnitus.

Material and Method: Patients with chronic unilateral tinnitus due to central causes will be randomly classified to one of five groups; 1 Hz, and 25Hz and sham group with total 2000 pulses at 100% resting motor threshold per session on the temporoparietal cortex contralateral or ipsilateral to the side of tinnitus for two weeks. The primary outcome of the treatment protocol will be the patients' own self rating of their symptoms using the TRI tinnitus questionnaire sheet, THI, measuring the residual inhibition and psychiatric morbidity monthly for 3 months.

THE SHORT-TERM IMPACT OF DIFFERENT RTMS PARAMETERS ON TINNITUS

Lorenz I., Müller N., Schlee W., Hartmann T., Keil J., and Weisz N.
University of Konstanz

Background: Tinnitus is the perception of sound in the absence of any external stimulus. People suffering from chronic tinnitus exhibit a significantly altered pattern of oscillatory brain activity, particularly reflected in an enhancement of power in the gamma frequency within the auditory cortices.

Repetitive transcranial magnetic stimulation (rTMS) of temporal areas has been studied as a treatment tool for chronic tinnitus for several years. Since the most suitable stimulation parameter is still a subject of discussion we systematically examined changes in oscillatory brain activity as well as in tinnitus perception after application of five different rTMS stimulation protocols.

Methods: Ten participants with chronic tinnitus were examined. They underwent five sessions of rTMS in which they received one of five stimulation parameters (1Hz, individual alpha frequency (IAF), continuous theta burst stimulation (TBSc), intermittent theta burst stimulation (TBSi), and Sham) in a randomized order using a single-blind study design. Participants were stimulated at the auditory cortex contralateral to their tinnitus sensation. Resting-state magnetencephalography (MEG) measurements pre and post rTMS (five minutes each) were recorded. Each parameter's potential success was determined by the reduction of temporal gamma power, the subjective tinnitus loudness, and the scores on a visual analogue scale assessing the tinnitus regarding different dimensions.

Results: Temporal gamma power is reduced after stimulation with 1Hz rTMS. The mean assessment of the tinnitus loudness is reduced to the greatest extend after stimulation with 1Hz rTMS and TBSc.

Conclusions: Those TMS parameters which are known to exert inhibiting influence on neuronal activity (TBSc, 1Hz) turned out to be most successful in reducing subjective tinnitus loudness and are currently applied in a ten-session therapy study.

TRANSCUTANEOUS ELECTRICAL STIMULATION ON PINNA AND MYOFASCIAL TRIGGER POINTS FOR RELIEF OF TINNITUS

MS Park, H Chung , JY Byun, SG Yeo
Dept of Otorhinolaryngology, College of Medicine, Kyunghee University, Seoul, Korea

Objectives: The transcutaneous electrical stimulation has been a method for managing myofascial trigger points (MTP). Recently it was reported that the pressing of MTP would modulate the tinnitus. Main objective of this study is comparing the effect of transcutaneous electrical stimulation on external pinna and MTP around the ear for relief of tinnitus.

Methods: 70 patients who have suffered from tinnitus more than 6 months were selected at Dept. of ORL, Kyunghee University, Korea.

In 40 patients transcutaneous electrical stimulation was performed on the external pinna at 2 times every week for 4 weeks. The stimulus was applied to 5 sites that we chosen on the auricle of ear with tinnitus. The duration of electrical stimulation was 30 seconds to each point. In 30 patients the same procedure was performed on the selected MTP. The MTP on Masseter, Digastic and Temporalis m. were selected for electrical stimulation. The MTP were identified by Travel and Simons criteria; presence of tout muscle band with sensitive spots when finger pressing.

All patients were requested to complete the questionnaires for Visual Analogue Scale (VAS) and Tinnitus Handicap Inventory (THI) before and 4wks after treatment.

Results: In pinna group 62% of patients received significant benefit based on an improvement of THI Score and VAS while 10% of patients had benefit In MTP group. The improvement duration of pinna group was within one month while In MTP group within 1hour in most patients. In pinna group electrical stimulation is more effective in patient with low frequency tinnitus or mild hearing loss ($p<<0.05$).

Conclusion: Transcutaneous electrical stimulation on the MTP around the ear showed less benefit compared with stimulation on pinna in tinnitus relief. Further trials are needed in different MTP sites in the future.

Audiological Treatment (C. Herraiz)

EFFECTS OF SEVERE UNILATERAL HEARING LOSS ON TINNITUS REHABILITATION

P. Davis, and P. Hanley
Nova Southeastern University, Fort Lauderdale, FL, USA, and Neuromonics Pty, Ltd, Sydney, Australia

Aims/Objectives: Severe or profound hearing unilateral hearing loss in the tinnitus ear has long been a great challenge for tinnitus clinics, with few viable non-invasive treatment options. One particular program has recently treated 32 of these patients, predominantly utilizing contralateral stimulation. The current cohort study presents their data, and compares it with other 438 bilaterally symmetrical patients,

Methods: Data was compiled from 470 patients over seven private practices. They utilized a particular tinnitus desensitization program that incorporates customized acoustic stimulation with a six-month counseling and support program1. When indicated, patients were categorized according to 11 pre-determined factors that

could negatively determine their prognosis, including high levels of hearing loss. These variables were held constant to ensure valid comparisons with those without other complicating factors.

Results: Two hundred and seventeen patients were identified as being free of those negative prognostic factors (Tier 1). Seventy-two % of the unilateral group had a Tinnitus Reaction Questionnaire (TRQ) improvement of >40%, while for Tier 1 it was 92%. The mean TRQ improvement in the Unilateral cohort was 55% (SD= 39) whilst in the Tier 1 it was 72% (SD=41). Audiometric data was found to display a similar pattern. Data from all patients will also be presented.

Conclusion: This data suggests that, despite the challenges, these unilateral patients can still be quite consistently well-treated with this new approach.

IS THE SOUND GENERATOR VOLUME CONTROL NEEDED FOR SOUND THERAPY WITH HEARING INSTRUMENT COMBINATION DEVICE?

Del Bo L.[1], Forti S.[2], Ambrosetti U.[2], Dyrlund O.[3]
[1]Fondazione Ascolta e Vivi, Milan, Italy; [2]Audiology Unit, Department of Scienze Chirurgiche Specialistiche, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e regina Elena, University of Milan, Italy; [3]GN Resound, Copenhagen, Denmark

Our previous studies demonstrated that new open ear combination prototype hearing instrument, was very useful in the tinnitus treatment. This instrument consists of an amplification part with advanced signal processing such as multi band wide dynamic rage compression, digital feedback suppression and noise reduction, and an advanced sound generator part.

This combination has been chosen to obtain optimal compensation for the subjects hearing loss and provide the most effective sound enrichment for use in TRT. This prototype was been modified: the receiver was moved to the ear (RITE) and the volume control for noise generator was removed.

Aim of this study is to evaluate if the new prototype can deliver better results than the previous one.

20 tinnitus patients were randomly divided in two groups: the first group is using the original prototype, the second using the new modified one without volume control and with RITE. THI and VAS were administered at the beginning, and they will be administered after 3 and 6 months.

Our hypothesis is that the missing of volume control doesn't affect the sound treatment efficacy while the RITE can improve the outcomes.

PHASE OUT TREATMENT IN PURE TONE AND NARROW BAND NOISE TINNITUS PATIENTS

Meeus O., Blaivie C., Heyndrickx K., Lambrechts P., De Ridder D., van de Heyning P.
University Department of Otorhinolaryngology and Head and Neck Surgery and Neurosurgery, Brain Research center Antwerp for Innovative & Interdisciplinary Neuromodulation (BRAI2N), Antwerp University Hospital (UZA), University of Antwerp, Belgium

Introduction: Phase shift treatment is a new tinnitus therapy that aims at sound cancelling via complete or partial residual inhibition. This technique is based on a theory advocating that the induction of a sound wave with a 180 degree phase shift compared to the sound experienced by the patient could result in sound cancelling, likely by negation of the cortical perception of tinnitus.

Aim: To determine the efficacy of the Phase Out treatment in pure tone and narrow band noise tinnitus patients.

Material and Methods: Comparative study in which we explore the effects of six weeks Phase Out therapy in pure tone tinnitus patients (PT) and narrow band noise tinnitus patients (NBN). The effects on tinnitus were assessed daily using three separate visual analogue scales (VAS). Moreover, the effect of Phase Out was assessed after six weeks treatment by means of the tinnitus questionnaire (TQ) and speech recognition in noise.

Results: 20 PT and 10 NBN were included in this study. While no differences in VAS were seen after therapy in NBN, a slight tinnitus increase could be demonstrated after Phase Out therapy in PT. This increase could be demonstrated for tinnitus loudness (p<<<0.01) and overall annoyance due to the tinnitus (p0.05).

Conclusion: In contrast to previous studies, no tinnitus relief could be demonstrated in pure tone tinnitus patients after six weeks of Phase Out therapy. Our results are discussed and compared to previous studies investigating the effects of Phase Out in tinnitus patients.

