Dear Colleagues,

TRI is glad to offer you the second newsletter of the year. As usual you'll find a collection of abstracts of recently published literature as well as a list of upcoming events and clinical trials. May this information be useful and inspiring for your work and don't hesitate to forward it to your colleagues and friends. The more we share the closer we'll get to the solution.

In the same context, we encourage you to contact us with any suggestion you might have, whether it is for TRI or this newsletter and we will be happy to include it in the next issue of the letter.

Finally, please note that the 3rd Tinnitus Research Initiative meeting will take place in Stresa, Italy, from June 24th to 26th, 2009. Through symposia, poster sessions, educational workshops and meet the expert sessions, it will cover all aspects of tinnitus research from basic science to clinical management. Save the date and join us!

Berthold Langguth    Benjamin Questier    Susanne Staudinger

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Image Source: www.photocase.de
NEWS

TRI Symposium at the EFNS 2008 in Madrid
Similarities between tinnitus and other CNS disorders suggest synergistic effects. Read about the TRI symposium at the EFNS on the topic “Tinnitus: a CNS disorder. Opportunities and needs of a big market” under www.tinnitusresearch.org

Meetings

The 3rd Tinnitus Research Initiative Meeting - From Clinical Practice to Basic Neuroscience and back. An international conference in Tinnitus - will take place from June 24th - 26 th, 2009 in Stresa, Italy. For detailed information please look at our website www.tinnitusresearch.org

Awards

Ana Belén Elgoyhen, leader of the pharmacological workgroup of TRI, is the Laureate 2008 for Latin America of the “L’oreal UNESCO for women in Science awards”.

Ricardo Figueiredo and Andréia Azevedo, Brasil, TRI grantees and members of the TRI pharma workgroup, have been awarded for the best oral presentation of their research project “Tinnitus treatment with piribedil guided by acoustic otoemissions and electrocochleography” at the V Congress of the Rio de Janeiro ENT Society.

Winfried Schlee, University of Konstanz, is the winner of the Young Investigator Award 2008 for the excellent presentation of his TRI-funded research project “Directed coherence in the Resting Tinnitus Brain” at the “International Conference on Biomagnetism”. This meeting is the most important specialized meeting in the field of magnetoencephalography (MEG) making this award a high scientific acknowledgment for Winfried Schlee and his coworkers Thomas Hartmann, Nadja Müller, Isabel Lorenz, Sarang Dalal and Nathan Weisz.

Tanit Sanchez was awarded as the President of the X International Tinnitus Seminars, to be hold in Aracaju, Brasil, 2011.

TRI funded projects

TRI Database of Tinnitus Citations

The database was launched at the 2nd TRI Meeting in Monaco, 2007. A replacement CD of a fully updated version was distributed at the IXth International Tinnitus Seminars in Gothenburg and is available from the TRI office, info@tinnitusresearch.org.

The database uses EndNote which is by far the most widely used reference management system in the world. If EndNote is not available from your academic institution then it can be downloaded as a “trial version” from the website. The TRI database library can then be opened. Even when the trial period is over the TRI library can still be used and expanded but that additional libraries cannot be added.

The TRI database is managed by research librarian, Sally Wheater. Updates with additional citations are readily available and are easy for you to add. To receive each set of updates as they become available you need to register only once tinnitus.citations@gmail.com. The updates will then be sent with simple instructions on how to add them to your tinnitus library.
Upcoming Meetings Meetings exclusively dedicated to Tinnitus are marked red

**Sixteenth Annual Management of the Tinnitus Patient Conference**
When: September 18 – 20, 2008
Where: University of Iowa, Iowa, USA
Contact: Gareth Smith, University of Iowa, USA
Phone: +1 319-356-2471
E-Mail: gareth-smith@uiowa.edu

**IAPA 2008 – The XIV International Symposium of Audiological Medicine**
When: September 18 – 21, 2008
Where: Ferrarra, Italy
Contact: Organizing Office: Meet and Work Srl
Piazza del Sole e della Pace 5, 35031 Abano Terme (Padova), Italy
Phone: +39 (0) 532 237038
Fax: +39 80) 532 247709
E-Mail: audiologia@unife.it
Detailed information: http://www.iapacongress2008.it

**International Tinnitus Forum: Translation Research in Tinnitus Therapy IV – Transcranial Magnetic Stimulation**
When: September 20, 2008
Where: Chicago, Illinois
Contact: Dr. Barbara Goldstein
Phone: +1 718-773-8888
E-Mail: metrc@inch.com
Detailed information: http://www.tinnituscenter.com

**The Jackson Laboratory – The Mouse as an Instrument for Ear Research III**
When: September 18 – 21, 2008
Where: Bar Harbor, Maine
Phone: +1 (0) 207-288-6803
E-Mail: barbara.donovan@jax.org
Detailed information: http://courses.jax.org/2008/earmeeting08.html

**IVX World Congress of Psychiatry**
When: September 20 – 25, 2008
Where: Prague, Czech Republic
Contact: GUARANT International spol. s r.o.
Opletalova 22, 110 00 Prague 1, Czech Republic
Phone: +420 284 001 444
Fax: +420 284 001 448
E-Mail: wpa@guarant.cz

**American Academy of Otolaryngology-Head & Neck Surgery – 112th AAO-NHS Annual Meeting and OTO Expo**
When: September 22 – 24, 2008
Where: Chicago, Illinois
Phone: +1 (0) 703-515-1530
E-Mail: aaomt2@aol.com
Detailed information: http://www.entnet.org/conferencesandevents/
International Hearing Society (IHS) – 57th Annual Convention and Expo
When: September 24 – 28, 2008
Where: Savannah, Georgia, USA
Phone: +1 (0) 734-522-7200
Detailed information: http://ihsinfo.org/IhsV2/Conv2008/Index.cfm

53rd International Congress of Hearing Aid Acousticians
When: October 15 – 17, 2008
Where: Leipzig, Germany
Contact: EUHA
PO Box 40 06
55030 Mainz, Germany
Phone: +49 (0) 61 31/ 28 30-0
Fax: +49 (0) 61 31/ 28 30-30
E-Mail: info@euha.org
Detailed information: http://www.euha.org

The Ear Foundation – Cochlear implants 2008: The State of the Art
When: November 7, 2008
Where: Nottingham, United Kingdom
Phone: +44 (0) 115 942 7800
Detailed information: http://www.earfoundation.org.uk

European Academy of Otology and Neuro-Otology – 4th Instructional Workshop
When: November 13 – 16, 2008
Where: Pueblo Español Congress Palace, Palma de Mallorca, Spain
E-Mail: orlcongresos@seorl.net
or Erwin.offeciers@gza.be

32nd MidWinter Meeting of the Association for Research in Otolaryngology (ARO)
When: February 14 – 19, 2009
Where: Marriott Waterfront Hotel, Baltimore, MD, USA
Contact: Alex Springer
E-Mail: aspringer@talley.com
Detailed information: http://www.aro.org/mwm/mwm.html
12. Jahrestagung der Deutschen Gesellschaft für Audiologie e.V.
When: March 11 – 14, 2009
Where: Innsbruck, Austria
Contact: Dt. Gesellschaft für Audiologie e.V. Geschäftsstelle
c/o Haus des Hörens
Marie-Curie-Str. 2
26129 Oldenburg
Phone: +49 (0)4 41/2172-500
Fax: +49 (0)4 41/2172-550
E-Mail: info@dga-ev.com
Detailed information: http://www.dga-ev.com

AudiologyNOW! 2009
When: April 1 – 4, 2009
Where: Dallas Convention Center, Dallas TX, USA
Contact: Brittany Kuntz
Fax: +49 (0)4 41/2172-550
E-Mail: bkuntz@audiology.org
Detailed information: http://www.audiologynow.org

IFOS 2009 – XIX World Congress of Oto-Rhino-Laryngology
When: June 1 – 5, 2009
Where: São Paulo ANHEMBI Convention Center
São Paulo - Brazil
E-Mail: info@ifossaopaulo2009.com.br
Detailed information: http://www.ifossaopaulo2009.com.br

Human Brain Mapping – 15th Annual Meeting
When: June 18 – 22, 2009
Where: San Francisco, CA, USA
Detailed information: http://www.humanbrainmapping.org/sanfrancisco2009

9th EFAS Congress
When: June 21 – 24, 2009
Where: Tenerife, Canary Islands, Spain
Contact: Magna Congresos
Ctra. Gral. Santa Cruz Laguna nº293 Edif. Cristina 2ºA
38320 La Cuesta - La Laguna - S/C de Tenerife
Canary Islands - Spain
Phone: +39 0 2 72001824
E-Mail: congresos@magnacongresos.com
Detailed information: http://www.efas2009.org
3rd Tinnitus Research Initiative Meeting – From Clinical Practice to Basic Neuroscience and back. An international conference on Tinnitus

When: June 24 – 26, 2009
Where: Stresa, Italy
Contact: Organizing Office: Fondazione Ascolta e Vivi
Via V. Foppa
20144 Milan, Italy
Phone: +39 0 2 72001824
E-Mail: info@faev.org
Detailed information: http://www.tinnitusresearch.org

Conference on Implantable Auditory Prostheses

When: July 12 – 17, 2009
Where: Granlibakken Conference Center
Lake Tahoe, California
Contact: John Middlebrooks, Chair
Kresge Hearing Research Institute
University of Michigan
E-Mail: jmidd@umich.edu
Detailed information: http://www.hei.org/ciap/index.html

27th Politzer Society Meeting

When: September 3 – 5, 2009
Where: The Queen Elisabeth II Conference Centre, London, UK
Contact: Sterling Events Ltd, 62 Hope Street
Liverpool L1 9BZ UK
Phone: +44 (0) 151 709 8979
Fax: +44 (0) 151 708 9861
Detailed information: http://www.politzerlondon.com

Medical Physics and Biomedical Engineering World Congress 2009

When: September 7 – 12, 2009
Where: ICM, International Congress Center Munich, Germany
Contact: JVDE CONFERENCE SERVICES
Stresemannallee 15
60596 Frankfurt am Main, Germany
Phone: +49 (0)69 - 63 08-229/ -477
Fax: +49 (0)69 - 96 31-52 13
E-Mail: wc2009@vde.com

American Academy of Otolaryngology, Head and Neck Surgery Annual Meeting

When: October 4 – 7, 2009
Where: San Diego, CA, USA
Detailed information: http://www.entnet.org
Recently published literature (articles of authors who are funded by TRI are marked in blue)

I Epidemiology

Personality and Perception of Tinnitus.
Ear Hear. 2008 Jul 1. [Epub ahead of print]

Welch D, Dawes PJ.
Dunedin Multidisciplinary Health and Development Research Unit, Departments of 1Preventive and Social Medicine; and 2ORL-HNS Dunedin School of Medicine, University of Otago, Dunedin, New Zealand.

OBJECTIVES: Tinnitus has high prevalence and a wide range of etiologies and of impacts on sufferers. Our objective was to develop understanding of the role of personality in the perception of tinnitus in the general population. As a theoretical basis for this, we combined elements of a general model of signal detection with the ideas of ignition (development) and promotion (neural transmission) of tinnitus, and considered plausible roles for personality factors within this conceptual framework. DESIGN: We interviewed a birth cohort of 970 people aged 32 yr sampled from the general population. On the basis of questioning, we divided them into three groups, those without tinnitus, those with occasional tinnitus (including those with transient tinnitus of very brief duration), and those who experienced tinnitus most of the time. We also established how annoying or distressing the tinnitus was, and assessed personality using the Multidimensional Personality Questionnaire. RESULTS: Tinnitus was experienced rarely by 38.2% and half the time or more by 6.8% of those studied. Men and women did not differ in the amount of tinnitus reported, but women were more likely to find it annoying. People from lower socioeconomic backgrounds were more likely to report tinnitus. People with tinnitus were more socially withdrawn, reactive to stress, alienated, and less Self-Controlled. People who were more annoyed by tinnitus were more socially withdrawn, and men were more stress reactive and alienated. CONCLUSIONS: Our interpretation of the findings is that personality influences the persistence of tinnitus by influencing the tendency to be aware of it. Consideration of personality factors may improve the ability to tailor tinnitus therapies, and the concept of awareness may benefit treatment outcomes by showing tinnitus sufferers a means of internalizing the locus of control over their symptoms.

Auditory evaluation in patients with type 1 diabetes.

Pessin AB, Martins RH, Pimenta Wde P, Simões AC, Marsiglia A, Amaral AV.
Departments of Otorhinolaryngology, Ophthalmology and Head and Neck Surgery, School of Medicine, São Paulo State University, Botucatu, Brazil.

OBJECTIVES: We performed a prospective clinical study of the cochleovestibular symptoms and the risk cofactors and characteristics of hearing loss in patients with type 1 diabetes. METHODS: Group 1 consisted of 40 patients with type 1 diabetes, and group 2 consisted of 20 control subjects without diabetes. All participants answered a questionnaire, and their medical records were reviewed. They also were submitted to otorhinolaryngological examinations and to auditory tests (pure tone audiometry and acoustic immitance and auditory brain stem response [ABR] tests). RESULTS: Dyslipidemia, hypertension, retinopathy, and diabetic neuropathy were not frequent in the patients of group 1, but incipient nephropathy was present in 47.5% of them. The most frequent cochleovestibular symptoms were tinnitus and hearing loss. Sensorineural hearing loss was found in 4 patients of group 1 and was predominantly bilateral, symmetric, and affecting the high frequencies, coexisting with normal vocal discrimination. These patients had a longer time from diabetes diagnosis and had poor glycemia control. A delay of ABR interpeak latency I-III was observed in 11.25% of the group 1 ears. All patients of group 2 presented normal audiograms and ABR tests. CONCLUSIONS: In group 1, the most frequent cochleovestibular symptoms were tinnitus and hearing loss. The sensorineural hearing loss was mild, symmetric, and predominantly high-frequency. A delay of ABR interpeak latencies was detected in the patients of group 1 who had normal audiometric thresholds.
BACKGROUND: Tinnitus, a ringing in the ear perceived only by the person concerned, occurs not only in the general population but also among patients suffering from schizophrenia. They may be afflicted by tinnitus and acoustic hallucinations at the same time. Misinterpreting their schizophrenic illness, patients prefer to consult a family doctor or an ear, nose and throat (ENT) specialist rather than a psychiatrist if they mistake their acoustic hallucinations for tinnitus. Conversely, in schizophrenia patients, tinnitus of recent onset can be mistaken for acoustic hallucination and may be treated with neuroleptics rather than by a symptom-oriented management approach. This paper aims to present treatment approaches and criteria for distinguishing between acoustic hallucinations, which occur often in schizophrenia, and tinnitus, and to highlight treatment options. PATIENTS AND METHODS: From October 1999 to October 2004, we investigated 31 schizophrenic inpatients (17 men [55%], 14 women [45%] aged between 29 and 60 years, mean: 44 years) suffering from tinnitus. A total of 11 patients were treated mainly for tinnitus in a specialized neurootological clinic, 11 were treated in a psychiatric clinic, and 9 patients were treated in a psychiatric day center. All patients were examined using psychiatric and neurootological standards. RESULTS: Differences were found between tinnitus and acoustic hallucinations in the patients’ descriptions and the audiometric outcomes. Tinnitus was mainly found in higher frequencies ranging from 4000 to 8000 Hz. Tinnitus was masked at an average of 9.3 dB and a maximum of 15 dB above the auditory threshold. Six patients (19%) had normal hearing, while ten patients (32%) had unilateral hearing loss and 15 patients had bilateral hearing loss. Hearing aids were indicated in 14 patients, but only five patients accepted them. CONCLUSION: Schizophrenic patients suffering from tinnitus benefit from basic standards of tinnitus treatment. However, psychiatric specialists should also provide the drug treatment that is often necessary as well as psychoeducation for schizophrenia.

A study of twenty-one cases of low-frequency noise complaints.

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From 203 cases of low-frequency complaints a random selection of twenty-one previously unsolved cases were investigated. The main aim of the investigation was to answer the question whether the annoyance is caused by an external physical sound or by a physically non-existing sound, i.e. low-frequency tinnitus. Noise recordings were made in the homes of the complainants, and the complainants were exposed to these in blind test listening experiments. Furthermore, the low-frequency hearing function of the complainants was investigated, and characteristics of the annoying sound was matched. The results showed that some of the complainants are annoyed by a physical sound (20-180 Hz), while others suffer from low-frequency tinnitus (perceived frequency 40-100 Hz). Physical sound at frequencies below 20 Hz (infrasound) is not responsible for the annoyance - or at all audible - in any of the investigated cases, and none of the complainants has extraordinary hearing sensitivity at low frequencies. For comparable cases of low-frequency noise complaints in general, it is anticipated that physical sound is responsible in a substantial part of the cases, while low-frequency tinnitus is responsible in another substantial part of the cases.
Occupational noise-induced tinnitus: does it affect workers’ quality of life?


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ENT Department, Faculty of Medicine, Kirikkale University, Kirikkale, Turkey. nbayarmuluk@yahoo.com

OBJECTIVES: This prospective study aimed to investigate the quality of life of workers in a steel factory.

METHODS: The study group was composed of 16 male workers with tinnitus and 30 ears. Fifteen male workers without tinnitus and 30 ears were included into the control group. Workers were evaluated by questionnaire, pure-tone audiometry, and the SF-36 Health Survey. In the study group, tinnitus loudness levels (TLLs) were found.

RESULTS: In the study group, the domains general mental health and role limitations owing to emotional problems were significantly lower than in the control group. Older age, industrial noise exposure over a long period, higher noise exposure during work, and hearing loss secondary to occupational noise caused workers to experience higher TLLs. Ear headers protected workers more than earplugs, and TLLs were lower. Important factors that affect workers’ quality of life are maximum exposed noise levels, daily and total noise exposure time, and exposure to continuous noise. Occupational noise-induced tinnitus mainly causes emotional disability rather than physical disability. Emotionally impaired QOL results may be due to tinnitus-related psychological problems.

CONCLUSION: Workers should have knowledge about the hazardous effects of noise. Periodic health checkups and regular seminars have great importance. Workers must be aware of other ototoxic factors, such as medications and noisy music. In the future, researchers should develop a screening method to detect those with a more hereditary affinity to hearing loss.

Prevalence of high frequency hearing loss consistent with noise exposure among people working with sound systems and general population in Brazil: a cross-sectional study.

BMC Public Health. 2008 May 7;8:151.

El Dib RP, Silva EM, Morais JF, Trevisani VF.
Urgency Medicine and Evidence-Based Medicine Department, Brazilian Cochrane Centre, Federal University of São Paulo, Brazil. re.lucci@terra.com.br

BACKGROUND: Music is ever present in our daily lives, establishing a link between humans and the arts through the senses and pleasure. Sound technicians are the link between musicians and audiences or consumers. Recently, general concern has arisen regarding occurrences of hearing loss induced by noise from excessively amplified sound-producing activities within leisure and professional environments. Sound technicians’ activities expose them to the risk of hearing loss, and consequently put at risk their quality of life, the quality of the musical product and consumers’ hearing. The aim of this study was to measure the prevalence of high frequency hearing loss consistent with noise exposure among sound technicians in Brazil and compare this with a control group without occupational noise exposure.

