### News

All of us, who see tinnitus patients day after day, have to deal with the difficulty that, with the currently available treatment possibilities, many tinnitus patients do not experience sufficient relief. When we ask patients what they expect from their clinician, they answer that they expect somebody who gives them hope. The question is: “Is it realistic to give our patients hope for better treatment possibilities in the near future?” and if so “On what is this hope based?”

First of all, our understanding of the pathophysiology of tinnitus seems to grow day by day, as evidenced by the number and quality of new studies in the last months, which are reported in this Newsletter. Moreover, the increasing availability of new diagnostic and treatment methods, e.g., in molecular biology, neuroimaging and brain stimulation, give hope that more and more patients can be helped in the future. Not only has our understanding, diagnosis and treatment options improved, but also the attitude towards tinnitus is changing. Thus, at present tinnitus is increasingly perceived as a potentially understandable and “solvable” problem. It is our firm ‘belief’ that ultimately a cure for tinnitus will be found. It is a matter of being ‘stubbom’ enough, of being persistent, driven and highly motivated even in the face of disappointments. If we keep on realizing that we can learn from our failures, we are already one step closer to a cure. Only if we keep trying, we will succeed one day.

In this issue of the newsletter, an article in honour of Joseph Toynbee is cited. Born in 1815 in London, his research in aural anatomy and physiology aimed at rescuing aural surgery from the quacks that infested the field, which was almost unanimously avoided by legitimate practitioners of surgery. But Toynbee was not only a visionary researcher and clinician (despite a very large practice, he managed to dissect more than 2000 ears). He also devoted himself to medical philanthropy and was especially concerned with public health and welfare. Tragically enough, his attempts to help his tinnitus patients brought him an untimely death. He had conceived the idea of introducing a mixture of chloroform and prussic acid into the tympanic cavity by means of the Valsalva manoeuvre. When he made the first trial with himself as subject, he was found dead on the couch of his consulting room.

The situation of ear surgery in the 19th century resembles to some extent the situation of tinnitus today, and it needs researchers and clinicians with the spirit of a John Toynbee to make a change. If Toynbee failed to find a tinnitus treatment for his patients, we should try to fail better and better calculate the risks, but not stop seeking for new means to cure tinnitus.

In 2010 TRI will continue to support this endeavor by providing a platform for all those sharing a common goal: finding a cure for tinnitus. We wish you all joyful holidays, and on behalf of the Tinnitus Research Initiative, its representatives and employees, to the fullest extent permitted by law, disclaim all warranties, express or implied, statutory or otherwise, including but not limited to all implied warranties of merchantability, non-infringement of third party rights, and fitness for a particular purpose. Specifically, TRI makes no representations or warranties as to the reliability, accuracy, timeliness or completeness of the information and content of this newsletter.

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**Image Source:** www.photocase.de
4th International TRI Tinnitus Conference.
Frontiers in Tinnitus Research.

June 9th - 11th, 2010, Dallas, TX, USA

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

Please register at http://www.utdallas.edu/research/tri/

Proposals for free talks, symposia and posters are welcome!

Deadline for abstract submission: January 31st, 2010

Conference Topics will include

- Clinical Management of Tinnitus
- Basic Neuroscience
- Sound therapy
- Hearing Aids
- Brain Stimulation
- Imaging, Neurofeedback
- Tinnitus Subtyping etc...

- Diagnosis
- Genetics, Pharmacology
- Auditory Training
- Electrical Stimulation of the cochlea
- Somatosensory Modulation
- Nutrition and Diet

Speakers who have already confirmed their participation

Dirk De Ridder, Belgium
Paul Fuchs, USA
Berthold Langguth, Germany
Aage Møller, USA
Ranulfo Romo, Mexico

Ana Belén Elgoyhen, Argentina
Tobias Kleinjung, Germany
Rodolfo Llinas, USA
Larry Roberts, Canada
Richard Salvi, USA

This Meeting is co-sponsored by the American Tinnitus Association
NEWS

RICHARD TYLER (USA) and CLAUDIA BARROS COELHO (Brazil)

Richard Tyler and Claudia Coelho received the Editor’s Award of the American Journal of Audiology for the best publication in 2008. The paper on “Identifying tinnitus subgroups with cluster analysis” meets the highest quality standards in research design, presentation, and impact for the given year. It is truly a high honor for Richard Tyler and Claudia Coelho together with their co-authors Pan Tao, Haihong Ji, William Noble, Anne K. Gehringer and Stephanie A. Gogel.

WINFRIED SCHLEE (Germany)

Award of the Schmieder Foundation 2008

Winfried Schlee received the Award of the Schmieder Foundation 2008 for his dissertation on tinnitus research “Towards a Global Model of Tinnitus Perception: Multiple Evidence for a Long-Range Cortical Tinnitus Network”.
Upcoming Meetings

Meetings exclusively dedicated to Tinnitus are marked red.

February 2010

33rd MidWinter Meeting of the Association for Research in Otolaryngology (ARO)
When: February 6 – 10, 2010
Where: The Disneyland Hotel Anaheim, California, USA
Contact: Alex Springer
E-Mail: aspringer@talley.com
Detailed Information: http://www.aro.org/mwm/mwm.html

March 2010

American Auditory Society, Annual Meeting
When: March 4 – 6, 2010
Where: Scottsdale, AZ, USA
Contact: American Auditory Society
Detailed Information: http://www.amauditorysoc.org/annual-meeting/reginfo.htm

DAGA 2010: 36. Jahrestagung der Deutschen Gesellschaft für Akustik DEGA
When: March 15 – 18, 2010
Where: Berlin, Germany
Contact: Dipl.-Ing. Judith Kokavec
Technische Universität Berlin
Institut für Strömungsmechanik und Technische Akustik
Einsteinufer 25
10587 Berlin
E-Mail: info2010@daga-tagung.de
Detailed Information: http://www.daga-tagung.de/2010

13. Jahrestagung der Deutschen Gesellschaft für Audiologie (DGA e.V.)
When: March 17 – 20, 2010
Where: Frankfurt, Germany
Contact: Deutsche Gesellschaft für Audiologie e.V., Geschäftstelle
c/o Haus des Hörens
Marie-Curie-Straße 2
26129 Oldenburg, Germany
Phone: 0049 (0)4 41 2172 500
Fax: 0049 (0)4 41 2172 550
E-Mail: info@dga-ev.com
April 2010

**AudiologyNOW ! 2010**
When: April 14 – 17, 2010
Where: San Diego, CA, USA
Detailed information: [http://www.audiologynow.org/](http://www.audiologynow.org/)

**159th Meeting of the Acoustical Society of America (ASA)**
When: April 19 – 23, 2010
Where: Miami, Florida, USA
Detailed information: [http://asa.aip.org/meetings.html](http://asa.aip.org/meetings.html)

May 2010

**81. Jahresversammlung der Deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V.**
When: May 12 – 16, 2010
Where: Rhein-Main-Hallen, Wiesbaden, Germany
Contact: Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie
Hittorfstr. 7
53129 Bonn, Germany
Phone: 0049 (0)2 28/23 17 70
Fax: 0049 (0)2 28/23 17 70
E-Mail: info@hno.org
Detailed information: [http://www.hno.org/veranstaltungen/ankuendigungen.html](http://www.hno.org/veranstaltungen/ankuendigungen.html)

June 2010

**ESPO 2010 European Society of Pediatric Otorhinolaryngology**
When: June 05 – 08, 2010
Where: Baluarte Conference Centre, Pamplona, Spain
Contact: Secretaría Científica, ORL Congresos, S.L.
C/ Fundadores, nº 13
28028 Madrid, Spain
Phone: 0034 91 575 93 93
Fax: 0034 91 431 26 92
E-Mail: ortcongresos@seorl.net

**Human Brain Mapping Annual Meeting**
When: June 06 – 10, 2010
Where: Barcelona, Spain
Detailed information: [www.humanbrainmapping.org](http://www.humanbrainmapping.org)
4th International TRI Tinnitus Conference. Frontiers in Tinnitus Research
When: June 9 – 11, 2010
Where: The Adolphus Hotel, Dallas, Texas, USA
E-Mail: dallas2010@tinnitusresearch.org
Detailed Information: http://www.utdallas.edu/research/tri/

4th World Congress of International Federation of Head and Neck Oncologic Societies (IFHNOS)
When: June 15 – 19, 2010
Where: Lotte Hotel, Seoul, Korea
Contact: IFHNOS 2010 Congress Secretariat
c/o Meci International Convention Services, Inc.
Rm. 1906, 19th floor, Daerung Post Tower #1 212-8 Guro-dong, Guro-gu
Seoul 152-790, Korea
Phone: 0082 2 2082 2310
Fax: 0082 2 2082 2314
E-Mail: ifhnos2010@ifhnos2010.org
Detailed information: http://www.ifhnos2010.org/

International Conference on Adult Hearing Screening (AHS) 2010
When: June 10 - 12, 2010
Where: Cernobbio, Italy
E-mail: ahs2010@polimi.it
Detailed Information: http://www.ahs2010.polimi.it/

CI2010 11th International Conference on Cochlear Implants and other Implantable Auditory Technologies
When: June 30 – July 03, 2010
Where: Stockholm International Fairs (Stockholmsmässan), Stockholm, Sweden
Contact: MCI Stockholm
Box 6911
102 39 Stockholm, Sweden
Phone: 0046 8 5465 1500
Fax: 0046 8 5465 1599
E-Mail: ci2010@mci-group.com
Detailed information: http://www.ci2010.com

Herbsttagung Arbeitsgemeinschaft Deutschsprachiger Audiologen und Neurootologen (ADANO)
When: September 16 – 19, 2010
Where: Zürich, Switzerland
Detailed information: http://www.hno.org/adano/tagungen.htm
International Symposium on Objective Measures in Auditory Implants
When: September 23 – 25, 2010
Where: St. Louis, MO, USA
Detailed information: https://cme.wustl.edu/om2010/

IAPA 2010 - XV International Symposium in Audiological Medicine
When: September 26 – 29, 2010
Where: Krakow Poland
Contact: Professor Mariola Sliwinska-Kowalska
Detailed Information: http://iapa-online.org/symposia/future-symposia/

American Academy of Otolaryngology, Head and Neck Surgery Annual Meeting
When: September 26 – 29, 2010
Where: Boston, MA, USA
Detailed information: http://www.entnet.org/ConferencesAndEvents/upcomingconferences.cfm

55th International Congress of Hearing Aid Acousticians
When: October 13 – 15, 2010
Where: Messe Hannover, Germany
Detailed information: http://www.euha.org

ASHA 2009 Annual Convention
When: November 18 – 20, 2010
Where: Philadelphia, PA, USA
Detailed information: http://www.asha.org/about/events/convention/
Recently published literature (articles of authors who are funded by TRI are marked in blue)

I Epidemiology

Ear symptoms in children with Fabry disease: data from the Fabry Outcome Survey.
J Inherit Metab Dis. 2009 Oct 27. [Epub ahead of print]

Keilmann A, Hajioff D, Ramaswami U; on behalf of the FOS Investigators.
Department for ENT and Communication Disorders, University Hospital, Langenbeckstr. 1, 55101, Mainz, Germany, keilmann@kommunikation.klinik.uni-mainz.de.

Background: Hearing loss and tinnitus are common symptoms in Fabry disease and increase in prevalence with age. This study aimed to provide an epidemiological description of hearing impairment and tinnitus in children with Fabry disease in the Fabry Outcome Survey (FOS), an international database to assess the natural history of Fabry disease and the efficacy of enzyme replacement therapy with agalsidase alfa. Methods: Signs and symptoms questionnaires were completed for 543 children with Fabry disease. Pure-tone audiograms were obtained from 101 children (53 girls, 48 boys). Results: On questioning, 33% of the children (n = 179) reported subjective hearing impairment. However, when assessed by age-appropriate audiometry, only 19 of 101 patients (19%) had a persistent hearing loss at least one frequency. Of these, 14 had a high-frequency hearing loss, 4 a pan-frequency hearing loss, and 1 a pattern typical of noise-induced loss. Of the 101 children with audiometry, 44 complained of tinnitus. Only 2 children reported sudden hearing loss, which was not verified by audiometry. Children with tinnitus had greater disease severity scores. Conclusions: Hearing loss is a well-known clinical manifestation in patients with Fabry disease. It was reported in significant numbers of children in the FOS signs and symptoms questionnaire, but confirmed in only 19% by formal audiometry. The subjective hearing impairment may have been due to middle-ear effusions in many cases. Tinnitus is a well-recognized symptom in Fabry disease and can present in childhood. The presence of tinnitus correlated with overall disease severity.

Physicians appeals on the dangers of mobile communication--what is the evidence? Assessment of public health data.

Zur Nieden A, Dietz C, Eikmann T, Kiefer J, Herr CE.
Institute of Hygiene and Environmental Medicine, Medical Centre, Faculty of Medicine, Justus-Liebig-University Giessen, Germany. anja.zur.nieden@hygiene.med.uni-giessen.de

In October 2002 German physicians appealed to persons in the field of health care, politicians and the public with „great concern“ („Freiburger Appell“, „Appeal of Freiburg“) claiming „soaring incidences of symptoms and diseases in the general population“ to be causally related to the „commence of radio (wave) burden“, i.e. due to mobile radio technology. This first example was followed by several further appeals published nationally and Europe-wide up until today. The aim of the present paper is an evaluation of the scientific literature and databases to check incidence and prevalence of symptoms and diseases stated in the appeals to have „dramatically increased“ or to have appeared in „greater frequency“ in adults. If the allegations were true a clear time-trend should show up since the start of widely-used mobile communication technology. The following health conditions were considered: Alzheimer's disease, dementia, sleep disturbances, tinnitus, cerebrovascular disease, ischemic heart-diseases, headache, migraine. Data on the incidence of these conditions were assessed from 1993 through at least 2005. For this, a systematic search by keywords was performed in the online-database of the National Library of Medicine (pubmed) and other national and international (European and US) databases. For none of the considered symptoms or diseases a „dramatic increase“ was found to have occurred since 1993. Because of the different diagnoses and terms used in the studies, direct
comparability is somewhat difficult. Indeed, with the data available no time related increases and surely no „dramatic increase“ can be identified, even if the limited comparability is considered. This analysis strongly suggests that the allegations of the quoted appeals are not supported by public health data.

Prevalence and characteristics of hearing problems in a working and non-working Swedish population.
J Epidemiol Community Health. 2009 Aug 19. [Epub ahead of print]
Hasson D, Theorell T, Westerlund H, Canlon B.

Sweden

BACKGROUND: Hearing problems are among the top ten most common burdens of disease and are projected to be become even more common by the year 2030. The aim of the present study was to give a current assessment of the prevalence of communication difficulties due to hearing loss and tinnitus, in the general Swedish working and non-working population in relation to gender, age, socioeconomic status (SES) and noise exposure. How prevalence is affected by (SES) has not been previously established. METHODS: A total of 18,734 individuals were invited to participate in the study, out of which 11,441 (61 %) enrolled. Of the participants 9,756 answered the questionnaire for those who work and 1,685 answered the version for non-workers. FINDINGS: The most important findings are that 31 % in the working population and 36 % in the non-working population report either hearing loss or tinnitus or both. The prevalence of hearing problems increases with age, is higher among men and persons with low self-rated SES, and co-varies with exposure to noise at work. Severe hearing problems are already present in men and women under 40 years of age who are exposed to work-related noise. Interpretation: Prevalence of hearing problems is far more common than previously estimated and is associated with socioeconomic status and noise exposure history. Hearing problems have a gradual onset that can take years to become recognized. In order to proactively intervene and prevent this deleterious, yet avoidable handicap, statistics need to be regularly updated.

Prevalence of noise induced hearing loss among traffic police in Dhaka Metropolitan City.
Sharif A, Taous A, Siddique BH, Dutta PG.

Department of Otolaryngology & Head-Neck Surgery, Mymensingh Medical College Hospital (MMCH), Mymensingh, Bangladesh.

The present study was done to determine the prevalence of noise induced hearing loss (NIHL) among the traffic police of Dhaka Metropolitan City. A cross sectional study was carried out among randomly selected 100 traffic police from January 2003 to June 2004, in the department of Department of Otolaryngology & Head-Neck Surgery, Bangabandhu Sheikh Mujib Medical University. Personal interview was taken from every respondent about the duration of exposure of noise (8 hours/day) in Dhaka City. Otological examination consists of 1) Otoscopy 2) Tuning fork test and 3) Pure tone audiometry. In this study 23 complaints of tinnitus or ringing in the ear and only 5% complaints of deafness. 24 respondents had mild to moderate high frequency sensorineural hearing loss, and affected mainly frequencies of 4-6 KHz. Among 20 mild hearing loss cases, 11/53(20.75%) have had duration of exposure between 6-10 years, 4/31 (12.9%) had duration of exposure between 11-15 years and 5/16(31.25%) had duration of exposure between 16-20 years. Among the 4 moderate hearing loss cases, 2/31 (6.45%) had duration of exposure of 11-15 years and 2/16(12.5%) had 16-20 years of noise exposure in Dhaka Metropolitan City. Among those who had exposure 6-10 years, 20% shows mild sensorineural hearing loss and those had exposure 11-20 years, 28% had mild to moderate sensorineural hearing loss. In the present series it is concluded that 24% of the respondent having mild to moderate sensorineural hearing loss due to noise exposure which is related with the duration of exposure.
Tinnitus incidence and characteristics in children with hearing loss

Celik, N.a, Bajin, M.D.a, Aksoy, S.b

a Department of Otorhinolaryngology-Head and Neck Surgery, Hacettepe University Hospital, Ankara 06100, Turkey, b Department of Otorhinolaryngology-Head and Neck Surgery Audiology Unit, Hacettepe University Hospital, Ankara 06100, Turkey

The objective of this study is to determine presence and prevalence of tinnitus in children with hearing loss under the age of eighteen in central Ankara. Materials and Methods All children were asked: „Do you hear any noises in your ears?“ If they answered „yes“ they were asked nine more questions. Associated symptoms, pitch, level and general descriptions were also noted. Results and Conclusion: Children with hearing loss had a high incidence of tinnitus. Even though they don't express, they have tinnitus and it effects their lives. By using a survey specific to tinnitus we can identify tinnitus in children with impaired hearing and develop new ways to manage their problems. Copyright © The mediterranean Society of Otology and Audiology.

II Pathophysiology

Bilateral subdural hematomas and hearing disturbances caused by spontaneous intracranial hypotension.
Srimanee D, Pasutharnchat N, Phanthumchinda K.

Division of Neurology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. Dukebrufen@yahoo.co.th

Spontaneous Intracranial Hypotension (SIH) is an uncommon headache syndrome. Patients classically present with orthostatic headache, tinnitus, and diplopia. The authors reported a 43 year-old man who presented with orthostatic headache, tinnitus, and hearing impairment for 3 months. Physical examination was unremarkable except for auditory impairment. The audiogram revealed minimal low-frequency neurosensori hearing loss suggesting a cochlear lesion. Computed tomography of the brain revealed bilateral thin chronic subdural hematomas. He underwent burr-hole surgery. Headache and auditory symptoms persisted and reevaluation of this syndrome was performed MRI of the brain showed diffuse smooth enhanced dura mater low lying position of midbrain, pons, medullar and cerebellar tonsil, as well as enlarged pituitary gland compatible with low CSF pressure syndrome. MRI of the whole spine could not demonstrate the site of CSF leakage. The patient was much improved after conservative treatments with hydration and bed rest. One year after treatment, he had no headache and only mild tinnitus was reported.

Mapping cortical hubs in tinnitus.
Schlee W, Mueller N, Hartmann T, Keil J, Lorenz I, Weisz N.

Dept of Psychology, Univ of Konstanz, 78457 Konstanz, Germany. winfried.schlee@uni-konstanz.de.

ABSTRACT: BACKGROUND: Subjective tinnitus is the perception of a sound in the absence of any physical source. It has been shown that tinnitus is associated with hyperactivity of the auditory cortices. Accompanying this hyperactivity, changes in non-auditory brain structures have also been reported. However, there have been no studies on the long-range information flow between these regions. RESULTS: Using Magnetoencephalography, we investigated the long-range cortical networks of chronic tinnitus sufferers (n = 23) and healthy controls (n = 24) in the resting state. A beamforming technique was
applied to reconstruct the brain activity at source level and the directed functional coupling between all voxels was analyzed by means of Partial Directed Coherence. Within a cortical network, hubs are brain structures that either influence a great number of other brain regions or that are influenced by a great number of other brain regions. By mapping the cortical hubs in tinnitus and controls we report fundamental group differences in the global networks, mainly in the gamma frequency range. The prefrontal cortex, the orbitofrontal cortex and the parieto-occipital region were core structures in this network. The information flow from the global network to the temporal cortex correlated positively with the strength of tinnitus distress. CONCLUSION: With the present study we suggest that the hyperactivity of the temporal cortices in tinnitus is integrated in a global network of long-range cortical connectivity. Top-down influence from the global network on the temporal areas relates to the subjective strength of the tinnitus distress.

**Significance of Serotonin Transporter Gene Polymorphism in Tinnitus.**

Otol Neurotol. 2009 Nov 17. [Epub ahead of print]


Departments of *Audiology and Otolaryngology, Faculty of Medicine, Gazi University, Besevler; double daggerDepartment of Otolaryngology, Kecioren Research and Training Hospital of the Ministry of Health; section signDepartment of Medical Biology and Genetics, Faculty of Medicine, Gazi University, Besevler; parallelDepartment of Otolaryngology, Ankara Numne Research and Training Hospital of the Ministry of Health, Ankara; and paragraph signDepartment of Medical Biology and Genetics, Faculty of Medicine, University of Mersin, Mersin, Turkey.

OBJECTIVES: To assess the role of serotonin transporter gene (SLC6A4) polymorphism in tinnitus. MATERIALS AND METHODS: Fifty-four consecutive patients experiencing subjective tinnitus and 174 healthy controls were allocated for the study. Psychoacoustic parameters of tinnitus were measured. Beck Depression Inventory was used to assess the depression level of the patients. Tinnitus Handicap Inventory was used to assess the severity of tinnitus. A visual analog scale was designed to measure the impact of tinnitus on quality of life of the patients. The 44-bp insertion-deletion in the promoter region (5-HTTLPR) and 17-bp variable number tandem repeats in the second intron of the serotonin transporter gene were assessed. RESULTS: No difference was found between the genotypes and allele frequencies of the patients and controls regarding variable number tandem repeats and SLC6A4 polymorphisms (p > 0.05). There was no association between the psychoacoustic parameters of tinnitus and SLC6A4 polymorphism (p > 0.05). There was a significant association between the 5-HTTLPR polymorphism and scores from the visual analog scale of the patients (p < 0.05). CONCLUSION: Generation of tinnitus signal is not associated with SLC6A4 polymorphism and possibly with serotonergic mechanisms. However, the „ll“ genotype variant of the SLC6A4 polymorphic promoter region seems associated with the limbic and autonomic nervous system symptoms of the patients with tinnitus. Therefore, serotonergic mechanisms may help explain the neurophysiological model of tinnitus, and serotonin replacement or serotonin reuptake inhibitors may increase the success rate of tinnitus treatment modalities based on the neurophysiologic model of tinnitus.


Kujawa SG, Liberman MC.

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Overexposure to intense sound can cause temporary or permanent hearing loss. Postexposure recovery of threshold sensitivity has been assumed to indicate reversal of damage to delicate mechano-sensory
and neural structures of the inner ear and no persistent or delayed consequences for auditory function. Here, we show, using cochlear functional assays and confocal imaging of the inner ear in mouse, that acoustic overexposures causing moderate, but completely reversible, threshold elevation leave cochlear sensory cells intact, but cause acute loss of afferent nerve terminals and delayed degeneration of the cochlear nerve. Results suggest that noise-induced damage to the ear has progressive consequences that are considerably more widespread than are revealed by conventional threshold testing. This primary neurodegeneration should add to difficulties hearing in noisy environments, and could contribute to tinnitus, hyperacusis, and other perceptual anomalies commonly associated with inner ear damage.