NOTCHED-MUSIC TRAINING FOR CHRONIC TONAL TINNITUS

Stracke H, Okamoto H, Lagemann L, Pantev C
Institute for Biomagnetism & Biosignalanalysis, Malmedyweg 15, 48149 Muenster, Germany

Background: Tinnitus is supposedly caused by maladaptive auditory cortex reorganization. Our previous work demonstrated that (i) focused neural activity in auditory cortex can be significantly attenuated by lateral inhibitory processes originating from adjacent neurons [1], and that (ii) tinnitus loudness in chronic tonal tinnitus patients can be significantly (~25%) diminished by the regular (i.e. daily), long-term (i.e. 12 months), low-impact (i.e. <<2 hours per day) passive listening to customized "notched music" (that does not contain energy in the frequency range centered at the individual tinnitus frequency) compared to placebo music treatment and no treatment control [2].

Aims: Here, we investigated whether such improvements in tinnitus loudness could also be achieved by means of a similar, but massive (i.e. 6 hours per day), attentive (i.e. top-down processing of the music via task), and short-term (i.e. week) notched-music training.

Methods: Tinnitus loudness was assessed psychometrically and audiometrically, tinnitus-related neural activity in auditory cortex was measured by MEG (N1m and auditory steady-state responses).

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

1. Pantev C, Okamoto H, Ross B, Stoll W, Ciurlia-Guy E, Kakigi R, Kubo T. Lateral inhibition and habituation of the human auditory cortex. Eur J Neurosci, 2004; 19:2337-2344.

2. Okamoto H, Stracke H, Thiede O, & Pantev C. Tailor-made music reverses maladaptive auditory cortex reorganization and alleviates tinnitus. Submitted for publication.

Corresponding author: Henning Stracke (hstracke@uni-muenster.de)

SPECIFIC EFFECTS AND PROGNOSTIC FACTORS OF HEARING AIDS ON TINNITUS

Myung-Whan Suh, Hyun-Ju Lee, Jeong-Beom Kim, Jae-Yun Jung, Chung-Ku Rhee
Department of Otolaryngology-Head & Neck Surgery, Dankook University College of Medicine

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.

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

Methods: 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, 3 week 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 decease 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.

ACOUSTIC STIMULATION IN TINNITUS TREATMENT FOR PATIENTS WITH SIGNIFICANT LEVEL OF HEARING LOSS

Tavora-Vieira D, Davis P, Miller S.
Medical Audiology Services, WA, Australia; Nova Southeastern University, FL, USA

Aims: High levels of hearing loss are an important challenge for tinnitus treatment based on acoustic stimulation. Patients with higher levels of hearing loss can be highly disturbed by tinnitus, but typically have not got sufficient relief from their hearing aids at night or during other quiet times (1). A particular tinnitus rehabilitation program, including counselling and a customized acoustic signal that provides relief and relaxation to the tinnitus sufferer has a standard protocol, which prescribes two months of acoustic stimulation with additional broadband signal (2). This cohort study aims to explore whether it is beneficial to extend that period for those patients with hearing loss >50 dB (average of 0.5, 1, 2, 4 KHz) in the worst ear.

Methods: Forty patients with moderate-severe hearing loss who are highly disturbed by tinnitus are being provided with the customized acoustic stimulus. They are advised to use the device for 2-4 hours a day during the time their tinnitus is more distressing, for at least six months.

Patients with higher levels of hearing loss will be streamed into the experimental group whilst the others will follow the regular protocol.

(1) Patients are kept for two months in phase one of the treatment, in which, the added broadband signal covers up their tinnitus to a high degree. This group is then moved to the second phase of the treatment, in which they are intermittently exposed to their tinnitus.

(2) Experimental Group: patients are kept in phase one of the treatment for an additional two months and then moved to the second phase.

Tinnitus disturbance is reassessed every two months with the Tinnitus Reaction Questionnaire., minimum masking level, and loudness discomfort levels, until completion at six months.

Results and Conclusion: Data on the first 22 patients completed suggests that the extended stimulation period is beneficial. The full dataset will be ready by the conference, and will be compared to previous studies.

QEEG CHANGES OF THE AUDITORY CORTEX FOLLOWING COCHLEAR IMPLANTATION TINNITUS IN SINGLE SIDED DEAFNESS (SSD)

Paul Van de Heyning°*, Olivier Meeus°, Andrea Kleine Punte°, Jan Van Ost*, Sven Vanneste* and Dirk De Ridder*
*°dept of Otorhinolaryngology, *BRAI²N, Antwerp University Hospital, University of Antwerp, Belgium,*

Email address corresponding author: paul.van.de.Heyning@uza.be

Background: Cochlear implantation in SSD with incapacitating tinnitus proved to be able to reduce tinnitus in a significant way when switched on (ref1). Switching off the CI make results in reappearance of the tinnitus. At the other hand tinnitus loudness is correlated with increased gamma-band band activity in the contralateral auditory cortex.

Objectives: To assess gamma-band activity in the contralateral auditory cortex in CI patients with tinnitus and SSD, and to analyse the influence of switching on and off the implant.

Methods: 22 patients were selected who received a cochlear implantation in the deaf ear for incapacitating the tinnitus for more than 36 months. All patients were implanted with a Medel cochlear implant (type Combi 40+ and Pulsar Ti100). The patients were fitted using a CIS or a fine structure strategy. Tinnitus was assessed using a comprehensive tinnitus assessment schedule comprising tinnitus characterization, pitch sensation, sensation level, visual analogue scale (VAS) for loudness, and the tinnitus questionnaire (TQ) following Goebel, which is a tinnitus specific quality of life questionnaire.

19 channel EEG (10-20 system) recordings were performed in relaxed state over 5 minutes with eyes opened in a sound proof and electromagnetically shielded room. Source analyses are performed on the different frequency bands, using LORETA. Correlations between subjective VAS scores and LORETA maps are obtained after normalisation of the source images, using

Results: EEG gamma band activities of the auditory cortex are correlated with changes of loudness induced by activation or desactivation of the CI.

Conclusions: The results may give further insights into tinnitus perception and lead to the validation of EEG recording with Loreta analysis as a tool to objectivate tinnitus.

Ref 1. van de Heyning,P.; Vermeire,K.; Diebl,M.; Nopp,P.; Anderson,I.; De Ridder,D Ann Otol Rhinol Laryngol 2008;177: 645-652

Disclosure: MED-EL GmbH, Innsbruck, Austria provided the implants.

Others
(E. Biesinger)

AUDIOLOGIC AND VESTIBULAR SYMPTONS IN FABRY DISEASE, CLINICAL PRESENTATION AND POSSIBLE SITE OF THE LESIONS

S. Carmona, R.C. Reisin, A. Pardal, C. Marchesoni, M. Birmingham, M. Moreno, S. Maira, P. Acosta
Institution, contact data AADELFA. (Asociación Argentina de Fabry y otras enfermedades lisosomales) Buenos Aires, Argentina

Introduction: Fabry Disease (FD) is an X-linked lysosomal disorder due to deficient activity of the enzyme alfa galactosidase A which leads to multisystemic storage of globotriaosylceramide with neurological, gastrointestinal, cardiac, renal, skin and ophthalmologic involvement. Recent reports (Palla et.al.2007, Carmona et al. 2008) showed that Neuro-otologic compromise is more common than it was previously believed, but clinical presentation and the exact site of the lesion has not been extensively evaluated. The proportion of affected females is not known.

Objective: To evaluate Neuro-otologic symptoms in patients with FD, the site of the involvement and the proportion of affected females.

Patients and Methods: We evaluated 20 consecutive patients with FD (6 males, mean age 32 years; 14 females, mean age 37 years; range 9-73 years)

One patient was excluded due to severe bilateral conductive hearing loss.

We investigated a history of vertigo, hearing loss and/or tinnitus

Neurophysiologic tests to evaluate the peripheral superior labyrinth we performed Horizontal Head Thrust Test and conventional calorics. The inferior labyrinth was evaluated using Vestibular Evoked Myogenic Potential (VEMP´s). Auditory function was tested using conventional pure tone audiometry with speech discrimination and Brainstem Auditory Evoked Potentials. Moreover Brain MRI was obtained to rule out Central Nervous System involvement.

Results: Symptoms: 3 patients were asymptomatic. Short spontaneous spells of vertigo were reported by 16 patients (80%). Hearing loss was referred by 9 patients (42%, in one it was fluctuating), tinnitus was present in 9 patients, taking both together the auditory symptoms affected 80% of the population.

13 /19 patients had both cochlear and vestibular symptoms (68%).

Lesion localization: 3 patients had normal studies. Neurootologic involvement was peripheral in 15 and central in 1. Only two patients showed a congruent peripheral unilateral involvement of the superior and inferior vestibular tests with compromise of the ipsilateral cochlea. The main finding was that in 15 subjects there was a lack of neural or vascular pattern in the involvement of the peripheral labyrinth.

Gender involvement: All but two of our females had Neuro-otologic abnormalities indicating a very high prevalence (85%) in this group.

Conclusions: Neuro-otologic involvement is frequent and under-recognized in FD, causing marked disability, and affecting both sexes. The site of the lesion is in the vestibular-cochlear labyrinth in the vast majority of the patients. There is no specific neural or vascular lesion pattern which is apparently a landmark of the FD suggesting multisystemic end organ damage.