METHODS: This was a cross-sectional study comparing 177 participants in two groups: 82 sound technicians and 95 controls (non-sound technicians). A questionnaire on music listening habits and associated complaints was applied, and data were gathered regarding the professionals’ numbers of working hours per day and both groups’ hearing complaint and presence of tinnitus. The participants’ ear canals were visually inspected using an otoscope. Hearing assessments were performed (tonal and speech audiometry) using a portable digital AD 229 E audiometer funded by FAPESP.

RESULTS: There was no statistically significant difference between the sound technicians and controls regarding age and gender. Thus, the study sample was homogenous and would be unlikely to lead to bias in the results. A statistically significant difference in hearing loss was observed between the groups: 50% among the sound technicians and 10.5% among the controls. This difference could be addressed to high sound levels. CONCLUSION: The sound technicians presented a higher prevalence of high frequency hearing loss consistent with noise exposure than did the general population, although the possibility of residual confounding due to unmeasured factors such as socioeconomic status cannot be ruled out.
Noise induced hearing loss and other hearing complaints among musicians of symphony orchestras.
Int Arch Occup Environ Health. 2008 Apr 11. [Epub ahead of print]

Jansen EJ, Helleman HW, Dreschler WA, de Laat JA.
ENT-Audiology, Academic Medical Center Amsterdam, Meibergdreef 9, Amsterdam, 1105 AZ, Netherlands, noor.jansen@amc.nl.

OBJECTIVES: An investigation of the hearing status of musicians of professional symphony orchestras. Main questions are: (1) Should musicians be treated as a special group with regard to hearing, noise, and noise related hearing problems (2) Do patterns of hearing damage differ for different instrument types (3) Do OAE have an added value in the diagnosis of noise induced hearing loss (NIHL) in musicians. METHODS: 241 professional musicians, aged between 23-64 participated. A brief medical history and the subjective judgment of their hearing and hearing problems were assessed. Musicians were subjected to an extensive audiological test battery, which contained testing of audiometric thresholds, loudness perception, diplacusis, tinnitus, speech perception in noise, and otoacoustic emissions. RESULTS: Most musicians could be categorized as normal hearing, but their audiograms show notches at 6 kHz, a frequency that is associated with NIHL. Musicians often complained about tinnitus and hyperacusis, while diplacusis was generally not reported as a problem. Tinnitus was most often localized utmost left and this could not be related to the instrument. It was usually perceived in high frequency areas, associated with NIHL. In general, musicians scored very well on the speech-in-noise test. The results of the loudness perception test were within normal limits. Otoacoustic emissions were more intense with better pure-tone thresholds, but due to large individual differences it can still not be used as an objective test for early detection of NIHL. CONCLUSIONS: Musicians show more noise induced hearing loss than could be expected on the basis of age and gender. Other indicators, such as complaints and prevalence of tinnitus, complaints about hyperacusis and prevalence of diplacusis suggest that musicians’ ears are at risk. Continuing education about the risks of intensive sound exposure to musicians, with the emphasis on the possible development of tinnitus and hyperacusis and the need for good hearing protection is warranted.

Questionnaire investigation of musicians’ use of hearing protectors, self reported hearing disorders, and their experience of their working environment.

Laitinen H, Poulsen T.
Heikki Helimäki Ltd, Helsinki, Finland. Heli.Laitinen@helimaki.fi

Musicians in symphony orchestras are exposed to harmful sound levels. Although research shows that industrial workers have a higher propensity to noise-induced hearing loss, musicians can also develop a hearing loss from noise exposure. Furthermore, musicians can suffer from tinnitus, hyperacusis, and distortion, among other hearing disorders, which can affect their work more severely than a hearing loss. This study investigated the use of hearing protectors, the prevalence of self-reported hearing disorders among musicians, and the importance of these hearing disorders to the musicians. The musicians at three Danish symphony orchestras were asked to complete a questionnaire on the topic. Results showed that Danish musicians are aware of the dangers of loud music, yet they rarely use hearing protectors and not always correctly; however, musicians with hearing disorders use hearing protectors more frequently. In addition, the musicians questioned suffered from different hearing disorders. Education is needed to change musicians’ opinion of hearing conservation and hearing protectors. The education must be directed to both the musicians and the administration of the symphony orchestras.
**Inner ear problems of Thai priest at Priest Hospital.**

Karnchanakas T, Tantanavat A, Sinsakontavat J.
Department of Ear Nose Throat, Priest Hospital, Bangkok, Thailand. tweporn@yahoo.com

BACKGROUND: The inner ear problems of Thai priest at Priest Hospital had never been reported previously, so Department of Ear Nose Throat try to correlate the metabolic disorder with inner ear problems. OBJECTIVES: 1) To study the fasting blood sugar (FBS), total cholesterol (T. Chol), low density lipoprotein (LDL), and triglyceride (TG), the factors expected to involve in inner ear problems of priests at Priest Hospital. 2) To compare the FBS, T. Chol, HDL, LDL, and TG of priests with inner ear problems at Priest Hospital. 3) To find the percentage of abnormal from FBS, T. Chol, LDL, and TG. MATERIAL AND METHOD: The study using 83 sampling of priests with inner ear problems and 107 priests as a controlled group. The research instruments used to collect data was the questionnaire which composed of general information, physical, ear-nose-throat and neurological examination, pure tone audiometry, brainstem evoke response audiometry (BERA) and the blood tests: FBS, T. Chol, TG, and LDL. The inner ear problems were composed of: 1) Dizziness 2) Hearing Loss 3) Tinnitus Aurium. The descriptive statistics were used to analyze the data from questionnaires and utilized frequency, percentage, standard deviation (S.D.) and t-test to achieve desired results. RESULTS: Priest at middle age and elderly with inner ear problems had greater FBS and TG than expected values of the control group. CONCLUSION: The middle age and elderly priests who had greater FBS and TG than expected values were sick with inner ear problems that causing dizziness, hearing loss and tinnitus aurium.

[**Tinnitus diagnosis and treatment on the basis of our experiences**]
[Article in Polish]

Olszewski J, Kowalska S, Kuśmierczyk K.
Klinika Otolaryngologii i Onkologii Laryngologicznej II Katedry Otolaryngologii UM w Łodzi. jolszewski@poczta.onet.pl

INTRODUCTION: The aim of the study was to analyse tinnitus diagnosis and treatment on the basis of our experiences. MATERIAL AND METHODS: 137 patients hospitalizated in Otolaryngology and Laryngological Oncology Clinic because of tinnitus (88 women - 64% and 49 men - 35,8%) were included to the study. The diagnostic procedures were unified that enabled put forward correct diagnosis. After history and otoscopy, detailed audiologic diagnostic procedures (pure tone audiometry, suprathreshold audiometry, speech audiometry, acoustic immittance measures, auditory brainstem responses) were taken. Electronystagmography and videonystagmography, tinnitus loudness match, head and neck radiologic examinations supplemented diagnostic procedures. Alternative tinnitus treatment options were applied. RESULTS: Study confirmed that tinnitus is the most frequent in patients above 50 years old (67,8% of participants). Tinnitus frequently coexist with bilateral sensorineural hearing impairment (69,1% of participants), 40,1% from analysed group of patients complained of tinnitus of medium frequencies and 30,6% of patients complained of high frequency tinnitus. 42,3% of participants suffered from vertigo. CONCLUSIONS: The risk of tinnitus increases in patients above 55 years old that suffer from metabolic conditions and cervical spondylosis. Tinnitus frequently coexist with bilateral sensorineural hearing impairment and are bilateral or they are noticeable in better hearing ear. The most beneficial to tinnitus is causal and symptomatic treatment with several methods application.
II Pathophysiology

Central nervous system neurodegeneration and tinnitus: a clinical experience. Part II: translational neurovascular theory of neurodegenerative CNS disease and tinnitus.

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Department of Otolaryngology, State University of New York, Downstate Medical Center, Brooklyn, NY 11203, USA. metrc@inch.com

The translation of a neurovascular hypothesis for Alzheimer’s disease to subjective idiopathic tinnitus (SIT) is presented as a challenge to the predominantly sensorineural view of SIT and its clinical application for tinnitus treatment. The concept of neurovascular dysfunction and neurodegeneration (ND) in SIT patients has been proposed and reported as an etiology in a particular subset of tinnitus patients with a diagnosis of medical-audiological tinnitus, through a medical-audiological tinnitus patient protocol, to be a predominantly central-type, severe, disabling SIT (n = 54 of 96). A medical-audiological ND tinnitus profile was the basis for selection of 18 SIT patients (n = 18 of 54) for nuclear medicine brain imaging (i.e., single-photon emission computed tomography or positron emission tomography, or both). Objective findings were reported in 16 of this cohort of 18 SIT patients selected for nuclear medicine imaging (88.9%). Classification of central nervous system (CNS) ND and tinnitus differentiated between (1) ND, nonspecific and of unknown etiology; (2) ND manifested by perfusion asymmetries in brain associated with ischemia (n = 11 of 18); and (3) ND CNS disease consistent with nuclear medicine criteria for senile dementia Alzheimer’s-type disease (n = 5 of 18). The diagnosis was associated with cerebrovascular disease (n = 16 of 18). The identification of pathological processes of inflammation and ischemia, linked to ND, in a particular cohort of SIT patients may provide a basis for establishing the medical significance and treatment of SIT and influence the clinical course of the tinnitus.

The THI questionnaire: psychometric data for reliability and validity of the Italian version.

Passi S, Ralli G, Capparelli E, Mammone A, Scacciatelli D, Cianfrone G.
Italian Association for Research on Deafness (AIRS), Italy. stefania.passi@libero.it

The main objective of this study was to determine reliability, validity, and reproducibility of the Italian version of the Tinnitus Handicap Inventory (THI) self-administered questionnaire aimed at evaluating the impact of tinnitus on the quality of life of subjects affected by this symptom. The questionnaire was presented to a sample of 443 subjects (285 men and 158 women; ages 19-86; mean age, 53) who were referred to our Tinnitus Centre in Rome and came from the entire national territory. All subjects reported as their main problem a tinnitus that had persisted for at least 6 months. Statistical analysis carried out on THI questionnaire results showed high internal consistency and reliability for the total scale (Cronbach’s alpha = .94). Despite the poor number of items, the THI proved useful for the functional scale (0.86), the emotional scale (0.89), and the catastrophic scale (0.75).

Tinnitus after cochlear implantation.
Auris Nasus Larynx. 2008 Jul 7. [Epub ahead of print]

Akdogan O, Ozcan I, Ozbek C, Dere H.
Ankara Numune Education and Research Hospital, 4th ENT Clinic, Attending Otolaryngolog Ankara, Turkey.

OBJECTIVE: The purpose of this study was to investigate properties of tinnitus which starts after cochlear implantation. Of the 17 adult patients in our cochlear implant group, four (23.5%) who had no pre-implantation tinnitus were eligible for the study. METHODS: Each patient was requested to complete a short questionnaire regarding his or her experience with tinnitus. Tinnitus match test was performed for each patient by using an Interacoustic Clinical Audiometer (model AC40; Assens, Denmark).
RESULTS: Tinnitus match test revealed a tinnitus frequency of a 4KHz for three and of a 6KHz for one patient. Mean value of the loudness score was calculated as 17.5dB SL. CONCLUSIONS: The results of this study emphasize the importance of counseling patients regarding risks of tinnitus after cochlear implantation.

Stability of Physiological Variables in Chronic Tinnitus Sufferers.
Appl Psychophysiol Biofeedback. 2008 Jul 4. [Epub ahead of print]
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The etiological tinnitus models propose that suffering can be caused and aggravated by heightened physiological arousal. Therefore psychophysiological treatments are applied. Stability of the measured parameters is essential for the use of biofeedback as well as to permit the attribution of changes to the administered treatment. The aim of our study was to investigate the 3-month reproducibility of psychophysiological parameters in 60 tinnitus patients. Using a repeated-measures design, the activity of these parameters was assessed twice during various stress and relaxation trials. The results showed that the measurements of frontalis, masseter and trapezius muscles were stable, while for the sternocleidomastoid, the skin conductance level (SCL) and the skin temperature retest-stability could not be evidenced. For all parameters, test-retest stability was weak for the relative scores. In conclusion, our study has important implications for applied psychophysiology research: (1) the measurement of EMG assessed in a clinical sample is stable over a 3-month interval; (2) in contrast, the measurements of SCL and skin temperature as well as all relative scores are less stable; and (3) the stability of EMG-parameters in our sample gives first hints that physiological changes can be attributed to an administered biofeedback treatment but further research is required.

Personality and Perception of Tinnitus.
Ear Hear. 2008 Jul 1. [Epub ahead of print]
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OBJECTIVES: Tinnitus has high prevalence and a wide range of etiologies and of impacts on sufferers. Our objective was to develop understanding of the role of personality in the perception of tinnitus in the general population. As a theoretical basis for this, we combined elements of a general model of signal detection with the ideas of ignition (development) and promotion (neural transmission) of tinnitus, and considered plausible roles for personality factors within this conceptual framework. DESIGN:: We interviewed a birth cohort of 970 people aged 32 yr sampled from the general population. On the basis of questioning, we divided them into three groups, those without tinnitus, those with occasional tinnitus (including those with transient tinnitus of very brief duration), and those who experienced tinnitus most of the time. We also established how annoying or distressing the tinnitus was, and assessed personality using the Multidimensional Personality Questionnaire. RESULTS:: Tinnitus was experienced rarely by 38.2% and half the time or more by 6.8% of those studied. Men and women did not differ in the amount of tinnitus reported, but women were more likely to find it annoying. People from lower socioeconomic backgrounds were more likely to report tinnitus. People with tinnitus were more socially withdrawn, reactive to stress, alienated, and less Self-Controlled. People who were more annoyed by tinnitus were more socially withdrawn, and men were more stress reactive and alienated. CONCLUSIONS:: Our interpretation of the findings is that personality influences the persistence of tinnitus by influencing the tendency to be aware of it. Consideration of personality factors may improve the ability to tailor tinnitus therapies, and the concept of awareness may benefit treatment outcomes by showing tinnitus sufferers a means of internalizing the locus of control over their symptoms.
Urocortin Expression in Mouse Cochlear Nucleus and Scarpa’s Ganglion.
Laryngoscope. 2008 Jun 25. [Epub ahead of print]

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OBJECTIVES/HYPOTHESIS: Clinical and basic studies have correlated tinnitus with stress. Although the etiology of tinnitus is unknown, the cochlear nucleus (CN) appears to play a role. To better understand the potential impact of stress on tinnitus and modulation of the central auditory system in general, the goal of the current study was to examine the presence and distribution of axon terminals containing urocortin in the CN of the mouse. STUDY DESIGN:: Prospective description of histological findings. METHODS: Three different forms of urocortin were labeled in brainstem sections collected from 10 wild-type mice by immunohistochemistry. Immunoreactive terminal fibers in the CN were digitally photographed, as well as reconstructed in the CN under a drawing tube attached to a light microscope. RESULTS: Specific staining was found in en passant type fibers scattered throughout the CN but situated mostly within the granule cell domains. Clusters of labeled fibers were observed in the nerve root. Labeled axons were observed in the three tracts known to carry olivocochlear fibers to the CN, as well as in the olivocochlear bundle itself. As the axons within the olivocochlear bundle departed the brainstem in the vestibular nerve, numerous labeled en passant fibers were observed among somata of the vestibular ganglion (Scarpa’s). Centrally, labeled axons were followed from the CN to the lateral superior olive, an established source of urocortin-positive efferents to the cochlea. These findings indicate that lateral olivocochlear efferents innervate the CN and Scarpa’s ganglion, and also that urocortin is likely a neuromodulator in particular CN circuits. CONCLUSIONS: The current study supports innervation of specific regions of the mouse CN and Scarpa’s ganglion by neurons expressing urocortin. The innervation may be one substrate by which stress modulates particular CN processes. Further studies are necessary to establish the role of urocortin in CN models of tinnitus.

The ‘multiplex model’ of Somatic Symptoms: Application to Tinnitus among Traumatized Cambodian Refugees.

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Somatic symptoms are a common clinical presentation of distress among ethnic populations in the USA, particularly traumatized refugees. In this article, we apply a ‘multiplex model’ of bodily experience to explain how a somatic symptom is evoked, amplified, and generates distress, particularly distress related to post-traumatic stress disorder. We illustrate the multiplex model's applicability to acute episodes of tinnitus (i.e., a buzzing-like sound in the ear) among Cambodian refugees, a common symptom in that group. The article demonstrates the importance of carefully examining somatic symptoms and associated meanings in distressed ethnic populations, especially traumatized refugees, and aims to contribute to a medical anthropology of somatic symptoms.

[DPOAE and lateral inhibition in chronic tinnitus]
[Article in German]

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INTRODUCTION: According to our audiological data, 90% of tinnitus patients have deficits in inner ear function as a generator of tinnitus, mainly in the outer hair cells (OHC). This can be verified by registration of distortion products of otoacoustic emissions (DPOAE). Thus, the main origin of tinnitus is peripheral, and most patients suffer from accompanying hearing loss, even though it is sometimes mild or subjectively not even felt. Whether or not the tinnitus is disturbing, however, is determined through further auditory processing of the "signal" tinnitus and its psychological validation.
With almost 50% of our tinnitus and hyperacusis patients, we find hyperfunctioning of the OHC, possibly originating from reduced or ineffective efferent control in the auditory pathway. Efferent activity can be measured by acoustic stimulation of the contralateral ear, which normally reduces the DPOAE amplitudes via efferent inhibition. METHOD AND PATIENTS: DPOAE were recorded with 67 tinnitus patients (127 ears) with and without contralateral acoustic stimulation. Twenty-one persons (41 ears) served as controls. RESULTS: With 64% of the tinnitus patients, DPOAE amplitudes were not reduced significantly, compared with 34% of the controls. The medium amplitude reduction for controls was 1.76 dB, whereas for the tinnitus patients it was significantly less (0.91 dB). CONCLUSION: For a considerable number of tinnitus patients, efferent control of OHC activity is restricted, but this seems to be confined to a certain type of tinnitus only.

Midazolam Reverses Salicylate Induced Changes in BDNF and Arg3.1 Expression: Implications for Tinnitus Perception and Auditory Plasticity.
Mol Pharmacol. 2008 Jun 4. [Epub ahead of print]
HNO Tuebingen.

Tinnitus is a phantom auditory perception, which can be induced via application of concentrated sodium salicylate, and is known to be associated with hearing loss and altered neuronal excitability in peripheral and central auditory neurons. The molecular features of this excitability has, however, been poorly characterized to date. Brain derived neurotrophic factor (BDNF), the activity-dependent cytoskeletal protein (Arg3.1, also known as Arc), and c-Fos are known to be affected by changes in excitability and plasticity. Using RT-PCR, in situ hybridization and immunohistochemistry, the expression of these genes was monitored in the rat auditory system following local (cochlear) and systemic application of salicylate. Induction of tinnitus and hearing loss was verified in a behavioural model. Regardless of the mode of salicylate application, a common pattern became evident: (1) BDNF mRNA expression was increased in the spiral ganglion neurons of the cochlea and (2) Arg3.1 expression was significantly reduced in the auditory cortex (AC). Local application of the GABAA receptor modulator midazolam resulted in the reversal not only of salicylate induced changes in cochlear BDNF expression, but also in cortical Arg3.1 expression, indicating that the tinnitus associated changes in cochlear BDNF expression trigger the decline of cortical Arg3.1 expression. Furthermore, local midazolam application reduced tinnitus perception in the animal model. These findings support Arg3.1 and BDNF as markers for activity changes in the auditory system and suggest a role of GABA-ergic inhibition of cochlear neurons in the modulation of Arg3.1 plasticity changes in the auditory cortex and tinnitus perception.