The role of anxiety sensitivity and behavioral avoidance in tinnitus disability.

Hesser H, Andersson G.

Department of Behavioural Sciences and Learning, Swedish Institute for Disability Research, Linköping University, Linköping, Sweden.

The purpose of this study was to investigate the role of anxiety sensitivity and behavioral avoidance in tinnitus distress and functioning. A cross-sectional sample of 283 individuals experiencing tinnitus was obtained from an epidemiological national survey study on hearing loss, dizziness, and tinnitus. The subjects completed a series of questionnaires measuring anxiety sensitivity, anxiety, and depression. They also answered questions regarding tinnitus distress, functioning, and avoidance. Results revealed a positive significant correlation between anxiety sensitivity and tinnitus distress. This relationship was not better explained by anxiety and depression symptoms. In addition, the findings provided support for a model where behavioral avoidance fully mediated the relationship between anxiety sensitivity and tinnitus functioning, and partially mediated the relationship between anxiety sensitivity and tinnitus distress. Implications for the role of anxiety sensitivity and behavioral avoidance in tinnitus research are discussed.

Final common pathway for tinnitus: theoretical and clinical implications of neuroanatomical substrates.

Shulman A, Goldstein B, Strashun AM.

Martha Entenmann Tinnitus Research Center, Forest Hills, New York, USA. metrc@inch.com

A final common pathway (FCP) for tinnitus has been hypothesized since 1989 for all clinical types of tinnitus, particularly subjective idiopathic tinnitus (SIT) of the severe disabling type. This was intended to explain the transformation-transition of the sensation of an aberrant auditory sensation-tinnitus (i.e., the sensory component)-to one of affect (i.e., the emotional-behavioral component) or, conversely, that an emotional-behavioral stimulus (affect) can result in the clinical manifestation of a sensation (a sensory stimulus). Understanding the pathophysiology of this transformation is fundamental for the diagnosis of tinnitus and the treatment of the patient, and it presents a dilemma to basic science, neuroscience, and clinical medicine. Clinically, tinnitus is not a unitary symptom; it constitutes many clinical types; can have its origin in the auditory or nonauditory systems and in the peripheral or central nervous system; and may be clinically manifest or subclinical. Accumulating evidence is presented to support the original hypothesis of an FCP. The resolution of this dilemma involves sensory processing (i.e., the integration, identification, and understanding of the ongoing, underlying, simultaneous, multiple associated brain function processes not only from one sensory modality but from multiple sensory modalities accompanying and associated with an FCP). In the FCP, the predominant brain function process is that of the sensory-affect transformation of a sensation and its conscious awareness by the affected patient. The neuroanatomical substrates identified in 1989 in tinnitus patients (reported originally in 1991 and published in 1995) are presented as a common framework for the hypothesis of an FCP. They further the understanding of the clinical heterogeneity of the tinnitus symptom, clinically manifest as multiple brain
functions associated with the clinical course of tinnitus patients, particularly those with SIT. The FCP provides a model for tinnitus theory, diagnosis, and treatment. The FCP is not a tinnitus theory. Specifically, it is a hypothesis that attempts to explain how an aberrant auditory sensory stimulus becomes transformed into one of affect and somatomotor response. The neuroanatomical substrates of the FCP provide a basis for the identification of the involved neurocircuits and neurochemistries. The physiology and biochemistry underlying the neuroanatomical substrates of the FCP provide a basis for translation for tinnitus diagnosis and treatment. The neuroanatomical substrates of the FCP are presented as algorithms of (1) components of a sensation (i.e., sensory, affect, and psychomotor), a translation from basic sensory physiology for tinnitus; (2) clinically manifest biophysiological brain functions and underlying processes associated with the tinnitus; (3) a model for investigation of metabolic-electrophysiological correlates for tinnitus; (4) the basis for an integrated theory of tinnitus and brain function (i.e., tinnitus dyssynchrony-synchrony theory; (5) a model for the identification of underlying neurocircuits and neurochemistries involved in brain for the sensory-affect transformation of an aberrant auditory stimulus (tinnitus); (6) a model for the selection-introduction of innovative therapies attempting tinnitus relief; and (7) its clinical translation for objective monitoring systems for the determination of the efficacy of modalities of therapy attempting tinnitus relief. The hypothesis of the FCP for tinnitus and the identified neuroanatomical substrates, when viewed in terms of the physiology of sensory processing, is considered to be expanded and broader in its application for all sensations, normal or aberrant.

[Peripheral and central audiological findings in patients with Vogt-Koyanagi-Harada syndrome] [Article in Spanish]

Instituto Nacional de Rehabilitación, Servicio de Audiología, México DF, México. danyallec@yahoo.com

OBJECTIVE: To identify and describe peripheral and central audiological abnormalities of patients with Vogt Koyanagi Harada syndrome. MATERIALS AND METHODS: Prospective, cross-sectional, observational, descriptive study. Vogt Koyanagi Harada patients referred from an ophthalmologic centre were assessed for signs and symptoms of auditory pathology. Peripheral audiological and central auditory processing tests were performed. To standardize the latter, methodological controls were matched for sex, age and audiometric chart. RESULTS: 21 patients were included (3 male, 18 female), mean age 40.7 years (+/-11.82). Nine of the 21 complained of tinnitus and nine suspected hearing loss. Exclusively or mainly sensorial abnormalities of pure tone audiometric chart were documented in 61.9% (mainly selective troughs at 4 and 8 kHz); 95.3% of patients had deficit in high-frequency audiometry. Five of the patients had sensorial disorders in the speech audiometry. No central auditory processing disorder was seen. CONCLUSIONS: Most of the patients with Vogt Koyanagi Harada syndrome had objective peripheral audiological abnormalities, although few revealed any symptoms.

Tinnitus and short-term serial recall in stable versus intermittent masking conditions.

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The relation between tinnitus and short-term memory performance in varying background sounds is not well understood. In the present study a sample of 18 persons with tinnitus completed a serial recall test in three conditions, silence, masking and intermittent masking. The performance of a matched control group without tinnitus was also investigated. Based on the literature on the „irrelevant sound effect“ we expected that the tinnitus group would perform worse during intermittent masking and that they would
score lower overall compared to the control group. Results revealed no statistically significant differences between the groups, nor any group interaction within sound conditions for the serial recall test. Groups did however differ regarding subjective measures of concentration problems, anxiety and depression. Results are discussed in relation to thought suppression and distraction from tinnitus.

**Voltage-gated sodium channel expression in rat spiral ganglion neurons.**

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The spiral ganglion neurons (SGN) provide the afferent innervation of the hair cells in the organ of Corti and relay auditory information from the inner ear to the brain. Voltage-gated sodium channels (Na(V)) initiate and propagate action potentials that encode this sensory information but little is known regarding the subtypes expressed in these cells. We have used RT-PCR and immunohistochemistry to study the compliment and anatomical distribution of Na(V) channels in rodent SGN. Na(V)1.1, Na(V)1.6 and Na(V)1.7 were all detected at the mRNA level. Fluorescence or streptavidin-horseradish peroxidase immunohistochemistry extended these findings, demonstrating predominant localisation of Na(V)1.6 and Na(V)1.7 on SGN cell bodies and Na(V)1.1 on axonal processes. Dual labelling with peripherin demonstrated higher Na(V)1.6 and Na(V)1.7 expression on Type I rather than Type II neurons. These results provide evidence for selective expression and variations in the distribution of VGSC in the rodent SGN, which may guide further studies into afferent function in the auditory pathway and therapeutic approaches for diseases such as hearing loss and tinnitus.

**[Caloric test in low-tone sensorineural hearing loss]**
[Article in Japanese]


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Acute low-tone sensorineural hearing loss (ALHL) is generally has a relatively good prognosis. We have often found in long-term following-up, however, that ALHL relapses, recurs or develops into Meniere’s disease. Diagnostic criteria of the Acute Altitude Deafness Research Group of the Ministry of Health, Labor, and Welfare of Japan, define ALHL as low-tone-disorder sensorineural hearing loss without vertigo in which cochlear symptoms -ear fullness, tinnitus, and deafness- develop suddenly. Over the last five years, we have treated 31 cases of ALHL, in about half of which neurotological examination showed potential peripheral vestibular dysfunction on testing positional nystagmus (a) with closed eyes and (b) in a dark room with open eyes, and by finding laterality in the peripheral labyrinth system on caloric test. These cases show high canal paresis -a maximum slow- phase eye velocity of caloric nystagmus exceeding 60%. These results, taken together, suggest that derangement extends to the peripheral labyrinth system in patients with ALHL.

**Cisplatin-based chemotherapy: Add high-frequency audiometry in the regimen.**

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BACKGROUND: Cisplatin-induced ototoxicity shows high interindividual variability and is often accompanied by transient or permanent tinnitus. It is not possible to identify the susceptible individuals before commencement of the treatment. We conducted a prospective, randomized and observational
study in a tertiary care centre and evaluated the effects of different doses of cisplatin on hearing.

MATERIALS AND METHODS: Fifty-seven patients scheduled for cisplatin-based chemotherapy were included in the study. All patients were divided into three groups depending on the dose of cisplatin infused in 3 weeks. RESULTS: The subjective hearing loss was found in seven patients, while six patients had tinnitus during the chemotherapy. The hearing loss was sensorineural, dose dependent, symmetrical, bilateral and irreversible. Higher frequencies were first to be affected in cisplatin chemotherapy. CONCLUSION: As use of high-frequency audiometry is still limited in research work only, we need a strict protocol of adding high-frequency audiometry in the cisplatin-based chemotherapy regimen.

Geldanamycin induces production of heat shock protein 70 and partially attenuates ototoxicity caused by gentamicin in the organ of Corti explants.
Yu Y, Szczepek AJ, Haupt H, Mazurek B.

BACKGROUND: Heat shock protein 70 (HSP70) protects inner ear cells from damage and death induced by e.g. heat or toxins. Benzoquinone ansamycin antibiotic geldanamycin (GA) was demonstrated to induce the expression of HSP70 in various animal cell types. The aim of our study was to investigate whether GA induces HSP70 in the organ of Corti (OC), which contains the auditory sensory cells, and whether GA can protect these cells from toxicity caused by a common aminoglycoside antibiotic gentamicin. METHODS: To address these questions, we used the OC explants isolated from p3-p5 rats. As a read-out, we used RT-PCR, ELISA and immunofluorescence. RESULTS: We found that GA at the concentration of 2 microM efficiently induced HSP70 expression on mRNA and protein level in the OC explants. Confocal microscopy revealed that HSP70 induced by GA is expressed by hair cells and interdental cells of spiral limbus. Preincubation of explants with 2 muM GA prior to adding gentamicin (500 microM) significantly reduced the loss of outer but not inner hair cells, suggesting different mechanisms of otoprotection needed for these two cell types. CONCLUSION: GA induced HSP70 in the auditory sensory cells and partially protected them from toxicity of gentamicin. Understanding the molecular mechanisms of GA otoprotection may provide insights for preventative therapy of the hearing loss caused by aminoglycoside antibiotics.

Plasticity at glycinergic synapses in dorsal cochlear nucleus of rats with behavioral evidence of tinnitus.

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Fifteen percent to 35% of the United States population experiences tinnitus, a subjective „ringing in the ears”. Up to 10% of those afflicted report severe and disabling symptoms. Tinnitus was induced in rats using unilateral, 1 h, 17 kHz-centered octave-band noise (116 dB SPL) and assessed using a gap-startle method. The dorsal cochlear nucleus (DCN) is thought to undergo plastic changes suggestive of altered inhibitory function during tinnitus development. Exposed rats showed near pre-exposure auditory brainstem response (ABR) thresholds for clicks and all tested frequencies 16 weeks post-exposure. Sound-exposed rats showed significantly worse gap detection at 24 and 32 kHz 16 weeks following sound exposure, suggesting the development of chronic, high frequency tinnitus. Message and protein levels of alpha(1-3,) and beta glycine receptor subunits (GlyRs), and the anchoring protein, gephyrin, were measured in DCN fusiform cells 4 months following sound exposure. Rats with evidence of tinnitus
showed significant GlyR alpha(1) protein decreases in the middle and high frequency regions of the DCN while alpha(1) message levels were paradoxically increased. Gephyrin levels showed significant tinnitus-related increases in sound-exposed rats suggesting intracellular receptor trafficking changes following sound exposure. Consistent with decreased alpha(1) subunit protein levels, strychnine binding studies showed significant tinnitus-related decreases in the number of GlyR binding sites, supporting tinnitus-related changes in the number and/or composition of GlyRs. Collectively, these findings suggest the development of tinnitus is likely associated with functional GlyR changes in DCN fusiform cells consistent with previously described behavioral and neurophysiologic changes. Tinnitus related GlyR changes could provide a unique receptor target for tinnitus pharmacotherapy or blockade of tinnitus initiation.

Tinnitus-provoking salicylate treatment triggers social impairments in mice.

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OBJECTIVES: Tinnitus (perception of sound in silence) strongly affects the quality of life of sufferers. Tinnitus sufferers and their relatives frequently complain about major social impairments. However, it is not known whether this impairment directly results from the occurrence of tinnitus or is the indirect expression of a preexisting psychological vulnerability. Using the well-characterized animal model of salicylate-induced tinnitus, we investigate in mice whether the occurrence of tinnitus can trigger social impairments. METHODS: Experiments were performed on 32 male Balb/C mice. Tinnitus was induced in mice using salicylate treatment. Social behavior was assessed in experimental and control animals using social interaction paradigm. Interaction time, number of social events, and number of nonsocial events were assessed in all animals. RESULTS: We demonstrate for the first time that treatment known to induce tinnitus triggers complex social impairments in mice. While salicylate-treated animals present a massive decrease in their overall social interactions compared to control untreated animals, they also display a paradoxal increase in the number of conspecific followings. CONCLUSION: Tinnitus can thus trigger a complex set of modifications of behavior, which will not only find their expression at the individual level, but also at the social level. Our results suggest that tinnitus can directly be a cause of psychosocial impairment in human and have strong implications for the clinical management of tinnitus sufferers.

Molecular aspects of tinnitus.
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Molecular changes caused by sensory trauma and subsequent structural alterations of the central nervous system are only beginning to be identified. In most cases, the generation of tinnitus can be linked to damage of the peripheral auditory system, probably even in cases where hearing impairment cannot be assessed by audiometry. Within a common view, acoustic trauma and salicylate induce abnormal excitability at the level of the brainstem, subcortical and cortical level that may be related to tinnitus. The present review summarizes studies emphasizing a crucial role of molecular events that occur in the cochlea exhibiting the potential to alter the network activity in distinct areas of the brain, including the limbic system. We proceed from the inner ear to the auditory cortex and discuss the recent molecular findings in the central auditory system as a secondary step of previous neuronal changes in the periphery.
Salicylate, an aspirin metabolite, specifically inhibits the current mediated by glycine receptors containing α1-subunits

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Background and purpose: Aspirin or its metabolite sodium salicylate is widely prescribed and has many side effects. Previous studies suggest that targeting neuronal receptors/ion channels is one of the pathways by which salicylate causes side effects in the nervous system. The present study aimed to investigate the functional action of salicylate on glycine receptors at a molecular level. Experimental approach: Whole-cell patch-clamp and site-directed mutagenesis were deployed to examine the effects of salicylate on the currents mediated by native glycine receptors in cultured neurones of rat inferior colliculus and by glycine receptors expressed in HEK293T cells. Key results: Salicylate effectively inhibited the maximal current mediated by native glycine receptors without altering the EC50 and the Hill coefficient, demonstrating a non-competitive action of salicylate. Only when applied simultaneously with glycine and extracellularly, could salicylate produce this antagonism. In HEK293T cells transfected with either α1-, α2-, α3-, α1β-, α2βα3-glycine receptors, salicylate only inhibited the current mediated by those receptors that contained the α1-subunit. A single site mutation of I240V in the α1-subunit abolished inhibition by salicylate. Conclusions and implications: Salicylate is a non-competitive antagonist specifically on glycine receptors containing α1-subunits. This action critically involves the isoleucine-240 in the first transmembrane segment of the α1-subunit. Our findings may increase our understanding of the receptors involved in the side effects of salicylate on the central nervous system, such as seizures and tinnitus. © 2009 The British Pharmacological Society All rights reserved.

III Diagnostics

Clinical spectrum of patients with erosion of the inner ear by jugular bulb abnormalities.
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OBJECTIVES/HYPOTHESIS: Anatomic variants of the jugular bulb (JB) are common; however, abnormalities such as large high riding JB and JB diverticulum (JBD) are uncommon. Rarely, the abnormal JB may erode into the inner ear. The goal of our study is to report a large series of patients with symptomatic JB erosion into the inner ear. STUDY DESIGN: Retrospective review in an academic medical center. METHODS: Eleven patients with JB abnormality eroding into the inner ear were identified on computed tomography (CT) scan of the temporal bone. RESULTS: Age at presentation was from 5 years to 82 years with six males and five females. The large JB or JBD eroded into the vestibular aqueduct (n = 9) or the posterior semicircular canal (n = 4). The official radiology report usually identified the JB abnormality; however, erosion into these structures by the JB was not mentioned in all but one case. All patients were symptomatic with five having conductive hearing loss (CHL) and three complaining of pulsatile tinnitus. Those with pulsatile tinnitus and four of five with CHL had erosion into the vestibular aqueduct. Vestibular evoked myogenic potential (VEMP) findings in three of six patients were consistent with dehiscence of the inner ear. CONCLUSIONS: High riding large JB or JBD can erode into the inner ear and may be associated with CHL and/or pulsatile tinnitus. CT scan is diagnostic and should be examined specifically for these lesions. As patients with pulsatile tinnitus may initially undergo a magnetic resonance imaging scan, identification of JB abnormality should prompt CT scan or VEMP testing to evaluate for inner ear erosion. Laryngoscope, 2010.
Vestibular schwannoma: when to look for it?

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Objectives:(1) To compare audiometric parameters in patients with vestibular schwannoma and in those with asymmetric hearing loss from other causes; and (2) to assess proposed screening criteria by comparing published protocols.Methods:Audiometric data from 199 vestibular schwannoma patients and 225 non-tumour patients were compared. Eight screening protocols were tested on these 424 patients.Results:Vestibular schwannoma and non-tumour patients with little or no hearing loss in the unaffected ear were inseparable; however, vestibular schwannoma patients with hearing loss in the unaffected ear had greater audiometric asymmetry, compared with non-tumour patients with the same pattern of hearing loss. The sensitivity of screening protocols varied from 73 to 100 per cent; parallelism was observed between sensitivity and screening rate.Conclusion:As regards vestibular schwannoma screening protocols, the best compromise between sensitivity and screening rate was offered by a criterion comprising either: (1) >/=20 dB asymmetry at two neighbouring frequencies, or unilateral tinnitus, or (2) >/=15 dB asymmetry at two frequencies between 2 and 8 kHz.

Spontaneous intracranial hypotension.

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Since the introduction of magnetic resonance imaging (MRI), spontaneous intracranial hypotension has been diagnosed much more frequently. The aim of this review is to discuss the symptoms and signs of the condition, in particular the characteristics of the associated headache, with sudden onset after sitting or standing, so that it can be included under the rubric of 'thunderclap headache'. This type of headache, like post lumbar puncture headaches, may be caused by cerebral vasodilatation and exacerbated by lowered pressure of the cerebrospinal fluid (CSF). Other symptoms include neck stiffness, nausea, vomiting, vertigo, tinnitus, deafness, and cognitive abnormalities. The clinical picture can sometimes mimic frontotemporal dementia, and the behaviour of some patients can sometimes be described as hypoactive-hypoalert, with somnolence, impaired attention, and stereotyped motor activity. Sagging of the brain, caused by leakage of the CSF, can cause lesions in the brainstem with stupor, gaze palsies, and cranial nerve palsies. The condition can be a risk factor for cerebral venous thrombosis because of slowing of the blood flow and distortion of the blood vessels. The clinical picture may well suggest the diagnosis, but the headache may possibly indicate a subarachnoid haemorrhage. However, MRI will help to confirm the diagnosis and to localize the site of the CSF leak. MRI myelograms are of particular value, but if they are equivocal a computed tomography myelogram should be performed. The leakage of CSF is due to a tear in the dura, most frequently where the spinal roots leave the subarachnoid space. If this does not heal with bedrest, an epidural blood patch or a percutaneous injection of fibrin glue may be needed. More information is required on long-term follow-up.
[A study on relationship between distortion product otoacoustic emissions and therapeutic effects in tinnitus]
[Article in Chinese]

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OBJECTIVE: To find mechanism of tinnitus and explore effective treatment for tinnitus. METHOD: The 133 tinnitus patients were assigned into two groups by relationship between Distortion product otoacoustic emissions and frequencies of tinnitus: relationship group (73 cases) and non-relationship group (60 cases). All 133 cases were treated with drug, such as injection of Lipo PGE1, Vitamine B1 and Vitamine B12. After 14 days of treatment the efficacy of the medicines in two groups was observed. RESULT: The effective rate of two groups mentioned above were 75.3% and 36.7% respectively (P < 0.01). Furthermore, effective rate was correlative to the course of the tinnitus. CONCLUSION: Drug therapy can be a choice for patients who have relationship between DPOAEs and frequencies of tinnitus, especially for acute tinnitus. Personalized treatment should be provided.

Is There a Correlation Between Vascular Loops in the Cerebellopontine Angle and Unexplained Unilateral Hearing Loss?
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OBJECTIVE: This study was a retrospective analysis of patients who had received magnetic resonance imaging scans of the internal auditory canal (IAC) to evaluate unexplained asymmetric hearing loss. The study aimed to correlate structural features of vascular loops formed by the anterior inferior cerebellar artery (AICA) within the cerebellopontine angle and IAC with asymmetric hearing loss. STUDY DESIGN: High-resolution thin-section T2 fast spin echo magnetic resonance imaging scans of 58 patients with asymmetric sensorineural hearing loss were obtained; the structure of the AICA was graded on both sides using 2 scoring systems. The grading senior head and neck radiologist was blinded to the clinical history. The first scoring system used was the Chavda classification, which is based on the anatomic location of the AICA loop. This system identified 92 loops within the cerebellopontine angle; 22 loops extending less than halfway into the IAC and 2 loops extending more than halfway into the IAC. A second classification system was used simultaneously to describe the extent of contact between the AICA loop and the vestibulocochlear nerve. The second system identified 24 loops that were not in contact with the nerve, 60 in which the loop was running adjacent to the nerve but not displacing it; 12 loops were identified that were displacing the vestibulocochlear nerve, and 24 loops were identified running between the facial and the vestibulocochlear nerve. Four loops were classified as both displacing the vestibulocochlear nerve and running between the facial and vestibulocochlear nerves. Tinnitus was present in addition to hearing loss. In 48 of the 58 patients, the statistical analysis was repeated for these patients. RESULTS: No statistically significant association was found between loops classified by the Chavda system and hearing loss. No statistically significant association was present between loops that made no contact with the nerve, ran adjacent to the nerve, or displaced the nerve. A statistically significant association was found between loops that ran between the facial and vestibulocochlear nerve and hearing loss, with a p value of 0.0162. The subset who had tinnitus in addition to hearing loss had
similar results, with the only significant association being found between loops running between the facial nerve and the vestibulocochlear nerve, and a p value of 0.0433 was obtained. CONCLUSION: A correlation between vascular loops and hearing loss did not exist in the majority of the patients in this study. The subset of patients that had a vessel between the facial and vestibular cochlear nerves deserve further investigation.

Auditory test result characteristics of subjects with and without tinnitus.