SLEEP COMPLAINTS IN SUFFERERS TINNITUS SMALL PATIENTS

Marciano E., Carrabba L., Longobardi A., Russo G., Di Pietro G., Giannini P.
Audiology Unit and Psychiatry Unit, Department of Neurosciences of the University of Naples " Federico II", Italy.

Significant relationship between tinnitus and insomnia in fifty patients sample referred to the Audiology Clinic of the University of Naples (Italy) Federico II Department of Neurosciences Italy from January to March 2008. Inclusion criteria were the following: ages ranging from 18 to 60 years, eight years of education to carry out tests. Ten subjects exclusion were due to age above sixty years and /or low education. A first questionnaire regarding sleep qualities were provided and twenty-four patients showed changes. Of these sufferers tinnitus seventeen underwent psychiatric evaluation end eight showed sleep clinically considerable disturbances and nine light complaints who required no intervention. Of eight with sleep difficulties fifty have started therapy using zolpidem or serotoninergic drugs. 55% of sufferers tinnitus patients show sleep complaints while at psychiatric evaluation and exhaustive tests alone 20% put in evidence clinically sleep disturbance while 12,5 of them require specific therapy. The following aim is the evaluation of the sleep therapy results to improve both sleep disturbance and reduce tinnitus perception. Moreover THI and Tinnitus Questionnaire were provided to tinnitus patients with sleep complaints for evaluation of peculiar features as to decide possible improvement of tinnitus as regards to sleep complaints

---

WEBSITE OF THE EUROPEAN FEDERATION OF TINNITUS ASSOCIATIONS (EUTI): CHARACTERISTICS OF THE TINNITUS RELEATED DISTRESS IN 15 DIFFERENT LANGUAGES OF THE TINNITUS-QUESTIONNAIRE (MINI-TQ12)

G. Goebel [1], H. Knoer [1], E. Knoer [1], E. Biesinger [2], C. Schaetz [2], W. Hiller [3]
[1]German Tinnitus League, Wuppertal, Germany, [3]University of Mainz, Germany, [2]European Tinnitus Association, Wuppertal, Germany

Background: The European Tinnitus Association (EUTI) was established in 2002 (Hans Knör). EUTI supports the foundation of tinnitus-associations and self-help groups with financial and conceptual aids and has the goal of bundling research interests in Europe. Little is known about differing characteristics of people with tinnitus in different nations. The Mini-TQ12 questionnaire provides an opportunity to address these questions.

Methods: In 2007 the EUTI initiated a pilot study to investigate the tinnitus-severity in different European nations (http://www.eutinnitus.com/country-selection.php). Basis of the investigation is the „MINI-TQ12". It is recommended as a psychometrically approved and solid tool for quick and economical assessment of subjective

tinnitus distress (Hiller & Goebel 2004). Correlation with the full TQ (Goebel & Hiller 1998; Hallam 1996) is > 0.90 and test-retest reliability is 0.89. Validity was confirmed by associations with general psychological symptom patterns. It was put on the EUTI homepage in 15 different languages in 2007. It is possible to differentiate four tinnitus-severity grades.

Results: The mean age of website users is 45 years. The mean MINI-TQ12-Score is about 13 points for both genders. (19% of the users rate the tinnitus as severity I (slight impairment), 28% severity II (medium), 31% severity III (severe) and 22% severity IV (very severe impairment). On all four levels of severity women show significantly lower scores. Differences between users with different native tongues will be presented at the meeting.

Conclusion: The distribution of the four levels of tinnitus severity is relatively even as counted on our website, which does not correspond to our previous experience with about 48,000 visitors of the German DTL website who are somewhat less affected.

Hiller W. Goebel G. Rapid assessment of tinnitus-related psychological distress using the Mini-TQ.

International Journal of Audiology, 2004; 43: 600-604

Address for correspondence: Gerhard Goebel (ggoebel@schoen-kliniken.de), Roseneck Center for Behavioral Medicine D-83209 Prien, Germany

---

TRI CONSENSUS FOR PATIENT ASSESSMENT AND OUTCOME MEASUREMENT

Berthold Langguth [1], Ron Goodey [2]
[1]Department of Psychiatry, Psychosomatics, and Psychotherapy, University of Regensburg, Germany
[2]Department of Surgery (Otolaryngology), The University of Auckland, Auckland, New Zealand

Chronic tinnitus, the phantom perception of sound, can be a debilitating and life-altering experience. Despite the enormous social and economic burden tinnitus causes, no well-established specific treatment for this disorder is available. Among the reasons for this unsatisfactory situation are the difficulties in assessing tinnitus as it is a purely self-report subjective phenomenon.

There is widespread recognition that consistency between research centers in the ways that patients with tinnitus are assessed and outcomes following interventions are measured would facilitate more effective co-operation and more meaningful evaluations and comparisons of outcomes. At the first Tinnitus Research Initiative meeting held in Regensburg in July 2006 an attempt was made through workshops to gain a consensus both for patient assessments and for outcome measurements. An increasing amount of clinical studies is performed according this consensus which increases the methodological quality, promotes cooperation between research centers and allows better comparability between studies.

TREATMENT OF TINNITUS IN A MULTIDISCIPLINARY CLINIC

V. Vielsmeier[1], T. Steffens[1], M. Landgrebe[2], E. Frank[2], J. Strutz[1], G. Hajak[2], B. Langguth[2], T. Kleinjung[1]
[1]Department of Otorhinolaryngology, University of Regensburg
[2]Department of Psychiatry and Psychotherapy, University of Regensburg

Aims: Recent neuroscientific research indicates that beside the peripheral and central auditory system also the somatosensoric system and nonauditory brain areas are involved in the pathophysiology of tinnitus. Since all these systems represent potential treatment targets, a coordinated multidisciplinary approach is needed to meet the requirements of tinnitus therapy. Such a concept has established at the University of Regensburg two years ago. It is based on a cooperation between the departments of otorhinolaryngology and psychiatry/psychotherapy with involvement of the departments of physiotherapy, dentistry, nuclear medicine, neurology, sleep medicine, neurosurgery and psychology.

Methods: The concept of a multidisciplinary tinnitus clinic, demographical and clinical characteristics of the patients and treatment options are presented.

Results: Standard diagnostic assessment involves completion of several questionnaires, anamnesis, ENT examination, audiologic assessment, neurologic and psychiatric exploration. In selected cases of somatic tinnitus additional investigations at the department of physiotherapy or of dental prosthetics are performed. In a case conference an individual treatment plan is established. Treatment possibilities include sound therapy, hearing aid recommendation, counseling and psychotherapy, transcranial magnetic stimulation, physiotherapy, pharmacotherapy and neurosurgical procedures. In the first two years 458 patients were treated in the Tinnitus Clinic at Regensburg.

Conclusions: The high demand for appointments reflects an enormous unmet need for multidisciplinary tinnitus clinics. Next steps are standardized assessment and outcome measurement for the different treatment procedures, collection of the data in an international database and the development of algorithms for diagnostics and treatment of the different forms of tinnitus in the framework of the Tinnitus Research Initiative Tinnitus Clinic network.

[not attending]

THE DIFFERENT RESPONS OF THE MAIN SYMPTOMS OF INNER EAR EXHAUSTION TO A SPECIFIC HIGH DOSAGE LOW LEVEL LASERTHERAPY

Lutz Wilden
L. Wilden, Private Office for Low Level Lasertherapie, Kurallee 16, D-94072 Bad Füssing, Germany Tel.: 0049-8531-980198, Fax.: 0049-8531-980119 e-mail: info@dr-wilden.de, www.dr-wilden.de

Object of examination: An evaluation of the course and the results of inner ear therapy of 5000 patients regarding the main symptoms of inner ear exhaustions loss of hearing, hyperacusis, dysacusis, pressure in the ear, tinnitus, otogenetic vertigo/Morbus Ménière.

Material and method: A statistical analysis of pre- and posttherapeutical audiometry controls, a clinical balance test, a regular questionnaire.

Results: An average significant improvement of the hearing capacity over all frequencies, a more significant improvement in the deep frequencies (0,125 kHz – 0,75

kHz) and in the high frequencies (6 kHz – 12 kHz) can be documented as well as a significant improvement of dysbalance and of the symptoms hyperacusis, dysacusis, pressure in the ear, tinnitus, otogenetic vertigo and Morbus Menière.

The different time structures of the improvements will be presented. Out of this different time patterns it is possible to lead the patients successful through the inner ear regeneration process.

It is possible to establish a biologically plausible correlation of the hearing improvement with the patients age and the duration of the inner ear exhaustion.

The highest correlation, however, was with the total amount of the transferred energy.

A new set up will be presented.

EARLY PATIENT EXPERIENCE WITH THE TIPA TINNITUS DEVICE

Winkler. P
Fairfield Hearing Clinic, Sydney, Australia

Introduction: The TIPA Tinnitus Device (TTD) is a hand held battery powered player using ear phone inserts to deliver the TIPA sound signal which was first published at the IXth International Tinnitus Seminars in Sweden in April 2008.

The TIPA signal is a series of complex, digitally engineered, non sinusoidal very low frequency sounds which have been found to produce prolonged residual inhibition in tinnitus patients. There are three different signals each lasting 3 minutes and are played in the sequence 1, 2, 1, 3. Clinical testing has shown that the sounds are synergistic in their ability to prolong residual inhibition (RI) if played in this order. This is an empirical observation and the underlying physiologic mechanisms are unknown.