Hormones and the auditory system: A review of physiology and pathophysiology.
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This review explores the potential role of hormones in modulating the auditory function. The review describes four groups of hormones (the hormones of the circadian cycle, reproduction, stress response and the fluid and electrolyte balance), their physiological variations, interactions, as well as the physiological basis for their effect on the auditory system. Possible contribution of hormones to pathophysiology of auditory dysfunctions, including hyperacusis, tinnitus, Menière’s disease and pre-menstrual auditory dysfunction, has also been discussed.
Tinnitus and inferior colliculus activity in chinchillas related to three distinct patterns of cochlear trauma.
J Neurosci Res. 2008 Apr 25. [Epub ahead of print]

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A longstanding hypothesis is that tinnitus, the perception of sound without an external acoustic source, is triggered by a distinctive pattern of cochlear hair cell (HC) damage and that this subsequently leads to altered neural activity in the central auditory pathway. This hypothesis was tested by assessing behavioral evidence of tinnitus and spontaneous neural activity in the inferior colliculus (IC) after unilateral cochlear trauma. Chinchillas were assigned to four cochlear treatment groups. Each treatment produced a distinctive pattern of HC damage, as follows: acoustic exposure (AEx): sparse low-frequency inner hair cell (IHC) and outer hair cell (OHC) loss; round window cisplatin (CisEx): pronounced OHC loss mixed with some IHC loss; round window carboplatin (CarbEx): pronounced IHC loss without OHC loss; control: no loss. Compared with controls, all experimental groups displayed significant and similar psychophysical evidence of tinnitus with features resembling a 1-kHz tone. Contralateral IC spontaneous activity was elevated in the AEx and CisEx groups, which showed increased spiking and increased cross-fiber synchrony. A multidimensional analysis identified a subpopulation of neurons more prevalent in animals with tinnitus. These units were characterized by high bursting, low ISI variance, and within-burst peak spiking of approximately 1,000/sec. It was concluded that cochlear trauma in general, rather than its specific features, leads to multiple changes in central activity that underpin tinnitus. Particularly affected was a subpopulation ensemble of IC neurons with the described unique triad of features. (c) 2008 Wiley-Liss, Inc.

Tinnitus and brain MRI findings in Japanese elderly.

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CONCLUSION: There is evidence of an inverse association between cerebral infarction and tinnitus in this study. The effects of cerebral infarction on tinnitus could be explained by a neurophysiological model of tinnitus. OBJECTIVES: We examined the relationship between tinnitus and brain MRI findings including cerebral infarction, brain atrophy, ventricular dilatation, and white matter lesions. SUBJECTS AND METHODS: This was a cross-sectional population-based study of 2193 subjects aged 41-82 years living in Aichi prefecture, Japan. Detailed questionnaires, pure tone audiometry, and brain MRI were performed. RESULTS: After adjusting for potential confounders in a multiple logistic analysis, cerebral infarction was inversely associated with tinnitus (odds ratio (OR)=0.649, 95% confidence interval (CI)=0.477-0.884). Cerebral infarctions of the basal ganglia (OR=0.542), thalamus (OR=0.441), and pons (OR=0.319) were especially associated with tinnitus. Brain atrophy, ventricular dilatation, and white matter lesions had no significant effects on the prevalence of tinnitus.

Development of hyperactivity after hearing loss in a computational model of the dorsal cochlear nucleus depends on neuron response type.

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Cochlear damage can change the spontaneous firing rates of neurons in the dorsal cochlear nucleus (DCN). Increased spontaneous firing rates (hyperactivity) after acoustic trauma have been observed in
the DCN of rodents such as hamsters, chinchillas and rats. This hyperactivity has been interpreted as a neural correlate of tinnitus. In cats, however, the spontaneous firing rates of DCN neurons were not significantly elevated after acoustic trauma. Species-specific spontaneous firing rates after cochlear damage might be attributable to differences in the response types of DCN neurons: In gerbils, type III response characteristics are predominant, whereas in cats type IV responses are more frequent. To address the question of how the development of hyperactivity after cochlear damage depends on the response type of DCN neurons, we use a computational model of the basic circuit of the DCN. By changing the strength of two types of inhibition, we can reproduce salient features of the responses of DCN neurons. Simulated cochlear damage, which decreases the activity of auditory nerve fibers, is assumed to activate homeostatic plasticity in projection neurons (PNs) of the DCN. We find that the resulting spontaneous firing rates depend on the response type of DCN PNs: PNs with type III and type IV-T response characteristics may become hyperactive, whereas type IV PNs do not develop increased spontaneous firing rates after acoustic trauma. This theoretical framework for the mechanisms and circumstances of the development of hyperactivity in central auditory neurons might also provide new insights into the development of tinnitus.

Effects of salicylate application on the spontaneous activity in brain slices of the mouse cochlear nucleus, medial geniculate body and primary auditory cortex.


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Salicylate is a well-known substance to produce reversible tinnitus in animals and humans as well. It has been shown that systemic application of salicylate changes the neuronal spontaneous activity in several parts of the auditory pathway. The effects observed in central auditory structures in vivo could be based upon the changed afferent cochlear input to the central auditory system or in addition by a direct action of salicylate onto neurons within the auditory pathway. A direct influence of local salicylate application on spontaneous activity of central auditory neurons has already been described for the inferior colliculus (IC) in brain slice preparations. As spontaneous activity within all key structures of the central auditory pathway could play an important role in tinnitus generation, the present study investigated direct effects of salicylate superfusion on the spontaneous activity of the deafferented cochlear nucleus (CN), medial geniculate body (MGB), and auditory cortex (AC) in brain slices. Out of 72 neurons, 73.4% responded statistically significantly to the superfusate by changing their firing rates. 48.4% of them increased and 51.6% decreased their firing rates, respectively. The mean change of firing rate upon salicylate superfusion was 24.4%. All responses were not significantly different between the brain areas. The amount of neurons which responded to salicylate and the mean change of firing rate was much higher in the IC than in the CN, MGB and AC. This contributes to the hypothesis that salicylate-induced tinnitus is a phantom auditory perception mainly related to hyperexcitability of IC neurons. However, the present results suggest that the individual, specific salicylate sensitivity of CN, MGB and AC neurons can modulate the salicylate-induced generation of tinnitus.

Plasma antidiuretic hormone in cases with the early onset of profound unilateral deafness.

Auris Nasus Larynx. 2008 Mar 6. [Epub ahead of print]

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OBJECTIVE: The p-ADH level in cases of juvenile unilateral profound deafness (JUPD) and the timecourse of the level were examined to investigate whether or not an increase of p-ADH is involved in the development of delayed endolymphatic hydrops (DEH) in JUPD. MATERIALS AND METHODS: In 90 consecutive patients with unilateral profound or total sensorineural deafness with the onset in early
childhood, pure-tone audiometric examination and the measurement of p-ADH and plasma osmolality (p-OSM) were followed up once or twice a year as far as possible. At every testing, we performed careful history-taking about episodic vertigo/dizziness, fluctuant hearing loss, and tinnitus in order to find out whether patients had experienced these clinical signs of the development of DEH. RESULTS: Means and standard deviation (S.D.) of p-ADH level and osmolality in all samples tested (n=368) were 7.3 +/- 7.0pg/mL (0.7-52.0pg/mL), and 288.6 +/- 4.4mOsm/L (273-306mOsm/L), respectively. The mean of p-ADH level was much higher than those previously reported in children and adolescents. High levels of p-ADH (over 5.0pg/mL) were often observed in subjects between 6 and 19 years of age, but not so frequently in subjects of 20 years of age or older. Long-term follow-up of p-ADH levels revealed that DEH frequently developed in cases with persistent elevation of p-ADH. CONCLUSIONS: The elevation of p-ADH is likely to promote the development of DEH in cases of JUPD, although the underlying mechanism remains to be elucidated.

Tinnitus aurium in persons with normal hearing: 55 years later.
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OBJECTIVE: The aim of this study was to investigate the effect of silence on the appearance of auditory phantom perceptions in normal-hearing adults, with specific emphasis on the influence of suggestion.

STUDY DESIGN: Cross-sectional survey.

SUBJECTS AND METHODS: Fifty-three normal-hearing young Caucasian adults were subjected to two 4-minute sessions in an anechoic sound chamber. In the first session the chamber was empty; in the second session the chamber contained a nonfunctioning loudspeaker. At the end of each session, subjects had to indicate which sounds they perceived from a list of 23 different sounds.

RESULTS: When the loudspeaker was not present, 83 percent of the participants reported that they experienced at least one sound, and the percentage increased to 92 percent when the loudspeaker was present.

CONCLUSION: These results confirm the emergence of tinnituslike perceptions in a nonclinical population in a silent environment and indicate that suggestive mechanisms play only a minor role in their generation.

[Possible triggers of decompensated chronic complex tinnitus with a therapeutic approach as relating to treatment of epilepsy]
[Article in German]
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Coxsackieviruses are responsible for numerable diseases in man. This is also the reason for the high prevalence of endemic infection rates in the population. Our analysis (working hypothesis) will focus on the participation of Coxsackieviruses in chronic decompensated, complex tinnitus. Examination of the Coxsackievirus antibody titers might reveal the extent to which a Coxsackieviruses-triggered disease of the central nervous system participates in the direct sequelae of tinnitus disorders. A spread of Coxsackieviruses to the auditory pathway might lead to an overstimulation of the auditory pathway, comparable to an epileptic lesion. Based on this assumption, treatment with an antiepileptic would make sense. The reasoning behind this working hypothesis is to find a potentially new diagnostic and therapeutic roadmap as a further guide for specialized clinics. The authors are well aware that previous results bear little relevance as they have been based on small case numbers.
The inner ear in patients with nasal allergy.

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BACKGROUND: The endolymphatic sac has been proposed as a target organ responsible for inner-ear symptom in allergic subjects. This is a report of inner-ear symptoms in patients with nasal allergy.

METHOD: Retrospective review of record charts of patients with known nasal allergy presenting to the otorhinolaryngology out-patient department of the University College Hospital, Ibadan in 5 years.

RESULT: Ear symptoms were found in 95/144 (66%) subjects with nasal allergy. This comprises of 41 males and 44 females (M: F = 1:1). Of these, itching of the external ear canal, hearing loss and tinnitus accounted for 63 (66%), 55 (58%) and 39 (41%), respectively, while vertigo was found in 12 (13%).

Peripheral vestibular signs of imbalance were seen in 11/95. The audiological assessment of 73 subjects revealed normal pure-tone average in 43 (59%), and sensorineural hearing loss (SHL) in 17 (23.3%). The severity of SHL was mild in 6/17, moderate in 7 and moderate-to-severe in 4. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated in 10/15 (67%) and 6/15 (40%), while the skin sensitivity test showed reactions to dust in 32, cold in 25, cockroach in 7, perfume in 11, vegetable oil in 1 and insecticide in 2. The clinical diagnoses were idiopathic tinnitus in 25 (26.3%), Idiopathic SHL in 17 (18%), cochlear hydrop in 6 (6%) and autoimmune inner-ear disease in 6 (6%).

CONCLUSION: This report suggests some peculiar predisposition to inner-ear pathology in patients with nasal allergy. However a longitudinal assessment of cochleovestibular features of nasal allergy subjects will help in its validation.

Residual Inhibition Functions Overlap Tinnitus Spectra and the Region of Auditory Threshold Shift.

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Animals exposed to noise trauma show augmented synchronous neural activity in tonotopically reorganized primary auditory cortex consequent on hearing loss. Diminished intracortical inhibition in the reorganized region appears to enable synchronous network activity that develops when deafferented neurons begin to respond to input via their lateral connections. In humans with tinnitus accompanied by hearing loss, this process may generate a phantom sound that is perceived in accordance with the location of the affected neurons in the cortical place map. The neural synchrony hypothesis predicts that tinnitus spectra, and heretofore unmeasured “residual inhibition functions” that relate residual tinnitus suppression to the center frequency of masking sounds, should cover the region of hearing loss in the audiogram. We confirmed these predictions in two independent cohorts totaling 90 tinnitus subjects, using computer-based tools designed to assess the psychoacoustic properties of tinnitus. Tinnitus spectra and residual inhibition functions for depth and duration increased with the amount of threshold shift over the region of hearing impairment. Residual inhibition depth was shallower when the masking sounds that were used to induce residual inhibition showed decreased correspondence with the frequency spectrum and bandwidth of the tinnitus. These findings suggest that tinnitus and its suppression in residual inhibition depend on processes that span the region of hearing impairment and not on mechanisms that enhance cortical representations for sound frequencies at the audiometric edge. Hearing thresholds measured in age-matched control subjects without tinnitus implicated hearing loss as a factor in tinnitus, although elevated thresholds alone were not sufficient to cause tinnitus.
Gly460Trp alpha-adducin mutation as a possible mechanism leading to endolymphatic hydrops in Ménière’s syndrome.

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OBJECTIVE: Ménière’s disease (MD) is an inner ear disorder characterized by recurrent episodic vertigo, hearing loss that is fluctuating in the first stages, aural fullness, and tinnitus. Raised endolymphatic pressure (hydrops) is commonly accepted as a causal condition. Approximately 90% of cases of MD are sporadic, whereas the remaining 10% of cases are linked to genetic factors. The ionic composition of endolymph may also depend on the activity of Na, K-ATPase. Adducin is a heterodimeric cytoskeleton protein consisting of 3 subunits (alpha, beta, and gamma) coded by 3 different genes (ADD1, ADD2, and ADD3). ADD1 Gly460Trp polymorphism is associated with salt-sensitive hypertension and increased Na-K pump activity in transfected cells. This study aims to verify the role of adducin in the development of MD. METHODS: We genotyped 28 patients affected by definite MD according to American Academy of Otolaryngology-Head and Neck Surgery Foundation criteria. Results were compared with those from 2 different control populations (normotensive control group from San Raffaele Hospital and general population group). RESULTS: We have not found any significant difference in the distribution of ADD2 C1797T and ADD3 IVS11+386A/G polymorphism genotypes. On the other hand, the frequency of ADD1 Trp allele is significantly increased in patients with MD compared with controls. CONCLUSION: We present data supporting the possibility that increased Na, K-ATPase activity may be one of the pathologic mechanisms inducing hyperosmolarity in endolymph which, in turn, may lead to hydrops.

Cortical excitability and transcallosal inhibition in chronic tinnitus: transcranial magnetic study.

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INTRODUCTION: It has been proposed that tinnitus may be caused by maladaptive plasticity of processing in the central auditory pathways, and that this may be due in part to a generalised deficit in NMDA-dependent glutamatergic synapses. STUDY AIM: To test this hypothesis, we used transcranial magnetic stimulation to assess the excitability of a number of well-defined synaptic connections in the motor cortex of patients with tinnitus. PATIENTS AND METHODS: Thirty-seven patients with chronic tinnitus and 12 normal age- and sex-matched volunteers were used as a control group. We measured resting and active motor thresholds (rMT/aMT) and the duration of the contralateral and ipsilateral cortical silent periods (CSP and ISP). Short interval intracortical inhibition (SICI) and intracortical facilitation (ICF) were evaluated using a paired pulse stimulation paradigm in the left (dominant) hemisphere. RESULTS: There was no difference between patients and healthy subjects in rMT or aMT or the onset latency of the ISP. The CSP was shorter in patients (P=0.046) whereas the ISP was longer than in healthy subjects (P=0.048) but there was no difference between the hemispheres nor any relation to tinnitus side in patients with predominantly unilateral symptoms. There was no difference in the time course of SICI/ICF between patients and control groups and no significant correlation between tinnitus handicap inventory (THI) score and any of the measures of cortical excitability. CONCLUSIONS: There are small changes in cortical excitability in patients with chronic tinnitus. However, given the number of factors we examined in each individual, such minor changes seem unlikely to be an important factor in development of clinical symptoms.
Vascular Loops at the Cerebellopontine Angle: Is There a Correlation with Tinnitus?

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BACKGROUND AND PURPOSE: Tinnitus is a common disorder, and the etiology remains mostly unclear. The purpose of this study was to investigate the causative effect of the vascular loop and compression of the vestibulocochlear nerve at the cerebellopontine angle in patients with unexplained tinnitus. MATERIALS AND METHODS: This study was approved by our institutional review board. Written informed consent was obtained from all participants. Fifty-eight patients with unexplained tinnitus and 44 age- and sex-matched asymptomatic controls were examined with temporal MR imaging. Besides the tinnitus and control groups, a third group was formed by asymptomatic sides of patients with unilateral tinnitus. A 3D fast imaging employing steady-state acquisition (3D-FIESTA) sequence was performed in addition to the regular pre- and postcontrast axial and coronal sequences. The anatomic type of vascular loop, the vascular contact, and the angulation of the vestibulocochlear nerve at the cerebellopontine angle (CPA) were evaluated by 2 experienced neuroradiologists. The chi(2) test was used for statistical analysis. RESULTS: No statistically significant differences were found between the patient and control groups for the anatomic type of vascular loop, the vascular contact, and the angulation of the vestibulocochlear nerve at the CPA (P > .05). CONCLUSION: Although 3D-FIESTA MR imaging correctly shows the anatomic relationships of the vestibulocochlear nerve, its vascular compression cannot be attributed as an etiological factor for tinnitus.

Salicylate enables cochlear arachidonic-acid-sensitive NMDA receptor responses.

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Currently, many millions of people treated for various ailments receive high doses of salicylate. Consequently, understanding the mechanisms by which salicylate induces tinnitus is an important issue for the research community. Behavioral testing in rats have shown that tinnitus induced by salicylate or mefenamate (both cyclooxygenase blockers) are mediated by cochlear NMDA receptors. Here we report that the synapses between the sensory inner hair cells and the dendrites of the cochlear spiral ganglion neurons express NMDA receptors. Patch-clamp recordings and two-photon calcium imaging demonstrated that salicylate and arachidonate (a substrate of cyclooxygenase) enabled the calcium flux and the neural excitatory effects of NMDA on cochlear spiral ganglion neurons. Salicylate also increased the arachidonate content of the whole cochlea in vivo. Single-unit recordings of auditory nerve fibers in adult guinea pig confirmed the neural excitatory effect of salicylate and the blockade of this effect by NMDA antagonist. These results suggest that salicylate inhibits cochlear cyclooxygenase, which increased levels of arachidonate. The increased levels of arachidonate then act on NMDA receptors to enable NMDA responses to glutamate that inner hair cells spontaneously release. This new pharmacological profile of salicylate provides a molecular mechanism for the generation of tinnitus at the periphery of the auditory system.

Learning about tinnitus from an animal model

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Several animal models of tinnitus have been developed in the past 20 years. The premise on which these models are based is that chronic tinnitus is most likely a primitive hearing disorder. Because no evidence indicates that higher-order cognitive skills are required to experience tinnitus, it is also likely that animals such as laboratory rats can experience tinnitus. Chronic tinnitus in humans commonly emerges after peripheral auditory damage caused by exposure to loud sound, ototoxic agents, or aging.
Tinnitus can be induced in animals using the same treatments. A significant advantage of using animals to study tinnitus is that the etiology of their disorder can be carefully controlled in a laboratory setting, a difficult task in human clinical studies. Although animals cannot describe their tinnitus verbally, their perception of sound, both objective and subjective, can be measured using psychophysical procedures. Furthermore, sensory processing and brain function can be determined with great detail in animals using a variety of measures. Over the past decade we have used our animal model of tinnitus to examine many fundamental aspects of tinnitus, including its sensory features, the time course of development, interactions with aging, neurophysiological correlates from cochlea to brain, and pharmacological treatment. Copyright © 2008 by Thieme Medical Publishers, Inc.