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Tinnitus is the perception of sound that does not have an acoustic source in the environment. Ascertaining the presence of tinnitus in individuals who claim tinnitus for compensation purposes is very difficult and increasingly becoming a problem. This study examined the potential to observe differences in loudness and pitch matches between individuals who experience tinnitus versus those who do not. This study follows a previous pilot study we completed that included 12 subjects with and 12 subjects without tinnitus. The current study included 36 subjects with and 36 without tinnitus. Results of this study revealed no significant differences between groups with regard to decibel sensation level (SL) loudness matches and within-session loudness-match reliability. Between-group differences revealed that the tinnitus subjects had (1) greater decibel sound pressure level loudness matches, (2) better between-session loudness-match reliability, (3) better pitch-match reliability, and (4) higher frequency pitch matches. These findings support the data from our pilot study with the exception that decibel SL loudness matches were greater for the tinnitus subjects in the pilot study. Tinnitus loudness and pitch matching may have some value in an overall battery of tests for evaluating tinnitus claims.

Quantitative analysis of cochlear active mechanisms in tinnitus subjects with normal hearing sensitivity: multiparametric recording of evoked otoacoustic emissions and contralateral suppression.

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OBJECTIVE: Aim of this study was to investigate the possible role played by outer hair cells and cochlear efferent system functionality when tinnitus develops in normal hearing ears. A multiparametric approach was used, entailing recording and analysis of a set of otoacoustic emissions (OAEs): distortion product (DPOAEs), transient evoked (TEOAEs) and efferent-mediated TEOAE suppression in the presence of contralateral acoustic stimulation (CAS). METHODS: Fifty-four subjects with normal hearing sensitivity participated in the study. Twenty-three suffered from chronic subjective tinnitus whereas thirty-one did not have tinnitus and acted as control subjects. DPOAEs were measured with eliciting tones of frequency ratio 1.22 and intensity 65 and 55dB SPL in the frequency range 0.5-8kHz. TEOAEs were recorded with the „linear” protocol using clicks at 60dB peak SPL both in the absence and in the presence of CAS at two different intensities. DPOAE amplitude, TEOAE amplitude, and TEOAE suppression were analysed as relevant parameters. RESULTS: Significantly reduced DPOAE amplitude in the frequency range 1.5-8kHz, lower TEOAE amplitude, and slightly decreased TEOAE suppression were measured in tinnitus subjects compared to non-tinnitus controls. In particular, 74% of tinnitus subjects exhibited abnormal DPOAEs, 13% had abnormal TEOAEs, whereas abnormal TEOAE suppression was found in 9% of patients. CONCLUSION: Overall, the present work revealed the presence of abnormal OAEs, in particular at higher frequencies, in tinnitus subjects with normal hearing sensitivity. A minor (i.e.,
sub-clinical) outer hair cell dysfunction, particularly in high-frequency cochlear regions, might thus be assumed in normal hearing tinnitus subjects. In order to better put in light the possible role played by outer hair cells in low-frequency cochlear regions, or by the cochlear efferent system, additional analyses would be needed.


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The objective of this study was to determine the psychometric properties of a Chinese (Cantonese) version of the Tinnitus Questionnaire (TQ), which is a psychometric self-report measure of perceived tinnitus-related distress. The subjects were 114 adults who attended audiology clinics with a primary or secondary complaint of tinnitus. They completed the Chinese versions of the TQ (TQ-CH), Short-Form 36 Health Survey (SF-36), and Hospital Anxiety and Depression Scale (HADS). The subjective severity of tinnitus and tinnitus-related problems were scored using rating scales. The TQ-CH and its subscales had good internal consistency reliability estimates (alpha=0.75-0.94), which were comparable to those of the original version. Significant correlations were observed between the TQ-CH and psychological distress, tinnitus-related problem ratings, and severity ratings. Factor analysis showed the high construct validity of the TQ-CH subscales. High test-retest reliability (intraclass correlation coefficient=0.96) was observed. The results suggest that the TQ-CH is a reliable and valid measure of general tinnitus-related distress that can be used in clinical settings to quantify the impact of tinnitus on daily living.


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We studied the relationship between tinnitus pitch and the audiogram in 195 patients. Patients with tone-like tinnitus reported a higher pitch (mean = 5385 Hz) compared to those with a noise-like quality (mean = 3266 Hz). Those with a flat audiogram were more likely to report: a noise-like tinnitus, a unilateral tinnitus, and have a pitch < 2000 Hz. The average duration of bilateral tinnitus (12 years) was longer than that of unilateral tinnitus (5 years). Older subjects reported a less severe tinnitus handicap questionnaire score. Patients with a notched audiogram often reported a pitch <or=8000 Hz. Subjects with normal hearing up to 8000 Hz tended to have a pitch >or=8000 Hz. We failed to find a relationship between the pitch and the edge of a high frequency hearing loss. Some individuals did exhibit a pitch at the low frequency edge of a hearing loss, but we could find no similar characteristics among these subjects. It is possible that a relationship between pitch and audiogram is present only in certain subgroups.

The Impact of Type D Personality on Health-Related Quality of Life in Tinnitus Patients Is Mainly Mediated by Anxiety and Depression. Otol Neurotol. 2009 Oct 7. [Epub ahead of print]

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OBJECTIVE: To evaluate the impact of Type D personality on health-related quality of life (HRQoL) and self-reported tinnitus-related distress in chronic tinnitus patients and whether this relationship is mediated by indicators of psychological distress (i.e., vital exhaustion, anxiety, and depression).
MATERIALS AND METHODS: Using a cross-sectional study design, 265 consecutive tinnitus patients were asked to complete the Hospital Anxiety and Depression Scale, the Maastricht Questionnaire, the Type D Scale (DS14), the Short-Form Health Survey 36, and the Tinnitus Reaction Questionnaire.

RESULTS: The prevalence of Type D was 35.5%. Type D patients were significantly more anxious, depressed, and vitally exhausted, and experienced more impaired HRQoL and increased tinnitus-related distress compared with non-Type D patients. Structural equation modeling showed that Type D personality directly increased symptoms of depression and anxiety, but not vital exhaustion. Type D was also a direct predictor of poor mental and physical HRQoL and increased tinnitus-related distress, although this influence was mainly mediated by symptoms of depression and anxiety. Anxiety, depression, and vital exhaustion had a direct influence on HRQoL and self-reported tinnitus-related distress, with a higher impact on mental HRQoL \( R = 0.74 \) compared with physical HRQoL \( R = 0.33 \). Vital exhaustion was a predictor of HRQoL and self-reported tinnitus-related distress; however, its influence was moderated by enhanced levels of anxiety and depression. CONCLUSION: Tinnitus patients with a Type D personality were more likely to be anxious and depressed and to experience poor HRQoL and increased self-reported tinnitus-related distress, with the impact of Type D mainly being mediated by symptoms of anxiety and depression, although Type D also exerted a direct influence on these outcomes. These findings underline that to reduce the impact of tinnitus on HRQoL and self-reported tinnitus-related distress, treatment should be directed toward reducing anxiety and depression, especially in patients with a Type D personality.

[Evaluation of superior semicircular canal dehiscence in patients with vertigo and tinnitus.]
[Article in Turkish]

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OBJECTIVES: The aim of the study was to investigate the presence of superior semicircular canal dehiscence (SSC) in patients with unknown etiology of vertigo/tinnitus. PATIENTS AND METHODS: This study was performed prospectively between December 2007 and March 2008. Fifty five patients (23 males, 32 females; mean age 44.5; range 36 to 74 year) with complaints of vertigo and/or tinnitus, of which we couldn’t establish the etiologies, were included in the study. Control group was consisted of 15 patients who didn’t have complaints of vertigo and/or tinnitus. A high resolution temporal bone computed tomography (CT) scan (1 mm slice thickness) was performed in all study groups (patients and controls). RESULTS: Thirty nine subjects (72%) had normal odiometric findings. Mild conductive hearing loss was present in 12 (22%) subjects. Two (3%) of the patients had moderate conductive hearing loss and the other two subjects (3%) had mixed type hearing loss. High resolution temporal bone CT scan revealed that 35 (65%) subjects had dehiscence around SSC otic capsule whereas 20 (35%) remaining patients yielded no dehiscence. Twenty one of 35 patients (60%) with dehiscence at SSC had minimum defect and 14 patients (40%) had significant defect. Bilateral defect was present in nine (64%) of 14 patients with significant defect but none of the subjects with minimum defect showed bilateral involvement. None of the control subjects exhibited SSC dehiscence with CT imaging. CONCLUSION: Semicircular canal dehiscence was found in 65% of the patients with unknown etiology of the vertigo and tinnitus. Physicians should evaluate the SSC dehiscence in patients with vertigo and tinnitus as an etiologic factor.
Head rotation evoked tinnitus due to superior semicircular canal dehiscence.
J Laryngol Otol. 2009 Sep 29:1-3. [Epub ahead of print]

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Introduction: Superior semicircular canal dehiscence affects the auditory and vestibular systems due to a partial defect in the canal's bony wall. In most cases, sound- and pressure-induced vertigo are present, and are sometimes accompanied by pulse-synchronous tinnitus. Case presentation: We describe a 50-year-old man with superior semicircular canal dehiscence whose only complaints were head rotation induced tinnitus and autophony. Head rotation in the plane of the right semicircular canal with an angular velocity exceeding 600 degrees/second repeatedly induced a 'cricket' sound in the patient's right ear. High resolution temporal bone computed tomography changes, and an elevated umbo velocity, supported the diagnosis of superior semicircular canal dehiscence. Conclusion: In addition to pulse-synchronous or continuous tinnitus, head rotation induced tinnitus can be the only presenting symptom of superior semicircular canal dehiscence without vestibular complaints. We suggest that, in our patient, the bony defect of the superior semicircular canal ('third window') might have enhanced the flow of inner ear fluid, possibly producing tinnitus.

Paroxysmal staccato tinnitus: a carbamazepine responsive hyperactivity dysfunction symptom of the eighth cranial nerve.
J Neurol Neurosurg Psychiatry. 2009 Sep 23. [Epub ahead of print]

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Hyperactive disorders related to neurovascular compression have been described for several cranial nerves of which trigeminal neuralgia and hemifacial spasm are the best known. The present report on four patients, in conjunction with previous reports, suggests that paroxysmal staccato tinnitus might be considered an auditory hyperactivity disorder for N. VIII. The present patients reported attacks, usually lasting 10-20 seconds, of loud monaural tinnitus with a staccato character (for example clattering or sounding like a machine-gun). The attacks occurred very frequently, sometimes every minute. The attacks were spontaneous, however, they were also provoked by certain head positions or by exposure to loud sounds. Most of the patients did not reveal any significant N. VIII sensory loss, and thus it is probably not advisable to rely on any specific test result for this diagnosis. Instead, it is suggested that a diagnosis of paroxysmal staccato tinnitus can be based on the history, since the symptoms are both stereotype and very specific. Further, low doses of carbamazepine, although not effective for the general population of tinnitus patients, relieved the symptoms.

A Compartment-Based Approach for the Imaging Evaluation of Tinnitus.
AJNR Am J Neuroradiol. 2009 Sep 17. [Epub ahead of print]

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SUMMARY: Tinnitus affects 10% of the US general population and is a common indication for imaging studies. We describe a sequential compartment-based diagnostic approach, which simplifies the interpretation of imaging studies in patients with tinnitus. The choice of the initial imaging technique depends on the type of tinnitus, associated symptoms, and examination findings. Familiarity with the pathophysiologic mechanisms of tinnitus and the imaging findings is a prerequisite for a tailored diagnostic approach by the radiologist.
[Aberrant internal carotid artery as a cause of pulsatile tinnitus: A difficult diagnosis in MRI?]
[Article in German]
HNO. 2009 Aug 22. [Epub ahead of print]

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We present the case of a 43-year-old patient with sensorineural hearing loss and the finding of an aberrant internal carotid artery in the left tympanic cavity that was causing pulsatile tinnitus. The aberrant vessel was initially invisible on magnetic resonance imaging (MRI) and was confirmed by high-resolution computed tomography and MR angiography (MRA). Recognition of an aberrant course of an internal carotid artery often requires a combination of MRI and MRA to establish the diagnosis and rule out other differential diagnoses.

[Distortion product otoacoustic emission levels and input/output-growth functions in normal-hearing individuals with tinnitus and/or hyperacusis]
[Article in Polish]


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The purpose of this study was to determine whether distortion product otoacoustic emissions (DPOAEs) can be used to distinguish among four groups with audiometrically normal-hearing sensitivity: (1) control adults without tinnitus or hyperacusis, (2) patients with tinnitus alone, (3) patients with hyperacusis alone, and (4) patients with both tinnitus and hyperacusis. Two types of DPOAE measures were evaluated: (1) the distortion product (DP-)gram measured with fixed primary levels as a function of frequency, and (2) DPOAE input/output (I/O) functions for a range of primary levels between 45 and 70 dB sound pressure level (SPL) at 1000, 2000, and 4000 Hz. DP-grams did not clearly distinguish between the control and patient groups. There was, however, a consistent trend for the three patient groups to have decreased average DP levels at 4000 and 6000 Hz; this notch in the DP-gram was not observed in the response configuration for the control group. In the three patient groups, 51 to 74% of these individuals had DP levels that were outside of the 95% confidence range for the control group. The average slopes of the I/O growth functions for each of the patient groups were consistently steeper than those for the control group; however, the slope values were indistinguishable among the patient groups. About 60% of the patients' DPOAE responses (in each group) were categorized as abnormal based on their slope values. Thus, DPOAE measures can be used with at least partial success to distinguish controls from patients with tinnitus, hyperacusis, or both tinnitus and hyperacusis, but not to discriminate among the respective patient groups. These findings suggest that the pathology represented among the patient groups is consistent at the level of the cochlea; however, diagnostic tests targeted at higher centers of processing are needed if the individuals in these groups are to be distinguished among themselves.

In all participants, DPOAEs with fixed primary levels as a function of frequency were measured. There was a consistent trend for the three patient groups to have decreased average DP-gram levels at 4000 and 6000 Hz; this notch in the DP-gram was not observed in the response configuration for the control group. In the three patient groups, 51 to 74% of these individuals had DP levels that were outside of the 95% confidence range for the control group. Thus, DPOAE measures can be used with at least partial success to distinguish controls from patients with tinnitus, hyperacusis, or both tinnitus and hyperacusis, but not to discriminate among the respective patient groups. These findings suggest that the pathology represented among the patient groups is consistent at the level of the cochlea; however, diagnostic tests targeted at higher centers of processing are needed if the individuals in these groups are to be distinguished among themselves.
Psychometric properties of the Chinese (Cantonese) Tinnitus Handicap Inventory.

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OBJECTIVES: To establish the reliability and validity of the Chinese (Cantonese) version of the Tinnitus Handicap Inventory to measure the self-perceived handicapping effect and severity of the condition in patients with chronic tinnitus. DESIGN: Cross-sectional psychometric validation study. SETTING: Audiology clinics in a hospital setting. PARTICIPANTS: Subjects were 114 adult Chinese who attended the audiology clinics with a complaint of tinnitus. MAIN OUTCOME MEASURES: Test-retest and internal consistency reliability; construct validity. RESULTS: The Chinese version of the Tinnitus Handicap Inventory and its subscales showed good internal consistency reliabilities (alpha = 0.72-0.94) that are comparable to those of the original version. High correlations were observed between the Tinnitus Handicap Inventory and psychological distress, tinnitus-related problem ratings and severity ratings. Factor analysis showed that the Chinese version of the Tinnitus Handicap Inventory has a unifactorial structure. A high degree of test-retest reliability was observed (intraclass correlation coefficient = 0.88). CONCLUSIONS: The results suggest that the Chinese (Cantonese) version of the Tinnitus Handicap Inventory is a reliable and valid measure of general tinnitus-related distress that can be used in clinical settings to quantify the impact of tinnitus on daily life.

Idiopathic sensorineural hearing disorders in adults--a pragmatic approach.

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Acute or progressive sensorineural hearing loss, with or without vertigo and tinnitus, has a considerable impact upon an individual's quality of life. Sensorineural hearing disorders are more commonly observed in patients with rheumatic disease than in the general population, are more likely to be accompanied by the presence of serum autoantibodies, and might respond to steroid therapy. A subgroup of these disorders seem to be immune mediated, but audiologic presentation and serologic testing do not enable this subgroup to be further defined. Rheumatologists should be prepared to manage patients with known rheumatic disease who develop acute hearing loss and to evaluate referred patients without known rheumatic illness experiencing progressive or refractory sensorineural hearing loss. In this article, we summarize the literature and outline a rational approach for the evaluation and treatment of such patients.

Tinnitus and normal hearing: a study on the transient otoacoustic emissions suppression.
[Brazilian J Otorhinolaryngol. 2009 May-Jun;75(3):414-9.]

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The workings of the auditory pathway of patients with tinnitus and normal hearing can be associated with an auditory efferent pathway dysfunction at the level of the superior olivary complex. Otoacoustic emission suppression with contralateral noise can represent an alternative to its evaluation. AIM: to investigate Transient Otoacoustic Emission suppression in normal hearing adults with and without tinnitus and to compare the two groups. STUDY DESIGN: cross-sectional contemporary cohort.
MATERIALS AND METHODS: we assessed 40 female individuals between 18 and 59 years of age, 20 without tinnitus and 20 with it. We studied the TOAE suppression with a contralateral white noise at 50 dBSPL.

RESULTS: TOAE amplitude was lower in the group with tinnitus. There was no difference between the groups with and without tinnitus in terms of TOAE suppression, except in the frequency of 1000 Hz in the left ear in the tinnitus group. CONCLUSION: the afferent system assessment may contribute to the topographic diagnosis of tinnitus; however, we still need further studies to establish the proper methodology and normative values to carry out these tests.

Measuring tinnitus loudness using constrained psychophysical scaling.

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PURPOSE: We measured tinnitus loudness using a new method of psychophysical scaling with the aim of introducing a potentially useful new procedure to the literature. METHOD: Fourteen adults reporting tinnitus were trained to use a standardized loudness scale, and then they used that response scale to assess loudness of nonstandard stimuli and of their tinnitus. We also measured tinnitus loudness and pitch using a computer-based matching procedure, and we measured the impact of tinnitus on daily living using the Tinnitus Handicap Inventory (THI; C. W. Newman, G. P. Jacobson, & J. B. Spitzer, 1996) for those 14 individuals and an additional 2 participants. Results and Conclusions Our 14 trained participants judged loudness similarly to normal hearing participants for pure tones at normal hearing, nontinnitus frequencies-implying that their judgments of tinnitus loudness were valid. Constrained scaling of tinnitus loudness yielded measurements that were substantially greater than the sensation level of sounds matched to tinnitus loudness. Our total of 16 participants fell into 2 groups on the basis of hearing loss, extent of abnormal loudness growth at the tinnitus frequency, and several aspects of tinnitus experience. Finally, as previously found, there was little correlation between tinnitus loudness, no matter how measured, and the impact of tinnitus on daily life as measured by the THI.

Evaluation of tinnitus patients with normal hearing sensitivity using TEOAEs and TEN test

Elsaeid Mohamed Thabet

Objectives: This study was designed to investigate the possibility of underlying cochlear damage whether outer hair cells (OHCs) or inner hair cells (IHCs) in tinnitus suffering patients with normal hearing sensitivity, using transient evoked otoacoustic emission (TEOAEs) and threshold equalizing noise (TEN) test, if any. Methods: Twenty patients suffering from unilateral tinnitus with normal hearing sensitivity participated in this study. Their other ear acted as control ears. They were subjected to full history taking, otoscopy, basic audiologic evaluation, TEOAEs and TEN test. Results: TEOAEs were abnormal in 85% of the tinnitus ears compared to 20% in control ears; this difference was statistically significant. The abnormal TEOAEs frequency bands in the tinnitus ears were statistically significant above 2000Hz when compared to the control ears and were more common for the 4000 and 5000Hz. This suggests that OHCs dysfunction may be important in the generation of tinnitus. TEN test demonstrated dead regions in the cochlea in 15% of the tinnitus ears only. This might be attributed to increased resistance of IHCs to damage compared to OHCs vulnerability. The affected frequency location was at 500Hz in 5%, 3000 and 4000Hz in 10% of tinnitus ears. Conclusion: This work has shown a higher prevalence of OAE abnormalities in tinnitus patients with normal hearing in contrast to TEN test denoting the more vulnerability of OHCs to damage.
**IV Imaging**

**Mapping cortical hubs in tinnitus.**

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**ABSTRACT:** BACKGROUND: Subjective tinnitus is the perception of a sound in the absence of any physical source. It has been shown that tinnitus is associated with hyperactivity of the auditory cortices. Accompanying this hyperactivity, changes in non-auditory brain structures have also been reported. However, there have been no studies on the long-range information flow between these regions.

RESULTS: Using Magnetoencephalography, we investigated the long-range cortical networks of chronic tinnitus sufferers (n = 23) and healthy controls (n = 24) in the resting state. A beamforming technique was applied to reconstruct the brain activity at source level and the directed functional coupling between all voxels was analyzed by means of Partial Directed Coherence. Within a cortical network, hubs are brain structures that either influence a great number of other brain regions or that are influenced by a great number of other brain regions. By mapping the cortical hubs in tinnitus and controls we report fundamental group differences in the global networks, mainly in the gamma frequency range. The prefrontal cortex, the orbitofrontal cortex and the parieto-occipital region were core structures in this network. The information flow from the global network to the temporal cortex correlated positively with the strength of tinnitus distress.

CONCLUSION: With the present study we suggest that the hyperactivity of the temporal cortices in tinnitus is integrated in a global network of long-range cortical connectivity. Top-down influence from the global network on the temporal areas relates to the subjective strength of the tinnitus distress.

**Tinnitus intensity dependent gamma oscillations of the contralateral auditory cortex.**

van der Loo E, Gais S, Congedo M, Vanneste S, Plazier M, Menovsky T, Van de Heyning P, De Ridder D.

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**BACKGROUND:** Non-pulsatile tinnitus is considered a subjective auditory phantom phenomenon present in 10 to 15% of the population. Tinnitus as a phantom phenomenon is related to hyperactivity and reorganization of the auditory cortex. Magnetoencephalography studies demonstrate a correlation between gamma band activity in the contralateral auditory cortex and the presence of tinnitus. The present study aims to investigate the relation between objective gamma-band activity in the contralateral auditory cortex and subjective tinnitus loudness scores.

**METHODS AND FINDINGS:** In unilateral tinnitus patients (N = 15; 10 right, 5 left) source analysis of resting state electroencephalographic gamma band oscillations shows a strong positive correlation with Visual Analogue Scale loudness scores in the contralateral auditory cortex (max r = 0.73, p<0.05). **CONCLUSION:** Auditory phantom percepts thus show similar sound level dependent activation of the contralateral auditory cortex as observed in normal audition. In view of recent consciousness models and tinnitus network models these results suggest tinnitus loudness is coded by gamma band activity in the contralateral auditory cortex but might not, by itself, be responsible for tinnitus perception.
Cortical Activation during a Pitch Discrimination Task in Tinnitus Patients and Controls - An fMRI Study.

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Chronic subjective tinnitus has been associated with aberrant activation of cortical areas involved in the perception of auditory information. This leads to the hypothesis that neural correlates of altered auditory perception may be found in tinnitus patients using functional magnetic resonance imaging. To study brain activation patterns due to acoustic stimulation in a pitch discrimination task, 6 tinnitus patients and 6 age-matched controls were investigated. Tones were presented binaurally at 5 beeps/s with three different frequencies in a block design. Using Statistical Parametrical Mapping, we found activation of secondary auditory areas in both groups. Furthermore, controls showed activation of the right-hemispheric anterior insula, whereas the middle frontal gyrus, putamen and left-hemispheric insula were activated in tinnitus patients. In the between-group analysis, activation of the caudate nucleus, superior frontal gyrus (Brodmann area 8) and cingular cortex was more pronounced in patients than in controls suggesting the perception of auditory inputs in a more emotional context in our patient group compared to controls. Copyright © 2009 S. Karger AG, Basel.