Methods: The TIPA signal was developed over a 5 year period using trial and error subjective testing in the author's solo ENT practice. Patients who experienced RI on initial testing were supplied with the TTD as soon as it received Australian regulatory approval on December 23rd 2008 which was 4 weeks before submitting this abstract.

Results: Patient P1 (63, male) has constant, unremitting, extremely disturbing tinnitus. His audiogram shows noise induced loss. After using the signal morning and evening for 12 days he then experienced 12 hours of complete RI. His life has been improved significantly.

Patient P2 (77, female) who has presbyacusis experiences 3 hours complete RI from a single exposure and uses the TTD at night to get to sleep without tinnitus.

Patient P3 (45, male) has had constant unremitting bilateral tinnitus since he was a teenager and has a normal audiogram. He usually experiences complete RI with TIPA lasting 48 hours. Using the device again as soon as the tinnitus returned he was able to achieve a 2 week tinnitus free period.

Conclusion: The concept that a tinnitus patient's life can be improved by such a simple measure is novel and is undergoing further investigation.

[not attending]

SOUND LOCALIZATION IN SPACE AND THE EFFECT OF INTERFERING AUDITORY STIMULATION IN TINNITUS: DIAGNOSTIC POWER OF THE AUDITORY REACTION PERIMETER ARP

Schmielau F
Institute for Medical Psychology and Special Neurorehabilitation, University of Lübeck, Lübeck (Germany)

Objectives: In Germany approximately 3 million patients suffer from chronic tinnitus. Symptoms such as the continuous presence of auditory phantom sensations, depression and sleep disorders frequently require medical and psychological measures to maintain a certain level of quality of life. Restriction of communication due to perception disorders is a central negative aspect in many tinnitus patients, especially under conditions of sound interference ("cocktail party effect") in daily living conditions, e.g. at work. Hearing devices frequently intensify that problem, deteriorating the ability to localize and understand.

Methods: To test sound localization in neurological and tinnitus patients, a spheric device, the Auditory Reaction Perimeter (ARP), has been developed, which permits measurements of 1. auditory evoked simple reaction times (aSRT) and 2. the accuracy of sound localization (SL) within the total space (F. Schmielau, European and US patent). On an aluminum tube construction of 1.60 m in diameter, 156 loudspeakers are homogeneously distributed on iso-azimuth and iso-elevation lines, to guarantee a 10 degree resolution within the total sphere.

In patients suffering from decompensated chronic tinnitus, hearing thresholds, auditory evoked brain stem potentials, aSRTs and SL were investigated. SL was tested with short (100 ms) sinusoidal and noise stimuli including interfering auditory stimulation. Measurements were repeated with the most recent hearing device. In one patient measurements were performed over a period of five years since tinnitus had been diagnosed.

Results: In general aSRTs were prolonged at least in part of the auditory space and SL accuracy was reduced significantly. In the interference situation an additional reduction of SL accuracy was observed. Patients at least did not profit from wearing their hearing devices.

Conclusion: Results and therapeutical approaches are discussed in the context of tinnitus models of neuronal plasticity.

POSTER PRESENTATION
JUNE 26, 2009, 12:55

Treatment 2
(A.B. Elgoyhen)

HYDROGEN PROTECTS AUDITORY HAIR CELLS FROM FREE RADICALS IN VIVO

R.T. Horie, T Nakagawa, Y.S. Kikkawa, S Kada, J Ito
Department of Otolaryngology-Head and Neck Surgery, Graduate School of Medicine,
Kyoto University, Kyoto, Japan
Corresponding to: Takayuki Nakagawa, MD, PhD
Department of Otolaryngology-Head and Neck Surgery, Graduate School of Medicine, Kyoto University,
Kawahara-cho 54, Shogoin, Sakyo-ku, 606-8507 Kyoto, Japan
Tel: +81-75-751-3346 Fax: +81-75-751-7225
E-mail: tnakagawa@ent.kuhp.kyoto-u.ac.jp.

Objectives: Reactive oxygen species (ROS) play a role in the degeneration of auditory hair cells due to aging, noise trauma, or ototoxic drugs. Hydrogenation is a fundamental deoxidation reaction in living organisms. In the neural system, hydrogen-rich water was shown to prevent superoxide formation in brain slices of vitamin C-depleted senescence marker protein 30 / gluconolactonase-knockout mice [1], and to prevent stress-induced impairments in learning tasks during chronic physical restraint in mice [2]. The current study thus examined the potential of hydrogen to protect auditory hair cells from ROS-induced damage. To examine the effect of hydrogen to protection of hair cells against ROS, we initially supplied hydrogen water to mice noise exposed. And we also evaluated that we supplied hydrogen water to DBA/2J mice to assess the potential of hydrogen to retard age-related hearing loss.

Methods: In the first study, CBA/N mice (4-10wks, male) were used (n=4, respectively). These mice were supplied hydrogen water for 14 days followed by noise exposure (8 kHz band noise at 100 dB SPL for 30 min or 120 dB SPL for 1 hour). Measurements of auditory brainstem responses at frequencies of 8, 16, 32 kHz were performed for cochlear function, and cochleae were collected on day 2 or 14 for histological analysis. And we investigated the expression of 4-hydroxynonenal (HNE) which is a lipid-peroxidation marker, and nitrotyrosine (NT) which is one of the products associated with protein nitration.

In the second study, DBA/2J mice (4wks, male) were used. These mice aged 4 weeks had been supplied hydrogen water. Measurements of auditory brainstem responses at frequencies of 8, 16, 32 kHz were performed for cochlear function once a month, and cochleae and several organs were collected appointed term for histological analysis. And we examined quantification of surviving inner hair cells and outer hair cells. And we investigated the expression of 4-HNE and NT.

Results and Conclusion: Hydrogen treatment significantly reduced the elevation or ABR thresholds against noise-induced hearing loss and age-related hearing loss. Histological analysis revealed that hydrogen treatment significantly prohibited the loss of hair cells and retard aging in several organs.

References: 1. Sato Y, Kajiyama S, Amano A, et al. Hydrogen-rich pure water prevents superoxide formation in brain slices of vitamin C-depleted SMP30/GNL knockout mice. Biochem Biophys Res Commun 2008; 375(3):346-350.

2. Nagata K, Nakashima-Kamimura N, Mikami T, Ohsawa I, Ohta S. Consumption of Molecular Hydrogen Prevents the Stress-Induced Impairments in Hippocampus-Dependent Learning Tasks during Chronic Physical Restraint in Mice. Neuropsychopharmacology 2008.

EFFECTS OF NERAMEXANE ON TINNITUS-RELATED HYPERACTIVITY IN THE DORSAL COCHLEAR NUCLEUS

Brian Budzyn and James A. Kaltenbach
Wayne State University, Detroit, Michigan and Cleveland Clinic Foundation, Cleveland, Ohio USA 44195

The pathomechanisms of tinnitus are not fully clarified. However, it has been observed that spontaneous activity (SpAc) of auditory neurons becomes elevated following exposure to intense sound. These increases resemble stimulus-driven activity and correlate with behavioral evidence of tinnitus. Based on these findings, it has been hypothesized that tinnitus amelioration might be possible by reducing the tinnitus-related increases in SpAc. NMDA receptors have been implicated in the induction of chronic hyperactivity in the nervous system; therefore we investigated the effects of NMDA receptor blockade on tinnitus related hyperactivity in the dorsal cochlear nucleus (DCN). Twelve hamsters were divided into 2 groups: One was exposed to intense sound (10 kHz, 115 dB SPL, 4 hrs) (n=7); the other served as controls (n=5). Approximately 14 days later, SpAc was recorded in the DCN of each animal before and after administration of the dual, NMDA and alpha9/10 receptor antagonist, neramexane (NER). Activity was averaged over 5 minute intervals from 5 to 20 minutes. Partial or complete recordings of activity before and after administration of control and/or NER solutions were obtained in 4 exposed and 4 control animals. Although the data are preliminary, NER administration (10 mg/kg i.p.) was often followed by decreases in the activity in the DCN. Some suppression also followed administration of saline, but the suppress ion caused by NER was stronger and more consistent. The results suggest that NER reduced activity by at least 25% more than saline. The effects of saline were confounded by the high level of activity fluctuation. In the control animals, NER, but not saline, also decreased SpAc. The results suggest that NMDA receptor blockade with NER may reduce the degree of tinnitus related hyperactivity in the DCN; however, confirmation of these findings must await testing of the dose response in more animals. (This work was supported by a grant from Merz Pharmaceuticals)

APPLICATION OF PDA TO TINNITUS TREATMENT

Kobayashi K, Sanders M, Searchfield G, Jepsen K, Morrison-low J, Coad G
261 Morrin Road, Glen Innes, Auckland, New Zealand / The University of Auckland

We set out to develop an effective means to apply auditory perceptual training in people experiencing tinnitus. The training paradigm needed to be inexpensive, accessible and easy to use. Not everyone attending tinnitus clinics have access to, or ability to use, personal computers

limiting the potential application of auditory training methods. This presentation describes the software, hardware, advantages and disadvantages of PDAs in the role of providing categorisation and discrimination training.