**Assessment and modification of the tinnitus-related cortical network**  

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Tinnitus refers to the perception of a sound in the absence of any physical source, and it is widely believed that this phantom sound is generated in the central nervous system. Thus the activation of neuronal cell assemblies is chronically changed in patients with an ongoing tinnitus perception. We used magnetoencephalography to investigate these changes in a resting condition. There was an increase of synchronized activity in the gamma and delta frequency range together with a decrease in the α band. Manipulation of these cortical networks by means of neurofeedback therapy resulted in a reduction of tinnitus loudness and distress. In this article we review the basic research and the clinical studies conducted in our laboratory and propose a model that explains the results and helps guide future research and therapy. Copyright © 2008 by Thieme Medical Publishers, Inc.

**Effects of high-intensity sound exposure on neurotransmitter chemistry in the central auditory system**  
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Exposure to intense sound often leads to tinnitus, the perception of a monotonous sound not actually present. Increased neural spontaneous activity in the central auditory system found in animal models of tinnitus should have a basis in their chemistry. Most chemical studies so far have focused on neurotransmitters, by which neurons communicate with each other, because alteration of this chemistry could easily lead to abnormal neural activity that might be perceived as tinnitus. Although increased spontaneous activity has been observed in the hamster dorsal cochlear nucleus (DCN) a month after intense tone exposure, we did not find increased glutamate concentrations in the 3 layers of the hamster dorsal DCN at that time. We did, however, find decreased glutamate concentrations 2 days after exposure that might correlate with slightly decreased spontaneous activity observed then. Others have provided evidence for decreased glutamate release in the chinchilla DCN 2 days after intense sound exposure. Other intense-sound-induced changes are increased choline acetyltransferase activity in some cochlear nucleus regions, increased acetylcholine receptor sensitivity in some DCN neurons, and some changes in the γ-aminobutyric acid (GABA) neurotransmitter system in the inferior colliculus. There is a need for more study of these and other neurotransmitter systems to determine their possible roles in tinnitus. Copyright © 2008 by Thieme Medical Publishers.
III Diagnostics

Central nervous system neurodegeneration and tinnitus: a clinical experience. Part II: translational neurovascular theory of neurodegenerative CNS disease and tinnitus.


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The translation of a neurovascular hypothesis for Alzheimer’s disease to subjective idiopathic tinnitus (SIT) is presented as a challenge to the predominantly sensorineural view of SIT and its clinical application for tinnitus treatment. The concept of neurovascular dysfunction and neurodegeneration (ND) in SIT patients has been proposed and reported as an etiology in a particular subset of tinnitus patients with a diagnosis of medical-audiological tinnitus, through a medical-audiological tinnitus patient protocol, to be a predominantly central-type, severe, disabling SIT (n = 54 of 96). A medical-audiological ND tinnitus profile was the basis for selection of 18 SIT patients (n = 18 of 54) for nuclear medicine brain imaging (i.e., single-photon emission computed tomography or positron emission tomography, or both). Objective findings were reported in 16 of this cohort of 18 SIT patients selected for nuclear medicine imaging (88.9%). Classification of central nervous system (CNS) ND and tinnitus differentiated between (1) ND, nonspecific and of unknown etiology; (2) ND manifested by perfusion asymmetries in brain associated with ischemia (n = 11 of 18); and (3) ND CNS disease consistent with nuclear medicine criteria for senile dementia Alzheimer’s-type disease (n = 5 of 18). The diagnosis was associated with cerebrovascular disease (n = 16 of 18). The identification of pathological processes of inflammation and ischemia, linked to ND, in a particular cohort of SIT patients may provide a basis for establishing the medical significance and treatment of SIT and influence the clinical course of the tinnitus.

Tinnitus Outcomes Assessment.
Trends Amplif. 2008 Jul 3. [Epub ahead of print]

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Over the past two decades, recognition has grown that measures for evaluating treatment outcomes must be designed specifically to have high responsiveness. With that in mind, four major types of tinnitus measures are reviewed, including psychoacoustic measures, self-report questionnaires concerning functional effects of tinnitus, various rating scales, and global outcome measures. Nine commonly used tinnitus questionnaires, developed in the period 1980-2000, are reviewed. Because of many similarities between tinnitus and pain, comparisons between pain and tinnitus measures are discussed, and recommendations that have been made for developing a core set of measures to evaluate treatment-related changes in pain are presented as providing a fruitful path for developing a core set of measures for tinnitus. Finally, the importance of having both immediately obtainable outcome measures (psychoacoustic, rating scales, or single global measures) and longer term measures (questionnaires covering the negative effects of tinnitus) is emphasized for further work in tinnitus outcomes assessment.

Comparison of auditory brainstem response results in normal-hearing patients with and without tinnitus.

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OBJECTIVE: To evaluate electrophysiologically the auditory nerve and the auditory brainstem function of patients with tinnitus and normal-hearing thresholds using the auditory brainstem response (ABR).
DESIGN: Case-control study. SETTING: Ambulatory section of the Department of Otolaryngology, Hospital de Base de Brasilia.
PATIENTS: Thirty-seven individuals with tinnitus and 38 without tinnitus, with ages ranging from 20 to 45 years and pure-tone thresholds of 25 dB or better at frequencies between 500 and 8000 Hz.

MAIN OUTCOME MEASURES: We compared the latencies of waves I, III, and V; the interpeak intervals I-III, III-V, and I-V; the interaural latency difference (wave V); and the V/I amplitude ratio between the 2 groups. RESULTS: Among the 37 patients in the study group, abnormal results were found in 16 (43%) in at least 1 of the 8 parameters evaluated. When we analyzed the latencies, although the values were on average in the normal range used in the present study, the tinnitus group presented a significant prolongation of the latencies of waves I, III, and V when compared with the control group. Furthermore, we found the interpeak I-III, III-V, and I-V values to be within the normal limits, but the interpeak III-V value was significantly (P = .003) enlarged in the study group compared with the control group. The V/I amplitude ratio found in the tinnitus group was within normal limits; however, a significant (P = .004) difference was found when the 2 groups were compared. The averages of the interaural latency difference (wave V) did not show significant differences in relation to the control group.

CONCLUSIONS: We conclude that, although the averages obtained in several analyzed parameters were within normal limits, the ABR results from the patients with and without tinnitus and normal hearing are different, suggesting that ABR might contribute to the workup of these patients. Our data show that there are changes in the central pathways in the study group. The meaning of these changes must be further investigated.

Non-pulsatile subjective tinnitus without hearing loss may be caused by undetectable sounds originating from venous system of the brain.

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Tinnitus is a common otologic symptom, which can interfere with the daily activities of life. Subjective tinnitus is perception of sound only heard by the patient. The most common type of tinnitus is non-pulsatile subjective tinnitus (NST), which is believed to originate from auditory pathway, mostly from central nervous system. This hypothesis proposes that an important percentage of NST cases are actually misdiagnosed venous type tinnitus cases. Recent studies have demonstrated that dural-jugular system is dominant only in the horizontal body position. Jugular flow is at maximum during this position possibly making any noise generated within the dural-jugular system louder. As body assumes more vertical positions it gradually leaves its function to the extrajugular venous system of the brain. When there is an objective and/or a pulsating sound it is easier to suspect a vascular etiology and diagnose it clinically or radiologically. However, if a vascular pathology causes a non-pulsatile complaint that can not be heard by the examiner or can not be detected clinically or radiologically, it is bound to be misdiagnosed as central tinnitus. Most NST cases experience their symptoms especially at night. Night time usually allows the combination of silent ambience and horizontal body position to take place. We believe that in some NST cases, especially those without hearing loss (HL), the main cause of tinnitus is venous in origin.

Characteristics, diagnosis and treatment of hypoglossal canal dural arteriovenous fistula: report of nine cases.
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INTRODUCTION: We report the characteristics, diagnosis and treatment of dural arteriovenous fistula (DAVF) of the hypoglossal canal in nine patients with this relatively rare vascular disorder. METHODS: Of 248 patients with intracranial DAVFs managed at our institution, nine patients (3.6%; four men, five women; mean age 62 years) were diagnosed with hypoglossal canal DAVF. We investigated patient characteristics with respect to clinical symptoms, neuroradiological findings, efficacy and complications related to endovascular treatment.
RESULTS: Seven patients had experienced head injury. All patients presented with pulsatile tinnitus. One patient displayed ipsilateral hypoglossal nerve palsy before treatment. MR angiography showed a “magic wand” appearance between the affected hypoglossal canal and the internal jugular vein in four patients. Angiography demonstrated an AV fistula on the medial aspect of the superior jugular bulb, mostly arising from the bilateral occipital, ascending pharyngeal and vertebral arteries with drainage to the internal jugular vein via the anterior condylar vein. Contralateral carotid injection accurately clarified the shunting point. Five patients underwent endovascular treatment: transarterial embolization (TAE; n = 2), transvenous embolization (TVE; n = 2), and TAE/TVE (n = 1). Complete shunt obliteration was achieved in four patients and shunt reduction in one. The remaining four patients were treated conservatively and the shunt had disappeared at follow-up. Postoperative hypoglossal nerve palsy occurred in one patient after TVE, possibly due to coil overpacking. CONCLUSION: The incidence of hypoglossal canal DAVF was not very low in our series. Contralateral carotid injection is an essential examination to provide an accurate diagnosis. TVE should be considered when access is available, although TAE is also appropriate for shunt reduction.

Prognostic model for predicting hearing recovery in idiopathic sudden sensorineural hearing loss.

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HYPOTHESIS: To aid in realistic counseling of patients at the time of their first visit concerning their chances for recovery, we created a simple prognostic model for predicting hearing recovery in idiopathic sudden sensorineural hearing loss (ISSHL). BACKGROUND: An important element of research on ISSHL is to identify prognostic factors for this disease. Many studies have described predictive indicators to identify patients with a good prognosis needing no or minimal treatment. Only a few of these studies have included a model for calculating the probability for patient recovery, which may be important for clinical work, but these prognostic tables have not achieved widespread use clinically. METHODS: Evaluation of an electronic patient data base of 541 patients with ISSHL. The standard treatment was carbogen inhalation (95% O2 and 5% CO2 8 times per day in duration of 30 min) and prednisone orally (100 mg in 1 morning dose) for 7 days. Factors that were analyzed included the patient’s age, the interval between the onset of symptoms and beginning of treatment, the presence or absence of vertigo and tinnitus, audiometric patterns, the severity of hearing loss, and hearing in the opposite ear. Hearing gain was expressed either as absolute hearing gain or as relative hearing gain. Significant recovery of hearing was defined as the final pure-tone audiometry of 30 dB or less (or the same as the pure-tone audiometry of the opposite ear). RESULTS: The absolute hearing gain was 15.1 dB. The mean relative hearing gain was 47%. Three hundred one (57%) patients had significant recovery of hearing, and 228 (43%) did not have significant recovery of hearing. Using step-wise multiple linear regression analysis, the most important factors for prognosis included severity of hearing loss, presence of vertigo, time between onset and treatment, the hearing of the other ear, and the audiogram shape (beta coefficient was -0.216, -0.231, 0.211, 0.113, and -0.064, respectively; constant, 0.968). A recovery expectancy table was developed using the data from this study. CONCLUSION: Based on a retrospective analysis, prognostic indicators for hearing recovery in ISSHL were found to be severity of hearing loss, presence of vertigo, time between onset and treatment, the hearing of the other ear, and the audiogram shape. We created a model for calculating the probability for hearing recovery based on the analysis of 529 patients with unilateral ISSHL.
Identification of predictors and development of a screening protocol for cerebello-pontine lesions in patients presenting with audio-vestibular dysfunction.

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OBJECTIVES: Magnetic resonance imaging (MRI) scanning in the investigation of cerebellopontine angle lesions represents a finite resource, the use of which needs to be carefully rationalised. Our aim was to identify predictive factors that can distinguish between patients with and without cerebellopontine angle lesions, and develop a screening protocol which could be useful in the clinical setting as an aid to clinical judgment. DESIGN: Case-control study. SETTING: Secondary care. PARTICIPANTS: Audio-vestibular features were collated on 136 patients (M : F 1.39 : 1) and 288 controls (M : F 1 : 1.1). INTERVENTION: Diagnostic by analysis of symptoms and audiometric data using logistic regression, receiver-operator characteristic curves and backwards elimination. MAIN OUTCOME MEASURES: Development of a predictive algorithm comprising those factors which are most strongly predictive of the presence of a cerebellopontine angle lesion. RESULTS: Positive predictors of a cerebellopontine angle lesion include the interaural threshold difference at 1 (P = 0.044) and 4 kHz (P = 0.034). The threshold in the better hearing ear at 0.25 kHz exerts a negative predictive (i.e. protective) effect (P = 0.005). The presence of tinnitus does not appear to influence the outcome on logistic regression. Although vertigo does exert an influence on the overall model, its impact is highly equivocal. CONCLUSIONS: We have identified audiometric factors which exert a positive and negative predictive influence on the presence of a cerebellopontine angle lesion, and audiovestibular symptoms which appear to exert little effect on the model. Our predictive equation represents a user-friendly standardised method of risk-stratification of patients within a general otolaryngology clinic.

Algorithm for evaluation of pulsatile tinnitus.

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CONCLUSIONS: Pulsatile tinnitus requires a careful physical examination and evaluation with selected imaging techniques to identify the origin of the symptoms. OBJECTIVE: To evaluate the incidence of identifiable anomalies in patients with pulsatile tinnitus. SUBJECTS AND METHODS: This was a retrospective chart review undertaken in a tertiary care center. Patients seen in the outpatient otolaryngology clinic with the chief complaint of pulsatile tinnitus were evaluated by physical examination and imaging including CT angiography. The outcome measure was the incidence of identifiable abnormalities on imaging studies. RESULTS: Fifty-four patients were seen between January 2002 and June 2007 with the chief complaint of constant pulsatile tinnitus, excluding those with chemodectomas. On the basis of physical examination and imaging, 14 were considered arterial, 23 venous, and 15 were indeterminate in origin. Among patients with venous tinnitus, sigmoid sinus diverticulum was the most common finding. Among patients with arterial tinnitus, carotid atherosclerotic disease was the most common. One patient had erosion of the cochlea by the carotid artery. Non-vascular entities identified include superior semicircular canal dehiscence and benign intracranial hypertension.

Transient and distortion product evoked oto-acoustic emissions in normal hearing patients with and without tinnitus.

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OBJECTIVE: To test the hypothesis that tinnitus begins with outer hair cell dysfunction by recording transient (TEOAE) and distortion product evoked (DPOAE) oto-acoustic emissions in patients with normal hearing with (study group, SG) and without tinnitus (control group, CG).
STUDY DESIGN: Case control study. SUBJECTS AND METHODS: SG had 32 patients with pure tone thresholds below 25 dB in the 500 to 8000 Hz interval. CG had 37 age- and gender-matched patients with similar thresholds. All patients had normal tympanograms and stapedial reflexes. TEOAE were recorded with wide band click in continuous mode at 80-dB peak SPL. DPOAE were recorded with f1/ f2 = 1.22 and intensities of 65 dB (f1) and 55 dB (f2) SPL. RESULTS: DPOAE were abnormal in 68.4% of SG and in 50% of CG (P = 0.036). TEOAE were abnormal in 70.2% of SG and in 16.10% of CG (P = 0.0001). CONCLUSION: SG had significantly higher prevalence of abnormal TEOAE and DPOAE than CG.

Spontaneous intracranial hypotension: the syndrome and its complications.

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Spontaneous intracranial hypotension (SIH) is a syndrome that was largely unknown until the advent of MRI. The incidence of SIH is estimated at 5 per 100,000, which is half the incidence of subarachnoid hemorrhage. The major feature is a postural headache of acute or subacute onset. This headache is absent or minimal when the patient is lying down and rapidly worsens to great intensity when the patient sits or stands. Other features may include nausea, vomiting, vertigo, tinnitus, and marked exacerbation by Valsalva maneuver. SIH is due to a leak of cerebrospinal fluid from a tear in the dural membrane, which occurs most often at the exit zones where the cervical spinal roots leave the subarachnoid space. Other leak sites may be the vestibular system, the cribriform plate, or the pituitary fossa. If the leak continues, the brain loses buoyancy within the cranial space and sags toward the foramen magnum. This, in turn, may produce subdural hygroma or hematoma, brainstem compression, focal cranial nerve palsies, or cerebellar tonsillar herniation. The initial therapy is generally strict bed rest. If this fails, an epidural blood patch is usually successful in sealing the leak and restoring brain buoyancy. A significant minority of patients require a repeat epidural blood patch. If the blood patch fails, a surgical approach may be needed. Repair of the leak and restoration of brain buoyancy will stop the postural headache and, in most cases, will reverse the complications.

[The relationship between tinnitus, personality, and depression]
[Article in German]

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OBJECTIVE: This study examines the relationship between personality characteristics, depression symptoms, demographic profile, and the amount of the tinnitus-related distress experienced. METHOD: 121 patients suffering from tinnitus were examined by unique testing in a tinnitus-practice via three questionnaires over a period of 22 months. RESULTS: A relationship between the severity of tinnitus-related distress and demographic profile as well as a relationship between depression symptoms and the severity of the tinnitus-related distress could be shown. Also, significant results were observed within the personality range in the areas of “impulsiveness,” “aggressiveness,” “demands,” “physical discomfort,” “health worries,” and “emotionality.” Discussion: Patients suffering severely from tinnitus represent a clinically relevant group for psychotherapeutic treatment. Especially persons with comorbid symptoms of depression should be screened regularly and offered additional psychotherapeutic or psychiatric treatment.
The aim of this study was to determine the validity of the Italian translation of the Tinnitus Handicap Inventory (THI) by Newman et al. in order to make this self-report measure of perceived tinnitus handicap available both for clinical and research purposes in our country and to contribute to its cross-cultural validation as a self-report measure of perceived severity of tinnitus. The Italian translation of the Tinnitus Handicap Inventory (THI) was administered to 100 outpatients suffering from chronic tinnitus, aged between 20 and 82 years, who attended the audiological tertiary centres of the University Hospital of Modena and the Regional Hospital of Treviso. No segregation of cases was made on audiometric results; patients suffering from vertigo and neurological diseases were excluded. Psychoacoustic characteristics of tinnitus (loudness and pitch) were determined and all patients also completed the MOS 36-Item Short Form Health Survey to assess self-perceived quality of life and the Hospital Anxiety and Depression Scale as a measure of self-perceived levels of anxiety and depression. The THI-I showed a robust internal consistency reliability (Cronbach’s alpha = 0.91) that was only slightly lower than the original version (Tinnitus Handicap Inventory-US; Cronbach’s alpha = 0.93) and its Danish (Cronbach’s alpha = 0.93) and Portuguese (Cronbach’s alpha = 0.94) translations. Also its two subscales (Functional and Emotional) showed a good internal consistency reliability (Cronbach’s alpha = 0.85 and 0.86, respectively). On the other hand, the Catastrophic subscale showed an unacceptable internal consistency reliability as it is too short in length (5 items). A confirmatory factor analysis failed to demonstrate that the 3 subscales of the THI-I correspond to 3 different factors. Close correlations were found between the total score of the Italian translation of the Tinnitus Handicap Inventory and all the subscales of the MOS 36-Item Short Form Health Survey (SF-36) and the Hospital Anxiety and Depression Scale scores indicating a good construct validity. Moreover, these statistically significant correlations (p < 0.005) confirmed that the self-report tinnitus handicap is largely related to psychological distress and a deterioration in the quality of life. On the other hand, it was confirmed that the tinnitus perceived handicap is totally independent (p > 0.05) from its audiometrically-derived measures of loudness and pitch thus supporting previous studies that focused on the importance of non-auditory factors, namely somatic attention, psychological distress and coping strategies, in the generation of tinnitus annoyance. Finally the results of the present study suggest that the THI-I maintains its original validity and should be incorporated, together with other adequate psychometric questionnaires, in the audiological examination of patients suffering from tinnitus and that psychiatric counselling should be recommended for the suspected co-morbidity between tinnitus annoyance and psychological distress.
IV Imaging

The role of the insula cortex in the final common pathway for tinnitus: experience using ultra-high-frequency therapy.