The auditory midbrain of people with tinnitus: abnormal sound-evoked activity revisited.

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Sound-evoked fMRI activation of the inferior colliculi (IC) was compared between tinnitus and non-tinnitus subjects matched in threshold (normal), age, depression, and anxiety. Subjects were stimulated with broadband sound in an „on/off“ fMRI paradigm with and without on-going sound from the scanner coolant pump. (1) With pump sounds off, the tinnitus group showed greater stimulus-evoked activation of the IC than the non-tinnitus group, suggesting abnormal gain within the auditory pathway of tinnitus subjects. (2) Having pump sounds on reduced activation in the tinnitus, but not the non-tinnitus group. This result suggests response saturation in tinnitus subjects, possibly occurring because abnormal gain increased response amplitude to an upper limit. (3) In contrast to Melcher et al. (2000), the ratio of activation between right and left IC did not differ significantly between tinnitus and non-tinnitus subjects or in a manner dependent on tinnitus laterality. However, new data from subjects imaged previously by Melcher et al. suggest a possible tinnitus subgroup with abnormally asymmetric function of the IC. The present and previous data together suggest elevated responses to sound in the IC are common among those with tinnitus and normal thresholds, while abnormally asymmetric activation is not, even among those with lateralized tinnitus.

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OBJECTIVES/HYPOTHESIS: Lidocaine is a local anesthetic that is known to suppress tinnitus via systemic or local application; however, this effect has only limited duration. The current study aimed to establish a method for the sustained delivery of lidocaine into the cochlea using poly lactic/glycolic acid (PLGA) microparticles. STUDY DESIGN: Experimental study. METHODS: Lidocaine-loaded PLGA microparticles were produced and their in vitro-release profiles were examined. The lidocaine concentrations in the perilymph were measured at different time points following the application of the lidocaine-loaded PLGA microparticles to the round-window membranes of guinea pigs. The possible adverse effects of the local application of lidocaine-loaded PLGA microparticles were also examined. RESULTS: The in vitro analyses revealed that the microparticles were capable of the sustained delivery of lidocaine. The in vivo experiments demonstrated the sustained delivery of lidocaine into the cochlear fluid, and the maintenance of high lidocaine concentrations in the perilymph for up to 3 days after application. Nystagmus and inflammation in the middle ear mucosa were not detected after the local application of lidocaine-loaded PLGA microparticles, although temporary hearing loss was observed. CONCLUSIONS: Lidocaine-loaded PLGA microparticles were shown to be capable of the sustained delivery of lidocaine into the cochlea, suggesting that they could be used for the attenuation of peripheral tinnitus. Laryngoscope, 2010.

Pharmacological approaches to the treatment of tinnitus.
Drug Discov Today. 2009 Nov 18. [Epub ahead of print]

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Tinnitus is the conscious perception of a phantom sound in the absence of an external source. For 1 in 100 of the general population, the condition severely affects quality of life. In spite of the fact that the market for a drug indicated for tinnitus relief is huge, there are still no FDA-approved drugs, and the quest for a tinnitus-targeted compound faces significant challenges. A wide variety of drugs have been used off-label to treat tinnitus sufferers, with limited but significant effects in subsets of patients. If the compounds being developed at present by the pharmaceutical industry finally reach the market, they will establish a turning point in the treatment of this pathology.

Transtympanic Steroids for Ménière's Disease.
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Herraiz C, Plaza G, Aparicio JM, Gallego I, Marcos S, Ruiz C.

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OBJECTIVE: To describe the long-term efficacy of transtympanic steroids (TTS) using methylprednisolone in the treatment of Ménière’s disease (MD). DESIGN: Descriptive prospective study.
MAIN OUTCOME MEASURES: Pure-tone average (PTA) corresponding to the conversational frequencies on the audiogram (0.5, 1, 2, and 3 kHz), visual analog scale on tinnitus annoyance, and number of vertigo spells 24 months after treatment. RESULTS: Thirty-four MD patients referred to a tertiary center were treated with TTS. All patients were diagnosed as probable or definitive MD (following American Academy of Otolaryngology-Head and Neck Surgery 1995 criteria) and treated by TTS (3 consecutive doses). Data from 32 patients were achieved after 12 months. Forty-eight percent of the patients reduced the PTA in 10 or more decibels, average improvement was 8.6 dB compared with initial PTA (p = 0.004). Tinnitus relief was achieved by 81.5% of the patients. Number of vertigo spells was reduced from 4.3 to 0.3 after 12 months (p = 0.002); 81% of the patients were free of vertigo spells, and 92.6% had 1 or less spells of vertigo. Data from 29 patients were achieved after 24 months. A reduction of PTA in 10 or more decibels was shown by the 33.3% of the sample, and PTA improved in 3.3 dB compared with initial PTA (nonsignificant). Tinnitus relief was achieved in 78% of the patients. Number of vertigo spells was reduced from 4.3 to 0.5 (p = 0.033). Seventy-eight percent of the cases were free of vertigo, and 96% had none or 1 spell. Because of an increase in any of the symptoms, 12 patients (35.2%) required retreatment with 1 or 2 series of TTS (1-3 doses) along the 2-year period. Two patients of the sample (6.25%) required transtympanic gentamicin for vertigo control due to lack of benefit with TTS (14 and 18 mo since TTS). CONCLUSION: Transtympanic steroids in this cohort were associated with good preservation of hearing. Tinnitus control is achieved in more than 70% of the patients, and number of vertigo spells can be dramatically reduced in more than 90% of the patients after a 24-month follow-up.

[A study on relationship between distortion product otoacoustic emissions and therapeutic effects in tinnitus]
[Article in Chinese]
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OBJECTIVE: To find mechanism of tinnitus and explore effective treatment for tinnitus. METHOD: The 133 tinnitus patients were assigned into two groups by relationship between Distortion product otoacoustic emissions and frequencies of tinnitus: relationship group (73 cases) and non-relationship group (60 cases). All 133 cases were treated with drug, such as injection of Lipo PGE1, Vitamine B1 and Vitamine B12. After 14 days of treatment the efficacy of the medicines in two groups was observed.
RESULT: The effective rate of two groups mentioned above were 75.3% and 36.7% respectively (P < 0.01). Furthermore, effective rate was correlative to the course of the tinnitus. CONCLUSION: Drug therapy can be a choice for patients who have relationship between DPOAEs and frequencies of tinnitus, especially for acute tinnitus. Personalized treatment should be provided.

The effects of alprazolam on tinnitus: a cross-over randomized clinical trial.
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BACKGROUND: Tinnitus remains a phenomenon with an unknown pathophysiology and for which few therapeutic measures are available. To date there has been insufficient evidence to support the use of alprazolam in the treatment of tinnitus. We sought to evaluate the efficacy of alprazolam for relief of tinnitus. MATERIAL/METHODS: Thirty-six tinnitus sufferers participated in this cross-over, randomized, triple-blind, placebo-controlled trial. Inclusion criteria included patients between ages 21 and 65, with a complaint of non-pulsatile tinnitus of more than 1 year duration. Patients with depressive or anxiety
disorders were excluded, as were those using hearing aids. Participants received alprazolam 1.5 mg daily versus placebo in each period. Primary outcome variables included the Tinnitus Handicap Inventory (THI), a Visual Analog Scale (VAS), and tinnitus loudness. RESULTS: Thirty patients completed the study. The average age of patients was 47.58 +/- 7.65 years. Alprazolam in comparison with placebo did not result in statistically significantly greater relief in THI score and tinnitus loudness. There was a significant improvement in VAS score in the alprazolam group compared with the placebo group (p<0.001). CONCLUSIONS: These results suggest that although alprazolam did not improve the THI score or sensation level of loudness significantly, it has a desirable effect on VAS. Further work is needed to determine the beneficial effects of alprazolam in distressed or depressed patients.

Effects of Selective Serotonin Reuptake Inhibitor on Treating Tinnitus in Patients Stratified for Presence of Depression or Anxiety.
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We evaluated the effects of a selective serotonin reuptake inhibitor, paroxetine, on treating tinnitus. Tinnitus patients stratified for the presence of depression and anxiety were studied retrospectively. Fifty-six patients were observed for more than 6 months. They were initially treated with paroxetine only at a dose of 10 mg/day for 2-4 weeks; thereafter, the dose was increased to 20 mg/day. Tinnitus distress was evaluated with the Tinnitus Handicap Inventory (THI) and with visual analog scales (VASs) for tinnitus loudness and annoyance. Depression and anxiety were measured with the Self-Rating Depression Scale (SDS) and the trait section of the State-Trait Anxiety Inventory (STAI). The patients were grouped according to their SDS and STAI scores, and each variable was compared at baseline and the 6-month follow-up. Changes among these variables were also examined to determine whether reduced tinnitus distress was related to the improvement of depression or anxiety. Patients with both depression and anxiety showed better results (decrease in THI, VASs, SDS and STAI scores) than patients with anxiety alone, or patients without depression and anxiety. In patients with depression and anxiety, changes in tinnitus variables and changes in depression and anxiety scores were strongly correlated. In other patients, however, changes in tinnitus variables and changes in depression and anxiety scores were not correlated. These results suggest that paroxetine is effective in treating distressed tinnitus patients with depression and anxiety by reducing their tinnitus severity as well as their depression and anxiety. Copyright © 2009 S. Karger AG, Basel.

Effects of extracochlear gacyclidine perfusion on tinnitus in humans: a case series.
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Gacyclidine, a non-competitive NMDA receptor antagonist, is a phencyclidine derivative with neuroprotective properties. It has been previously safely administered intravenously to acute traumatic brain-injured patients. Experiments in guinea pigs have shown that local administration of gacyclidine to the cochlea can suppress salicylate-induced tinnitus. Thus, we thought that patients with therapy-resistant sensorineural tinnitus might benefit from a local therapy with gacyclidine. As a compassionate treatment, we administered aqueous gacyclidine solution via a Durect RWmuCath(TM) into the round window niche in six patients with unilateral deafness associated with tinnitus. The response of each patient to the drug treatment was given a numerical value by the use of a visual analogue scale (VAS) on a scale of 0-10 for tinnitus intensity, where 0 represented no tinnitus and 10 represented unbearable tinnitus-intensity or -annoyance (subjective).
After constant perfusion of gacyclidine for 40-63 h, four out of six patients experienced a temporary relief from their tinnitus. No serious side effects were recorded in any of the cases. Gacyclidine might present a potent drug for the suppression of sensorineural tinnitus in humans and therefore should be considered for future double-blinded, placebo-controlled clinical trials. For lasting effective treatment, controlled intracochlear and long-term delivery of the drug seems to be necessary. Further studies investigating the toxicological effects of gacyclidine intracochlear perfusion as well as different dosages and therapy durations are under way to ensure the safety of the drug for long-term human use and warrant clinical trials.

Emerging pharmacotherapy of tinnitus.

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Tinnitus, the perception of sound in the absence of an auditory stimulus, is perceived by about 1 in 10 adults, and for at least 1 in 100, tinnitus severely affects their quality of life. Because tinnitus is frequently associated with irritability, agitation, stress, insomnia, anxiety and depression, the social and economic burdens of tinnitus can be enormous. No curative treatments are available. However, tinnitus symptoms can be alleviated to some extent. The most widespread management therapies consist of auditory stimulation and cognitive behavioral treatment, aiming at improving habituation and coping strategies. Available clinical trials vary in methodological rigor and have been performed for a considerable number of different drugs. None of the investigated drugs have demonstrated providing replicable long-term reduction of tinnitus impact in the majority of patients in excess of placebo effects. Accordingly, there are no FDA or European Medicines Agency approved drugs for the treatment of tinnitus. However, in spite of the lack of evidence, a large variety of different compounds are prescribed off-label. Therefore, more effective pharmacotherapies for this huge and still growing market are desperately needed and even a drug that produces only a small but significant effect would have an enormous therapeutic impact. This review describes current and emerging pharmacotherapies with current difficulties and limitations. In addition, it provides an estimate of the tinnitus market. Finally, it describes recent advances in the tinnitus field which may help overcome obstacles faced in the pharmacological treatment of tinnitus. These include incomplete knowledge of tinnitus pathophysiology, lack of well-established animal models, heterogeneity of different forms of tinnitus, difficulties in tinnitus assessment and outcome measurement and variability in clinical trial methodology.

Protective effect of ursolic acid from Cornus officinalis on the hydrogen peroxide-induced damage of HEI-OC1 auditory cells.

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The fruits of Cornus officinalis have been used in traditional oriental medicine for treatment of inner ear diseases, such as tinnitus and hearing loss. In the present study, we investigated the protective effect of C. officinalis on hydrogen peroxide-induced cytotoxicity in HEI-OC1 auditory cells. The results from bioassay-guided fractionation of methanol extract of C. officinalis fruits showed that ursolic acid is a major active component. Ursolic acid (0.05-2 microg/ml) had protective effect against the HEI-OC1 cell damage and reduced lipid peroxidation in a dose-dependent manner. In addition, pre-treatment with ursolic acid significantly attenuated the decrease of activities of catalase (CAT) and glutathione peroxidase (GPX), but superoxide dismutase (SOD) activity was not significantly affected by ursolic acid. These results indicate that ursolic acid protects hydrogen peroxide-induced HEI-OC1 cell damage through inhibition of lipid peroxidation and induction of antioxidant enzymes, CAT and GPX, and may be one of the active components responsible for these effects of C. officinalis fruits.
Intratympanic methylprednisolone injections for subjective tinnitus.

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OBJECTIVES: This study aimed to determine whether intratympanically injected methylprednisolone is effective in treating subjective tinnitus refractory to medical treatment. STUDY DESIGN: Prospective, randomised, placebo-controlled, single-blinded study. METHODS: Seventy adult patients with subjective tinnitus of cochlear origin were randomly assigned to receive intratympanic injection of either methylprednisolone or saline solution. The treatment protocol comprised three intratympanic injections, one per week for three weeks. Improvement in tinnitus severity was measured by a self-rated tinnitus loudness scale and by the tinnitus severity index, at baseline and two weeks after the last injection. RESULTS: Data for 59 patients were available for analysis. There was no significant difference between the two treatment groups regarding age, sex, pure tone average, pretreatment tinnitus intensity, tinnitus laterality or tinnitus duration. There was a significant post-treatment improvement in self-rated tinnitus loudness scale results in both groups. No significant post-treatment changes in the tinnitus severity index individual and total scores were observed in either group. The most frequently encountered side effects were pain during injection, vertigo, a burning sensation around the ear and in the throat, and a bitter taste. A burning sensation and bitter taste were observed more often in the methylprednisolone group compared with the placebo group. CONCLUSION: The results of this study indicate that intratympanic methylprednisolone has no benefit, compared with placebo, for the treatment of subjective tinnitus of cochlear origin refractory to medical treatment.

Persistent tinnitus induced by tricyclic antidepressants.

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Recently a case of unilateral tinnitus after a short course of low-dose amitriptyline has been described. Here we report on a similar case of a patient who developed persisting tinnitus after a short course of low-dose trimipramine. Review of the literature and of a large database of side-effects revealed that the occurrence of persistent tinnitus after a short course of anti-depressant therapy seems to be rare. The mechanisms by which tricyclic antidepressants may induce tinnitus are still incompletely understood, but both central and peripheral effects may be involved.

Vasodilators and vasoactive substances for idiopathic sudden sensorineural hearing loss
Cochrane Database of Systematic Reviews, Issue 4, 2009

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Idiopathic sudden sensorineural hearing loss (ISSHL) is sudden hearing loss where clinical assessment fails to reveal a cause. Hearing loss may vary from partial to total loss, and is usually accompanied by tinnitus. It has been frequently considered that ISSHL may have a vascular origin (i.e. is related to the blood circulatory system) and vasodilators and rheological substances are widely used as treatments. Vasodilators are drugs which widen blood vessels and thus improve blood flow. Vasoactive/rheological substances increase flow through blood vessels in other ways (such as by altering the viscosity of fluid). We found three trials, involving 189 participants, which showed improvement in hearing thresholds in those treated with vasodilators compared to control groups. However, as the number of patients included
in the studies was small, and there were differences in the type, dosage and duration of vasodilator treatment used in each of these studies, the results could not be combined to reach a conclusion. The effectiveness of vasodilators in the treatment of ISSHL could not be proven. Further research is needed.

**Antioxidant micronutrient impact on hearing disorders: concept, rationale, and evidence**


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Purpose: Although auditory disorders are complex conditions, device-related modalities dominate current treatment. However, dysfunction from the central cortex to the inner ear apparatus is increasingly thought to be related to biochemical pathway abnormalities and to free radical-induced oxidative damage and chronic inflammation. Therefore, considering appropriate biologic therapy as an adjunct to standard care against these damaging factors may provide rational expansion of treatment options for otolaryngologists and audiologists. Methods: This review outlines the biologic concepts related to some auditory and vestibular conditions and details the current rationale for utilizing antioxidants for a spectrum of hearing disorders. The strategy is based on the authors’ collective experience in antioxidant science and supported with published research, pilot animal data and preliminary clinical observations. Results: A comprehensive micronutrient approach was developed to exploit these pathways, and demonstrated safety and efficacy against oxidative damage and inflammation and clinically relevant neuroprotection. Cooperative research with Department of Defense institutions used prospective, randomized designs to show (1) reduction in oxidative damage measured in plasma and urine over six months, (2) protection against oxidative damage during 12 weeks of intense military training, (3) protection against inflammation after total body blast exposure (rodents), (4) strong neuroprotection against chemically-induced Parkinson’s disease (rodents), (5) nerve VIII function improvement after concussive head injury in military personnel, and (6) tinnitus improvement in majority of patients after 90-day evaluation. Conclusion: This systematic review of biologic strategies against hearing disorders combined with new animal and human observations may provide a rational basis for expanding current practice paradigms. © 2009 Elsevier Inc. All rights reserved.

**Simvastatin and Ginkgo biloba in the treatment of subacute tinnitus: a retrospective study of 94 patients**


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Objectives: Studies suggest that hypercholesterolemia promotes the development of inner ear disorders such as tinnitus. However, the underlying pathomechanisms are still not clearly defined. Methods: A retrospective study was performed to assess whether a reduction of serum cholesterol by 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors may result in a relief of subacute tinnitus. Remission rates of 58 patients were investigated after 4 months of treatment with simvastatin (40 mg). Results were compared to treatment with Ginkgo biloba (120 mg; n = 36) as control group. Differences between tinnitus score at the day of first treatment and after 4 months were used as main outcome measure. Results: After treatment with simvastatin or G biloba, tinnitus score decreased from 41.3 ± 10.4 to 37.4 ± 17.3 and from 44.7 ± 11.2 to 41.2 ± 8.7, respectively. However, independently of the treatment regimen, differences of tinnitus scores were considered not significant. Conclusions: After administration of simvastatin over 4 months, this retrospective study has shown no significant efficacy in treatment of subacute tinnitus. For a more conclusive answer, further prospective, double-blind, and placebo-controlled studies with a larger number of patients are needed. © 2009 Elsevier Inc. All rights reserved.
VI Auditive Stimulation

Changes in the tinnitus handicap questionnaire after cochlear implantation.  

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PURPOSE: To determine (a) changes in the Tinnitus Handicap Questionnaire (THQ) for patients using  
cochlear implants, (b) differences between patients who receive total or partial relief, and (c) identifiable  
characteristics of those who report tinnitus after implantation. METHOD: Pre- and postoperatively,  
244 adults were administered the THQ when they reported tinnitus. RESULTS: Of the 153 patients  
who had tinnitus preoperatively, 94 (61%) patients reported total suppression and 59 (39%) reported  
a partial reduction. In 91 patients who did not have tinnitus before implantation, 11 (12%) reported  
tinnitus postimplantation. The THQ score decreased from 41% preimplant to 30% postimplant. The  
largest reductions involved social handicap and hearing. Patients with a more severe hearing loss  
might be more likely to experience an exacerbation of their tinnitus. We were not able to clearly identify  
differences between patients who received total or partial relief and the characteristics of patients who  
reported tinnitus after implantation. Those who acquired tinnitus had the shortest duration hearing loss  
(5.6 years) and were the oldest (63 years). The average THQ score of patients getting tinnitus was 29%.  
CONCLUSIONS: Most tinnitus patients benefit from receiving a cochlear implant.

Phase-shift treatment for tinnitus of cochlear origin.  
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Phase-shift treatment is a new tinnitus therapy that aims at sound cancelling. This technique is based  
on a theory advocating that the induction of a sound wave with a 180 degrees phase-shift compared to  
the sound experienced by the patient could result in sound cancelling, likely by negation of the cortical  
perception of tinnitus or residual inhibition, which can be partial or complete. The aim of our study is  
to compare the effect of phase-shifting generated by the tinnitus phase-out device between pure tone  
tinnitus patients (PTP) and narrow band noise tinnitus patients (NBNP). In present comparative study,  
we explore the effects of phase-shifting during 6 weeks of phase-out therapy in PTP and NBNP. Thirty-  
five tinnitus patients were included in the study. Twenty-one patients had pure tone tinnitus and 14  
patients had narrow band noise tinnitus. The effects on tinnitus were assessed using three separate  
visual analogue scales (VAS), the tinnitus questionnaire, the hyperacusis questionnaire, the Beck  
depression inventory, a categorical scale and audiometric measurements. While no differences in VAS  
were seen after therapy in NBNP, tinnitus increase could be demonstrated in PTP. This increase could  
be demonstrated for tinnitus loudness (p = 0.002) and tinnitus annoyance (p = 0.014). In conclusion,  
implementation of phase-shifting did not lead to significant sound cancelling. Our results are discussed  
and compared to previous studies investigating the effects of phase-out in tinnitus patients.
Clinical observation of the relationship between tinnitus masking curve and masking therapy result
[Article in Chinese]

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**OBJECTIVE:** To observe the relationship between the tinnitus masking curve and the effect of masking therapy, so as to select an effective treatment method. **METHOD:** Detect 108 (137 ear) tinnitus patients, and all the patients accept masking therapy. **RESULT:** The type I and III of the tinnitus masking curve were the highest percentage. In residual inhibition test type I and III had the highest positive rate, and masking therapy was the best treatment for type I and III. The residual inhibition test was positive correlation to the effect of masking therapy. **CONCLUSION:** The effectiveness of different types of masking curve are different in patients with the treatment of masking, patients should be provided with personalized treatment on masking curve and residual inhibition test.

Management of hearing impairment in adults
[Article in French]

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Hearing impairment, mainly the deafness with possible distortions, assorted with tinnitus concerns about 4 million of the French population. It can be of variable severity. Deafness is an invisible disability until we must answer a question. The permanent improvement of the computer and microelectronics sciences benefit to the prosthetic devices: cochlear implants compensate for complete hearing loss, hearing aids are hidden by being miniaturized, being partially or totally implantable. The management of disability is not limited to this material part: human assistance and assistive devices are part of the armory. Rest to continue and to increase the financial support. This claim is obviously not specific to disability hearing although the hearing aid is only refunded 138 Euro per device for a unit cost from 1300 Euro to 2500 Euro with an observed lifetime of 4 or 5 years.

Estimation of factors influencing the results of tinnitus retraining therapy.