Palm Tungsten E2 (200MHz CPU, 320x320 TFT), 1GB secure digital (SD) card and inner ear headphones were used for the home training. Software was programmed by LabVIEW 8.0 PDA Module. Stimuli in the SD card were presented with a PCM audio format. Trade-off of length, frequency limit and resolution was required due to memory restrictions. The trainer set up the auditory training parameters individually before the patient used the device. The graphical user interface was quite instinctive so patients could start training immediately at home. The training result and time stamp were automatically recorded in the SD card so the trainer would be able to analyse it after all training was completed.

We have successfully used PDAs as the hardware interface in the use of digital audio files for attention training (1) and for LabVIEW software based frequency discrimination and categorisation training programs. The size of program and stimuli were restricted by the memory size and the processing had some time delay due to play sound files (stimuli). However, the effects were reasonably negligible with our training design.

The PDA and LabVIEW software have proven to be a stable platform for implementing sound based tinnitus treatment. The software and recommendations for hardware are available to researchers by contacting the authors (tinnitus@auckland.ac.nz).

Reference: 1. Searchfield, G. D., Morrison-Low, J., & Wise, K., Progress in Brain Research, 2007; 166: 441-460

PREVENTING CHRONIC TINNITUS - MUSIC THERAPY FOR PATIENTS SUFFERING FROM IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

Lageman, L., Okamoto, H., Stracke, H. & Pantev, C.
Institute for Biomagnetism and Biosignalanalysis, Malmedyweg 15, D-48149 Muenster

Idiopathic sudden sensorineural hearing loss (SSNHL) is not only a frightening and worrisome disease in acute state, but also often leads to maladaptive cortical reorganization associated with chronic hearing loss and tinnitus. On the one hand maladaptive cortical reorganization can trigger tinnitus; on the other hand the brain's capability to change structure and function can be used to treat tinnitus. In this project we developed a novel treatment approach for SSNHL patients who often suffer from acute tinnitus in order to prevent manifestation of maladaptive cortical reorganization and tinnitus chronification. In animal studies it had been shown, that cats being impaired from noise trauma recovered better with regard to cortical structures when placed in an acoustically enriched environment, than cats in the control group which were lacking extra auditory stimulation. Our novel treatment strategy is inspired by this concept of an "enriched acoustic environment" as well as by the concept of "constraint-induced behavioral therapy" known from stroke therapy and is aiming at reversal of maladaptive reorganization. In addition to the usual medical treatment by means of corticosteroids and Pentoxifylline, patients suffering from unilateral SSNHL receive a therapy consisting of active and passive music-listening. Furthermore patients have their healthy ear sealed thus being forced to make use of the diseased ear. By this we try to prevent maladaptive cortical reorganization which stems from deprivation of sensory input. The course of recovery of the patients was documented by subjective psychometric measures such as audiometry as well as by objective measures such as magnetoencephalography. Results seem promising, giving hope that the musical training can aid recovery and prevention of chronic tinnitus as well as decrease the dose of drugs given.

TINNITUS TREATMENT WITH AMITRIPTILINE: SPECIAL MODALITY AND TIMETABLE

R. Vergara and M. Vergara
Fundacion Ciencia y Tecnologia, carrera 36 A No 61 28 Bogotà - Colombia

Amitriptiline has been widely used for tinnitus treatment (1). Ten permanent Tinnitus patients were treated with special doses and time table of Amitriptiline (2). Three ladies and seven men received Amitriptiline one day per week, in a form of a cure that lasted 28 hours and they took 12.5 mg every 4 hours.

The cure began at 6 pm one day until 10 pm the next day. Treatment lasted 4 weeks. In nine patients lower the tinnitus intensity within this period of time, one patient did no t lower the tinnitus intensity.

Two patients were free of tinnitus during a while longer than 24 hours after the second cure. Patients have to choose the day to take the treatment because they have to reduce the usual activities, they can not drive a car and they have to be free of risk activities.

Patients felt sleepy and dry mouth. No one had addiction. From the above we conclude we can cure tinnitus through a therapeutic intervention on the neural system, where the energy source of the sound tinnitus source, is located.

REFERENCES:

1. House, J. TINNITUS SIMPOSIUM, AAOHNS ANNUAL MEETING, Los Angeles, 2005.

2. TINNITOLOGIA, Vergara, R. www.lulu.com. 2008.

Imaging (N. Weisz)

PET IMAGING FOR CORTICAL HYPERACTIVITY IN TINNITUS PATIENTS: INTERIM ANALYSIS

L.I. Geven, E. de Kleine, A.T.M. Willemsen, A.M.J. Paans, P. van Dijk
Department of Otorhinolaryngology / Head and Neck Surgery, University Medical Center Groningen, Groningen, the Netherlands, Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, the Netherlands

Objective: Tinnitus is believed to be the result of plastic changes and reorganisation processes in the auditory pathway and brain structures, most likely caused by deprivation of input. With Positron Emission Tomography (PET) increases in neural activity can be demonstrated. In published literature asymmetric metabolic activity in the auditory cortex was noted, irrespective of various tinnitus localisations. The objective of this study was to measure the difference in cortical activity in chronic bilateral tinnitus patients compared to healthy control subjects with the use of [18F]deoxyglucose (FDG)-PET scanning.

Methods: FDG-PET scanning was performed in 12 chronic tinnitus patients and 12 control subjects, all right-handed. The tinnitus was bilateral in all patient cases. Subjects were scanned for 20 minutes, after an uptake time of 30 minutes in a resting state. Auditory input was prevented by ear plugs and a sound-isolating headphone. Analysis was done with SPM5, False Discovery Rate (FDR) p <<0.05.br>

Results: No significant difference was found on voxel-level between tinnitus patients and control subjects in this interim analysis.

Conclusion: So far no significant difference could be detected between patients and control subjects on a voxel level. In this ongoing study we will include more study subjects for better matching. In the existing literature concerning FDG-PET and tinnitus, mostly asymmetry indices were used to analyse the difference in activity of the auditory cortex. Therefore, further analysis of the right and left auditory cortex activity, including a region-of-interest analysis, will be done before a final conclusion will be drawn in this interim analysis.

TONOTOPIC CHANGES IN THE AUDITORY CORTEX IN UNILATERAL TINNITUS PATIENTS: AN FMRI STUDY

S. Kovacs, D. De Ridder, R. Peeters, S. Sunaert
Department of Radiology, University Hospitals of the Catholic University Leuven, Herestraat 49, 3000 Leuven, Belgium

Previously, reduced fMRI activity was demonstrated in the auditory cortex (AC) of unilateral tinnitus patients. This was suggested to reflect plasticity effects within the AC (1). At present, our goal is to study the tonotopy of this plasticity effect in the AC by means of fMRI.

20 patients with unilateral tonal tinnitus (12 right- and 8 left-sided) and 20 healthy volunteers were scanned on a 3T MRI scanner. An EPI silent gap sequence was used during the stimulation paradigm. This paradigm consisted of a blocked design in which white noise filtered through either a narrow or a wide bandpass and tones were binaurally presented. The stimuli were either the tinnitus frequency experienced by the patients e.g. 8000Hz (TF-session) or a different frequency e.g. 1000Hz (OF-session). Healthy volunteers were stimulated with identical frequencies.

Significant fMRI activity was found bilaterally in the AC in both sessions for all subjects. In the AC, a higher fMRI activity for the OF-session than for the TF-session was shown. For the TF-session, a significant decrease of activity was found in the left AC for all patients. No such decrease was observed for the OF-session. The activity within either AC cannot be explained by sex, age, tinnitus side or tinnitus loudness. Moreover, the decreased fMRI activity in the TF session cannot be attributed to hearing loss, since no correlation was found between the decreased fMRI activity and dB loss on the TF. However, the fMRI activity in the left AC correlated significantly with the patient's total score on the TQ, intrusiveness and emotional plus cognitive distress subscores.

The decreased fMRI activity is a tonotopic effect in unilateral tinnitus patients, as we only find such a decrease for the TF-session. This study provides further support for the view of decreased fMRI activity as a reflection of plasticity effects within the AC of unilateral tinnitus patients.

1 Smits et al., Neuroradiology 2007;49(8):669-679

NEURAL DIFFERENCES BETWEEN PURE TONE AND NOISE-LIKE TINNITUS

Mark Plazier, Sven Vanneste, Jan Ost, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning, Marco Congedo, Dirk De Ridder
University Hospital Antwerp, Dept. of Brai²n, Belgium

BACKGROUND: The perception of tinnitus knows a high prevalence in the general population and 1-2% suffers from a high amount of distress. Tinnitus can be perceived as a variety of sounds. Among them we find pure tones, white noise and narrow band noise. These latter two noise are also named noise-like tinnitus

AIMS: The differences in the neural generators of tinnitus in pure tone tinnitus compared to noise-like tinnitus are analyzed.