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The insula cortex (Brodmann’s 13-16) has distinct auditory and multisensory areas that have been identified through imaging to be active or hypoactive in cases of severe tinnitus. As such, the insula is a candidate for inclusion in the final common pathway (FCP) for tinnitus. The insula has connections with the prefrontal and auditory cortices, amygdala, thalamus, parabrachial nucleus, orbitofrontal cortex, striate, cuneus, and cerebellum. The insula, as part of the medial temporal lobe system—which also includes the amygdala and the hippocampus—modulates its metabolic activity after high-frequency stimulation. The FCP is characterized by numerous areas in the lemniscal and extralemniscal pathways, including the auditory regions in the thalamus, the cortex, and the cerebellum. It is suggested that elements of the FCP, formulated into a general model of tinnitus, should be considered as beads on a string in designing treatment strategies. This view is the direct result of our past and recent new experiences using ultra-high-frequency sound therapy in cases of severe disabling tinnitus, presented at this time. Behaviorally, tinnitus symptoms decrease by self-report and changes in minimal masking levels with high-frequency sound therapy. The use of multisensory vibration stimulation (somatosensory and high-frequency jointly) should also be explored to maintain or reprogram the auditory cortical map and induce activity in the FCP circuit, including the parabrachial nucleus and the insula, which may be the physiological substrate of tinnitus behavioral tests.

Functional imaging of unilateral tinnitus using fMRI.

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CONCLUSIONS: This article shows that the inferior colliculus plays a key role in unilateral subjective tinnitus. OBJECTIVES: The major aim of this study was to determine tinnitus-related neural activity in the central auditory system of unilateral tinnitus subjects and compare this to control subjects without tinnitus. SUBJECTS AND METHODS: Functional MRI (fMRI) was performed in 10 patients (5 males) with unilateral tinnitus (5 left-sided, 5 right-sided) and 12 healthy subjects (6 males); both groups had normal hearing or mild hearing loss. fMRI experiments were performed using a 3T Philips Intera Scanner. Auditory stimuli were presented left or right and consisted of dynamically rippled broadband noise with a sound pressure level of 40 or 70 dB SPL. The responses of the inferior colliculus and the auditory cortex to the stimuli were measured. RESULTS: The response to sound in the inferior colliculus was elevated in tinnitus patients compared with controls without tinnitus.
Multimodal therapy for chronic tinnitus.

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From 2001 to 2006, we performed a retrospective study of patients suffering from chronic unilateral or bilateral tinnitus that was previously ineffectively treated by oral drugs [betahistine (Betaserc), extract of Ginkgo biloba (EGb 761), tanakan (Tebokan), and cinnarizine-dimenhydrinate (Arlevert), singly or in combination]. We divided 150 tinnitus patients (80 men, 70 women) into seven treatment groups. Treatments consisted of application of intravenous pentoxifylline, lidocaine, or vinpocetine (Cavinton) and combination of these agents with physiotherapy and soft laser. Mean duration (+/- standard deviation) of tinnitus in these patients was 7.4 +/- 6.0 years; their mean age was 55.6 +/- 12.5 years. The aim of our study was to compare treatment modalities and define their effectiveness for tinnitus relief. The most effective treatment was defined as a combination of Cavinton and physiotherapy. We evaluated pure lidocaine infusion therapy as ineffective. None of the treatment modalities had an objective correlate of improvement, though improvement was reported by a visual analog scale.

Intratympanic gentamicin therapy for control of vertigo in unilateral Meniere's disease: a prospective, double-blind, randomized, placebo-controlled trial.
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Conclusions. Intratympanic application of gentamicin is a relatively safe and efficient treatment for the reduction of complaints of vertigo attacks associated with Meniere's disease. The treatment also reduces the severity of the perceived aural fullness. Objective. To investigate the effectiveness of intratympanic gentamicin treatment in patients with unilateral Meniere's disease. Subjects and methods. In a prospective, double-blind, randomized, placebo-controlled clinical trial subjects scored vertigo complaints, aural fullness and tinnitus, before, during and up to 1 year after treatment. Hearing loss was monitored with pure tone audiometry. Results. Gentamicin treatment resulted in a significant reduction of the score for vertigo complaints and the score for perceived aural fullness. A small increase in hearing loss (average 8 dB) was measured in the gentamicin group.

Intratympanic dexamethasone for refractory sudden deafness
[Article in Chinese]
Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2008 Apr;22(7):309-311.

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OBJECTIVE: To observe the clinical efficacy of intratympanic dexamethasone (IT-DEX) for sudden deafness (SD) which were inefficient and contraindicated for systemic steroid. METHOD: Thirty-four patients who were inefficient and contraindicated for systemic steroid were treated by IT-DEX (5 g/L) for 4 times within 12 days. The improvement of auditis, tinnitus and stuffy were observed. And the results between the different influencing factor such as age, sex and course of disease were compared by statistical analysis. RESULT: 1) For total patients, the effective power of auditis, tinnitus and stuffy were 52.9%, 58.8% and 82.4% respectively. And the patients who treated within 2 weeks result in higher effective power of auditis and tinnitus than those having been treated for more than 2 weeks, but there was no significant difference between these two groups (P >0.05). 2) For the patients who were inefficient and contraindicated for systemic steroid, the audile effective power of them were 44.4% and 62.5% respectively.
CONCLUSION: IT-DEX can treat refractory SD effectively and safely. It is an effective treatment for the patients who were contraindicated for systemic steroid, and it could be used for salvage for the patients who were inefficient for systemic steroid.

Midazolam Reverses Salicylate Induced Changes in BDNF and Arg3.1 Expression: Implications for Tinnitus Perception and Auditory Plasticity.
Mol Pharmacol. 2008 Jun 4. [Epub ahead of print]
HNO Tuebingen.

Tinnitus is a phantom auditory perception, which can be induced via application of concentrated sodium salicylate, and is known to be associated with hearing loss and altered neuronal excitability in peripheral and central auditory neurons. The molecular features of this excitability has, however, been poorly characterized to date. Brain derived neurotrophic factor (BDNF), the activity-dependent cytoskeletal protein (Arg3.1, also known as Arc), and c-Fos are known to be affected by changes in excitability and plasticity. Using RT-PCR, in situ hybridization and immunohistochemistry, the expression of these genes was monitored in the rat auditory system following local (cochlear) and systemic application of salicylate. Induction of tinnitus and hearing loss was verified in a behavioural model. Regardless of the mode of salicylate application, a common pattern became evident: (1) BDNF mRNA expression was increased in the spiral ganglion neurons of the cochlea and (2) Arg3.1 expression was significantly reduced in the auditory cortex (AC). Local application of the GABAA receptor modulator midazolam resulted in the reversal not only of salicylate induced changes in cochlear BDNF expression, but also in cortical Arg3.1 expression, indicating that the tinnitus associated changes in cochlear BDNF expression trigger the decline of cortical Arg3.1 expression. Furthermore, local midazolam application reduced tinnitus perception in the animal model. These findings support Arg3.1 and BDNF as markers for activity changes in the auditory system and suggest a role of GABA-ergic inhibition of cochlear neurons in the modulation of Arg3.1 plasticity changes in the auditory cortex and tinnitus perception.

I.V. ropivacaine compared with lidocaine for the treatment of tinnitus.
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BACKGROUND: I.V. lidocaine has been used to ameliorate tinnitus, but in general its effect has been limited. The longer acting local anaesthetic ropivacaine may be more effective. METHODS: A total of 19 randomized, double-blind, cross-over study patients suffering from chronic tinnitus were given a 30 min i.v. infusion of ropivacaine or lidocaine 1.5 mg kg(-1) at an interval of 2-3 months. The intensity of tinnitus was evaluated on tinnitus handicap inventory (THI) scale and on the visual analogue scale (VAS). Plasma ropivacaine and lidocaine concentrations were determined. RESULTS: In both treatments, the infusion decreased the VAS score significantly. At the end of infusion, a > or =50% reduction in VAS score was observed in five patients by ropivacaine and in one patient by lidocaine, but this effect was sustained for 1 h only in three patients. However, the THI scores did not differ significantly within or between treatments. On the post-infusion day, three patients after ropivacaine and five after lidocaine treatment had > or =30% improvement in the THI score. Four weeks later, one patient after ropivacaine and two after lidocaine had a > or =30% reduction in the THI score. One patient developed seizures soon after ropivacaine infusion from which he recovered uneventfully. His plasma concentration of ropivacaine was 1817 ng ml(-1). The highest individual ropivacaine and lidocaine concentrations were 3483 and 1680 ng ml(-1), respectively. CONCLUSIONS: Temporary clinically significant alleviation of tinnitus was observed only in a few individuals after both i.v. ropivacaine and lidocaine. The toxicity of ropivacaine limits its usefulness.
Hormones and the auditory system: A review of physiology and pathophysiology.  

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This review explores the potential role of hormones in modulating the auditory function. The review describes four groups of hormones (the hormones of the circadian cycle, reproduction, stress response and the fluid and electrolyte balance), their physiological variations, interactions, as well as the physiological basis for their effect on the auditory system. Possible contribution of hormones to pathophysiology of auditory dysfunctions, including hyperacusis, tinnitus, Menière’s disease and pre-menstrual auditory dysfunction, has also been discussed.

[Expression patterns of non-viral transfection with GFP in the organ of Corti in vitro and in vivo. Gene therapy of the inner ear with non-viral vectors]  
[Article in German]  
HNO. 2008 May;56(5):524-529.

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BACKGROUND: Diseases of the inner ear such as presbycusis, tinnitus, sudden hearing loss, and vertigo affect many patients, but so far there are no specific therapy options. Gene therapy might become a potential modality of treatment. Viral vectors are standard in animal models to date. Future considerations, however, call for a further evaluation of non-viral transfection methods.

MATERIAL AND METHODS: The non-viral transfection agents Metafectene, Superfect, Effectene, and Mirus TransIT were incubated with a plasmid coding for GFP. In vivo, the plasmid-agent mix was injected via the membrane of the round window, and 48 h later the inner ear was perfused, harvested, decalcified, and histologically evaluated for GFP expression. RESULTS: Cationic lipids (Metafectene) and dendrimers (Superfect) were able to transfect cells in the area of the organ of Corti and lead to GFP expression. The polyamine (Mirus TransIT) did show expression of GFP in the area of Rosenthal’s canal and in the area of the inner hair cell. The combination of a non-liposomal lipid with a DNA condensing component (Effectene) did not show transfection of the organ of Corti. In the area of the spiral ganglia cells, GFP expression was seen with all the transfection agents. CONCLUSIONS: Non-viral transfection agents are able to introduce a reporter gene in cells of the inner ear in vitro and in vivo. There are, however, differences in the efficiency of the transfection. They might be an alternative in gene therapy of the inner ear. Further investigations to elucidate their potential are needed.

Tinnitus treatment with memantine.  

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OBJECTIVE: To evaluate efficacy and safety of memantine in the treatment of tinnitus. STUDY DESIGN: Prospective, randomized, double-blind crossover study. SUBJECTS AND METHODS: A total of 60 patients with tinnitus were randomized into a double-blind, placebo-controlled, prospective crossover study. Patients each received up to 20 mg memantine and placebo for 90 days, separated by a 30-day washout period. Treatment effects were assessed by using the Tinnitus Handicap Inventory (THI). A total of 43 patients completed the trial. RESULTS: There was no significant improvement of THI score after memantine treatment compared with placebo. A possible tendency for delayed effects of memantine was observed. The incidence of side effects during memantine treatment was 9.4 percent, leading to interruption of treatment in all cases. CONCLUSION: This study does not provide evidence to recommend memantine for the treatment of tinnitus. A possible late effect of the drug should be evaluated in further studies with longer observation periods.
VI Auditive Stimulation

Tinnitus treatment with customized sounds.

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Recent studies have indicated that the pathophysiological basis for tinnitus may be abnormal activity in the auditory areas of the brain rather than aberrant activity in the periphery. Tinnitus-related activity leads to changes in tonotopic representation in auditory cortex. However, such reorganization can be reversed through training-induced changes in the response pattern of cortical neurons. We address this problem by using customized sounds that reproduce the subjective experience to reduce overactive auditory circuits. The results of two preliminary studies indicate that customized sound therapy (CST*) aimed at this central dysfunction reduces tinnitus quickly and safely. Participants described immediate relief, showed changes on the Tinnitus Handicap Questionnaire, and reported changes in hearing threshold within 3 weeks. We also saw changes in the intensity dependence of the auditory N100 in tinnitus patients, supporting the idea that tinnitus reflects a reorganization of tonotopic maps in the auditory cortex. The main correlate of this reorganization was the enhanced contrast between responses to the perceived tinnitus pitch and tones approximately one octave lower. After 3 weeks of CST, the intensity dependence to the tinnitus pitch decreased, making these responses more similar to those from normal subjects responding to tones in the same frequency.

The role of the insula cortex in the final common pathway for tinnitus: experience using ultra-high-frequency therapy.

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The insula cortex (Brodmann’s 13-16) has distinct auditory and multisensory areas that have been identified through imaging to be active or hypoactive in cases of severe tinnitus. As such, the insula is a candidate for inclusion in the final common pathway (FCP) for tinnitus. The insula has connection with the prefrontal and auditory cortices, amygdala, thalamus, parabrachial nucleus, orbitofrontal cortex, striate, cuneus, and cerebellum. The insula, as part of the medial temporal lobe system—which also includes the amygdala and the hippocampus—modulates its metabolic activity after high-frequency stimulation. The FCP is characterized by numerous areas in the lemniscal and extralemniscal pathways, including the auditory regions in the thalamus, the cortex, and the cerebellum. It is suggested that elements of the FCP, formulated into a general model of tinnitus, should be considered as beads on a string in designing treatment strategies. This view is the direct result of our past and recent new experiences using ultra-high-frequency sound therapy in cases of severe disabling tinnitus, presented at this time. Behaviorally, tinnitus symptoms decrease by self-report and changes in minimal masking levels with high-frequency sound therapy. The use of multisensory vibration stimulation (somatosensory and high-frequency jointly) should also be explored to maintain or reprogram the auditory cortical map and induce activity in the FCP circuit, including the parabrachial nucleus and the insula, which may be the physiological substrate of tinnitus behavioral tests.

Treatment of Tinnitus with a Customized, Dynamic Acoustic Neural Stimulus: Underlying Principles and Clinical Efficacy
Trends Amplif. 2008 Jul 9. [Epub ahead of print]

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Tinnitus has been challenging to treat with consistently positive results. The Neuromonics Tinnitus Treatment is a newly available approach to the treatment of clinically significant, problematic tinnitus (and reduced sound tolerance) that was developed with the intention of simultaneously addressing the
auditory, attentional, and emotional processes underlying the condition. It uses a prescribed acoustic stimulus, customized for each patient’s individual audiometric profile, which provides a broad frequency stimulus to address the effects of auditory deprivation, promotes relief and relaxation with the intention of reducing engagement of the limbic system/amygdala and autonomic nervous system, and applies the principles of systematic desensitization to address the attentional processes. This article describes the underlying principles behind this approach. It also summarizes evidence for clinical efficacy from controlled clinical studies and from a private practice clinical setting, where it has been shown to provide consistently positive outcomes for patients meeting suitability criteria.

**Cortical reorganisation and tinnitus: principles of auditory discrimination training for tinnitus management.**
Eur Arch Otorhinolaryngol. 2008 Jun 28. [Epub ahead of print]

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Scientific evidence has proved reorganisation processes in the auditory cortex after sensorineural hearing loss and overstimulation of certain tonotopic cortical areas, as we see in auditory conditioning techniques. Acoustic rehabilitation reduces the impact of these reorganisation changes. Recent theories explain tinnitus mechanisms as a negative consequence of neural plasticity in the central nervous system after a peripheral aggression. Auditory discrimination training (ADT) could partially reverse the wrong changes in tonotopic representation and improve tinnitus. We discuss different studies and their efficacy on tinnitus perception and annoyance. Indications, method, dose and sound strategy need to be implemented.

**Clinical application of long-term intensity and pitch matches in fluctuating low-frequency hearing loss.**

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The purpose of this study was to measure changes in intensity and pitch matches to better assess disease activity in fluctuating hearing loss. Long-term suprathreshold audiometry was carried out at home on a subject with a unilateral fluctuating low-frequency hearing loss during a period when the subject demonstrated no symptoms and a period when the subject reported hearing loss, aural pressure, and tinnitus. Daily measurements of binaural intensity and pitch matches were made. Day-to-day fluctuations were clearly accentuated during the period when the subject experienced symptoms. Specifically, deviations from the reference tone were only observed for binaural pitch matches at 1 kHz during the period without symptoms; however, highly fluctuating binaural intensity and pitch matches were observed at 0.25 kHz during the period with symptoms. These fluctuations were not observed in a normal-hearing group. The results suggest that long-term measurements of binaural intensity and pitch matches can be used to monitor disease activity in fluctuating low-frequency hearing loss.

**[Music therapy in chronic tonal tinnitus. Heidelberg model of evidence-based music therapy]**
[Article in German]

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Tinnitus has a very high prevalence, with more than one million patients in the German population needing treatment for it. About 50% of them suffer from so-called tonal tinnitus, i.e., tinnitus with a well-defined frequency. Although tinnitus is one of the most common symptoms in ENT medicine, the existing treatments are polypragmatic and often lack a scientific foundation. Based on this fact, a novel music therapy concept was developed, evaluated, and scientifically
substantiated (with psychological, audiological, and functional imaging procedures in the diagnosis and treatment). The advantages of the described therapy are the integration of known and well-proven acoustic and psychotherapeutic techniques. They were converted to specific music therapy interventions (resonance training, neuroauditive cortex reprogramming, and tinnitus desensitization). More than 190 patients suffering from chronic tonal tinnitus were effectively treated. The results indicate that the therapy is highly advantageous in terms of treatment duration, effectiveness, and follow-up stability compared with customary interventions. Furthermore, the results of brain imaging strongly suggest the usefulness of further investigation and discussion in the realm of neuronal tinnitus modeling.