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**CONCLUSION:** The factors of tinnitus loudness and Tinnitus Handicap Inventory (THI) score in tinnitus patients have the potential to relate to therapeutic results of tinnitus retraining therapy (TRT). **OBJECTIVES:** To confirm what factors in tinnitus influence the results of TRT. **PATIENTS AND METHODS:** Twelve factors were investigated in 53 patients with tinnitus, examining the relationship between these factors and the results of TRT. A THI score was determined before and 6 months after TRT introduction (pre- and post-TRT). Moreover, the change of THI score from pre- to post-TRT (delta THI) was referred to as the therapeutic effect of TRT. Based on the 12 factors, subjects were respectively divided into two groups, comparing delta THI between groups. **RESULTS:** Two groups of greater tinnitus loudness and higher THI score showed significant increases in delta THI, indicating that two factors of tinnitus loudness and THI score were related to the therapeutic effect of TRT.
Transtympanic electrical stimulation for immediate and long-term tinnitus suppression.

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Tinnitus is a common symptom which often becomes disabling, affecting the emotional and psychosocial dimensions of life. There are many reports describing tinnitus suppression or attenuation through electrical stimulation of the ear, provided either by cochlear implants or by transtympanic stimulation. Our study project aims to assess the effects of electrical promontory stimulation (EPS) on persistent disabling tinnitus. We enrolled 11 patients affected by postlingual monoaural or binaural profound hearing loss and disabling tinnitus in the worse ear. EPS was performed with direct continuous positive current delivered by an active platinum-iridium needle electrode connected to a promontory stimulator device. The short-term effect on tinnitus was assessed during and immediately after the stimulation. Long-term effects were estimated after one month by comparing pre- and post-EPS Tinnitus Handicap Inventory (THI) scores. Immediately after EPS, five patients (45.4%) reported complete suppression and four (36.4%) reported attenuation of tinnitus. Two patients (18.2%) said it was unchanged. After one month, the THI score was reduced in five patients (45.4%) and remained unchanged in the other six patients (54.6%). The beneficial effects of EPS on tinnitus might be explained by interference with tinnitus generating circuits such as the dorsal cochlear nucleus and the inferior colliculus and by modification of cortical activity. EPS is to be considered a worthwhile attempt at tinnitus suppression, and could help select candidates for the positioning of an implantable electrical stimulator that might provide longer-term beneficial effect on tinnitus.

The windowed sound therapy: a new empirical approach for an effective personalized treatment of tinnitus.

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We auditorily stimulated patients affected by subjective tinnitus with broadband noise containing a notch around their tinnitus frequency. We assessed the long-term effects on tinnitus perception in patients listening to notched noise stimuli (referred to as windowed sound therapy [WST]) by measuring the variation of subjects' tinnitus loudness over a period of 2-12 months. We tested the effectiveness of WST using non-notched broadband noise and noise of water as control sound therapies. We found a significant long-term reduction of tinnitus loudness in subjects treated with notched noise but not in those treated with control stimulations. These results point to the importance of the personalized sound treatment of tinnitus sufferers for the development of an effective tinnitus sound therapy.

Curing tinnitus with a Cochlear Implant in a patient with unilateral sudden deafness: a case report.
Cases J. 2009 May 18;2:7462.

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Cochlear implantation is a routine procedure for patients with bilateral profound sensorineural hearing loss. Some reports demonstrated a suppression of tinnitus as a side-effect after implantation. We describe the case of a 55-year-old man suffering from severe right-sided tinnitus in consequence of sudden right-sided deafness. Multiple therapeutic efforts including intravenous steroids and tympanoscopy with grafting of the round window remained unsuccessful. One year after onset of symptoms right-sided cochlear implantation was performed, which resulted in a complete abolishment of tinnitus after activating the implant. Severe unilateral tinnitus after sudden deafness might represent a new indication for cochlear implantation.
Association between tinnitus retraining therapy and a tinnitus control instrument

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Objective: Tinnitus retraining therapy (TRT), which is an adaptation therapy for tinnitus based on the neurophysiological model proposed by Jastreboff in 1990, consists of directive counseling and acoustic therapy with a tinnitus control instrument (TCI) or other devices. For the past 5 years, our hospital has administered TRT characterized by the use of a TCI. Method: In this study, we reviewed the clinical course of patients with tinnitus who presented to our outpatient clinic for tinnitus and hearing loss during the 3-year period from April 2004 to March 2007 and underwent TRT with a TCI. Among 188 patients with tinnitus (105 males and 83 females), 88 patients (51 males and 37 females, excluding dropouts) who purchased a TCI and continued therapy were included in the study. Results: Significant improvement in Tinnitus Handicap Inventory (THI) and Visual Analogue Scale (VAS) scores was found as early as 1 month of treatment and later compared with those on initial examination, suggesting that TRT with a TCI may be an effective treatment for tinnitus. Among the noises generated by the TCI, the sound pressure output from the TCI was set at just below tinnitus loudness level both of the first adjustment and the second adjustment. Speech noise and white noise were frequently selected, whereas high-frequency noise and pink noise were infrequently selected. Speech noise was most frequently selected at the first adjustment, and the number of patients selecting white noise increased at the second adjustment. The results that we compared the two also revealed that the mean hearing level and tinnitus loudness levels were higher in the white noise group than in the speech noise group, which suggested that the inner ear disorder was more harder in the white noise group. Both the THI score and VAS grade improved after 1 month of treatment in the speech noise group, whereas improvement in these parameters was observed in the white noise group after 6 months of treatment. These results suggest that it took much longer for the patients in the white noise group to improve. Conclusion: Significant improvement in THI and VAS scores was found as early as 1 month of treatment and later compared with those on initial examination, suggesting that TRT with a TCI may be an effective treatment for tinnitus. It resulted that many patients chose the speech noise or the white noise. And also it was indicated that noise generators set at just below mixing point with tinnitus are more effective. In this study, however, speech noise was often selected probably because of the reduced output at high frequencies and the level of comfort. As white noise produces greater sound volume, patients tended to switch from other therapeutic sound to white noise at the second adjustment. These findings may help administer acoustic therapy in the future.

Cochlear reimplantation due to electrode problems
Practica Oto-Rhino-Laryngologica Volume 102, Issue 10 (Oct 2009):825-829

Hori, Sa, Sato, Tb, Fukutsuji, Kb, Imai, Tb, Ueda, Tb, Naito, Yb, Shinohara, Sb, Fujiwara, Kb, Kikuchi, Mb, Tona, Ya, Yamazaki, Hb, Hospital, SGb

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We report two cases of cochlear reimplantation due to electrode problems. Case 1: A 76-year-old woman, complaining right-ear tinnitus in the 8 years following CI22 cochlear implantation in the right ear, was found in an X-ray examination to have the electrode array bending near the cochlear stoma. In cochlear reimplantation using a CI22 device upgraded to CI24RCS, fibrous tissue around the stoma and in the cochlear basal turn was removed and the electrode was replaced. Her speech perception score improved thereafter and tinnitus was reduced. Case 2: A 6-year-old boy with bilateral inner ear malformation presented with right facial spasm and decreased speech recognition 2 years and 4 months after right-ear cochlear implantation. An X-ray examination showed slight electrode slipout, so we inserted a CI24M device upgraded to CI24RCS, after which his speech perception score improved. Cochlear reimplantation was thus proved to be safe and effective in cases of electrode problems.
VII Brain Stimulation

Burst stimulation of the auditory cortex: a new form of neurostimulation for noise-like tinnitus suppression.

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Object Tinnitus is an auditory phantom percept related to tonic and burst hyperactivity of the auditory system. Two parallel pathways supply auditory information to the cerebral cortex: the tonotopically organized lemniscal system, and the nontonotopic extralemniscal system, which fire in tonic and burst mode, respectively. Electrical cortex stimulation is a method capable of modulating activity of the human cortex by delivering stimuli in a tonic or burst way. Burst firing is shown to be more powerful in activating the cerebral cortex than tonic firing, and bursts may activate neurons that are not activated by tonic firing.

Methods Five patients with an implanted electrode on the auditory cortex were asked to rate their tinnitus distress and intensity on a visual analog scale before and after 40-Hz tonic and 40-Hz burst (5 pulses at 500 Hz) stimulation. All patients presented with both high-pitched pure tone and white noise components in their tinnitus. Results A significantly better suppression for narrowband noise tinnitus with burst stimulation in comparison with tonic stimulation (Z = -2.03, p = 0.04) was found. For pure tone tinnitus, no difference was found between tonic and burst stimulation (Z = -0.58, p = 0.56). No significant effect was obtained for stimulation amplitude (Z = -1.21, p = 0.23) and electrical charge per pulse (Z = -0.67, p = 0.50) between tonic and burst stimulation. The electrical current delivery per second was significantly different (Z = -2.02, p = 0.04). Conclusions Burst stimulation is a new form of neurostimulation that might be helpful in treating symptoms that are intractable to conventional tonic stimulation. Further exploration of this new stimulation design is warranted.

Efficacy and safety of bilateral continuous theta burst stimulation (cTBS) for the treatment of chronic tinnitus: design of a three-armed randomized controlled trial.

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BACKGROUND: Tinnitus, the perception of sound and noise in absence of an auditory stimulus, has been shown to be associated with maladaptive neuronal reorganization and increased activity of the temporoparietal cortex. Transient modulation of tinnitus by repetitive transcranial magnetic stimulation (rTMS) indicated that these areas are critically involved in the pathophysiology of tinnitus and suggested new treatment strategies. However, the therapeutic efficacy of rTMS in tinnitus is still unclear, individual response is variable, and the optimal stimulation area disputable. Recently, continuous theta burst stimulation (cTBS) has been put forward as an effective rTMS protocol for the reduction of pathologically enhanced cortical excitability. METHODS: 48 patients with chronic subjective tinnitus will be included in this randomized, placebo controlled, three-arm trial. The treatment consists of two trains of cTBS applied bilaterally to the secondary auditory cortex, the temporoparietal association cortex, or to the lower occiput (sham condition) every working day for four weeks. Primary outcome measure is the change of tinnitus distress as quantified by the Tinnitus Questionnaire (TQ). Secondary outcome measures are tinnitus loudness and annoyance as well as tinnitus change during and after treatment. Audiologic and speech audiometric measurements will be performed to assess potential side effects. The aim of the present trial is to investigate effectiveness and safety of a four weeks cTBS treatment on chronic tinnitus and to compare two areas of stimulation. The results will contribute to clarify the therapeutic capacity of rTMS in tinnitus. TRIAL REGISTRATION: The trial was registered with the clinical trials register of http://www.clinicaltrials.gov (NCT00518024).
Transcranial magnetic stimulation (TMS) in tinnitus patients.

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The objective of this paper is to present Transcranial Magnetic Stimulation (TMS), a new and highly promising technique in tinnitus modulation. We conducted a Pubmed and Web of Science search using the words ‘Tinnitus’, ‘TMS’ and ‘Transcranial Magnetic Stimulation’. We report on the most relevant studies relating to the effects and stimulation parameters of TMS in tinnitus patients. It has already proved possible to reduce tinnitus using TMS and rTMS in selected patient populations with specific stimulation parameters. Intrinsic and extrinsic factors were shown to determine the amount of tinnitus reduction. Though many studies point out that tinnitus reduction can be obtained using TMS, a lot of questions still remain concerning stimulation parameters and optimal patient selection.

Deep brain stimulation effects in patients with tinnitus.

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OBJECTIVE: To report deep brain stimulation (DBS) effects in patients with tinnitus. STUDY DESIGN: Case series with chart review. SETTING: Tertiary medical center. SUBJECTS AND METHODS: Seven patients implanted with DBS systems for movement disorders who also reported having tinnitus were interviewed about their tinnitus conditions. Four were available for testing in a specialized tinnitus clinic with their DBS systems turned off or on. Testing included matching of self-rated and psychoacoustically measured tinnitus loudness to measure the impact of DBS on tinnitus. RESULTS: Three of the seven patients reported reduced tinnitus loudness when DBS was turned on. Of the four patients tested in the clinic, results indicated that DBS of the ventralis intermedius nucleus of the thalamus caused decreases in tinnitus loudness in two patients with relatively prolonged residual inhibition. CONCLUSION: These results suggest that DBS of nonauditory thalamus structures may provide tinnitus relief for some patients.

Influence of tonic and burst transcranial magnetic stimulation characteristics on acute inhibition of subjective tinnitus.
Otol Neurotol. 2009 Sep;30(6):697-703.

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OBJECTIVE: Transcranial magnetic stimulation (TMS) is already broadly used in different areas of neuroscience research. In the last years, special attention was drawn to TMS in tinnitus. The aim of our study is to investigate the stimulation characteristics of TMS in tinnitus patients, in particular the effect of tonic and burst stimulation of the superior temporal lobe. STUDY DESIGN: Prospective sham-controlled study. SETTING: Tertiary referral center. PATIENTS: Fifty tinnitus patients were included in the study. Thirty-one patients had pure-tone tinnitus, and 19 patients had noise-like tinnitus. STUDY DESIGN: Transcranial magnetic stimulation was performed in 1 session of 200 pulses at different frequencies. Stimuli were delivered to the auditory cortex region contralateral to the tinnitus side. Tonic and burst stimulations were delivered at different frequencies. Patients were asked to rate the acute tinnitus reduction after TMS on a visual analog scale.
VIII Behavioral Therapy

Consequences of controlling background sounds: the effect of experiential avoidance on tinnitus interference.

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OBJECTIVE: Masking by the use of sounds has been one of the most commonly applied means of coping with tinnitus. The ability to control auditory stimulation represents a potentially important process involved in tinnitus masking strategies. Little is, however, known about the consequences of control on tinnitus experience. The present study investigated the effects of control of background sounds (type and loudness) on perceived intrusiveness of tinnitus and cognitive performance. DESIGN: Using an experimental design with a series of trials, participants with clinically significant tinnitus (N = 35) were randomly assigned to 1 of 2 experimental manipulation conditions (control of sounds vs. no control of sounds). Measures: Self-reported tinnitus interference and the Digit-Symbol subtest served as dependent measures. RESULTS: Latent growth curve modeling showed that individuals assigned to the condition with control exhibited faster growth rates on tinnitus interference (increased interference) and demonstrated slower rates of improvement on cognitive performance measures over trials compared to individuals assigned to the condition with no control. CONCLUSION: These results suggest that efforts to control tinnitus through sounds can be associated with increased disability in individuals with tinnitus.
comparable in both groups. CONCLUSION: In acute tinnitus, distraction and relaxation training should be conducted as a complement to standard medical treatment, especially in high-risk patients demonstrating abnormal psychopathological status, since treatment results can be improved in this way.


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This study tested a theoretical model of tinnitus-related distress and of general distress that involved acceptance of tinnitus symptoms and emotional intelligence as factors that may protect against such distress. One hundred and sixty-two tinnitus sufferers from throughout Australia completed measures of acceptance of tinnitus symptoms, emotional intelligence, tinnitus-related distress, and general distress. As hypothesized, greater acceptance of tinnitus symptoms was associated with less tinnitus-related distress. Emotional intelligence was not associated with tinnitus distress. Greater acceptance and less tinnitus distress were both associated with less general distress, and the association between acceptance and general distress was mediated by tinnitus-related distress. The findings, which provide partial support for the tested model, may have implications for efforts to assist distressed tinnitus sufferers.

Real-time fMRI feedback training may improve chronic tinnitus. Eur Radiol. 2009 Sep 16. [Epub ahead of print]

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OBJECTIVES: Tinnitus consists of a more or less constant aversive tone or noise and is associated with excess auditory activation. Transient distortion of this activation (repetitive transcranial magnetic stimulation, rTMS) may improve tinnitus. Recently proposed operant training in real-time functional magnetic resonance imaging (rtfMRI) neurofeedback allows voluntary modification of specific circumscribed neuronal activations. Combining these observations, we investigated whether patients suffering from tinnitus can (1) learn to voluntarily reduce activation of the auditory system by rtfMRI neurofeedback and whether (2) successful learning improves tinnitus symptoms. METHODS: Six participants with chronic tinnitus were included. First, location of the individual auditory cortex was determined in a standard fMRI auditory block-design localizer. Then, participants were trained to voluntarily reduce the auditory activation (rtfMRI) with visual biofeedback of the current auditory activation. RESULTS: Auditory activation significantly decreased after rtfMRI neurofeedback. This reduced the subjective tinnitus in two of six participants. CONCLUSION: These preliminary results suggest that tinnitus patients learn to voluntarily reduce spatially specific auditory activations by rtfMRI neurofeedback and that this may reduce tinnitus symptoms. Optimized training protocols (frequency, duration, etc.) may further improve the results.


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Several disorders that involve motor and sensory disturbances such as chronic pain, tinnitus, stroke or dystonia are also characterized by changes in the sensory and motor maps in the sensorimotor cortices.
This article reviews training procedures that target these maladaptive changes and the behavioral and cortical changes that accompany them. In addition, we will discuss factors that influence these training procedures and discuss new developments. These procedures include training of perceptual abilities, motor function, direct cortical stimulation as well as behavioral approaches and have been shown to reorganize the altered sensory and motor maps. Treatments that combine several modalities such as imagery or mirror treatment as well as use of prostheses also have beneficial effects. Further research must elucidate the mechanisms of these plastic changes and relate them to disorders and treatments.

A Cluster Randomised Trial of an Internet-Based Intervention Program for Tinnitus Distress in an Industrial Setting.
Cogn Behav Ther. 2009 Aug 12:1. [Epub ahead of print]

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The effectiveness of a therapist-supported Internet intervention program for tinnitus distress in an industrial setting was evaluated using a cluster randomised design. Fifty-six Australian employees of two industrial organisations were randomly assigned, based on their work site (18 work sites from BP Australia and five from BHP Billiton), to either a cognitive behavioural therapy (CBT) program or an information-only control program. Participants were assessed at pre- and postprogram, measuring tinnitus distress, depression, anxiety, stress, quality of life, and occupational health. The CBT program was not found to be superior to the information program for treating tinnitus distress. A high attrition rate and small sample size limit the generalisability of the findings, and further developments of the program and assessment process are needed to enhance engagement and compliance.

Long-Term Improvement in Tinnitus after Modified Tinnitus Retraining Therapy Enhanced by a Variety of Psychological Approaches.

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This work evaluates an enhanced tinnitus retraining therapy (TRT) for patients with chronic tinnitus based on different group therapeutic interventions in a day hospital setting. Therapy for chronic tinnitus is intended to improve the way patients cope with tinnitus by learning how to reduce tinnitus-induced impairments. Short-term and long-term changes in stress variables and tinnitus-related distress were investigated using 3 psychometric instruments. Patients received 7 consecutive days of a multidisciplinary therapy at the Charité University Hospital in Berlin. The data were assessed before and after therapy, either immediately or after 3, 6 or 12 months. As a control, we used scores of tinnitus patients from the waiting list, and compared these to the scores of the therapy group 3 months after the end of treatment. The main factors of the modified TRT were Jacobson's progressive muscle relaxation, physiotherapy, education via lectures and training of selective attention, as well as changes of appraisal, mental attitude and behavior towards tinnitus. The therapy resulted in a significant reduction in both short-term and long-term tinnitus-related distress and psychometric stress variables, with the latter being more reduced in patients with higher initial scores. Moreover, our study revealed differences in psychometric parameters concerning duration of tinnitus, age and gender, which may explain the different outcomes of therapy. The outpatient setting enables the patients to test, practice and transfer strategies into their everyday life.
Chronic Tinnitus: Which Kind of Patients Benefit from an Outpatient Psychotherapy?
Psychother Psychosom Med Psychol. 2009 Jul 21. [Epub ahead of print]

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BACKGROUND: Psychotherapy proved to be effective in the treatment of chronic tinnitus sufferers. We investigated, which patient and symptom characteristics predicted the treatment outcome. PATIENTS AND METHODS: 95 patients underwent a CBT based treatment including biofeedback elements. Predictors were identified by the use of regression analysis. Outcome was defined as changes in tinnitus annoyance, intensity, duration, the number of responder and the end-state-functioning. RESULTS: More than 80% of the participants significantly improved. Positive predictors found in the analysis were an active and non-sceptical treatment expectancy. If patients suffered from depressive disorder, outcome was slightly reduced. CONCLUSION: Most tinnitus patients benefit from outpatient psychotherapy. Positive treatment expectancy should be increased at the beginning of the treatment. Patients who are sceptical should be informed about potential positive treatment results. In the case of affective disorder, additional treatments should be considered.

The effectiveness of bibliotherapy in alleviating tinnitus-related distress
Journal of Psychosomatic Research [Article in Press]

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Objective: The present study examined the efficacy of bibliotherapy in assisting individuals experiencing distress related to tinnitus. Methods: One hundred sixty-two tinnitus sufferers from Australia participated in a study designed to examine the effectiveness of a cognitive-behaviorally based self-help book in reducing distress. To maximize the ecological validity of the findings, we excluded no individuals interested in treatment for tinnitus-related distress. Results: The experimental condition lost 35% of participants at postassessment, compared to 10% in the control group. In an analysis of participants who completed postintervention assessment, those assigned to the intervention condition, who received a tinnitus self-help book, showed significantly less tinnitus-related distress and general distress 2 months later compared to those assigned to the waiting list control condition. The intervention group’s reduction in tinnitus-related distress and general distress from preintervention to postintervention 2 months later was significant, and these participants maintained a significant reduction in distress on follow-up 4 months after they received the tinnitus self-help book. A long-term follow-up of all participants, who at that time had received the book at least a year previously, showed a significant reduction in tinnitus distress. Although these group differences and pre-post changes were significant, effect sizes were small. Intention-to-treat analyses showed no significant effect for between-groups analyses, but did show a significant effect for the 1-year follow-up pre-post analysis. Conclusion: Information on the effectiveness of using a self-help book, without therapist assistance, in alleviating distress is important, as bibliotherapy can provide inexpensive treatment that is not bound by time or place. © 2009.
IX Somatic Tinnitus

Eye movement abnormalities in somatic tinnitus: Fixation, smooth pursuit and optokinetic nystagmus.
Auris Nasus Larynx. 2009 Nov 16. [Epub ahead of print]

Kapoula Z, Yang Q, Vernet M, Bonfils P, Londero A.
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OBJECTIVE: Smooth pursuit (SP), optokinetic nystagmus (OKN) and fixation were investigated in five subjects with somatic tinnitus modulated by eye movements, jaw or neck. METHODS: Eye movements were recorded with the EyeLink II video system. RESULTS: (1) Fixation was characterized by high frequency and amplitude of saccade intrusions; (2) SP had low gain particularly in the vertical direction, and it was characterized by high frequency of catch-up saccades with high amplitude, including predictive saccades; (3) OKN also had low gain particularly in the vertical direction. Each subject showed abnormality for more than one type of eye movement, and for specific directions. CONCLUSIONS AND SIGNIFICANCE: The results suggest mild dysfunction of cortical-subcortical and cerebellar structures involved in the control of these eye movements. Particularly deficits for vertical pursuit eye movements and fixation instability in line with cerebellar signs. Further studies of more patients with or without modulated tinnitus are in progress.