METHODS: EEG recordings were acquired with 19 electrodes and one bipolar electrode to track eye movements. Acquisition was preformed with MITSAR amplifiers at a sampling rate of 500 Hz in an eyes closed situation for three minutes. An average reference montage was chosen. Artefacts were removed manually and by Independent Component Analysis.

sLORETA transformations were made and Current Density measurements were compared for different frequency bands. A between-subjects t-test comparison was preformed between the acute and the chronic group for each frequency band. Results were formulated with a significance of p <<.05.br> 12 patients were selected all suffering from tinnitus, 6 of the patients suffered from a pure tone tinnitus and 6 patients suffered from narrow band noise tinnitus, perceived at the left side.

RESULTS: In the comparison of pure tone tinnitus and narrow band tinnitus we found differences in the less delta (1.5-3.5 Hz) and theta activity (4-7 Hz) in right dorsal prefrontal cortex for noise-like tinnitus, and overactivation in the orbito- and ventro-lateral prefrontal cortex for the high frequencies, namely beta 5 (28-32 Hz) and gamma (32-44 Hz)

CONCLUSION: Differences in the type of tinnitus perception influence the neural structures involved in the perception of tinnitus. Knowledge of these findings can lead to more accurate therapeutic strategies.

UNILATERAL PERCEPTION OF TINNITUS AND BILATERAL PERCEPTION OF TINNITUS: PRILIMENARY RESULTS ON THE NEURAL CORRELATES

Mark Plazier, Sven Vanneste, Jan Ost, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning, Dirk De Ridder, Marco Congedo
University Hospital Antwerp, Dept. of Brai²n, Belgium

BACKGROUND: The perception of tinnitus knows a high prevalence in the general population and 1-2% suffers from a high amount of distress. Tinnitus can present itself as a left-sided, right-sided, bilateral and holocranial phantom sound. The side of perception can have impact on the appliance of therapy.

AIMS: The neural generators of tinnitus related to unilateral or bilateral perception of tinnitus are analyzed.

METHODS: EEG recordings were acquired with 19 electrodes and one bipolar electrode to track eye movements. Acquisition was preformed with MITSAR amplifiers at a sampling rate of 500 Hz in an eyes closed situation for three minutes. An average reference montage was chosen. Artefacts were removed manually and by Independent Component Analysis.

sLORETA transformations were made and Current Density measurements were compared for different frequency bands. A between-subjects t-test comparison was preformed between the acute and the chronic group for each frequency band. Significant results were formulated with a p <<.05.br> 12 patients were selected all suffering from tinnitus, all of the patients suffered from a narrow band noise perception, 6 of them on the unilateral at the left side and 6 of them experienced a bilateral perception.

Differences in neural activity between these two groups were objectivated.

RESULTS: In the comparison between unilateral and bilateral perception of tinnitus we found differences more actrivation in right dorsal lateral prefrontal cortex (alpha 8-12 Hz), right orbitoprefrontal cortex (beta2 16-20 Hz), and right auditory cortex (beta 3 20-24 Hz; gamma 32-44 Hz), and less activation in the right auditory cortex (alpha 8-12 Hz) and the precuneus (beta2 16-20 Hz), anterior cingulated and dorsal anterior cingulate (gamma 32-44 Hz)

CONCLUSION: Differences between the neural correlates for unilateral and bilateral tinnitus might play an important role in the treatment of tinnitus by means of neuromodulation.

VISUAL ANALOGUE SCALE (VAS) FOR TINNITUS INTENSITY AND ITS REPERCUSSIONS ON THE NEURAL NETWORK

Mark Plazier, Sven Vanneste, Jan Ost, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning, Marco Congedo, Dirk De Ridder
University Hospital Antwerp, Dept. of Brai²n, Belgium

BACKGROUND: The perception of tinnitus knows a high prevalence in the general population and 1-2% suffers from a high amount of distress. One way to get the subjective intensity is to score it on a Visual Analogue Scale (VAS).

METHODS: EEG recordings were acquired with 19 electrodes and one bipolar electrode to track eye movements. Acquisition was preformed with MITSAR amplifiers at a sampling rate of 500 Hz in an eyes closed situation for 3 minutes. An average reference was chosen. Artefacts were removed manually and by ICA.

With E-LORETA beam forming 6 regions of interest were selected based on earlier findings using whole brain sLORETA imaging in tinnitus patients (BA22, BA36, BA46, BA10, BA24, BA13). A current density trend analysis was performed related to the VAS intensity. Significant trends were formulated with a p<<.05.br> 16 patients with unilateral left-sided narrow band noise tinnitus were analyzed. The group was divided in 8 patients with tinnitus of recent onset (<4 years) and 8 patients with chronic tinnitus> 4 years). The VAS intensity ranged from 2-9. The duration of tinnitus varies among the patients and suppression by TMS decreases in time. The VAS trend analysis was made for the regions of interest for and differences between current density at increasing VAS were noted.

RESULTS: In tinnitus of recent onset a significant increase in gamma and theta activity is noted in the left auditory cortex, as well as changes in the amygdala-parahippocampal cortex (APHC), the cingulate (BA24) and frontal cortex (BA10).

In chronic tinnitus a significant increase of theta and alpha bands at the left auditory cortex is found as well as increased theta and gamma activity at the right auditory cortex. The APHC and BA24 show differences in activity

CONCLUSION: These results suggest different amount of activity in increasing VAS on the proposed structures. The duration of tinnitus changes the structures influenced by VAS.

LEFT-SIDED TINNITUS COMPARED TO RIGHT-SIDED TINNITUS: IS THERE A DIFFERENCE?

Sven Vanneste, Mark Plazier, Jan Ost, Elsa van der Loo, Tomas Menovsky, Paul van de Heyning, Dirk De Ridder, Marco Congedo
Brai²n, University Antwerp, Wilrijkstraat 10, 2650 Edegem

BACKGROUND: The perception of tinnitus knows a high prevalence in the general population and 1-2% suffers from a high amount of distress. Tinnitus can present itself as a left-sided, right-sided, bilateral and holocranial perception.

AIMS: Analyze the neural generators of tinnitus related to the side of perception.

METHODS: EEG recordings were acquired with 19 electrodes and one bipolar electrode to track eye movements. Acquisition was preformed with MITSAR amplifiers at a sampling rate of 500 Hz in an eyes closed situation for three minutes. An average reference montage was chosen. Artefacts were removed manually and by Independent Component Analysis.

sLORETA transformations were made and Current Density measurements were compared for different frequency bands. A between-subjects t-test comparison was preformed between the acute and the chronic group for each frequency band. Significant results were formulated with a p<<.05.br> 14 patients were selected all suffering from tinnitus, all of the patients suffered from a narrow band noise perception, 7 of them on the left side and 7 of them at the right side. Differences in neural activity between these two groups were analyzed.

RESULTS: If we compare left sided tinnitus to right sided tinnitus we see a decrease of theta-band activity in the right auditory cortex and a decrease in alpha-band activity in the left auditory cortex, combined with an increased gamma-band activity.

In the posterior cingulated cortex we found a decrease of high beta-band activity and the para-hippocampal cortex shows a right-sided decrease of gamma activity.

CONCLUSION: Differences between left- and right-sided tinnitus were objectivated with this study. This might be important for the determination of the side of therapy in auditory cortex implantation and TMS.

Somatosensory Tinnitus (T. G. Sanchez)

EVALUATION OF BOTULINUM TOXIN IN THE TREATMENT OF SOMATOSENSORY TINNITUS

Herraiz C, Diges I, Aparicio JM
Hospital Universitario Fundacion Alcorcon, Madrid

Introduction: Somatosensory tinnitus includes those tinnitus generated after a somatosensorial injure or those tinnitus that can change their characteristics with orofacial or neck movements. We propose the use of botulinum toxin A for the management of this type of tinnitus. The mechanism is based on the action through the autonomous nerve system (ANS), all along the somatosensorial pathway. The effect on the multimodal crossing sites could have an indirect modulation on the auditory pathways and therefore, reduce tinnitus perception. The toxin could also decrease the emotional reaction through the parasympatic system.

Our objective: has been the evaluation of the effectiveness of botulinum toxin A on somatic tinnitus patients, compared with a placebo group after a two-month follow-up period (RCT).

Method: Inclusion criteria are patients that refer tinnitus after a somatosensorial injury (whiplash syndrome, dental or temporomandibular joint (TMJ) disorders) or tinnitus that can modify its loudness or pitch with somatic manoeuvres (orofacial movements, TMJ and cervical movements. Tinnitus evaluation includes a visual analogue scale on tinnitus loudness (VAS), a Spanish validation of the Tinnitus Handicap Inventory (THI, Newman 1996, Herraiz 2001) and the tinnitus somatic modulation test (Levine 2004). We also report hyperacusis and hearing loss measurement (psicoacoustic and handicap). For outcome evaluation we use three parameters: the question "is your tinnitus better, same or worse due to the treatment?", the VAS and the THI scores. We perform the Injection of 20 units of Botulinum Toxin A or placebo in three places of the retroaural origin

Results: Since now, twenty-five patients have been enrolled in the study. Other nine patients have rejected to participate in the trial due to the potential risks of the drug. Botox patients and the placebo group will be compared according to tinnitus relief and tinnitus somatic modulation test modifications.