**Treatment of tinnitus with a customized acoustic neural stimulus: a controlled clinical study.**


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In patients with tinnitus, achieving consistently positive treatment results is a challenge. We conducted a controlled clinical study of a new treatment approach (Neuromonics Tinnitus Treatment) that involves the use of a customized neural stimulus. This stimulus is delivered to the patient in the form of a pleasant acoustic sensation that is spectrally modified according to each patient’s individual audiometric profile. This treatment approach is provided as part of a structured rehabilitation program. In our study, patients who received the customized stimulus (Neuromonics group) reported significantly greater and more consistent alleviation of tinnitus symptoms than did patients who participated in a counseling and support program with and without delivery of a broadband noise stimulus (Noise+Counseling group and Counseling-Only group, respectively). After 6 months of treatment, 86% of the Neuromonics patients met the minimum criterion for clinical success, defined as an alleviation of tinnitus disturbance of at least 40% (as determined by the Tinnitus Reaction Questionnaire score). By contrast, only 47 and 23% of the Noise+Counseling and Counseling-Only groups, respectively, reported a successful result according to this criterion. Mean improvements in tinnitus disturbance scores in the Neuromonics, Noise+Counseling, and Counseling-Only groups were 66, 22, and 15%, respectively. The differences between the Neuromonics group and the control groups were statistically significant. Significant differences were observed in other clinical outcomes. Patient reports of user acceptability were more consistently positive in the Neuromonics group.

**Incidence and quality of vertigo symptoms after cochlear implantation.**

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Objectives: To assess the incidence of vestibular disturbance in patients after cochlear implantation, and to evaluate the quality of vertigo symptoms. Study design: Prospective, observational study. Setting: Cochlear implant centre at a tertiary referral university hospital, Munich, Germany. Patients: Forty-seven adult patients undergoing unilateral cochlear implantation between 2003 and 2007. Methods: Patients were interviewed post-operatively about vertigo symptoms, using a specifically designed questionnaire. Questionnaire data were used to define patient subgroups based on probable vertigo aetiology. Cochlear implantation was performed via a retroauricular, transmastoidal approach. Thirty-six implants were Cochlear Nucleus 24 devices and 11 were MedEl devices. Results: Twenty-one (45 per cent) patients reported vertigo symptoms following cochlear implantation. The time of onset was directly post-operatively in the majority of patients. In 90 per cent, the symptoms suggested an otogenic origin. The majority of patients reported paroxysmal vertigo with a duration of seconds to minutes. Typical concomitant symptoms were tinnitus, fluctuating hearing loss and vegetative reactions. Serious disablement by vertigo was rare. Conclusion: Exposing patients to the risk of possible balance disorders associated with cochlear implantation is justified in view of the hearing rehabilitation achieved, even with today’s broader indications for cochlear implantation. However, patients should in any case be informed about the possibility and quality of post-operative vertigo symptoms.
Intervention for restricted dynamic range and reduced sound tolerance.

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Hyperacusis is an abnormal condition of sound intolerance that may cause some persons to reject amplified sound from their hearing aids. A significant secondary benefit reported for many patients receiving Tinnitus Retraining Therapy (TRT) is increased Loudness Discomfort Levels (LDLs). TRT involves both counseling and sound therapy (i.e., daily exposure to soft sound from bilateral noise generators (NGs)). We implemented a randomized, double-blind, placebo-controlled clinical trial to assess the efficacy of TRT as an intervention to improve sound tolerance in hearing-aid eligible persons with hyperacusis and/or restricted dynamic ranges. Subjects were assigned to one of four treatment groups: 1) full treatment, both counseling and NGs, 2) counseling and placebo NGs, 3) NGs without counseling, and 4) placebo NGs without counseling. They were evaluated at least monthly, typically for five months or more, on a variety of audiometric tests, including LDLs, the Contour Test for Loudness, and word recognition measured at comfortable and loud levels. Over 80% of the subjects assigned to full treatment achieved significant benefit (defined as shifts of greater than 10 dB in LDLs or the Contour Test uncomfortable level); whereas, most subjects assigned to a partial treatment group did not benefit from their treatment. [Supported by NIH].

Establishing a tinnitus clinic in your practice.

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PURPOSE: While tinnitus is very common among the hearing impaired population, specific treatment for tinnitus is not provided in most clinics. This article provides a plan for establishing a tinnitus treatment program that can be implemented in stages at most audiology clinics. METHOD: Preparation for establishing a tinnitus clinic includes having an overall plan regarding the type and degree of tinnitus management. Assessment involves a measurement of tinnitus and of the reaction a patient has to the tinnitus, including the use of handicap questionnaires. Management typically involves some form of counseling and sound therapy. Four problematic areas in tinnitus management are thoughts and emotions, hearing and communication, sleep, and concentration. CONCLUSIONS: Licensed audiologists generally have the essential training necessary to provide counseling and sound therapy to treat tinnitus patients. We introduce 3 levels of treatment implementation, depending on whether the patient is curious, concerned, or distressed. Follow-up and referrals might be necessary in more severe cases. Finally, the development of a tinnitus clinic centers around establishing a need for individual treatment, creating a treatment plan, estimating the need for additional staff and resources, reimbursement options, and assessing the effectiveness of the program.
Hearing aids and tinnitus therapy: a 25-year experience.
J Laryngol Otol. 2008 Mar 20;20:1-5. [Epub ahead of print]

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Objectives:(1) To assess the subjective tinnitus perception of patients with audiologically proven hearing loss presenting to a tinnitus clinic, both before and after hearing aid provision; (2) to investigate subjective tinnitus perception in patients with unilateral and bilateral hearing loss; and (3) to assess the impact on tinnitus perception, if any, of a digital hearing aid programme in patients provided with hearing aids.


Setting: University teaching hospital otolaryngology department.

Participants: A total of 2153 consecutive patients attending a consultant-delivered specialist tinnitus clinic.

Main outcomes measures: A visual analogue scale was used to assess the degree of tinnitus perception improvement, if any, comparing before versus after unilateral or bilateral aiding (in those with audiometrically proven hearing loss). A further assessment compared the effect of digital hearing aid programme introduction on symptomatic tinnitus perception in patients provided with unilateral or bilateral aids.

Results: A total of 1440 patients were given hearing aids (826 unilateral and 614 bilateral). There was little difference in tinnitus perception, comparing overall aiding results in unilaterally or bilaterally aided patients. Overall, 554 (67 per cent) of unilaterally aided patients and 424 (69 per cent) of bilaterally aided patients reported some improvement in their tinnitus perception following aiding.

There was a statistically significant improvement in tinnitus perception, comparing analogue aids with digital hearing aids, following introduction of a digital hearing aid programme in 2000, in both unilaterally (p < 0.001) and bilaterally (p < 0.001) aided patients.

Conclusions: Provision of hearing aids in patients with audiometrically demonstrable hearing loss can play a very important part in tinnitus control. The additional improvement in tinnitus control observed following introduction of programmable digital aids had a summative effect in the management of these patients.

Using therapeutic sound with progressive audiologic tinnitus management.

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Management of tinnitus generally involves educational counseling, stress reduction, and/or the use of therapeutic sound. This article focuses on therapeutic sound, which can involve three objectives: (a) producing a sense of relief from tinnitus-associated stress (using soothing sound); (b) passively diverting attention away from tinnitus by reducing contrast between tinnitus and the acoustic environment (using background sound); and (c) actively diverting attention away from tinnitus (using interesting sound).

Each of these goals can be accomplished using three different types of sound-broadly categorized as environmental sound, music, and speech-resulting in nine combinations of uses of sound and types of sound to manage tinnitus. The authors explain the uses and types of sound, how they can be combined, and how the different combinations are used with Progressive Audiologic Tinnitus Management. They also describe how sound is used with other sound-based methods of tinnitus management (Tinnitus Masking, Tinnitus Retraining Therapy, and Neuromonics).
VII Brain Stimulation

Maintenance repetitive transcranial magnetic stimulation can inhibit the return of tinnitus.

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OBJECTIVES/HYPOTHESIS: A single patient was tested to examine the safety and feasibility of using maintenance sessions of low-frequency repetitive transcranial magnetic stimulation (1 Hz rTMS) to reduce tinnitus loudness and prevent its return over time. STUDY DESIGN: Interrupted time series with multiple replications. METHODS: Tinnitus loudness was assessed using a visual analogue rating (VAR) with 0 = no tinnitus, and 100 = loudest tinnitus experienced; 1,800 TMS pulses delivered at 1 Hz and 110% of motor threshold were administered over the posterior, superior lateral temporal gyrus of the subject’s right hemisphere until subjective tinnitus fell to a VAR of 25. TMS was reapplied as tinnitus returned to a VAR of 25 or higher. Cerebral metabolism was measured using positron emission tomography before and after treatment. RESULTS: In this patient, tinnitus could be reduced to a VAR of 6 or lower each time it reoccurred using one to three maintenance sessions of rTMS. Tinnitus loudness remained at or below a VAR of 25 and was reported to be unobtrusive in daily life when last assessed 4 months after the third and final round of maintenance treatment. Asymmetric increased cerebral metabolism in the right hemisphere reduced following treatment and as tinnitus improved. Maintenance treatment was well tolerated with no side effects. CONCLUSIONS: Although a case study cannot establish treatment efficacy, this study demonstrates for the first time that it is feasible to use maintenance rTMS to manage chronic tinnitus. Maintenance rTMS might impede cortical expansion of the tinnitus frequency into adjacent cortical areas, but group studies are necessary to confirm this speculation.


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BACKGROUND: Chronic tinnitus is a frequent condition, which can have enormous impact on patient’s life and which is very difficult to treat. Accumulating data indicate that chronic tinnitus is related to dysfunctional neuronal activity in the central nervous system. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive method which allows to focally modulate neuronal activity. An increasing amount of studies demonstrate reduction of tinnitus after repeated sessions of low-frequency rTMS and indicate that rTMS might represent a new promising approach for the treatment of tinnitus. However available studies have been mono-centric and are characterized by small sample sizes. Therefore, this multi-center trial will test the efficacy of rTMS treatment in a large sample of chronic tinnitus patients. METHODS/DESIGN: This is a randomized, placebo-controlled, double-blind multi-center trial of two weeks 1 Hz rTMS-treatment in chronic tinnitus patients. Eligible patients will be randomized to either 2 weeks real or sham rTMS treatment. Main eligibility criteria: male or female individuals aged 18-70 years with chronic tinnitus (duration > 6 months), tinnitus-handicap-inventory-score > or = 38, age-adjusted normal sensorineural hearing (i.e. not more than 5 dB below the 10% percentile of the appropriate age and gender group (DIN EN ISO 7029), conductive hearing loss < or = 15dB. The primary endpoint is a change of tinnitus severity according to the tinnitus questionnaire of Goebel and Hiller (baseline vs. end of treatment period). A total of 138 patients are needed to detect a clinical relevant change of tinnitus severity (i.e. 5 points on the questionnaire of Goebel and Hiller; alpha = 0.05; 1-beta = 0.80). Assuming a drop-out rate of less than 5% until the primary endpoint, 150 patients have to be randomized to guarantee the target number of 138 evaluable patients.
The study will be conducted by otorhinolaryngologists and psychiatrists of 7 university hospitals and 1 municipal hospital in Germany. DISCUSSION: This study will provide important information about the efficacy of rTMS in the treatment of chronic tinnitus. TRIAL REGISTRATION: Current Controlled Trials ISRCTN89848288.

**Combined temporal and prefrontal transcranial magnetic stimulation for tinnitus treatment: a pilot study.**

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OBJECTIVES: Low-frequency repetitive transcranial magnetic stimulation (rTMS) of the temporal cortex has been proposed as a new treatment strategy for patients with chronic tinnitus. However, functional abnormalities in tinnitus patients also involve brain structures used for attentional and emotional processing, such as the dorsolateral prefrontal cortex. Therefore, we have developed a new rTMS treatment strategy for tinnitus patients that consists of a combination of high-frequency prefrontal and low-frequency temporal rTMS. STUDY DESIGN: A total of 32 patients received either low-frequency temporal rTMS or a combination of high-frequency prefrontal and low-frequency temporal rTMS. Treatment effects were assessed with a standardized tinnitus questionnaire (TQ). RESULTS: Directly after therapy there was an improvement of the TQ-score for both groups, but no differences between groups. An evaluation after 3 months revealed a remarkable benefit from the use of combined prefrontal and temporal rTMS treatment. CONCLUSION: These results support recent data that suggest that auditory and nonauditory brain areas are involved in tinnitus pathophysiology.

**Tinnitus and transcranial magnetic stimulation**

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Tinnitus is a frequent disorder that is very difficult to treat. Both functional imaging studies in patients and electrophysiological studies in animals suggest that hyperactivity in the central auditory system due to increased synchronicity may cause tinnitus. Targeted modulation of tinnitus-related cortical activity has been proposed as a promising new treatment. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive method that can focally modulate cortical activity. This technique has been used to diagnose and treat tinnitus. Single sessions of high-frequency rTMS over the temporal cortex have been used to suppress tinnitus transiently and could become a useful predictor for treatment outcome of epidural stimulation. Another approach uses rTMS as a treatment for tinnitus by applying repeated sessions of low-frequency rTMS to induce a lasting reduction of excitability in the auditory cortex. Beneficial effects of treatment have been consistently demonstrated in several controlled studies. However, results are characterized by high interindividual variability and only moderate effect sizes. Convincing evidence indicates that rTMS represents a promising tool for diagnosis and treatment of tinnitus. Further development of this technique will depend on a more detailed understanding of the neurobiological effects that mediate the clinical effects of TMS. Copyright © 2008 by Thieme Medical Publishers, Inc.
VIII Behavioral Therapy

Differential outcome of a multimodal cognitive-behavioral inpatient treatment for patients with chronic decompensated tinnitus.

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We examined 179 inpatients with severe chronic tinnitus for tinnitus-related distress and psychological dysfunction after treatment. We conducted a prospective, nonrandomized, noncontrolled study. We calculated treatment outcome in tinnitus-related distress, depression, and somatic complaints by analysis of variance with repeated measurement at admission, at discharge, and at 3, 6, and 12 months after treatment. Additionally, on the basis of reduction in tinnitus-related distress, responders and nonresponders were determined. We compared the effects of treatment for both groups on tinnitus-related distress, depression, and somatic complaints. In our entire sample, tinnitus-related distress, depression, and somatic complaints decreased significantly at discharge. After discharge, all patients showed improvement for up to 12 months as compared to their condition at admission. Of the 179 severely distressed patients, 67% were found to have improved clinically at discharge, and 47% still benefited after 12 months. In comparison to the nonresponders, the responders displayed less depression, fewer physical complaints, and fewer body-related anxieties at each measuring point. The only distinguishing factors between responders and nonresponders were their age and the extent of their psychosocial stress. Limitations of the study and consequences for treatment of chronic tinnitus patients are discussed.

Cortical reorganisation and tinnitus: principles of auditory discrimination training for tinnitus management.
Eur Arch Otorhinolaryngol. 2008 Jun 28. [Epub ahead of print]

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Scientific evidence has proved reorganisation processes in the auditory cortex after sensorineural hearing loss and overstimulation of certain tonotopic cortical areas, as we see in auditory conditioning techniques. Acoustic rehabilitation reduces the impact of these reorganisation changes. Recent theories explain tinnitus mechanisms as a negative consequence of neural plasticity in the central nervous system after a peripheral aggression. Auditory discrimination training (ADT) could partially reverse the wrong changes in tonotopic representation and improve tinnitus. We discuss different studies and their efficacy on tinnitus perception and annoyance. Indications, method, dose and sound strategy need to be implemented.

[Neurootologic and psychosomatic habituation therapy. Treatment approaches in chronic tinnitus]
[Article in German]

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Modern tinnitus therapy, especially for chronic tinnitus accompanied by psychosomatic disturbances, is based on an understanding of the controlled network of auditory perception. The symptom of tinnitus derives from damage or defective coding in this system, mainly the inner ear. It becomes an independent disease as a result of disturbed auditory perception with pathologic evaluation and emotional association in the cortex. We present different therapeutic approaches based on these models.
The therapy aims to eliminate or diminish the symptom of tinnitus through retraining, cognitive restructuring, or enhancement of efferent filter mechanisms in the auditory pathway. Psychosomatic stabilization of patients is an important preliminary condition for effective habituation; therefore, an integrative neurootologic and psychosomatic therapy is proposed that requires an interdisciplinary therapeutic team and can be mostly carried out in an outpatient setting.

**Tinnitus: one problem that can be solved.**


**Mattia GM.**

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The author explains the origin of idiopathic or subjective tinnitus. After more than ten years of research (at a personal centre and at Rome University “La Sapienza” Faculty of Medicine ...) we have solved more than 80% of tinnitus problems for a thousand people. We have found that the perceived sound can be a source of stress and can be recorded in the brain as “dangerous”. We illustrate that a psychological and neurological rehabilitation implemented in a multifactors approach can give health and offer a new normal quality of life. With biofeedback EEG, EMG and GSR we are implementing our therapy. The biofeedback helps people understand the effects of stress on tinnitus and how to manage this stress to optimize performance and improve health. Previous studies have shown an enhancement of human performance and faster rehabilitation when physiological measures (respiration rate, heart rate, skin conductance, temperature, and surface electromyography) were fed back in sessions of Autogenic Training.

**Establishing a tinnitus clinic in your practice.**


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**PURPOSE:** While tinnitus is very common among the hearing impaired population, specific treatment for tinnitus is not provided in most clinics. This article provides a plan for establishing a tinnitus treatment program that can be implemented in stages at most audiology clinics. **METHOD:** Preparation for establishing a tinnitus clinic includes having an overall plan regarding the type and degree of tinnitus management. Assessment involves a measurement of tinnitus and of the reaction a patient has to the tinnitus, including the use of handicap questionnaires. Management typically involves some form of counseling and sound therapy. Four problematic areas in tinnitus management are thoughts and emotions, hearing and communication, sleep, and concentration. **CONCLUSIONS:** Licensed audiologists generally have the essential training necessary to provide counseling and sound therapy to treat tinnitus patients. We introduce 3 levels of treatment implementation, depending on whether the patient is curious, concerned, or distressed. Follow-up and referrals might be necessary in more severe cases. Finally, the development of a tinnitus clinic centers around establishing a need for individual treatment, creating a treatment plan, estimating the need for additional staff and resources, reimbursement options, and assessing the effectiveness of the program.

**Pros and cons of tinnitus retraining therapy.**


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**CONCLUSIONS:** A significant reduction in the Tinnitus Handicap Inventory (THI) was obtained as early as 1 month after implementation of tinnitus retraining therapy (TRT). Over half of our patients either could not tolerate the tinnitus control instrument (TCI) or obtained a poor result in the TRT trial. Candidates for TRT should thus be restricted to patients who can use the TCI.
OBJECTIVES: TRT has been regarded as a promising therapy for tinnitus, although there have been very few studies to determine which patients are most likely to benefit from TRT. The aim of the present study was to demonstrate TRT’s pros and cons based on our experience. SUBJECTS AND METHODS: The subjects were 217 patients with intractable tinnitus. Of those, 84 tolerated TRT and 79 were followed for 6 months. The remaining subjects did not undergo TRT. Japanese translations of the THI and visual analogue scale of annoyance caused by tinnitus (VAS) were administered to evaluate the effect of TRT. RESULTS: The average THI score at the beginning of the treatment was 48.8, but it was 36.3 (p<0.01) 1 month after starting the treatment and 28.3 (p<0.005) after 6 months.