Stomatognathic adaptive motor syndrome is the correct diagnosis for temporomandibular disorders.
Med Hypotheses. 2009 Nov 10. [Epub ahead of print]

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Temporomandibular disorder is a generic and inadequate conception to be used as a diagnosis. It fails to express the etiology or the pathophysiology and it is mainly associated with the anatomical site. Moreover, the clinical condition presents a mandibular motor problem and not a joint problem. The hypothesis presents the new diagnosis stomatognathic motor adaptive syndrome, which comprehend a motor response and the adaptive processes it induces. Inadequate occlusal contacts cause the mandible to shift in order to reach an ideal intercuspal position. The condylar displacements are proportional to such movements. Temporomandibular joint (TMJ) receptors respond to the capsular mechanical stress and the information reaches the trigeminal sensory nuclei. The mandibular modified position seems to be relevant information and may interfere with catecholaminergic neurotransmission in basal ganglia. The main motor responses comprise increased jaw muscle tone, decreased velocity of movements and incoordination. The overload of muscle function will produce adaptive responses on many stomatognathic structures. The muscle adaptive responses are hypertonia, pain, fatigue and weakness. Temporomandibular joint presents tissue modification, disc alteration and cracking noise. Periodontium show increased periodontal membrane, bone height loss and gingival recession. Teeth manifest increased wear facets, abfraction and non-accidental fractures. The periodontal and teeth adaptive processes are usually identified as occlusal trauma. The altered stomatognathic functions will show loss of velocity during mastication and speech. Fatigue, weakness in jaw muscle and difficulties to chew hard food are related to hypertonia. Incoordination between stomatognathic muscles groups is found, causing involuntary tongue/cheek biting and lateral jaw movements on speech. Otologic complaints, as aural fullness and tinnitus, are related to the tensor tympani muscle, innervated by the trigeminal nerve.
**INTRODUCTION AND OBJECTIVES:** Temporomandibular disorders are associated with symptoms such as tinnitus, vertigo, sensation of hearing loss, ear fullness and otalgia. The connection and dysfunction of the tympanic tensor muscle and palate veil tensor muscle seems to be associated with the aforementioned symptoms. We seek to demonstrate and explain this connection through the morphometry of these structures.

**METHODS:** We studied 22 paired blocks and 1 left side of human temporal bone. Digital measurements were made of the tensor muscles of the hammer and stapes.

**RESULTS:** The average length of the stapedial muscle was 5.8mm SD 0.61, and that of the hammer tensor was 19.69mm SD 1.07. Anatomical connections were found in all the samples between the tensor muscles of the palate veal and of the hammer through a common tendon.

**CONCLUSIONS:** There is a need for an interdisciplinary management between physician and specialized dentist in cases of craniofacial pain.

**The effect of a new treatment based on somatosensory stimulation in a group of patients with somatically related tinnitus.**


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The aim of this study was to evaluate the effect of a new treatment consisting of stretching, posture training, and auricular acupuncture immediately and at a 3-month followup. This method has not been tested previously. From an original pool of 41 potential subjects, we recruited 24 (12 men, 12 women; ages 18-70 years) into this study and divided them from a waiting list into either a treatment group or a control group. We measured mobility of neck and posture; measured severity of tinnitus by the Klockhoff test and the visual analog scale (VAS); and measured grade of anxiety and depression with the Hospital Anxiety and Depression Scale. We also used the Mann-Whitney U-test to determine statistical significance. The statistical analysis demonstrated a significant decrease of tinnitus in the treatment group as compared with the control group, according to the VAS before and after treatment (p < .001) and at follow-up after 3 months (p < .01). We also observed a significant decrease of tinnitus according to the Klockhoff test before and after treatment (p < .001) and at follow-up after 3 months (p < .01). Our study indicates that this method, based on somatosensory stimulation, may be a useful and alternative treatment of somatic tinnitus.

**Symptoms and signs of temporomandibular disorders in patients with sudden sensorineural hearing loss**


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Sudden sensorineural hearing loss (SSH) usually affects one ear and leads to life long deafness in some cases. There are many theories about the origin of the condition but the etiology and pathophysiology are still unknown. However, tinnitus and vertigo frequently occur in patients with SSH, but are also
frequent symptoms reported by patients with temporomandibular disorders (TMD). We hypothesized that TMD symptoms and signs are frequent in SSH patients. The objective of this study was therefore to investigate the presence of TMD symptoms and signs in SSH patients compared with healthy individuals. The groups, matched by gender and age, consisted each of 9 females and 6 males. Both groups answered a questionnaire about TMD symptoms and a clinical examination which included maximum voluntary mouth opening, temporomandibular joint sounds, tenderness to digital palpation of the TMJs and selected masticatory muscles, intermaxillary relations and dental occlusion was performed. The SSH patients reported significantly higher rates of pain in the head and face region and pain during mandibular movements as well as of aural symptoms compared with the control group. There was also a statistically significant difference between the groups in the number of masticatory muscles tender to digital palpation, as well as in some occlusal variables. In conclusion, this study shows that self-reported symptoms and clinical signs of TMD are more frequent in patients with SSH than in healthy controls. © Axelson et al.

X Surgical Treatment

Otoneurological management of petrous apex cholesterol granuloma.
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OBJECTIVE: The aim of the study is to review the management of petrous apex cholesterol granuloma. The surgical approaches for drainage or total removal and the wait and see policy were analyzed, and outcomes were evaluated. METHODS: Retrospective charts of 27 patients managed for petrous apex cholesterol granuloma with a minimum follow-up of 12 months were analyzed in a quartenary skull base center. Presenting symptoms and signs were recorded, and radiologic imaging was evaluated. Management options included wait and see policy and surgery by several approaches. RESULTS: The mean age of patients affected by the lesion was 38.8 years. The mean follow-up was 56.7 months. Patients complained of hearing loss, vertigo, tinnitus, diplopia, hemifacial spasm, trigeminal neuralgia, and facial paresthesia. Twelve patients were managed by wait and see policy, and in this category, only one lesion showed growth during the follow-up. Depending upon size and location, 15 patients were surgically treated by infralabyrinthine approach (9 patients), infratemporal type B approach (3 patients), combined infratemporal type B transotic approach (2 patients), and transotic approach (1 patient). One recurrence was recorded during the follow-up. CONCLUSIONS: Radiologic evaluation is required for diagnosis and management. Patients with good hearing can be treated by infralabyrinthine approach. Infratemporal fossa type B approach is advocated in patients with extensive disease and internal carotid artery involvement. Wait and see policy is recommended for asymptomatic cases. Drainage and permanent ventilation are the goals of treatment. Complete removal is indicated in selected cases where placement of drainage tube is not feasible.

Jugular Foramen Tumors: Clinical Characteristics and Treatment Outcomes.
Otol Neurotol. 2009 Sep 24. [Epub ahead of print]
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OBJECTIVE: To describe the diagnosis, management, and treatment outcome of jugular foramen (JF) tumors. STUDY DESIGN: Retrospective chart review. METHODS: Charts of the 83 patients diagnosed with JF tumors between January 1997 and May 2008 were reviewed. Presenting symptoms, otologic and neurotologic examination, audiologic thresholds, treatment procedure, surgical technique, tumor size and classification, and postoperative complications were recorded. Facial nerve function was
graded using the House-Brackmann scale. Extent of tumor removal was determined at time of surgery, followed by routine radiographic follow-up. RESULTS: The mean age of patients with JF tumors was 48.5 years (standard deviation, 16.3 yr), and women (79.5%) outnumbered men (20.5%). Most had glomus jugulare (GJ) tumors (n = 67, 80.7%); 9 patients had lower cranial nerve schwannomas (10.8%), and 7 patients had meningiomas (8.4%). The most frequent initial symptoms included pulsatile tinnitus (84.3%), conductive hearing loss (75.9%), and hoarseness (34.9%). Sixty-one patients (73.5%) underwent surgery, 18.1% had radiotherapy, and 8.4% were observed. Total tumor removal was achieved in 81% of surgery cases. New lower cranial nerve (CN) deficits occurred after surgery in 18.9% of GJ, 22.2% of schwannoma, and 50% of the 4 meningiomas. At last follow-up, 88.1% of surgical patients had normal or near-normal (House-Brackmann I or II) facial function. CONCLUSION: Total resection of GJ tumors, meningiomas, and lower CN schwannomas can be a curative treatment. However, subtotal removal may be required to preserve CN function, vital vascular structures, and the brainstem. Postoperative radiotherapy is used to control residual tumor. When postoperative complications develop in patients, early rehabilitation is important to decrease mortality and morbidity. Therefore, patients should be closely followed.

**Quality of life in postoperative vestibular schwannoma patients.**

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OBJECTIVES/HYPOTHESIS: To quantify the postoperative quality of life (QOL) in patients following vestibular schwannoma surgery in a new multidisciplinary skull base unit. STUDY DESIGN: Cross-sectional study. METHODS: The Australian Short Form 36 (SF-36) quality of life health questionnaire was administered to 121 consecutive patients surgically treated for vestibular schwannoma between 1999 and 2007 at Westmead Hospital, New South Wales, Australia. QOL scores were calculated using a standardized process across the eight SF-36 health domains and compared to sex- and age-matched healthy Australian population. RESULTS: An 81% response rate (98 patients) was obtained. The postoperative QOL in vestibular schwannoma patients was significantly less than the appropriate matched healthy Australian population in one health domain of role physical limitation (P < .05). Analysis of preoperative patient factors (age, gender) and surgical factors such as tumor size (cutoff points of 15 mm or 25 mm) together with, surgical approach (translabyrinthine and retrosigmoid) showed no significant difference in QOL outcomes for each of these variables (P < .05). CONCLUSIONS: Results indicate that patients following vestibular schwannoma surgery reported near equivalent QOL as the healthy population. Advances in surgical techniques and experiences have minimized morbidities associated with vestibular schwannoma surgery. Significant physical role limitation encountered postoperatively may relate to facial nerve dysfunction, vestibular dysfunction, tinnitus or hearing loss that may persist after surgery. Careful patient selection, as well as, appropriate preoperative counselling, multidisciplinary follow-up and rehabilitation should be offered to all surgical candidates. A measured approach should still be considered for patients with small, slow growing tumors with minimal symptoms.

**Treatment of Dural Arteriovenous Fistulas Presenting as Pulsatile Tinnitus.**
Otol Neurotol. 2009 Sep 2. [Epub ahead of print]

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OBJECTIVE: To describe the clinical picture and treatment of dural arteriovenous fistulas (DAVFs) presenting as pulsatile subjective tinnitus. STUDY DESIGN: Review of prospectively collected data.
SETTING: Academic referral center. PATIENTS: Fourteen patients with clinically and radiographically diagnosed DAVFs. INTERVENTIONS: Treated by endovascular route. MAIN OUTCOME MEASURES: Treatments, clinical course, complications, and evolution were evaluated. RESULTS: All patients presented with sleep-disruptive pulsatile tinnitus. Other symptoms included severe headaches, papilledema, proptosis, blepharoptosis, visual disturbances, and hemiparesis. Cortical venous drainage was present in 4 cases. Endovascular treatment was performed at least once by the arterial route in 14 patients and the venous route in 4 patients. The origin of tinnitus was always a vessel in or above the petrous bone. When these arteries or veins could not be visualized in the final control, the tinnitus disappeared. In the patients whose tinnitus returned, a vessel in the petrous bone could always be seen. There was no mortality. CONCLUSION: Endovascular treatment is an effective and safe treatment of DAVFs presenting as tinnitus.

[The comparative analysis of clinical symptomatology before and after the operation of otosclerosis]
[Article in Serbian]
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INTRODUCTION: Otosclerosis is a progressive osteodystrophic disease of the osseous capsule of the labyrinth which leads to the fixation of the stapes and partial deafness. The progressive hearing loss followed by ear tingling--tinnitus and vertigo is of great importance for this disease. The aim of the work was to determine the changes of clinical symptomatology before and after the operative treatment of otosclerosis. MATERIAL AND METHODS: The study included 32 subjects between 25 and 60 years of age affected by otosclerosis who had undergone surgical treatment at the VMA (Military Medical Academy) Clinic, Department of Otolaryngology in Belgrade. Besides the clinical examination and detailed case history, audiometry and tympanometry examinations were performed. During the postoperative period the clinical symptomatology was evaluated and audiomtery examinations were performed in order to determine the effect of the surgical intervention. RESULTS: Of the total number of 32 subjects, partial deafness was present in all of them before the operation, whereas tinnitus, vertiginous disturbances and otalgia were found in a certain number of the subjects. During the postoperative period a partial recovery was found in a larger number of the subjects in relation to the total hearing recovery. During the postoperative period tinnitus of lower intensity was found in a greater number of the subjects, whereas the number of those without tinnitus was smaller. The problem of vertiginous disturbances as well as otalgia were not found during the postoperative period. CONCLUSION: By following the changes of the clinical symptomatology we came to the conclusion that surgical treatment of otosclerosis results in the reduction and disappearance of subjective disturbances, tinnitus, vertigo and otalgia and leads to the partial or complete hearing recovery.

Transarterial embolization of intracranial dural arteriovenous fistulas with direct cortical venous drainage using ethylene vinyl alcohol copolymer (Onyx).
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PURPOSE: This communication concerns the new possibilities and technical aspects of using ethylene vinyl alcohol copolymer (Onyx, EVAC) for endovascular treatment of intracranial dural arteriovenous fistulas with direct cortical venous drainage (DAVF-CVs). PATIENTS AND METHODS: Five patients with symptomatic DAVF-CVs were treated primarily with transarterial embolization using Onyx. RESULTS: All patients had complete obliteration of their DAVFs with a single Onyx injection that resulted in passage of embolic agent to the draining vein. One asymptomatic technical adverse event occurred (a broken
microcatheter on retrieval). On clinical follow-up (mean 12.6 months, range 1-27 months), two patients with intracranial hemorrhage and one patient with cerebellar symptoms improved significantly after treatment, with residual symptoms that did not affect independence. One patient had remission of tinnitus and headache but developed seizures, and one patient was asymptomatic. Imaging follow-up (mean 4 months, range 1-7 months) did not show any revascularization. CONCLUSION: Embolization with Onyx represents a significant improvement in the endovascular treatment of DAVF-CVs. Cases that would not be effectively treated with cyanoacrylate or particles can be cured by embolization alone.

XI  Holistic

XII  Review

Tinnitus: etiology, classification, characteristics, and treatment.

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Tinnitus is the perception of sound with the absence of acoustic stimulus. It affects approximately 10% of the population. This is a symptom with a broad differential diagnosis. In some cases, tinnitus impacts significantly on patients’ activities of daily living. Understanding how to differentiate between subjective and objective tinnitus is essential to the evaluation and management of these patients. The various causes of each type of tinnitus will be discussed. This review presents a general approach to tinnitus in order to facilitate timely diagnosis and management of this complex symptom.

[The significance of stress: Its role in the auditory system and the pathogenesis of tinnitus.]
[Article in German]
HNO. 2009 Oct 2. [Epub ahead of print]

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Emotional stress is often associated with auditory phenomena such as hyperacusis, tinnitus, Ménière’s disease and vertigo. Stress develops as a result of a person’s attempts to come to terms with the increased or unexpected demands of his or her environment. Stress serves to protect one from physical danger and to temporarily increase one’s performance in order to increase the probability of survival. Sleep and appetite are particularly reduced, while anxiety increases. The mental changes induced by stress may contribute to the onset or exacerbation of tinnitus. The following links exist between the auditory and stress systems: the limbic system, which regulates instinctive behavior and emotions, is linked to the auditory system via the medial geniculate body (amygdala). The hypothalamus, which is the integrative center of the endocrine and autonomic systems, is linked to the auditory system via the inferior colliculus. The reticular system, which is focused on the behavior pattern of attention and excitement, projects serotonergic fibers to all pathways of the auditory system, ranging from the cochlea to the auditory cortex.
Review paper: more than ringing in the ears: a review of tinnitus and its psychosocial impact.

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AIM AND OBJECTIVES: To provide an overview of tinnitus, current management and its psychosocial impact offering strategies for managing acute and chronic tinnitus in practice. BACKGROUND: Tinnitus, characterised by the perception of sound in the absence of external stimuli, is experienced by about 10% of the population at some time in their lives. It may be temporary/longstanding; approximately 5% adults experience severe, persistent tinnitus affecting their lifestyle. Although many adjust successfully, others are disabled by the condition. Though often unrecognised, tinnitus affects many patients regardless of their presenting illness. DESIGN: A literature review including descriptive, theoretical and empirical material. Databases were searched using the keyword ‘tinnitus’ providing diverse information which was used to address the research questions. RESULTS: Tinnitus represents more than ‘simple’ ringing in the ears and may be accompanied by many distressing changes. It may be acute or chronic. It is difficult to treat, care may be directed towards management rather than cure. Many patients are, however, told that ‘nothing can be done’. Relevance to clinical practice. Despite the high prevalence of tinnitus, there is a paucity of relevant nursing literature suggesting that there is an information deficit amongst nurses. The information provided shows that understanding the full impact of the condition and identification of patients’ needs are essential to effective care. Strategies to help affected patients are given. CONCLUSIONS: Tinnitus, a widespread, often intractable condition, affects millions of people; there is considerable debate about its causes. Tinnitus is distressing and may be severe enough to affect lifestyle and quality of life. Affected patients need considerable support and advice on healthcare options, encouragement to try different treatments and recognition that help and hope are available. Though patients may have to learn to live with tinnitus, the most important thing is that they recognise that help is available.

XIII Others

The effect of tightened hearing protection regulations on military noise-induced tinnitus.

Mrena R, Savolainen S, Kiukaanniemi H, Ylikoski J, Mäkitie AA.
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The objective of this study was to investigate the effect of tightened hearing protection regulations on tinnitus in the Finnish Defence Forces. The initial study group comprised 252 officers and non-commissioned officers (NCOs), of which 229 were included in the final study group. Subjective symptoms of tinnitus and audiometric test results for these officers and NCOs examined before retirement, from 1984 to 1986 (Period I), and 2003 to 2005 (Period II), were reviewed. Changes in tinnitus reports between the two time periods, during which regulations had been revised, were investigated. Prevalence of tinnitus showed a decline both in officers (from 68% to 63%) and in NCOs (from 76% to 72%) between the two study periods, in accordance with tightened hearing protection regulations. The Cox regression analysis showed a significantly decreased hazard ratio for constant or disturbing tinnitus for Period II. Tinnitus prevalence, especially constant or disturbing tinnitus, in the Finnish Defence Forces was diminished by tightened hearing protection regulations. Tinnitus might be more persistent than hearing loss and does not necessarily improve in direct relation to hearing loss after protective measures.
Health state valuation methods and reference points: the case of tinnitus.


Happich M, Moock J, von Lengerke T.

Helmholtz Zentrum München-German Research Center for Environmental Health, Institute of Health Economics and Health Care Management (IGM), Munich, Germany.

OBJECTIVES: Many studies support the finding that patients, compared to the general public, valuate a given health condition differently. Based on Prospect Theory, this difference can be explained by adaptation processes resulting in differences in individual reference points. Using tinnitus as a case in point, our objective is to analyze empirically to what extent differences in risk attitudes (as a proxy to reference points) mediate differences in health valuations. METHODS: Two hundred ten tinnitus patients and a similar number of unaffected persons indicated their willingness to undergo, hypothetically, an intervention (surgery or treatment) that would either improve or worsen the condition, thus revealing their risk attitudes. Utilities were elicited using three different methods: visual analogue scale (VAS), time trade-off (TTO), and standard gamble (SG). Repeated measure analysis of variance was used to test for mediation of utility differences by reference points. RESULTS: Health status (affected-unaffected) has a significant effect on tinnitus utilities and risk attitude; at the same time, the latter is significantly associated with utilities. Adjusting for risk attitude, differences by health status disappear for SG and TTO, and are alleviated for VAS. CONCLUSION: Reference points in terms of risk attitudes are a potential confounder in the valuation of health states. Taking into account theoretical predictions and issues in measuring SG, TTO, and risk attitudes, these results cast doubt on the construct validity of SG and TTO, and point to the need to recognize and further clarify the role of reference points in health valuation research.

Chapter 4 neurology in the bible and the talmud.


Feinsod M.

The Bible, a major pillar of Western Civilization consists of Hebrew Scriptures, assembled over a millennium and accepted as of divine origin. The Talmud is a compendium of Jewish laws, covering every possible aspect of life, analyzed in depth from 200 BCE to 600 CE, becoming the foundation of Jewish existence. The all-encompassing character of the books provides numerous medical problems and observations that appear in various connotations. When in need to clarify various legal dilemmas, the Talmudic sages displayed astoundingly accurate anatomical knowledge and were pioneers in clinical-pathological correlations. The descriptions of „neurological“ events in the Bible are very precise but show no evidence of neurological knowledge. Those reported in the various tractates of the Talmud are evidence of a substantial medical knowledge, marked by Hellenistic influence. Subjects such as head and spinal injuries, epilepsy, handedness neuralgias aphasia tinnitus and tremor were discussed in depth. This chapter is an updated collection of the studies, extracting observations and discussions of neurological manifestations from the ancient texts.

Brazilian young adults and noise: attitudes, habits, and audiological characteristics.


Zoccoli AM, Morata TC, Marques JM, Corteletti LJ.

Graduate Program in Communication Disorders, Universidade Tuiuti do Paraná, Brazil.

The objective of this study was to examine behaviors and attitudes of Brazilian teenagers towards noise, and determine their audiological characteristics. Participants were 245 young persons (14 to 18 years old) who attended private school. Behaviors and attitudes were measured using the validated Portuguese version of the Youth Attitude to Noise Scale (YANS). Pure-tone audiometry was used to evaluate the hearing of a sub-sample of 24 participants. Music played through personal media players
was the most common exposure reported. A substantial percentage of participants reported temporary tinnitus (69%) after attending discos, music concerts, and listening to music through headphones. Tinnitus complaints were more frequent among females (41%) than males (27%). Four participants (1.6%) reported use of a hearing protector. Among a subsample of 24 participants, two (8%) young women had bilateral audiometric notches. YANS scores in the present study were slightly lower than those obtained in Sweden and the US, indicating a more negative attitude towards noise. Gender, age, country, and/or region are variables that will influence exposure to noise or music and possibly hearing outcomes.


Zazzio M.


Abstract Objective: The aim of this study was to investigate if laser therapy in combination with pulsed electromagnetic field therapy/repetitive transcranial magnetic stimulation (rTMS) and the control of reactive oxygen specimens (ROS) would lead to positive treatment results for hyperacusis patients. Background Data: Eight of the ten patients treated for tinnitus, who were also suffering from chronic hyperacusis, claimed their hyperacusis improved. Based upon that, a prospective, unblinded, uncontrolled clinical trial was planned and conducted. ROS and hyperacusis pain thresholds were measured. Materials and Methods: The patients were treated twice a week with a combination of therapeutic laser, rTMS, and the control and adjustment of ROS. A magnetic field of no more than 100 μT was oriented behind the outer ear, in the area of the mastoid bone. ROS were measured and controlled by administering different antioxidants. At every treatment session, 177-504 J of laser light of two different wavelengths was administered toward the inner ear via meatus acusticus. Results: The improvements were significantly better in the verum group than in a placebo group, where 40% of the patients were expected to have a positive treatment effect. The patients in the long-term follow-up group received significantly greater improvements than the patients in the short-term follow-up group. Conclusion: The treatment is effective in treating chronic hyperacusis.

XIV Case Reports

Aggressive intracranial dural arteriovenous fistula presenting with cerebrospinal fluid rhinorrhea: case report.

Willems PW, Willinsky RA, Segev Y, Agid R.

Division of Neuroradiology, Department of Medical Imaging, Toronto Western Hospital, Toronto, Canada. pwawillems@gmail.com

OBJECTIVE: This is the first report of an aggressive dural arteriovenous fistula presenting with rhinorrhea. It demonstrates the importance of recognizing increased intracranial pressure, and its underlying cause, as the predisposing factor to a spontaneous cerebrospinal fluid leak because this carries implications for management. CLINICAL PRESENTATION: Ten years after minor trauma and directly after an intercontinental flight, a 43-year-old woman presented with rhinorrhea. Right-sided pulsatile tinnitus had been present for the past 9 years. Imaging demonstrated an intracranial dural arteriovenous fistula of the right transverse sinus with cortical venous reflux. Magnetic resonance imaging findings indicated long-standing increased intracranial pressure. INTERVENTION: The fistula was treated by endovascular means, using both transvenous and transarterial approaches, which led to immediate relief of the tinnitus and resolution of the rhinorrhea within 4 days.
CONCLUSION: A dural arteriovenous fistula should be included in the differential diagnosis of underlying causes of increased intracranial pressure when examining a patient with a cerebrospinal fluid leak. Treatment of the fistula should precede attempts to treat the rhinorrhea, especially if the fistula has cortical venous reflux.