EFFICACY OF DEACTIVATION OF MYOFASCIAL TRIGGER POINTS IN PATIENTS WITH BOTH TINNITUS AND MYOFASCIAL PAIN

Rocha CACB; Nascimento AF; Sanchez TG
Tinnitus Research Group of the University of São Paulo Medical School, Brazil

Aims/Objectives: Different treatments have been proposed to control tinnitus, but the discrepant and unsatisfactory results among many centers reflect the need of new therapeutic approaches. The objective of this study is to evaluate the efficacy of both myofascial trigger point deactivation and home orientations for tinnitus control in a population with tinnitus and myofascial pain.

Methods: A double blind placebo control randomized clinical trial was carried out so as to verify the efficacy of a treatment based on 10 sessions of MTP deactivation, in tinnitus patients by means of comparison with a placebo treatment in a control group. All of them underwent interviews with an otologist, audiologist and physiotherapist. The later evaluated, randomized and treated both groups, while a blind researcher evaluated tinnitus and pain before the first and after the fifth and tenth sessions. The real treatment was performed through digital pressure in each MTP (8 possible muscles) and some home orientations. In the control group the physiotherapist pressed adjacent non-tender muscle fibers of the same muscle presenting MTP, and no home orientations were prescribed.

Results: 17 patients from the experimental group and 9 patients from the control group were analyzed before the beginning of the treatment and after ten weeks. Through gender, age and time of tinnitus onset between groups, randomization proved effective. The analyzed results were: (1) variation of tinnitus loudness ($p < 0,001$); (2) variation of pain intensity ($p < 0,001$); (3) variation of scores in the THI scale ($p = 0,01$) and (4) variation of the number of active MTP ($p < 0,001$).

Conclusion: MTP deactivation treatment was deemed effective in relation to tinnitus relief when a control group was compared to an experimental group.

TENDER POINTS CAN ALSO EVOKE SOMATOSENSORY MODULATION OF TINNITUS

Rocha CACB; Sanchez TG
Tinnitus Research Group, Otolaryngology Department, University of São Paulo School of Medicine, São Paulo, Brazil

Objectives: Tinnitus is often modulated by muscle contractions of head and neck muscles. Recently, we have shown the influence of trigger points in tinnitus modulation. Trigger points are self-sustaining hyperirritable foci in skeletal muscles or fascia, which are characteristic of patients with myofascial pain syndrome. Likewise, tender points are discreet areas of pain on body surface that can be identified in many people. While tender points hurt whenever touched and cause local pain, trigger points must refer pain to another area. We aimed to demonstrate that tender points can also modulate tinnitus.

Methods: As part of a major project for treating patients with tinnitus and regional pain, we selected preliminary unexpected data to present. All patients were subject to medical and audiological evaluation, a questionnaire on both tinnitus and pain, and to bilateral digital pressure of 8 muscles of head and neck and shoulder girdle. Tinnitus modulation was deemed present when there was any immediate change in loudness/pitch during palpation of each muscle.

Results: Out of 39 patients evaluated, 33 (84.6%) presented association of trigger and tender points, 4 (10.2%) had only trigger points and 2 (5.1%) had only tender points in every muscle evaluated. Surprisingly, 23 out of the 35 patients with tender points (65.7%; 58.9% of the whole sample) had tinnitus modulation during their pressure. Among them, 20 (86.9%) had tinnitus modulation both by tender and trigger points, and 3 (13.1%) only modulated tinnitus by tender points.

Conclusion: Like myofascial trigger points, tender points can also modulate tinnitus and should also be included as a factor of influence of the somatosensory tinnitus subgroup. This might be another aspect of the well known evidences of the relation between tinnitus and chronic pain. Further ongoing research will demonstrate whether or not the deactivation of tender points, isolated or associated to myofascial trigger points, is worthwhile in relation to tinnitus relief.

SOMATOSENSORY MODULATION OF TINNITUS: A THREE-PHASE STUDY FROM PREVALENCE TO TREATMENT

Tanit G Sanchez, Daniela B Lima, Marcos Venturini, Maria E Pedalini
Tinnitus Research Group of University of São Paulo

OBJECTIVES: Somatosensory modulation is a clinical characteristic of a subgroup of tinnitus patients. This 3-phase study aims to 1) establish the prevalence and reproducibility of somatosensory modulation through muscle contractions and pressure of trigger points in head and neck, 2) standardize an international protocol for somatosensory modulation, 3) check the efficacy of repetitive muscular training and transelectrical nerve stimulation for managing somatosensory modulation.

METHODS: The ongoing first phase included consecutive subjects with constant tinnitus, and excluded those with somatosounds or using drugs for pain or muscle relaxants. Procedures included anamnesis, ENT exam, THI, VAS, audiometry with tinnitus loudness and MML, cervical RX, and 96 muscle contractions (active, passive and against resistance) and pressure of trigger points in test (T1) and retest (T2) after one week. Tinnitus group was formed with 75 patients (68% females, mean age=59y, 53% unilateral)

and a matched control group is under formation (n=6; 66% females, mean age 51y).

RESULTS: In the tinnitus group, 80% were able to modulate with at least one movement during T1, with reproducibility in 56% in T2. When grouped by the respective cranial nerves, modulation was most commonly evoked by XI (rotation to the right; 48,58%), VII (tight eye closure; 42%), and V nerves (clenching teeth; 41,94%). TMJ movements evoked modulation in 48%, and the trigger points, in 42,6% of the cases. Movements against resistance evoked more modulation than passive maneuvers when TMJ was tested, but not in the neck. In control group, just one volunteer modulated tinnitus up to now (chin protrusion forward and to the right). Updated sample will be presented at Stresa.

CONCLUSION: The first phase of the study showed that the prevalence of somatosensory modulation through head and neck muscle contractions and trigger points is 80%, but the reproducibility of the phenomenon is 56% of the cases.

SOMATOSENSORY TINNITUS AND TONIC TENSOR TYMPANI SYNDROME (TTTS)

Westcott M
Dineen and Westcott Audiologists

Introduction: TTTS is an involuntary anxiety-based condition where the central reflex threshold for tensor tympani muscle activity is reduced, causing a continual spasm and triggering symptoms that include somatosensory tinnitus. TTTS can lead to dysfunction of the trigeminal nerve innervating the tensor tympani muscle.

A hypothesis is presented that TTTS may be a crucial component of the somatosensory tinnitus pathway. This paper is a research review with case study presentations exploring the link between TTTS and somatosensory tinnitus, TMD and hyperacusis.

Research review: Ramirez investigated the anatomical/physiological connections and the central/peripheral mechanisms in TMD patients with secondary aural symptoms, emphasising TTTS involvement and trigeminal nerve dysfunction [1].

Shore considers that somatosensory neurons may stir excessive neuron activity in the cochlear nucleus due to an inflamed trigeminal system in TMD [2]. It is proposed that this process also occurs with TTTS, albeit with a different aetiology.

Case Studies: The development and rehabilitation of TTTS symptoms including somatosensory tinnitus is shown.

Discussion: TTTS symptoms in TMD are stable, with no hyperacusis. In TTTS where the aetiology is an anxiety/trauma response to sound, hyperacusis is present and symptoms are exacerbated by intolerable sounds. Proposed central and peripheral mechanisms of these clinical findings are discussed.

Conclusion: This research review and my clinical findings support a link between TTTS and somatosensory tinnitus, with further research warranted to clarify the underlying pathway.

[1] Ramirez LM, Ballesteros LE, Sandoval GP. Topical Review: Temperomandibular disorders in an integral otic syndrome model. Int J Aud 2008: 47:215-227

[2] Shore SE, Koehler S, Oldakowski M, Hughes LF, Syed S. Dorsal cochlear nucleus responses to somatosensory stimulation are enhanced after noise-induced hearing loss. Eur J Neurosci 2008 27:155-168

POSTERS OF ORAL PRESENTATIONS

CLINICAL DEVELOPMENT OF NEW DRUGS FOR THE TREATMENT OF TINNITUS USING THE EXAMPLE OF NERAMEXANE

Althaus M* for the NERAMEXANE TINNITUS STUDY GROUP
**Merz Pharmaceuticals, Frankfurt, D-60318 Germany*

TINNITUSBOOK: A PROPOSAL FOR AN ADVANCED SCIENTIFIC WEB COMMUNITY FOR TINNITUS RESEARCH

G. Attanasio[a,f], P. Ciccarese[b,c], E. Wu[e], T. Clark[b,c,d], E. Pecis[f], R. Filipo[a]
[a]Dept. Neurol and Otolaryngol, Univ La Sapienza, Rome,IT; [b]Massachusetts Gen. Hosp., Boston,MA; [c]Harvard Med. School, Boston,MA; [d]Harvard Initiative in Innovative Computing, Cambridge,MA; [e]Alzheimer Res. Forum Found., Boston,MA; [f]Acufeni.net web por

THE TINNITUS DISABILITY INDEX: A NOVEL MEASURE FOR TINNITUS-RELATED DISABILITY

Cima RFF, Joore MA, Anteunis LJC, Maes IH, Vlaeyen JWS

ANALYSIS OF THE CORRELATION BETWEEN AUDIOMETRIC THRESHOLDS, PSYCHO-ACOUSTIC MEASURES AND VALIDATED QUESTIONNAIRES IN TINNITUS PATIENTS

Figueiredo RR, Rates MA, Azevedo AA, Oliveira PM,Navarro P
OTOSUL,Otorrinolaringologia Sul-Fluminense, Volta Redonda,RJ, Brazil; Clinica de Tratamento e Pesquisa em Zumbido, Belo Horizonte,MG,Brazil

EFFECTS OF CAFFEINE IN TINNITUS: PRELIMINARY DATA

Figueiredo RR, Azevedo AA, Rates MA, Moreira RKP, Oliveira PM, Navarro P
OTOSUL,Otorrinolaringologia Sul-Fluminense,Volta Redonda,RJ,Brazil;Clínica de Tratamento e Pesquisa em Zumbido, Belo Horizonte,MG, Brazil; Serviço de Otorrinolaringologia da Santa Casa de Misericórdia,Belo Horizonte,MG,Brazil.