[The relationship between tinnitus, personality, and depression]  
[Article in German]  
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OBJECTIVE: This study examines the relationship between personality characteristics, depression symptoms, demographic profile, and the amount of the tinnitus-related distress experienced. METHOD: 121 patients suffering from tinnitus were examined by unique testing in a tinnitus-practice via three questionnaires over a period of 22 months. RESULTS: A relationship between the severity of tinnitus-related distress and demographic profile as well as a relationship between depression symptoms and the severity of the tinnitus-related distress could be shown. Also, significant results were observed within the personality range in the areas of “impulsiveness,” “aggressiveness,” “demands,” “physical discomfort,” “health worries,” and “emotionality.” Discussion: Patients suffering severely from tinnitus represent a clinically relevant group for psychotherapeutic treatment. Especially persons with comorbid symptoms of depression should be screened regularly and offered additional psychotherapeutic or psychiatric treatment.

IX Somatic Tinnitus

Multimodal therapy for chronic tinnitus.  
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From 2001 to 2006, we performed a retrospective study of patients suffering from chronic unilateral or bilateral tinnitus that was previously ineffectively treated by oral drugs [betahistine (Betaserc), extract of Ginkgo biloba (EGb 761), tanakan (Tebokan), and cinnarizine-dimenhydrinate (Arlevert), singly or in combination]. We divided 150 tinnitus patients (80 men, 70 women) into seven treatment groups. Treatments consisted of application of intravenous pentoxifylline, lidocaine, or vinpocetine (Cavinton) and combination of these agents with physiotherapy and soft laser. Mean duration (+/- standard deviation) of tinnitus in these patients was 7.4 +/- 6.0 years; their mean age was 55.6 +/- 12.5 years. The aim of our study was to compare treatment modalities and define their effectiveness for tinnitus relief. The most effective treatment was defined as a combination of Cavinton and physiotherapy. We evaluated pure lidocaine infusion therapy as ineffective. None of the treatment modalities had an objective correlate of improvement, though improvement was reported by a visual analog scale.
The role of the cervical spine and the craniomandibular system in the pathogenesis of tinnitus. Somatosensory tinnitus

Article in German

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The causes of tinnitus, vertigo, and hearing disturbances may be pathological processes in the cervical spine and temporomaxillary joint. In these cases, tinnitus is called somatosensory tinnitus (SST). For afferences of the cervical spine, projections of neuronal connections in the cochlear nucleus were found. A reflex-like impact of the cervical spine on the cochlear nucleus can be assumed. The tinnitus treatment concept of the Charité University Hospital in Berlin involves the cooperation of ENT specialists with many other disciplines in an outpatient clinic. A standardized examination protocol has been established, and physical therapy has been integrated into the interdisciplinary tinnitus treatment. For tinnitus-modulating therapy of muscular trigger points, local anesthetics as well as self-massage or treatment by a physiotherapist or osteopath are useful.

Modified Muncie technique: osteopathic manipulation for eustachian tube dysfunction and illustrative report of case.


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In eustachian tube dysfunction, the eustachian tube fails to open sufficiently, resulting in a difference between the air pressure inside and outside the middle ear. This condition can cause pain and hearing loss and may lead to barotitis media, oitis media, tinnitus, and vertigo. Although several treatment options are available, from antibiotics to surgery, little documentation of osteopathic manipulative techniques exists. The current report discusses various treatment options, including the modified Muncie technique—a type of myofascial release administered inside the patient’s mouth—for patients with eustachian tube dysfunction and its symptoms. An illustrative case of a 37-year-old woman who complained of intermittent vertigo and who was treated with this technique is included.

Otological and vestibular symptoms in patients with low grade (Quebec grades one and two) whiplash injury.

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Objective: To establish the prevalence of new vestibular and otological symptoms in a group of patients who had sustained a low grade (Quebec grades one or two) whiplash injury. Methods: A retrospective review of the case records of 109 patients undergoing assessment by a single practitioner for the purposes of compiling a medicolegal report on their whiplash injury. Results: Four patients complained of short-lived, non-specific dizziness symptoms in the acute phase following their original injury. There were no reports of vertigo, tinnitus or hearing loss after a mean period of 149 days following the whiplash injury. Conclusions: No patients reported otological or persistent vestibular symptoms in the acute phase following their whiplash injury. This suggests that caution should be exercised when attributing these symptoms to such an injury. Before whiplash injuries are admitted as an aetiological factor in the development of such symptoms, other causes should be excluded.
Otologic symptoms of temporomandibular disorder and effect of orofacial myofunctional therapy.

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The aim of this study was to investigate the frequency of otologic symptoms and their relationship to orofacial signs and symptoms of temporomandibular disorder (TMD), and the effect of orofacial myofunctional therapy. The study was conducted on eight asymptomatic subjects (Group C) and 20 subjects with articular TMD, randomly distributed over two groups: one treated using orofacial myofunctional therapy (OMT Group) and a control group with TMD (Group CTMD). Patient selection was based upon the Research Diagnostic Criteria for TMD (RDC/TMD). All subjects submitted to a clinical examination with self-reporting of symptom severity, and to orofacial myofunctional and electromyographic evaluation at diagnosis and again, at the end of the study. Correlations were calculated using the Pearson test and inter- and intragroup comparisons were made (p < 0.05). In the diagnosis phase, subjects with TMD reported earache (65%), tinnitus (60%), ear fullness (90%), and 25% of the asymptomatic subjects reported tinnitus. The otologic symptoms were correlated with tenderness to palpation of the temporomandibular muscles and joints and with orofacial symptoms. Only the OMT group showed a reduction of otologic and orofacial symptoms, of tenderness to palpation and of the asymmetric index between muscles. OMT may help with muscle coordination and a remission of TMD symptoms.

Transcutaneous electrical stimulation of subjective tinnitus. A placebo-controlled, randomized and comparative analysis.

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AIM: The effect of the transcutaneous application of the electrical stimulus on tinnitus perception has been reviewed in a placebo-controlled, randomized and comparative analysis to eventually determine the outcome of the therapeutic role of the therapy. METHOD: There are 42 patients who were randomized into 2 groups according to their order of admission. Group A consists of 31 patients who were subjected to transcutaneous electrical stimulation 3 times a week for 1 month. Group B includes 11 patients who had electrical stimulus attachment but where no stimulus was given (placebo group). The stimulator is a custom-made device which generates direct and alternative current in 10-200 Hz frequency. An alternative low-frequency (not >100 Hz) pulsed current was used for tinnitus therapy through a preauricular skin electrode. The amplitude of stimulus ranged between 50 and 2,000 mA. The pulse frequency was 30 Hz. Each session lasted for 25 min for both groups. Statistical analysis was performed. RESULT: The rate of improvement following the therapy was 42.8% (18/42) in the electrical therapy group and 28.5% (4/14) in the placebo group. CONCLUSION: Electrical suppression of the tinnitus does not offer a promising outcome for patients with tinnitus in the presented study. 2008 S. Karger AG, Basel
Topical review: temporomandibular disorders in an integral otic symptom model.  

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The literature has closely observed otic symptoms (and other craniofacial complaints) in temporomandibular disorders; however, there is little evidence for an association between the two. This review tries to provide an integrated biological basis for otic symptoms in temporomandibular disorders from both anatomical and physiological points of view; it also attempts to enlarge the view of one of the ranges of central and peripheral mechanisms involved. The pathophysiology of common symptoms is integrated within different health specialties through basic science. This review is not based on a structured selection of randomized controlled trials; rather, it deals with perspectives of otic symptoms triggered or exacerbated by stomatognathic dynamics.

Somatosensory pulsatile tinnitus syndrome: somatic testing identifies a pulsatile tinnitus subtype that implicates the somatosensory system.  

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A new tinnitus syndrome is described: high-pitched, cardiac-synchronous tinnitus, whose pulsations are suppressed by strong contractions or compressions of the neck and jaw muscles (somatic testing). 14 cases, 6 non-lateralized and 8 unilateral, are reported. In the non-lateralized cases, onset was bilateral. In the one intermittent case, while her tinnitus was absent her pulsatile tinnitus could be induced by somatic testing. No etiology was found from physical examination, imaging, or ancillary testing. Because these cases of pulsatile tinnitus can be both induced and suppressed by activation of the somatosensory system of the head or upper lateral neck, we propose that this syndrome is occurring from (a) cardiac synchronous somatosensory activation of the central auditory pathway or (b) failure of the somatosensory-auditory central nervous system interactions to suppress cardiac somatosounds.

X Surgical Treatment

Superior Canal Dehiscence Plugging Reduces Dizziness Handicap.  
Laryngoscope 2008 Jul 10. [Epub ahead of print]

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OBJECTIVES/HYPOTHESIS: To compare dizziness handicap inventory (DHI) scores before and after surgery for plugging of superior canal dehiscence (SCD). The size of the dehiscence as measured during surgery, subject age, vestibular-evoked myogenic potentials threshold, and degree of conductive hearing loss (CHL) were also considered. STUDY DESIGN: Retrospective. METHODS: Nineteen adults with SCD who underwent surgery to plug the SCD via middle fossa approach were studied. Pre- and postoperative DHI scores were compared, and correlations between DHI scores and other clinical measures were assessed. RESULTS: Average preoperative DHI score was 44 +/- 24 (mean +/- SD). Postoperative DHI score was significantly lower at 18 +/- 15 (P < .01). Only two subjects had a higher DHI score after surgery. Subjects who had a preoperative DHI score below 30 did not have any significant change in their DHI score after surgery, whereas those with a preoperative DHI score >/=30 had an improvement by an average of 39 +/- 16 after surgery. There were no correlations between either preoperative DHI score or the change in DHI score after surgery and HL, age, vestibular-evoked myogenic potentials threshold, or dehiscence size. CONCLUSIONS: DHI scores significantly decreased after SCD plugging. Subjects who had the largest decrease in DHI scores were those with high preoperative DHI scores.
Subjects who chose to undergo SCD plugging because of nonvestibular symptoms such as conductive HL, tinnitus, or autophony generally had lower preoperative DHI scores and did not experience large improvements in DHI scores. The SCD plugging procedure offers an improvement in DHI score that is comparable with that of other procedures for peripheral vestibular dysfunction.

**Stereotactic radiation techniques in the treatment of acoustic schwannomas.**

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Medical decision-making is based on benefit-to-cost analysis. Optimally, treatment obtains a high degree of benefit while minimizing the physical, social, and financial costs. The goals of the treatment of acoustic schwannomas are prohibiting tumor growth and alleviation of symptoms caused by damage to local structures. These symptoms-tinnitus, ataxia, and hearing loss-secondary to eighth nerve dysfunction, as well as symptoms arising from damage to adjacent structures such as the facial nerve, trigeminal nerve, or pons, can be caused by tumor growth or treatment. Determination of optimal therapy must also take into account an understanding of the natural history of the disease, because acoustic schwannomas are slow-growing benign tumors that when left untreated, usually enlarge over time and cause problems.

**Incidence and quality of vertigo symptoms after cochlear implantation.**
J Laryngol Otol. 2008 Jun 4:1-5. [Epub ahead of print]

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Objectives: To assess the incidence of vestibular disturbance in patients after cochlear implantation, and to evaluate the quality of vertigo symptoms. Study design: Prospective, observational study. Setting: Cochlear implant centre at a tertiary referral university hospital, Munich, Germany. Patients: Forty-seven adult patients undergoing unilateral cochlear implantation between 2003 and 2007. Methods: Patients were interviewed post-operatively about vertigo symptoms, using a specifically designed questionnaire. Questionnaire data were used to define patient subgroups based on probable vertigo aetiology. Cochlear implantation was performed via a retroauricular, transmastoidal approach. Thirty-six implants were Cochlear Nucleus 24 devices and 11 were MedEl devices. Results: Twenty-one (45 per cent) patients reported vertigo symptoms following cochlear implantation. The time of onset was directly post-operatively in the majority of patients. In 90 per cent, the symptoms suggested an otogenic origin. The majority of patients reported paroxysmal vertigo with a duration of seconds to minutes. Typical concomitant symptoms were tinnitus, fluctuating hearing loss and vegetative reactions. Serious disablement by vertigo was rare. Conclusion: Exposing patients to the risk of possible balance disorders associated with cochlear implantation is justified in view of the hearing rehabilitation achieved, even with today’s broader indications for cochlear implantation. However, patients should in any case be informed about the possibility and quality of post-operative vertigo symptoms.

**Characteristics, diagnosis and treatment of hypoglossal canal dural arteriovenous fistula: report of nine cases.**
Neuroradiology. 2008 Apr 25. [Epub ahead of print]

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INTRODUCTION: We report the characteristics, diagnosis and treatment of dural arteriovenous fistula (DAVF) of the hypoglossal canal in nine patients with this relatively rare vascular disorder. METHODS: Of 248 patients with intracranial DAVFs managed at our institution, nine patients (3.6%; four men, five women; mean age 62 years) were diagnosed with hypoglossal canal DAVF. We investigated patient characteristics with respect to clinical symptoms, neuroradiological findings, efficacy and complications related to endovascular treatment. RESULTS: Seven patients had experienced head injury. All patients presented with pulsatile tinnitus. One patient displayed ipsilateral hypoglossal nerve palsy before treatment.
MR angiography showed a “magic wand” appearance between the affected hypoglossal canal and the internal jugular vein in four patients. Angiography demonstrated an AV fistula on the medial aspect of the superior jugular bulb, mostly arising from the bilateral occipital, ascending pharyngeal and vertebral arteries with drainage to the internal jugular vein via the anterior condylar vein. Contralateral carotid injection accurately clarified the shunting point. Five patients underwent endovascular treatment: transarterial embolization (TAE; n = 2), transvenous embolization (TVE; n = 2), and TAE/TVE (n = 1). Complete shunt obliteration was achieved in four patients and shunt reduction in one. The remaining four patients were treated conservatively and the shunt had disappeared at follow-up. Postoperative hypoglossal nerve palsy occurred in one patient after TVE, possibly due to coil overpacking.

CONCLUSION: The incidence of hypoglossal canal DAVF was not very low in our series. Contralateral carotid injection is an essential examination to provide an accurate diagnosis. TVE should be considered when access is available, although TAE is also appropriate for shunt reduction.

**Microvascular decompression of cochleovestibular nerve.**

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The role of microvascular decompression (MVD) in the management of trigeminal neuralgia, hemifacial spasms and glossopharyngeal neuralgia is well-established. However, controversy persisted as to the use of MVD in cochleovestibular neurovascular compression syndrome. This report provides a review of all the published studies on MVD of the eighth (8th) nerve in alleviating cochleovestibular symptoms and presents three additional patients who underwent MVD of the eighth nerve for tinnitus or vertigo. Nineteen studies were identified. Five were case reports. The remaining have sample sizes ranging from 4 to 207 patients. Quantitative and qualitative reviews of all studies were performed, focusing on the selection criteria for surgery, efficacy and safety of the procedure. Selection criteria for surgery were variable. No standardised outcome measures were used and all studies rely on patient subjective assessment of surgical outcome. Nonetheless, the results suggest that MVD of the eighth nerve produces good outcome with low morbidity in selected cases.

**Erbium: yttrium-aluminum-garnet laser stapedotomy--a safe technique.**
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OBJECTIVE: To standardize the technical parameters of the erbium: yttrium-aluminum-garnet (Er:YAG) laser stapedotomy. STUDY DESIGN: Retrospective study of all patients with otosclerosis who underwent stapedotomy from January 2002 to January 2006. SUBJECTS AND METHODS: The charts of 152 consecutive patients who underwent stapedotomy were reviewed. The patients were stratified into two groups, according to the instrument used. Stapedotomies were performed in group A, with the OPMI TwinEr:YAG laser; and in group B with manual microperforators. RESULTS: No statistically significant differences were found over all measured frequencies, between pre- and postoperative bone conduction thresholds, in each group. At the last postoperative follow-up, vertigo and nystagmus were not detected; two patients in group A and one patient in group B showed persistent tinnitus. CONCLUSION: Er:YAG laser stapedotomy is a safe and effective procedure, with no damage of the inner ear when strict adherence to the safety parameters is observed. The Er:YAG laser is definitively suitable for stapes surgery, and represents a useful and safe tool in the armamentarium of otological microsurgery.
Multidisciplinary treatment of a large cerebral dural arteriovenous fistula using embolization, surgery, and radiosurgery.

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Dural arteriovenous fistulae are rare lesions composed of abnormal connections between meningeal arteries and the dural sinuses or lepto-meningeal veins. Treatment is challenging because of the small size and wide distribution of the myriad sites of fistulous connection. We present a case of a dural arteriovenous fistula presenting with visual deterioration, pulsatile tinnitus, and intracranial hypertension that was successfully treated with a multidisciplinary approach combining angiographic, surgical, and radiosurgical intervention. This is one of the largest of these formidable lesions treated in this fashion that has been reported.

XI Holistics

Tinnitus: a philosophical problem.

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Anatomical, physiological and metabolic properties of tinnitus have been identified and a comprehensive theory isimmerging. The key elements and their interaction are presented in a general fashion highlighting areas of concern such as needed details of individual biosusceptibility and the need for continued tinnitus modeling for predictions as an aid in the development of effective treatment modalities. Nonetheless, there remains something of the uniqueness of tinnitus as a personal experience. The use of the final common pathway (FCP) as a unifying principle in diagnosis and treatment is presented.

[Clinical observation on warming-removing obstruction needling method for treatment of sudden tinnitus and deafness]
[Article in Chinese]

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OBJECTIVE: To compare therapeutic effects of acupuncture at Fengchi (GB 20) as main with warming-removing obstruction needling method and routine acupuncture on sudden tinnitus and deafness.

METHODS: Sixty-two cases were randomly divided into a warming-removing obstruction needling method group (n=32) and a routine acupuncture group (n=30). The warming-removing obstruction needling method group were treated with acupuncture at Fengchi (GB 20) as main point with warming-removing obstruction needling method, in combination with local, distant points of ear with twirling uniform reinforcing-reducing method used; and the routine acupuncture group were treated with acupuncture at local and distant points of ear with twirling uniform reinforcing-reducing method adopted. After treatment for 3 courses, their therapeutic effects were compared and followed-up. RESULTS: The cured-markedly effective rate, the effective rate and the recurrence rate were 90.6%, 96.9% and 3.4% in the warming-removing obstruction needling method group, and 60.0%, 80.0% and 22.2% in the routine acupuncture group, with a very significant difference in the cured-markedly effective rate (P<0.01) and with a significant difference in the effective rate and the recurrence rate (P<0.05) between the two groups. CONCLUSION: The therapeutic effect of the warming-removing obstruction needling method group is significantly better than that of the routine acupuncture group with lower recurrence rate after cure.
XII Review

Treatments for tinnitus.

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The various forms of treatment for tinnitus that have been tested in properly controlled trials can be classified as pharmacological, acoustic-physical, and psychological. In clinical trials, no pharmacological agent has been shown to have lasting effect on the presence or severity of tinnitus, although there are promising signs in an animal model. Acoustic devices do not seem to influence tinnitus, although appropriately fitted hearing aids may slightly reduce its prominence. Of physical treatments, cortical implantation may hold some promise of being effective for tinnitus suppression in selected cases. A psychological treatment that has emerged as consistently beneficial is cognitive-behavior therapy in terms of affecting overall well-being and reducing level of tinnitus annoyance.