**Pulsatile tinnitus from a spontaneous carotid-jugular fistula: case report.**
Huang CF.

Department of Neurosurgery/Neuro-Medical Scientific Center, Buddhist Tzu Chi General Hospital, Taichung Branch, Taiwan. discover_paris@hotmail.com

INTRODUCTION: We describe a patient who presented with unilateral objective pulsatile tinnitus (PT) from an unusual spontaneous fistula between the internal carotid artery (ICA) and the internal jugular vein (IJV).

CASE REPORT: The 56-year-old woman presented with unilateral PT without antecedent trauma. A blowing bruit, synchronous with the pulse, was audible with stethoscopic examination of the right carotid, mastoid, and orbital regions. The duplex ultrasound showed high velocity flow over the right ICA. Right carotid angiography demonstrated a high-flow fistula between the ICA and the IJV. The patient received treatment with endovascular embolization, with coils, and the PT disappeared.

DISCUSSION: Unilateral objective PT should be carefully evaluated for arteriovenous communications within the head and neck region. Although a fistula between the ICA and the IJV is rare, this arteriovenous fistula should be included in the differential diagnosis of pulsatile tinnitus. Noninvasive color duplex ultrasonography, rather than conventional angiography or CT arteriography, and venography, could be the primary diagnostic tool of choice with the suspicion of carotid artery abnormality in patients with normal otoscopic and neurologic examinations.

[A case of traumatic middle meningeal arteriovenous fistula on the side of the head opposite to the injured side]
[Article in Japanese]

Department of Neurosurgery, National Hospital Organization Disaster Medical Center, Tokyo, Japan.

A rare case of a traumatic middle meningeal arteriovenous fistula on the side of the head opposite to the injured side was reported. A 21-year-old man was admitted to our hospital after a traffic accident in which the right side of his head was hit. CT scans and MR images on admission showed a right temporal bone fracture, traumatic subarachnoid hemorrhage, and a left frontal lobe contusion. Three months after the head injury, he complained of tinnitus and exophthalmos. One year after the head injury, left external carotid angiograms showed a dural arteriovenous fistula fed by the left dilated middle meningeal artery and draining into the middle meningeal vein. Early filling of the sphenoparietal sinus, cavernous sinus, superior ophthalmic vein, and the cortical vein were also detected. Transarterial embolization of the left middle meningeal fistula was performed, resulting in the disappearance of the lesion. The postoperative course was uneventful.
Intraosseous cavernous angioma of the petrous bone.

Sade B, Lee DK, Prayson RA, Hughes GB, Lee JH.
Brain Tumor Institute, The Cleveland Clinic Foundation, Cleveland, Ohio.

Objective: Intraosseous cavernous angioma (CA) of the petrous bone is rare and preoperative diagnosis can be challenging, especially when its epicenter is outside the internal auditory canal (IAC) or geniculate ganglion. Methods: A 45-year-old man presented to our clinic with right-sided hearing loss, tinnitus, and unsteadiness. Neuroimaging revealed a right posterior petrous mass. Aggressive subtotal resection with decompression of the IAC was achieved through a right suboccipital craniotomy. Histopathological findings were consistent with CA. Conclusion: As was the case with this patient, we believe that CA should be included in the differential diagnosis of petrous region pathology with bony involvement. Surgery is warranted due to its expansive nature and to decompress the adjacent neural structures.

Epidermal inclusion cyst of the styloid process: a case report.

Nair DR, Pai PS, Chaturvedi P, Kumar R, Juvekar SL.
Department of Head and Neck Services, Tata Memorial Centre, Mumbai, India.

We report an unusual case of epidermal inclusion cyst of the styloid process which presented to us with decreased hearing and tinnitus. The patient underwent complete excision via a combined postaural cervical approach. The unusual location of the tumor and the absence of a history of trauma or intervention in that area added confusion to the diagnosis, which was finally made on histopathology.

Endolymphatic hydrops and therapeutic effects are visualized in 'atypical' Meniere’s disease.

Miyagawa M, Fukuoka H, Tsukada K, Oguchi T, Takumi Y, Sugiura M, Ueda H, Kadoya M, Usami S.
Department of Otorhinolaryngology, Shinshu University School of Medicine, Matsumoto, Japan.

A 53-year-old male with fluctuating low frequency sensorineural hearing loss and tinnitus, but without vertigo, was evaluated by MRI obtained by intratympanic injection of a gadolinium-based contrast agent (GBCA) before and after the administration of isosorbide. The endolymphatic hydrops was semiquantitatively evaluated by a 3.0-T MR scanner. For quantification, the affected side/contralateral side ratios were calculated. A gadodiamide (a kind of GBCA)-enhanced space surrounding the endolymph in the affected side with a 0.50 ratio (which may have represented endolymphatic hydrops) improved after isosorbide therapy to a 0.98 ratio. Thus, endolymphatic hydrops was demonstrated in a patient with 'atypical' Meniere’s disease (MD), suggesting that at least some atypical MD may share similar etiology with, and therefore be a continuum of, MD. Also, therapeutic effects could be visualized by using MRI. Therefore, MRI-based diagnosis of MD-related disease will be a powerful tool not only because of its precision but also its usefulness for therapeutic evaluation.
Tinnitus in postherpetic neuralgia.
J Headache Pain. 2009 Oct 23. [Epub ahead of print]

De Marinis M, Santilli V.
Department of Neurological Sciences, Sapienza University of Rome, Viale dell’ Università 30, 00185, Rome, Italy, m.de.marinis@mclink.it.

We describe a woman who developed postherpetic neuralgia (PHN) located on the skin areas of the left ophthalmic division of the fifth cranial nerve without ocular involvement. PHN was associated with tinnitus, which was located ipsilaterally to the painful side and increased in proportion to the intensity of pain. Tinnitus was responsive to treatment with duloxetine, 60 mg daily, and subsided when the PHN resolved. This is the first description of tinnitus in PHN.

[Objective tinnitus and essential palatal tremor in children: report of a case]
[Article in French]

Daval M, Cohen M, Mari I, Ayache D.
Fondation Adolphe de Rothschild, Unité d’Otologie-Otoneurologie, Paris, France.

Palatal tremor is a rare neurotological disorder responsible for objective tinnitus in children. Palatal tremor may be symptomatic of an underlying neurological disease or essential when a cause cannot be identified. We report a case of an essential palatal tremor in a 10-year-old girl complaining of clicking tinnitus. No treatment was undergone as she was not obviously bothered by the ear-clicking sound. Different treatment modalities have been used for distressing tinnitus related to palatal myoclonus. Recently several publications reported satisfactory results with botulinum toxin injection, which seems to be the treatment of choice.

Petrous apex cholesterol granuloma presenting as endolymphatic hydrops: a case report.

Kim HC, An YS, Ahn JH.
Department of Otolaryngology, Asan Medical Center, Ulsan University School of Medicine, Seoul, Korea.

A petrous apex cholesterol granuloma (PACG) is the most common lesion of the petrous apex mass. Affected patients present with various symptoms such as hearing loss, vertigo, headache, tinnitus, facial spasms, and diplopia. We report the case of a 32-yr-old man with a PACG, who was first misdiagnosed with Ménière’s disease. He was placed on a low-salt diet, and prescribed medication from another hospital, for several months, but the symptoms persisted and worsened. The patient presented to the emergency room complaining of left facial twitching and numbness. To rule out a central neurological lesion, temporal bone magnetic resonance imaging was carried out and a 2.5 cm mass with high signal intensity on T1- and T2-weighted imaging, without gadolinium enhancement, was found. Because of the hearing and facial problems, we drained cholesterol-bearing material via an infralabyrinthine approach using a computer aided image-guided surgical device, the BrainLAB(R). After the operation, the vertigo and hearing loss were no longer present. It is likely that the patient’s Ménière’s disease-like symptoms were due to the compression of the endolymphatic sac by a PACG.
Lightning strike to a vehicle causing acute acoustic trauma.

HNO. 2009 Sep 19. [Epub ahead of print]

Angerer F, Hoppe U, Schick B.

Hals-Nasen-Ohren-Klinik, Kopf- und Halschirurgie, Universitätsklinikum Erlangen, Deutschland.

The cochlea and vestibular organ is often affected in lightning strikes. A lightning strike to a motor vehicle with cochlear injury has not been described hitherto in the literature. We report the case of a 44-year-old male patient with sensorineural hearing loss and tinnitus after his car was struck by lightning. While hearing loss recovered using intravenous therapy, tinnitus persisted 6 months after the lightning strike. Cochlear injuries as an acute acoustic trauma have to be considered in lightning strikes and can occur when a car is struck by lightning.

Extradural plasmacytoma of temporal bone: report of 2 cases and review of literature.


1st Department of Otorhinolaryngology-Head and Neck Surgery, ENT Department, AHEPA University Hospital, Aristotle University of Thessaloniki, 54636 Thessaloniki, Greece.

OBJECTIVE: The aim of the study was to report 2 cases of extradural plasmacytoma (EP) with localization to middle ear that were diagnosed and managed in our department. METHODS: The first patient was a 60-year-old man with progressive hearing loss, tinnitus, recurrent episodes of otalgia, and otorrhea in his right ear during the last 2 years. The second patient was a 66-year-old man who presented with aural fullness in his right ear and a mild pain in the region of right mastoid. Mild hearing loss and episodes of dizziness with sensation of falling for about 6 months were reported in the clinical history. CONCLUSIONS: The prognosis of EP is considered favorable in regard to the solitary bone plasmacytoma and multiple myeloma (MM). The differential diagnosis of EPs from other plasma cell dyscrasias and especially from MM is considered essential. It is a radiosensitive tumor and, especially for EPs of temporal bone, the combined treatment of surgery resection and postoperative radiation seems to provide the best local control and the lower risk of occurrence. The therapeutic strategy includes a close follow-up of the patients because of the risk of occurrence and/or dissemination into MM. The 10-year survival rate reaches 70% with the appropriate therapy.

Neuro-Behçet’s disease with dizziness.

Auris Nasus Larynx. 2009 Aug 18. [Epub ahead of print]

Sugita-Kitajima A, Koizuka I.

Department of Otolaryngology, St. Marianna University, School of Medicine, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan.

A 30-year-old man had complete-type Behçet’s disease since he was 23 years old. Disease signs and symptoms were well controlled. After experiencing no symptoms for some years, however, he experienced dizziness, headache, fever, dysarthria, right facial nerve palsy, and right tinnitus. He showed spontaneous horizontal-rotatory nystagmus directed toward the right side, and upbeat nystagmus. T2-weighted and fluid-attenuated inversion recovery MRI showed slight hyperintense signals in the medulla oblongata, pons, and left midbrain. Neurological involvement in Behçet’s disease was diagnosed.
Acute hearing loss, dysarthria, dysphagia, and a rubbery intraoral mass in an 18-year-old woman.

Aitken L, Levin D, Blau A, Lewin MR.
The Arizona College of Osteopathic Medicine of Midwestern University, Glendale, AZ, USA.

Rhabdomyosarcoma is the most common soft tissue tumor of childhood, frequently presenting in the head and neck, genitourinary tract, or extremities. We present a case of rhabdomyosarcoma in which an 18-year-old woman presented with abrupt onset unilateral hearing loss, tinnitus, dysarthria, dysphagia, and a new painless red bump on the palate. With an alveolar subtype and older age, both predictors of poor prognosis, early recognition of disease of these symptoms is vital.

Recovery of sensorineural hearing loss following operative management of a posterior fossa arachnoid cyst. Case report.

Jayarao M, Devaiah AK, Chin LS.
Department of Neurosurgery, Boston Medical Center, Boston, Massachusetts, USA.

Arachnoid cysts are benign, intraarachnoid cysts filled with cerebrospinal fluid that are usually encountered in the middle cranial fossa. If present in the posterior fossa, they usually produce nonspecific signs and symptoms such as headaches, dizziness and vertigo. We report the rare presentation of a young girl with right-sided sensorineural hearing loss and tinnitus secondary to a right cerebellopontomedullary arachnoid cyst. The patient underwent a suboccipital retrosigmoid (retromastoid) craniectomy with fenestration of the arachnoid cyst. Subsequently, the patient experienced improvement in hearing with near-complete resolution of sensorineural hearing loss. To the authors’ knowledge, postoperative near-complete resolution of hearing loss secondary to posterior fossa arachnoid cysts in a pediatric patient has not been previously reported. The authors also review the literature with respect to posterior fossa arachnoid cysts and discuss their clinical features, diagnosis, and management.

Postpartum vertigo and superior semicircular canal dehiscence syndrome.

Ogutha J, Page NC, Hullar TE.
Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Missouri 63110, USA.

BACKGROUND: Superior semicircular canal dehiscence is a recently described cause of imbalance, hearing loss, and tinnitus. Symptoms may begin after abrupt changes in intracranial or middle ear pressure. CASE: This patient presented with a 6-year history of imbalance, hearing loss, and pulsatile tinnitus beginning when she was pushing during labor. A temporal-bone computed tomography scan showed a dehiscence of the superior semicircular canal. Surgical repair of the dehiscence through the middle cranial fossa resulted in immediate resolution of the patient's symptoms, and she returned to full activity within 3 weeks. CONCLUSION: Superior semicircular canal dehiscence is recognized increasingly as a cause of multiple otologic symptoms. Obstetricians and gynecologists with patients complaining about postpartum vertigo should inquire about symptom onset and focus their questions around events during the second stage of labor. Patients with symptoms of dehiscence should be referred to a neurootologist for treatment, including possible surgical repair.
Idiopathic intracranial hypertension in a young male

Walden, J\textsuperscript{a}, Skorin, L\textsuperscript{b}

\textsuperscript{a}Pacific University, College of Optometry, Forest Grove, OR, United States, \textsuperscript{b}Albert Lea Medical Center, Mayo Health System, 404 West Fountain Street, Albert Lea, MN 56007, United States

Idiopathic intracranial hypertension, also known as pseudotumor cerebri, is a condition typically associated with young, obese females.\textsuperscript{1-3} Due to this higher prevalence in females, this condition has been studied and reported much more in females than males. Patients usually present with a complaint of headache, transient visual obscurations, tinnitus, and diplopia.\textsuperscript{1-3} Papilledema is seen upon dilated fundus examination, and there is an absence of other pathology causing increased intracranial pressure.\textsuperscript{1-3} While these signs and symptoms do occur in males with idiopathic intracranial hypertension, the presentation and course of this disease in males appears to be slightly different compared to females. This report discusses a case of idiopathic intracranial hypertension in a young, obese male.

A case of unilateral sudden deafness following dissection of the basilar artery

Okada, M\textsuperscript{a}, Hyodo, J\textsuperscript{a}, Gyo, K\textsuperscript{a}, Kobayashi, T\textsuperscript{b}

\textsuperscript{a}Ehime University, Graduate School of Medicine, \textsuperscript{b}Ehime Prefectural Central Hospital

A 55-year-old woman suddenly noticed right hearing loss and tinnitus. Several days later, she lost consciousness, and was referred to Ehime Prefectural Central Hospital. Computed tomography (CT) showed subarachnoidal hemorrhage at the right cerebellopontine angle. However, subsequent CT-angiography and four-vessel cerebral angiography could not detect the exact cause of hemorrhage, such as aneurysm and arterial dissection. When she regained consciousness a few days later, she noticed worsening of right hearing loss and dizziness. Pure-tone audiogram showed complete deafness in the right ear. Distortion product otoacoustic emission and auditory brainstem response were not elicited in the right ear. Caloric test demonstrated canal paresis of the right ear with normal response in visual suppression. There were no neurological deficits other than right VIIIth nerve damage. Cerebral infarction and vasospasm were negative in magnetic resonance imaging (MRI) and MR-angiography performed on the 5th day. One month after onset, four-vessel angiogram demonstrated stenosis of the basilar artery near the branching site of AICA. These findings suggested that her deafness and disequilibrium were due to inner ear ischemia caused by dissection of the basilar artery, which also caused subarachnoidal hemorrhage.
## Multi-Site Evaluation of Progressive Tinnitus Management

<table>
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### Purpose
This multi-site study will evaluate the implementation of Progressive Tinnitus Management (PTM), which combines both Audiology and Psychology approaches to Tinnitus Management. Those Veterans who require intervention for tinnitus have different levels of need, and this progressive approach gives them the appropriate level of intervention.

### Condition(s)
Tinnitus

### Interventions
- Procedure: Progressive Tinnitus Management
- Procedure: Usual Care

### Study type and design
Interventional; Treatment, Randomized, Open Label, Parallel Assignment, Efficacy Study

### Official title:
Multi-Site Evaluation of Progressive Tinnitus Management

### Arms
1: Experimental: Progressive Tinnitus Management  
2: Usual Care

### Assigned Interventions
1: Procedure: Progressive Tinnitus Management  
The program follows a five-level “progressive intervention” model that addresses the various needs of tinnitus patients in a systematic and hierarchical manner—from initial contact with a VA provider through long-term treatment. The five levels of progressive intervention are: 1) Triage; 2) Audiologic Evaluation; 3) Group Education; 4) Interdisciplinary Evaluation; 5) Individualized Support  
2: Procedure: Usual Care  
VA audiologists typically (a) perform an audiologic evaluation; (b) fit hearing aids if necessary; and (c) provide basic information about tinnitus in the form of one-time, one-on-one informational counseling and/or a tinnitus handout. We therefore will provide these procedures for subjects who are randomized to receive usual care. Usual care subjects also can be referred for other clinical services as deemed appropriate.

### Primary Outcomes
- Tinnitus Handicap Inventory [Time Frame: Baseline, 6 months (from Baseline), 12 months (from Baseline)] [Designated as safety issue: No]

### Secondary Outcomes
- SF-36V [Time Frame: Baseline, 6 months (from Baseline), 12 months (from Baseline)] [Designated as safety issue: No]  
- Tinnitus & Hearing Survey [Time Frame: Baseline, 6 months (from Baseline), 12 months (from Baseline)] [Designated as safety issue: No]
## Detailed description

**Objectives.** We currently are completing a single-site pilot project to develop and evaluate Progressive Tinnitus Management (PTM). PTM takes into account the fact that most Veterans who complain of tinnitus do not require extensive intervention. The method thus is “progressive” in that a hierarchical approach is used to provide clinical services only to the degree needed by individual patients. Preliminary analyses of our pilot data provide evidence that PTM is an effective and efficient means of providing tinnitus management services to Veterans. Importantly, The Veterans Affairs (VA) Audiology and Speech Pathology Program Office has tentatively identified PTM as a standardized method of tinnitus management for use at all VA medical centers. It is essential to more definitively evaluate PTM for routine application at VA medical centers. Accordingly, the specific aim of this study is to conduct a randomized clinical trial at multiple VA medical centers to evaluate the effectiveness and clinical utility of PTM as compared to usual care.

**Plan.** The 3-year study will be based at the VA National Center for Rehabilitative Auditory Research (NCRAR), and PTM will be implemented and evaluated in a randomized clinical trial at the Memphis VA Medical Center and at the VA Connecticut Healthcare System (West Haven). During months 0-6: (a) All clinical materials for conducting PTM will be modified (especially with the addition of Cognitive-Behavioral Therapy - CBT); (b) training materials will be developed (the web-based PTM training program for VA audiologists will be updated; PTM training will be developed for VA psychologists); (c) by random selection, five audiologists (two in Memphis, three in West Haven) will be identified to conduct PTM and five (two in Memphis, three in West Haven) will be identified to conduct usual care; (d) the five PTM audiologists and the West Haven psychologist will receive PTM training (the West Haven study psychologist will develop the training). By month 7, the randomized clinical trial will be implemented at the two VA sites and will continue through year 3.

**Methods.** Prior to conducting the clinical trial, PTM will be modified to incorporate critical components of CBT at all levels of intervention so as to address the psychological effects of tinnitus. Qualifying Veteran subjects (n=150 at each site) will be randomized into either PTM or usual care. Self-perceived tinnitus handicap will be evaluated pre- and post-intervention for each subject using the Tinnitus Handicap Inventory. The five audiologists and two psychologists who participate in this study will be interviewed to determine their level of satisfaction with the PTM protocol to which they are assigned. Evaluation of the program will determine its efficacy, and will identify areas of needed improvement.

Although quantitative efficacy data are not yet complete, a great deal has been learned from the study for which the current proposed study would be a continuation. A preliminary process evaluation has

<table>
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<td>Study start</td>
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<tr>
<td>Expected primary completion date</td>
<td>December 2012 (Final data collection date for primary outcome measure)</td>
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revealed mostly positive results of implementing the PTM protocol at the James A. Haley (Tampa) Veterans’ Hospital. The process evaluation has already indicated a number of changes that need to be made to the protocol, and those changes will be made for the continuation study.

Relevance to VA’s Mission. Although tinnitus is the second most common service-connected disability, most VA medical centers do not provide comprehensive clinical services for Veterans suffering from tinnitus. This study will extend our current work, which has focused on the development of a comprehensive tinnitus management protocol that can be implemented efficiently in VA hospitals. Further development of PTM has the potential of providing needed tinnitus services to Veterans across the country for a relatively small cost and with minimal impact on individual VA hospitals.

<table>
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**Eligibility Inclusion Criteria**

Inclusion criteria include Veterans who:

1. are eligible for audiology services at their respective VAMC;
2. report the chronic presence of tinnitus (i.e., they have tinnitus that they can usually hear when they listen for it in a quiet room);
3. report that their tinnitus is at least a “small” problem; and
4. are willing to give verbal consent.

**Eligibility Exclusion Criteria**

Individuals will not be enrolled in this study if they:

1. are not Veterans;
2. have received previous tinnitus services at their VAMC;
3. report that their tinnitus is “no problem”;
4. are currently involved in tinnitus litigation; or
5. are unable (for any reason) to fulfill all of the requirements of the study.

**Contact**

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Tara Zaugg, (503) 220-8262 ext 56608; tara.zaugg@va.gov

**Locations**

VA Connecticut Health Care System (West Haven), West Haven, Connecticut, United States, 06516
VA Medical Center, Portland, Portland, Oregon, United States, 97201
VA Medical Center, Memphis, Memphis, Tennessee, United States, 38104

**Study chairs or principal investigators**

James Henry, PhD, VA Medical Center, Portland

**Study ID Numbers**

C7213R
Exploring Voluntary Control of Tinnitus

Current status | currently recruiting participants
---|---
Sponsors and collaborators | Washington University School of Medicine
Information provided by | National Institute on Deafness and Other Communication Disorders (NIDCD)
ClinicalTrials.gov Identifier | NCT00973648
Purpose | This pilot study aims to increase the understanding of tinnitus through the identification of potentially altered brain networks in patients who are able to voluntarily control or alter their tinnitus. Upon completion of this study, new knowledge will be gained about the changes in brain activity in people who are able to modify their tinnitus.
Condition(s) | Tinnitus
Study type and design | Observational; Cohort, Cross-Sectional
Official title: | Exploring Voluntary Control of Tinnitus: A Pilot Study
Detailed Description | Certain patients report that they are able to modulate the loudness or pitch of their tinnitus temporarily through various means, including attention re-direction or somatosensory mechanisms such as oral facial movements or head turn. This subset of patients may represent a unique opportunity for the researcher to gain insight into the mechanisms responsible for tinnitus. Neural activity in the brain has been linked to increases in blood flow and blood oxygenation. These changes in the concentration of oxyhemoglobin versus deoxyhemoglobin alter the magnetic resonance signal of blood which may then be detected using an appropriate MR pulse sequence as blood-oxygen-level-dependent (BOLD) contrast. In addition to increases in blood flow due to evoked neural activity, the brain exhibits continuous low frequency spontaneous activity. These fluctuations tend to be synchronous in functionally related, but spatially distinct, regions of the brain even when not performing a prescribed task. The phrase functional connectivity has been used to implicate the neural activity that facilitates the coordinated activity of functionally related brain regions.
This study will use functional connectivity magnetic resonance imaging (fcMRI) to measure the network of synchronous brain activity in patients with tinnitus. Several targeted networks are those linked to the auditory system, attention, and control systems and the emotion systems linked to prefrontal cortex. Previously, functional MRI (fMRI) used changes in blood flow and blood oxygenation within the brain to detect which isolated regions of the brain were active during a task.
The goal of functional connectivity research is to describe a pattern of interactions or a picture of the connectivity that occurs within distinct regions of the brain when the individual is not involved in a task.