MEASURING TINNITUS: A RE-EVALUATION OF THE DIMENSIONALITY AND CONGRUENT VALIDITY OF THE 12 ITEMS TINNITUS HANDICAP INVENTORY

Goertelmeyer R[1], Suckfuell, M[2], Wittmann, W[3]
[1]Merz Pharmaceuticals Frankfurt, [2]Ludwig-Maximilians-Universitaet Muenchen, [3]Universitaet Mannheim

RNID – WORKING TOWARDS A CURE

D Goldman, J Robinson and R Holme
RNID, London, UK

NEW DIET FOR TINNITUS: ADENOSINE DIET

M.A. Lopez-Gonzalez, F. Esteban
Hospital Universitario Virgen del Rocio, Sevilla, Spain

ATTENTIONAL EFFECTS ON EXCITATORY AND INHIBITORY NEURAL ACTIVITY IN THE HUMAN AUDITORY CORTEX

Okamoto H, Stracke H, Pantev C
Institute for Biomagnetism and Biosignalanalysis, Westfalian Wilhelms-University Münster, Münster 48149, Germany

SPECTRAL PROFILE OF TINNITUS CAN BE PREDICTED FROM HIGH-RESOLUTION AUDIOGRAM AND DPOAE FOR A SUBSET OF SUBJECTS

Xiang Zhou, Simon Henin, Glenis Long, Lucas C. Parra
City University of New York

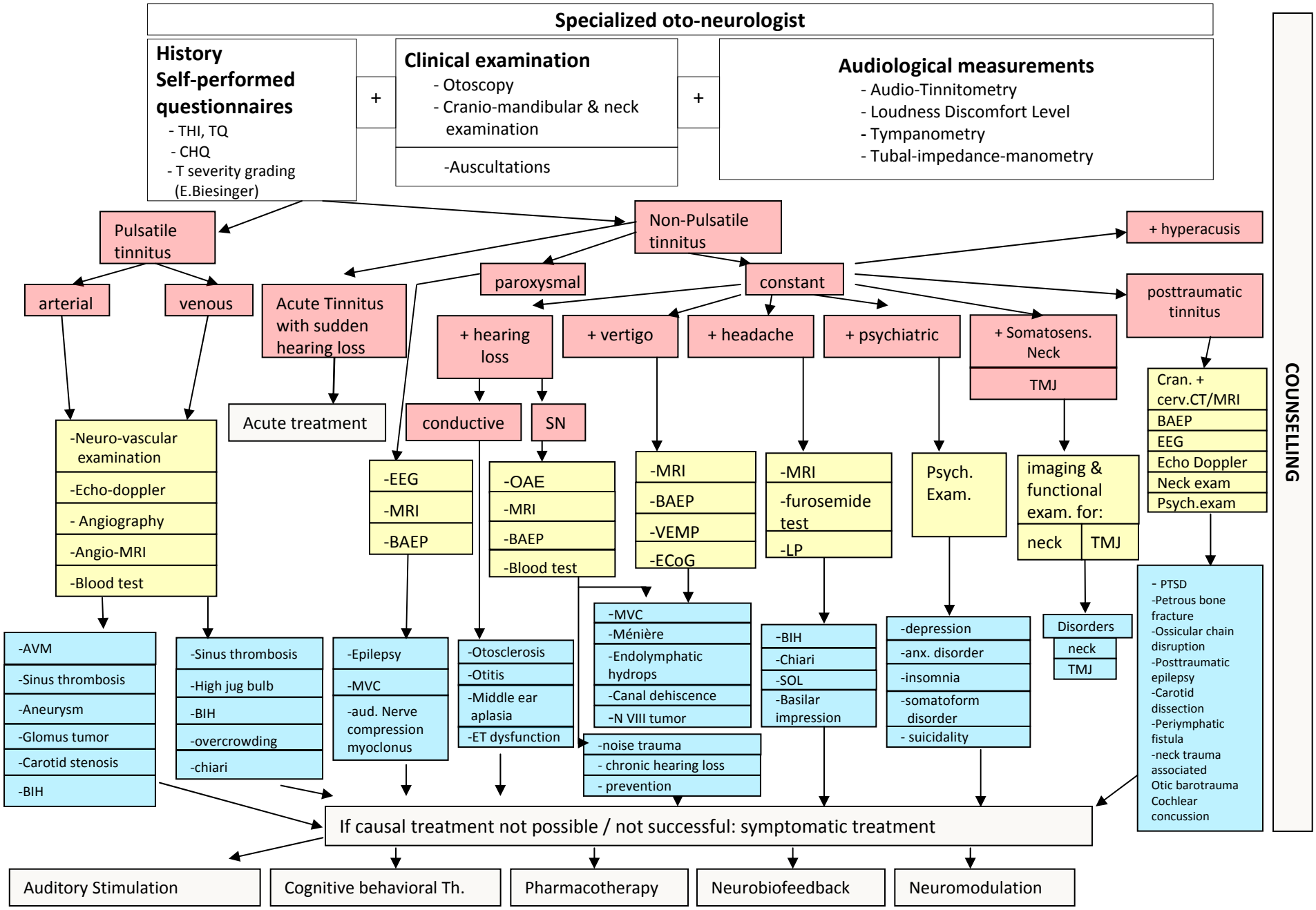
EFFECTS OF NERAMEXANE ON IONOTROPIC A9A10 NICOTINIC RECEPTORS AND HUMAN NMDA (NR1A/2A) - RELEVANCE FOR TINNITUS

C.G. Parsons [1], K.E. Gilling [1], G. Rammes [2], B. Elgoyhen [3], P.V. Plazas [3]
[1]Merz Pharmaceuticals, Frankfurt, D-60318 Germany; [2]Clinical Neuropharmacology, Max Planck Institute of Psychiatry, Munich, D-80804 Germany; [3]Instituto de Investigaciones en Ingenieria Genetica y Biologia Molecular, Buenos Aires, Argentina.

A COGNITIVE MODEL OF TINNITUS AND HYPERACUSIS

O. Wagenaar, M. Wieringa, **J. Verschuure**
Erasmus MC- University Medical Center Rotterdam, Netherlands

INDEX OF AUTHORS


Specialized oto-neurologist
History
Self-performed questionnaires
- THI, TQ
- CHQ
- T severity grading (E.Biesinger)
+
Clinical examination
- Otoscopy
- Cranio-mandibular & neck examination
-Auscultations
+
Audiological measurements
- Audio-Tinnitometry
- Loudness Discomfort Level
- Tympanometry
- Tubal-impedance-manometry
Pulsatile tinnitus
Non-Pulsatile tinnitus
arterial
venous
Acute Tinnitus with sudden hearing loss
paroxysmal
constant
+ hyperacusis
posttraumatic tinnitus
+ hearing loss
+ vertigo
+ headache
+ psychiatric
+ Somatosens. Neck
TMJ
Acute treatment
conductive
SN
-Neuro-vascular examination
-Echo-doppler
- Angiography
-Angio-MRI
-Blood test
-EEG
-MRI
-BAEP
-OAE
-MRI
-BAEP
-Blood test
-MRI
-BAEP
-VEMP
-ECoG
-MRI
-furosemide test
-LP
Psych. Exam.
imaging & functional exam. for:
neck
TMJ
Cran. + cerv.CT/MRI
BAEP
EEG
Echo Doppler
Neck exam
Psych.exam
-AVM
-Sinus thrombosis
-Aneurysm
-Glomus tumor
-Carotid stenosis
-BIH
-Sinus thrombosis
-High jug bulb
-BIH
-overcrowding
-chiari
-Epilepsy
-MVC
-aud. Nerve compression myoclonus
-Otosclerosis
-Otitis
-Middle ear aplasia
-ET dysfunction
-MVC
-Ménière
-Endolymphatic hydrops
-Canal dehiscence
-N VIII tumor
-noise trauma
- chronic hearing loss
- prevention
-BIH
-Chiari
-SOL
-Basilar impression
-depression
-anx. disorder
-insomnia
-somatoform disorder
- suicidality
Disorders
neck
TMJ
- PTSD
-Petrous bone fracture
-Ossicular chain disruption
-Posttraumatic epilepsy
-Carotid dissection
-Periymphatic fistula
-neck trauma associated
Otic barotrauma
Cochlear concussion
COUNSELLING
If causal treatment not possible / not successful: symptomatic treatment
Auditory Stimulation
Cognitive behavioral Th.
Pharmacotherapy
Neurobiofeedback
Neuromodulation

TRI HISTORY AND TARGETS