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>Changes in brain neural activity between before and after tinnitus modulation as detected on functional connectivity MRI. [Time Frame: After completion of functional connectivity MRI] [Designated as safety issue: No]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected total Enrollment</td>
<td>15</td>
</tr>
<tr>
<td>Study start</td>
<td>August 2009</td>
</tr>
<tr>
<td>estimated study completion date</td>
<td>July 2010</td>
</tr>
<tr>
<td>Estimated Primary Completion Date</td>
<td>July 2010 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 Years to 80 Years</td>
</tr>
<tr>
<td>Gender</td>
<td>both</td>
</tr>
<tr>
<td>Accepts health volunteers</td>
<td>no</td>
</tr>
<tr>
<td>Sampling Method</td>
<td>Non-Probability Sample</td>
</tr>
<tr>
<td>Study Population</td>
<td>Speciality clinic Community health centers Solicitation of participants from American Tinnitus Association and Acoustic Neuroma Society Research database</td>
</tr>
</tbody>
</table>
| Eligibility Inclusion Criteria | • Adults, between the ages of 18 and 80 years.  
• Idiopathic, subjective, troublesome, unilateral or bilateral, non-pulsatile tinnitus of 6 month’s duration or greater.  
• Patient has some voluntary control over their tinnitus, whether through attention redirection or somatosensory control, such as orofacial movements or head turn.  
• Able to give informed consent.  
• English-speaking |
| Eligibility Exclusion Criteria | • Patients with tinnitus related to cochlear implantation, retrocochlear lesion, or other known anatomic/structural lesions of the ear and temporal bone.  
• Patients with hyperacusis or misophonia (hyper-sensitivity to loud noises).  
• Patients with cardiac pacemakers, intracardiac lines, implanted medication pumps, implanted electrodes in the brain, or other intracranial metal objects with the exception of dental fillings or any other contraindication for MRI scan.  
• Patients with an acute or unstable medical condition including all individuals with any significant heart disease, history of seizures, pneumonia, recent hip fracture (within 3 months), acute GI bleed, uncontrolled hypertension, or other disorders which would require stabilization prior to initiation of imaging.  
• Patients with a history of a brain-related injury or brain-related illness such as increased intracranial pressure, brain mass, Huntington’s chorea). |
- Patients currently taking psychoactive drugs that cannot be suspended for several days prior to imaging.
- Weight over 350 pounds.
- Patients with a history of claustrophobia.
- Patients who have an inability to lay flat for 1 hour.
- Patients with tinnitus related to Workman’s Compensation claim or litigation-related event.
- Patients whose ability to give informed consent is in question.
- Any exclusions from radiology screening.

**Contact**

Funmi T. Okuyemi, MD, 314-362-4356; okuyemio@ent.wustl.edu
Marie T. Scott, BA, 314.362.5296; scottm@ent.wustl.edu

**Locations**

Washington University School of Medicine, St. Louis, Missouri, United States, 63110

**Principal investigator**

Jay F. Piccirillo, MD

**Responsible party**

Washington University (Jay F. Piccirillo, MD)

**Study ID Numbers**

09-0481

**Last Updated**

September 8, 2009

**Record first received**

September 8, 2009

**ClinicalTrials.gov Identifier**

NCT00973648

**Health Authority**

United States: Federal Government

### Efficacy, Safety, Tolerability of Neramexane in Patients With Subjective Tinnitus

**Current status**

currently recruiting patients

**Sponsors and collaborators**

Merz Pharmaceuticals GmbH

**Information provided by**

Merz Pharmaceuticals GmbH

**ClinicalTrials.gov Identifier**

NCT00955799

**Purpose**

The purpose of this study is to investigate the safety and efficacy of neramexane mesylate in the treatment of subjective tinnitus in comparison to placebo.

**Condition(s)**

Subjective Tinnitus

**Interventions**

Drug: Neramexane mesylate
Drug: Placebo

**Phase**

III

**Study type and design**

Interventional; Treatment, Randomized, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Placebo Control, Parallel Assignment, Safety/Efficacy Study

**Official Title**

A Randomized, Double-Blind, Placebo-Controlled, Clinical Evaluation of the Efficacy, Safety and Tolerability of Neramexane in Patients With Subjective Tinnitus
<table>
<thead>
<tr>
<th>Arms</th>
<th>Neramexane mesylate: Experimental Double-blind treatment period of 29 weeks up to 75 mg Neramexane mesylate per day Placebo: Placebo Comparator Placebo: identical placebo tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assigned Interventions</td>
<td>Drug: Neramexane mesylate Double-blind treatment period of 29 weeks up to 75 mg Neramexane mesylate per day Drug: Placebo Double-blind treatment period of 29 weeks placebo</td>
</tr>
<tr>
<td>Primary Outcomes</td>
<td>TBF-12 (Tinnitus-Beeinträchtigungs-Fragebogen-12 &quot;Tinnitus Handicap Inventory-12&quot;) total score change from baseline to end of treatment, TSSw [Time Frame: Screening, Baseline, week 5, 11, 17, 29] [Designated as safety issue: No]</td>
</tr>
<tr>
<td>Secondary Outcomes</td>
<td>See above TBF-12 factorial scores, individual responder rate, Tinnitus Rating Scale, APSA Questionnaire, safety parameters, population pharmacokinetics, optional pharmacogenetics [Time Frame: 29 weeks] [Designated as safety issue: Yes]</td>
</tr>
<tr>
<td>Expected total Enrollment</td>
<td>400</td>
</tr>
<tr>
<td>Study start</td>
<td>September 2009</td>
</tr>
<tr>
<td>Estimated Study Completion Date</td>
<td>August 2011</td>
</tr>
<tr>
<td>Estimated Primary Completion Date</td>
<td>August 2011 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 Years to 75 Years</td>
</tr>
<tr>
<td>Gender</td>
<td>both</td>
</tr>
<tr>
<td>Accepts health volunteers</td>
<td>no</td>
</tr>
<tr>
<td>Eligibility Inclusion Criteria</td>
<td>Patients aged between 18 and 75 years with a clinical diagnosis of first onset, persistent (i.e., tinnitus should never be absent for &gt; 24 hours in a row), subjective, uni- or bilateral subacute tinnitus</td>
</tr>
<tr>
<td>Eligibility Exclusion Criteria</td>
<td>• Clinical diagnosis of intermittent or pulsatile tinnitus • Patients who have tinnitus as a concomitant symptom of an otological/neurological disease (such as otitis media, Menière’s disease, otosclerosis, etc)</td>
</tr>
<tr>
<td>Contact</td>
<td>Janos Csikos, MD, 0049 69 1503 ext 0</td>
</tr>
<tr>
<td>responsible party</td>
<td>Merz Pharmaceuticals GmbH ( Dr. Janos Csikos )</td>
</tr>
<tr>
<td>Study ID Numbers</td>
<td>MRZ 92579/TI/3003, EudraCT Number 2009-011246-25</td>
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<tr>
<td>Last Updated</td>
<td>November 13, 2009</td>
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<tr>
<td>Record first received</td>
<td>August 6, 2009</td>
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<td>ClinicalTrials.gov Identifier</td>
<td>NCT00955799</td>
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<td>Health Authority</td>
<td>United States: Food and Drug Administration</td>
</tr>
<tr>
<td>Current status</td>
<td>currently recruiting patients</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Sponsors and collaborators</td>
<td>NeuroSystec Corporation</td>
</tr>
<tr>
<td>Information provided by</td>
<td>NeuroSystec Corporation</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00957788</td>
</tr>
</tbody>
</table>

**Purpose**

This research study involves an experimental drug (NST_001) and a delivery system. The main purpose of this research study is to investigate the safety of NST-001, delivered directly to the inner ear for the treatment of tinnitus.

**Condition**

Tinnitus

**Intervention**

Drug: NST-001

**Phase**

I

**Study type and design**

Interventional; Treatment, Non-Randomized, Open Label, Uncontrolled, Parallel Assignment, Safety/Efficacy Study

**Official title**

Safety and Feasibility Study of NST - 001 in Inner Ear Using Neuroject Injection Set for the Treatment of Tinnitus

**Arms**

- Cohort 0: Experimental
- Cohort 1: Experimental
- Cohort 2: Experimental
- Cohort 3: Experimental

**Assigned Interventions**

- Drug: NST-001 Comparison of different dosages of drug.
- Drug: NST-001 Comparison of different dosages of drug.
- Drug: NST-001 Comparison of different dosages of drug.
- Drug: NST-001 Comparison of different dosages of drug.

**Primary Outcomes**

Subjects will be followed for identification and frequency of drug or procedure-related adverse events. [Time Frame: At each follow-up visit.][Designated as safety issue: Yes]

**Secondary Outcomes**

Observe any effect on tinnitus as determined by the visual analog scale, subject tinnitus diary, and investigator interview. [Time Frame: At each follow-up visit.][Designated as safety issue: No]

**Expected total Enrollment**

24

**Study start**

January 2009

**Estimated Study Completion Date**

December 2010
Estimated Primary Completion Date | December 2010 (Final data collection date for primary outcome measure)
--- | ---
Participants (age) | 18 Years to 70 Years
Gender | both
Accepts health volunteers | no
Eligibility Inclusion Criteria | • Patients able to provide voluntary consent.
• Severe tinnitus in one ear that began no more one year ago.
• Ear to be treated must be deaf or have profound hearing loss.
• Subjects with cardiac disease or hypertension, must have table disease for at least 6 months.
• Subject must have intact cochlear nerve on the ear to be treated.
• Women of childbearing potential (i.e., not post-menopausal or surgically sterilized) must agree to use adequate birth control methods as recommended by the study physician.
Eligibility Exclusion Criteria | • Current diagnosis of bilateral tinnitus.
• Current diagnosis or history of pancreatitis.
• Females that are pregnant or lactating.
• Use of investigational drugs within the previous 30 days.
• History of drug dependency or other substance abuse.
contact: | Randall Sanabria, MD, 661-702-6880; rsanabria@neurosystec.com
Thomas Lobl, PhD, 661-702-6880; tlobl@neurosystemc.com
Location | France, Cedex, Hôpital Avicenne, Bobigny, Cedex, France, 93009
Principal investigator | Bruno Frachet, MD, Hôpital Avicenne
Responsible party | NeuroSystec Corporation ( Randall Sanabria - Director Clinical Projects )
Study ID Numbers | NST-CP-02
Last Updated | August 17, 2009
Record first received | August 10, 2009
ClinicalTrials.gov Identifier | NCT00957788
Health Authority | France: Afssaps - French Health Products Safety Agency; France: French Data Protection Authority

**Study of Low Level Laser Therapy and Tinnitus Relief**

Current status | terminated
Sponsors and collaborators | Erchonia Medical, Inc.
Information provided by | Erchonia Medical, Inc.
ClinicalTrials.gov Identifier | NCT00845975
---|---
Purpose | The purpose of this study is to determine if low level laser light therapy might help to relieve tinnitus in adults.
Condition(s) | Tinnitus
Interventions | Device: Hearing Laser#1
Device: Hearing Laser #2
Study type and design | Interventional; Treatment, Randomized, Double Blind (Subject, Investigator, Outcomes Assessor), Placebo Control, Parallel Assignment, Efficacy Study
Detailed Description | Tinnitus is the perception of sound, such as a ringing or hissing, that occurs in the ears or head in the absence of external stimuli. About 40-50 million people in the United States report experiencing tinnitus; 10-12 million have sought medical help for their tinnitus, with 2.5 million reporting their tinnitus as debilitating. As a result of the distressing nature of tinnitus, it is often accompanied by anxiety, depression and sleep difficulties.
Tinnitus is most often caused by sensorineural hearing loss due to presbyacusis (aging) or noise damage. It is believed that the tinnitus results when spurious neuro-electrical signals are produced by diseased, degenerated or damaged cochlear hair cells and interpreted by the brain as tinnitus.
There is presently no cure for tinnitus. Current management strategies include using other external sounds to distract from the tinnitus, teaching relaxation and stress reduction techniques, and prescription medications to help ease stress, anxiety, depression and sleep difficulties. However, in general, current tinnitus management techniques are only minimally effective. It is believed that low level laser light therapy may offer a simple, non-invasive means of relieving the symptoms of tinnitus. In theory, low level laser light penetrates targeted tissues to stimulate the mitochondria in underlying cells to produce energy through the production of ATP (adenosine triphosphate). In turn, the enhanced ATP fuels cellular energy and enhances blood flow to the cochlear hair cells (cilia) to assists in regulating the electrical signals disrupted by the diseased and/or degenerated cochlear hair cells. With the taming of the spurious electrical signals, the brain no longer has a basis to perceive the noise known as tinnitus.
Arms | A: Placebo Comparator
B: Experimental
Assigned Interventions | Device: Hearing Laser #2
Comparison of active low level light therapy lasers with placebo devices.
Device: Hearing Laser#1
Comparison of active low level light therapy lasers with placebo devices.
<table>
<thead>
<tr>
<th><strong>Primary Outcome Measures</strong></th>
<th>Change from baseline to study endpoint in the Total score on the Tinnitus Handicap Inventory (THI). [ Time Frame: one week ] [ Designated as safety issue: No ]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary Outcome Measures</strong></td>
<td>Beck Depression Inventory-II (BDI-II)Spielberger State-Trait Anxiety Inventory - Trait portion [ Time Frame: 4 weeks ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td><strong>Expected total Enrollment</strong></td>
<td>19</td>
</tr>
<tr>
<td><strong>Study start</strong></td>
<td>August 2008</td>
</tr>
<tr>
<td><strong>Estimated Study Completion Date</strong></td>
<td>November 2008</td>
</tr>
<tr>
<td><strong>Estimated Primary Completion Date</strong></td>
<td>November 2008 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td><strong>Participants (age)</strong></td>
<td>18 Years and older</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>both</td>
</tr>
<tr>
<td><strong>Accepts health volunteers</strong></td>
<td>yes</td>
</tr>
</tbody>
</table>
| **Eligibility Inclusion Criteria** | • Total score on the Tinnitus Handicap Inventory (THI) of at least 20.  
• Tinnitus is on-going; present for more than 50% of the time over the past 6 months.  
• Subject has been previously evaluated by a qualified health care professional for tinnitus and received a diagnosis of etiology of tinnitus related to hearing impairment and/or noise exposure and/or unknown.  
• Any existing hearing loss stable over the past 12 months.  
• Willingness to abstain from partaking in other, non-study procedures indicated to lessen tinnitus and/or its perception, with the exclusion of wearing hearing aids for those subjects who enter the study using hearing aids, throughout the course of study participation.  
• Willing and able to refrain from engaging in activities or work involving loud noise exposure, such as hunting, rock concerts and work situations that involve working around loud machinery, construction sites, etc., throughout the course of study participation.  
• 18 years or older.  
• Male or female.  
• English as primary spoken language. |
| **Eligibility Exclusion Criteria** | • Presence of any of the following or in the subject’s medical history:  
• physical trauma or surgery to the head or neck  
• uncontrolled hypertension  
• current or prior surgically removed acoustic neuroma middle ear infection/active drainage from the ear and/or history of either within the previous 90 days  
• impacted cerumen  
• thyroid disease  
• vascular disorders  
• TMJ disorder  
• nutritional deficiency  
• aneurysm |
- multiple sclerosis
- Episodic or infrequent tinnitus
- Somatic or pulsatile tinnitus
- Prior history of sudden hearing loss and/or fluctuating hearing levels.
- Consistent use of any of the following drugs within the past 30 days:
  - NSAIDS; aspirin and other salicylates; Lasix and ther “loop”diuretics; “mycin” antibiotics such as vancomycin; quinine and related drugs; Chemotherapy agents such as cis-platin.
- Acute or chronic vertigo/dizziness.
- Prior diagnosis of central auditory processing disorder.
- Ménière’s disease.
- Tympanic membrane perforation or tubes.
- Prior stapedectomy
- Prior mastoidectomy.
- Otosclerosis.
- Otosyphilis.
- Labyrinthitis.
- Auditory nerve damage.
- Stapedius myoclonus syndrome.
- Brain and/or brainstem injury.
- Cochlear implant.
- Photosensitivity disorder.
- Active/open infection, wound or other external trauma to the areas to be treated with the Hearing Laser.
- Pregnant or lactating.
- Serious mental health illness such as dementia or schizophrenia; psychiatric hospitalization in past two years.
- Developmental disability or cognitive impairment that would make it difficult for the subject to partake in the clinical study, including adequate comprehension of the informed consent form and ability to record the necessary measurements.
- History of drug or alcohol abuse.
- Involvement in litigation and/or a worker’s compensation claim and/or receiving disability benefits related to tinnitus and/or hearing loss.
- Participation in research in the past 30 days.

Locations
- United States, California, McDonald Hearing Aid Center, Sacramento, California, United States, 95825

Principal investigator
- Louis A Looper, MA, CCC-A, McDonald Hearing Aid Centers

Responsible party
- Erchonia Medical, Inc. (Mr. Steven Shanks, President)

Study ID Numbers
- TS-001

Last Updated
- June 25, 2009

Record first received
- February 16, 2009

ClinicalTrials.gov Identifier
- NCT00845975

Health Authority
- United States: Institutional Review Board
### Current status

enrolling patients by invitation only

### Sponsors and collaborators

London School of Hygiene and Tropical Medicine  
University of Cambridge  
University of Liverpool

### Information provided by

London School of Hygiene and Tropical Medicine

### ClinicalTrials.gov Identifier

NCT00916305

### Purpose

In 1986 The Medical Research Council estimated that 4 million UK adolescents were at risk of hearing damage from over-exposure to loud music from personal audio players (PAPs), gigs, clubs, pubs and festivals. Since that time social noise exposure is estimated to have tripled to 19% of young people. The European Commission commissioned a report that estimated 5-10% of personal audio player users are risking permanent hearing loss and tinnitus by listening to music at high volumes for more than 1 hour a day for 5 years or more. Up to 246 million PAPs were sold in Europe in 2008, and 200 million mobile phones, many of which now have built-in audio players. Nevertheless, a recent survey showed that only 8% of young people identify hearing loss as a health problem. The Royal National Institute for the Deaf (RNID) undertook two surveys of young people in the UK to analyse listening behaviours as part of their “Don’t Lose the Music” campaign. As a consequence they offer listening advice given by flyers at events and online at the dedicated website. There have been no studies to confirm if such advice is effective in reducing noise exposure.

Aim: This study will pilot a methodology for a randomised controlled trial to test the effectiveness of a publically-available online video in changing the listening habits of young music lovers i.e. reduce the volume and number of hours of exposure.

Hypothesis: A video and adapted sound track demonstrating the experience of noise-induced hearing loss and tinnitus accessed online will change the listening habits of 18-25 year-olds.

### Condition

Noise-induced Hearing Loss and Tinnitus

### Intervention

Other: Modified Audio video  
Other: Audio video

### Study type and design

Interventional; Prevention, Randomized, Single Blind (Outcomes Assessor), Active Control, Single Group Assignment, Efficacy Study

### Official title

Pilot Study of an Intervention Among Young People to Prevent Noise-induced Hearing Loss and Tinnitus

### Detailed Description

Participants aged 18-25 years will be recruited by approaching staff at the LSHTM for recommendations of offspring or friends. Staff will be given information about the study and asked to provide an email address if the recruits are willing.

After obtaining informed consent online, participants will be randomized to active intervention i.e. an audio video demonstrating

- Normal hearing
- Temporary hearing damage after one night at a loud club
- Noise-induced hearing loss after repeated exposure (e.g. repeated clubbing for several months)
- Tinnitus related to noise exposure

Controls will watch the same video with an unaltered soundtrack.

Baseline data on listening habits and volumes will be collected prior to the intervention and again at 2 and 4 weeks. All data will be collected using an online system (survey monkey). At no point will researchers meet participants who will also not be known to each other.

Compliance will be assessed as participants will have to give a comment at the end of listening to the intervention.

Primary outcome: reduction is the proportion of time young people spend listening to music at a dangerous level i.e. equivalent to >80dB for 8 hours per day for 5 days a week

<table>
<thead>
<tr>
<th>Arms</th>
<th>A) Modified Audio video: Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The active intervention will be an audio video with 3 parts: 1) unaltered music. 2) the same music, but after modification to mimic noise induced hearing loss after one night at a loud club 3) hearing loss after repeated exposure to loud music 4) noise-induced tinnitus</td>
</tr>
<tr>
<td></td>
<td>B) Control: Sham Comparator</td>
</tr>
<tr>
<td></td>
<td>Participants will listen to the same music as the other arm, but only the track with unaltered music.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assigned Interventions</th>
<th>A) Other: Modified Audio video</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The active intervention will be an audio video with 3 parts: 1) unaltered music. 2) the same music, but after modification to mimic noise induced hearing loss after one night at a loud club 3) hearing loss after repeated exposure to loud music 4) noise-induced tinnitus</td>
</tr>
<tr>
<td></td>
<td>Other: Audio video</td>
</tr>
<tr>
<td></td>
<td>The active intervention will be an audio video with 3 parts: 1) unaltered music. 2) the same music, but after modification to mimic noise induced hearing loss after one night at a loud club 3) hearing loss after repeated exposure to loud music 4) noise-induced tinnitus</td>
</tr>
<tr>
<td></td>
<td>B) Other: Audio video</td>
</tr>
<tr>
<td></td>
<td>The active intervention will be an audio video with 3 parts: 1) unaltered music. 2) the same music, but after modification to mimic noise induced hearing loss after one night at a loud club 3) hearing loss after repeated exposure to loud music 4) noise-induced tinnitus</td>
</tr>
</tbody>
</table>

| Primary Outcome Measures | Reduction in dangerous listening behaviour defined as Daily Personal Noise Exposure in dB (LEPD) :to be safe this should total less than 80dB [Time Frame: 5 months] [Designated as safety issue: No] |

<table>
<thead>
<tr>
<th>Expected total Enrollment</th>
<th>164</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study start</td>
<td>July 2009</td>
</tr>
<tr>
<td>Estimated Study Completion Date</td>
<td>November 2009</td>
</tr>
<tr>
<td>Estimated Primary Completion Date:</td>
<td>October 2009 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 Years to 25 Years</td>
</tr>
<tr>
<td>Gender</td>
<td>both</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>Accepts health volunteers</td>
<td>yes</td>
</tr>
</tbody>
</table>
| Eligibility Inclusion Criteria | • between 18 and 25 years of age  
• used a portable listening device this year  
• normal hearing  
• no family history of hearing loss starting before 60 years of age |
| Eligibility Exclusion Criteria | • recurrent or recent hearing loss, tinnitus or ear disease  
• hearing loss beginning before 60 years of age in an immediate member of family |
| Location             | United Kingdom, London School of Hygiene and Tropical Medicine, London, United Kingdom, WC1E 7HT |
| Study director       | Andrew Smith, MB ChB, London School of Hygiene and Tropical Medicine |
| Responsible Party    | London School of Hygiene and Tropical Medicine (Professor) |
| Study ID Numbers     | Gilbert deafness 1                         |
| Last Updated         | July 24, 2009                             |
| Record first received | June 5, 2009                              |
| ClinicalTrials.gov Identifier | NCT00916305                |
| Health Authority     | United Kingdom: Research Ethics Committee  |