The role of audiologic evaluation in progressive audiologic tinnitus management.

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Progressive Audiologic Tinnitus Management (PATM) is based on the premise that tinnitus is managed most efficiently using a hierarchy of clinical services that address different levels of need. PATM includes five levels of management: (a) triage; (b) audiologic evaluation; (c) group education; (d) tinnitus evaluation; and (e) individualized management. This article provides an overview of PATM and focuses on the procedures that make up the Level 2 Audiologic Evaluation. The evaluation is conducted to assess the potential need for medical, audiologic (hearing loss, tinnitus, hyperacusis), and/or mental health services. The Tinnitus Handicap Inventory, Hearing Handicap Inventory, and Tinnitus and Hearing Survey are used to differentiate effects of tinnitus and hearing loss. If indicated, patients are interviewed with the Tinnitus-Impact Screening Interview. Patients requiring amplification receive hearing aids. Often, management of hearing loss at Level 2 addresses any problems that were attributed to the tinnitus, which obviates further tinnitus-specific intervention.

Strategies for managing patients with tinnitus: A clinical pathway model
Semin Hearing 2008 Aug 29 (3):300-309

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Tinnitus is a distressing symptom affecting the health-related quality of life of many individuals. Yet most audiologists feel ill equipped in providing clinical services to these patients. This article presents an overview of a clinical pathway for patients seen in the multidisciplinary Tinnitus Management Clinic at the Cleveland Clinic. The model illustrates an efficient approach for managing patients with varying levels of perceived tinnitus severity and annoyance by sequencing patient care and intervention strategies. After providing a general overview of the clinical pathway, three unique components of the model are highlighted: (1) benefits of a Group Education Session; (2) usefulness of the Sound Therapy Option Profile, a new tool designed to guide the clinician in selecting the most appropriate sound therapy device for a given patient; and (3) participation of a psychologist and neurologist on the multidisciplinary management team. Copyright © 2008 by Thieme Medical Publishers, Inc.
Hyperbaric oxygen therapy seems to enhance recovery from acute acoustic trauma.

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Conclusion. The average recovery of hearing and cessation of tinnitus was significantly better after hyperbaric oxygen therapy (HBOT) than after normobaric oxygen therapy (NBOT). HBOT can be valuable adjuvant therapy for patients with acute acoustic trauma (AAT). Objectives. AAT was one of the early indications for the use of HBOT. The rationale of administering oxygen to patients with AAT is based on experimental studies showing that noise exposure results in cochlear hypoxia, which could be compensated by HBOT. The aim of this study was to investigate the efficacy of HBOT in patients with AAT. Patients and methods. We compared the recovery from hearing impairment and tinnitus in 60 ears treated with HBOT with 60 ears treated with NBOT. The HBOT was given daily for 1-8 days. There were no significant differences in clinical or audiological data between HBOT and NBOT groups. Results. The average recovery of hearing both at high and speech frequencies was significantly better and tinnitus persisted less commonly after the HBOT than after the NBOT. Normal hearing at the end of the follow-up period was regained in 42 ears in the HBOT group and in 24 ears in the NBOT group (p<0.01).

The roadmap to a cure, who pays for basic science, and the future of tinnitus research

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The American Tinnitus Association (ATA) exists to cure tinnitus through the development of resources that advance tinnitus research. A large part of the population suffers from tinnitus, yet private donations to tinnitus research remain limited. This article explains who pays for tinnitus research: industry, government, and private and public philanthropy. To encourage larger donations, donors who suffer from tinnitus need to see a clear connection between their financial support of research and future treatments. An expanded version of the "Roadmap to a Cure," adopted in its original form by the ATA, is offered as a vehicle to show how donor contributions can make a difference. Finally, this article gives an overview of certain issues of academic priority in research and the growing role of the financial value of intellectual property, and it explores how these issues relate to advancing tinnitus research. Copyright © 2008 by Thieme Medical Publishers, Inc.

Dangerous Decibels: Partnership for preventing noise-induced hearing loss and tinnitus in children
Semin Hearing 2008 Aug 29 (1):102-110

Martin WH
Oregon Hearing Research Center, Department of Otolaryngology/Head and Neck Surgery, Oregon Health and Science University, Portland, OR, United States

Oregon Health & Science University’s Oregon Hearing Research Center, in conjunction with the Oregon Museum of Science and Industry, the Portland State University School of Community Health, the Veterans Affairs National Center for Rehabilitative Auditory Research, and the American Tinnitus Association, formed a public health partnership to address the problem of noise-induced hearing loss and tinnitus. The Dangerous Decibels partnership has received funding from several private foundations and public sources. This support enabled the development of a wide range of activities including exhibits, educational outreach, educator training, and research. All of the Dangerous Decibels activities communicate three educational messages: What are sources of dangerous sounds? What are the consequences of being exposed to dangerous sounds? How can I protect myself from dangerous sounds?
Cultural and social perspectives on attitudes, noise, and risk behavior in children and young adults
Semin Hearing 2008 Aug 29 (1):29-41

Erlandsson SI1, Holmes A2, Widén SE1, Bohlin M1
1 Division of Psychology and Organizational Studies, Department of Social and Behavioral Sciences, University West, Trollhättan, Sweden, 2 Department of Communicative Disorders, College of Public Health and Health Professions, University of Florida, Gainesville, FL, United States

Interdisciplinary research is critical to the prevention of hearing loss in children and young adults. To meet that goal, this paper focuses on the relationship between the prevalence of noise-induced hearing loss, attitudes to noise and exposure, and how hearing protection use seems to be linked to cultural and socioeconomic factors. Results of a series of studies point to attitudes as one explanatory factor. Additionally, the experience of hearing symptoms such as tinnitus and noise sensitivity increases the likelihood that adolescents and young adults will choose to wear earplugs when attending clubs or discos. This behavior can be referred to as an important “trigger” mechanism for the development of health-related behavior. Some general theories on health behavior are discussed to understand the role attitudes play for hearing prevention in young people. Finally, the finding that adolescents seeking professional help for tinnitus appear to have strong fears related to anxious thoughts and reactions associated with the condition is addressed. These fears can be a sign of a phobic reaction, something that most often first appears during adolescence. For these reasons, interdisciplinary research in the investigation of tinnitus distress and hearing conservation in young people seems to be the most relevant approach. Copyright © 2008 by Thieme Medical Publisher, Inc.

Hearing-loss prevention practices should be taught in schools

Folmer RL
Department of Otolaryngology, Oregon Health and Science University, Portland, OR, United States, National Center for Rehabilitative Audiology Research, Veterans Administration Medical Center, Portland, OR, United States

Children are often exposed to excessive levels of sound, such as loud music, firearms, power tools, and noisy toys. Such exposure puts children at risk for developing noise-induced hearing loss (NIHL) and tinnitus. For more than 30 years, health policy agencies and numerous experts in hearing science have recommended teaching hearing-loss prevention practices to children in schools as a way to reduce the prevalence of NIHL. Despite these recommendations, basic hearing-loss prevention information that could prevent countless cases of NIHL remains conspicuously absent from most school curricula. At least 10 organizations produce or use a variety of materials in a comprehensive hearing-loss prevention curriculum for school-age children. At least 18 additional organizations produce or disseminate materials (Web-based, video, or printed matter) that could be used to teach hearing-loss prevention in classrooms. Therefore, adequate materials and curricula are available for presenting this information to school-age children. It is time to implement the repeated recommendations of experts by providing hearing-loss prevention instruction in all of our nation’s schools on a regular basis. These educational efforts should eventually help to reduce the prevalence of NIHL, which is a fully preventable condition. Copyright © 2008 by Thieme Medical Publishers, Inc.
Venous Hum Causing Tinnitus: Case Report and Review of the Literature.
Anderson JE, Teitel D, Wu YW.
Hearing one’s own heart murmur has been reported in adults, but has not been reported in the pediatric literature. This study reports the case of a young child who clearly heard her own venous hum, causing her to complain of pulsatile tinnitus. This entity should be included in the differential diagnosis of pulsatile tinnitus and by doing so pediatricians and cardiologists may avoid ordering unnecessary diagnostic procedures.

Acute hearing loss from scuba-diving holidays: Diagnosis and treatment of barotrauma of the inner ear.
HNO 2008 Jul 12. [Epub ahead of print]
Brocks C, Wollenberg B, Graefe H.
Klinik und Poliklinik für Hals, Nasen- und Ohrenheilkunde und plastische Operationen, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Ratzeburger Allee 160, 23538, Lübeck, Deutschland, carsten.brocks@uk-sh.de.
A 35-year-old diver noticed hearing loss and tinnitus after his diving holiday. He presented to the Lübeck clinical practice for divers, and we found vascular injections on the eardrum. Audiometry showed a high-degree hearing loss of 40-60 dB. Under the assumption of a perilymphatic fistula, we performed a tympanoscopy with covering of the oval and round windows. Bone-conduction hearing improved immediately postoperatively to 25 dB. A postoperative rheological infusion treatment was given. After 6 months the diver was assessed fit to dive with almost normal inner ear function.

Fluctuating response of a cystic vestibular schwannoma to radiosurgery: case report.
de Ipolyi AR, Yang I, Buckley A, Barbaro NM, Cheung SW, Parsa AT.
Department of Neurological Surgery, Brain Tumor Research Center, University of California at San Francisco, San Francisco, California, USA.
OBJECTIVE: A vestibular schwannoma (VS) is a benign tumor of the VIIIth cranial nerve that can often be treated by microsurgery or radiosurgery and demonstrates high tumor control rates. Radiosurgery is typically performed as gamma knife surgery (GKS), although other modalities are being applied with increasing frequency. A differentiating feature in responsiveness to microsurgery or GKS is whether the VS is cystic or solid. A cystic VS is less responsive to GKS than a solid VS, representing a challenging clinical problem. GKS treatment of a cystic VS usually results in sustained expansion, sustained regression, or transient expansion followed by sustained regression. In this article, we report an atypical fluctuating course of a cystic VS after GKS, ultimately requiring surgical intervention.
CLINICAL PRESENTATION: A 66-year-old woman presented with asymmetric hearing loss and tinnitus. Magnetic resonance imaging revealed a 2.0-cm unilateral cystic VS within the cerebellopontine angle. INTERVENTION: After GKS with a 12-Gy dose to the 50% isodose line, the tumor expanded transiently to 3.2 cm and then regressed to 1.0 cm over the next 2 years. She presented several months later with new-onset dizziness, ataxia, and facial numbness. Magnetic resonance imaging revealed a 3.2-cm multicystic VS that compressed the brainstem. After microsurgical tumor excision, the patient’s symptoms abated. CONCLUSION: Our case report is a novel demonstration that a cystic VS that has regressed after GKS is still at risk for expansion. The mechanisms responsible for radiation-induced cystic tumor expansion have not been thoroughly elucidated. The risk of unpredictable tumor enlargement should be discussed with patients when considering GKS for cystic tumors.
Clinical application of long-term intensity and pitch matches in fluctuating low-frequency hearing loss.

Jonas Brannstrom K, Grenner J.
Department of Clinical Sciences, Lund University, Sweden. jonas.brannstrom@med.lu.se

The purpose of this study was to measure changes in intensity and pitch matches to better assess disease activity in fluctuating low-frequency hearing loss. Long-term suprathreshold audiometry was carried out at home on a subject with a unilateral fluctuating low-frequency hearing loss during a period when the subject demonstrated no symptoms and a period when the subject reported hearing loss, aural pressure, and tinnitus. Daily measurements of binaural intensity and pitch matches were made. Day-to-day fluctuations were clearly accentuated during the period when the subject experienced symptoms. Specifically, deviations from the reference tone were only observed for binaural pitch matches at 1 kHz during the period without symptoms; however, highly fluctuating binaural intensity and pitch matches were observed at 0.25 kHz during the period with symptoms. These fluctuations were not observed in a normal-hearing group. The results suggest that long-term measurements of binaural intensity and pitch matches can be used to monitor disease activity in fluctuating low-frequency hearing loss.

[Pediatric otosclerosis: case report and literature review]
[Article in Portuguese]

Salomone R, Riskalla PE, Vicente Ade O, Boccalini MC, Chaves AG, Lopes R, Felin Filho GB.
Hospital CEMA.

Otospongiosis is an osteodystrophy of the temporal bone, characterized by disordered neoformation and deposition of bone, characterized by the presence of a progressive conductive, sensorineural or mixed hearing loss and tinnitus. Typically, otospongiosis presents as a slowly progressive conductive hearing loss in the third to fourth decade of life. Uncommonly children and adolescents may also have conductive or sensorineural hearing loss caused by otosclerosis. We describe a case of an 11-year-old patient, with progressive unilateral conductive hearing loss for 5 years. The otoscopic examination revealed a positive Schwartz’s sign in the left ear. Audiometry, impedanciometry and CT scan showed characteristics that suggested otospongiosis. We reviewed clinical aspects, diagnosis and the therapeutic approach for otospongiosis in children.

Pulsatile tinnitus in a case of traumatic temporal extradural arteriovenous fistula: Carotid duplex sonography findings before and after embolization.
J Clin Ultrasound. 2008 Jun 17. [Epub ahead of print]

Tan TY, Lin YY, Schminke U, Chen TY.
Department of Neurology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, 123 Ta-Pei Road, Niao-Sung Hsiang, Kaohsiung 833, Taiwan.

Carotid duplex sonography (CDS) is regarded as a screening tool for lateral dural arteriovenous fistulae (AVF). However, data on evaluating long-term effects of endovascular treatment are limited. We report the CDS findings in the feeding arteries of a traumatic temporal extradural AVF before and after transarterial embolization. Volume flow of the left common carotid artery was greater than the right (433 ml/minute versus 294 ml/minute right) and the resistance index of the left external carotid artery was lower than the right (0.69 left versus 0.84 right). Both parameters returned to normal 4 months after embolization, thus confirming successful endovascular treatment. (c) 2008 Wiley Periodicals, Inc. J Clin Ultrasound, 2008.
[A Dural Fistula as a Rare Cause for a Pulse-synchronized Tinnitus aurium.]
[Article in German]
Laryngorhinootologie. 2008 Jun 5. [Epub ahead of print]

Brocks C, Bela C, Gaebel C, Wollenberg B, Sommer K.
Universitätsklinikum Schleswig Holstein, Campus Lübeck, Klinik für Hals-Nasen- und Ohrenheilkunde
(Direktorin: Prof. Dr. med. Barbara Wollenberg).

Pulse-synchronized tinnitus aurium is commonly caused by vascular processes within the area of the temporal bone. With a microphone or a stethoscope in the external ear or on the mastoid perceptible noises can be heard by the physician. The most important differential diagnoses of an objective tinnitus are paraganglioma of the glomus jugulare or the glomus tympanicum, vascular stenosis, arteriovenous malformations, aneurysms and atypical findings of the bulb of the temporal bone. In case of a pulse-synchronized tinnitus purposeful use of neuroradiological diagnostic can lead to a correct diagnosis. The indication for invasive intervention of dural fistulas depends on the number and the hemodynamic relevance of these fistulas and on individual suffering of the patient. Even if it does not succeed, all to embolize AV-short-circuits, it is possible to reduce the intensity of the tinnitus in order to continue with conservative therapy.

Aberrant ectatic internal carotid artery in the middle ear.

Safdar A, Hughes JP, Walsh RM.
Department of Otolaryngology-Head and Neck Surgery, Beaumont Hospital, Dublin, Ireland. adnan_safdar@hotmail.com

We report the case of a 34-year-old man with pulsatile tinnitus and a reddish mass in the anteroinferior quadrant of the middle ear. Physical examination and imaging were unable to establish a diagnosis, so an exploratory tympanotomy was performed. Exploration revealed the presence of an ectatic aberrant internal carotid artery in the middle ear. Aberrations of the internal carotid artery in the middle ear are rare. Even so, our case is unusual in that all initial investigations had failed to establish the diagnosis. This case highlights the limitations of modern imaging techniques in certain situations.

Embolisation of an extensive arteriovenous malformation of the temporal region as an alternate treatment: case report.

Aslan S, Yavuz H, Cagici AC, Kizilkilic O.
Department of Otorhinolaryngology, Baskent University, Ankara, Turkey. drsundus@hotmail.com

OBJECTIVES: To report the case of a spontaneous arteriovenous malformation involving the auricula, external auditory meatus, middle ear and part of the petrous apex, and also to provide updated information about its management. CASE REPORT: A 33-year-old woman presented complaining of accelerated growth of a retro-auricular swelling during her latest pregnancy, together with pain, pulsatile tinnitus and ear discharge. An arteriovenous malformation occupying the right auricula, external auditory canal, mastoid process of the temporal bone and the lateral half of the petrous segment was diagnosed, using temporal computerised tomography and magnetic resonance imaging. The lesion was embolised with polyvinyl alcohol particles at angiography. Excision of the arteriovenous malformation nidus was performed. Three years post-operatively, magnetic resonance imaging showed no residual lesion or recurrence at the temporal bone and petrous apex, although a few scanty, serpiginous, vascular remnants had persisted. CONCLUSIONS: In the head and neck, arteriovenous malformations usually occur intracranially; they are rare outside the cranium. To our knowledge, there have been no previously published cases of such an extensive arteriovenous malformation involving the temporal region. Apropos of our case, the definition, clinical findings, diagnostic approaches and therapeutic management of arteriovenous malformations are discussed.
Musical hallucinations after left temporal lobectomy.

Williams VG, Tremont G, Blum AS.
Department of Psychiatry, Warren Alpert Medical School of Brown University, RI, USA.

BACKGROUND: Musical hallucinations (MHs) are rare and most often described in patients with hearing loss, female sex, older age, and various brain pathologies, including epilepsy. CASE HISTORY: We describe a unique case in which, after successful left temporal lobectomy for refractory epilepsy and subsequent ototoxic therapies, a 49-year-old man experienced the onset of songs replaying constantly in his mind for days to weeks. He had intractable partial epilepsy since age 26. Presurgical neurodiagnostic evaluations revealed a left temporal focus, left hippocampal magnetic resonance imaging abnormalities, bilateral language representation, and cognitive deficits lateralized to the left hemisphere. He underwent a partial left temporal lobectomy but required repeated antibiotic courses for postoperation bone flap infections, resulting in tinnitus. Surgery led to near seizure-freedom, plus improved cognitive and emotional function. Pathology revealed focal cortical dysplasia. Six months postsurgery, during antibiotic treatment, he began to hear songs replaying in his head, which increased in frequency over ensuing years. CONCLUSIONS: We report, to our knowledge, the first case of MHs associated with temporal lobectomy for epilepsy. This patient had multiple risk factors for these unwanted musical experiences, including epilepsy, mild neuropsychiatric dysfunction, and tinnitus plus hearing loss. Possible mechanisms for MHs are discussed.

Pulsatile tinnitus: A harbinger of a greater ill?
Head Neck. 2008 Jul 18. [Epub ahead of print]

Liess BD, Lollar KW, Christiansen SG, Vaslow D.
Department of Otolaryngology-Head and Neck Surgery, University of Missouri School of Medicine, Columbia, Missouri.

BACKGROUND.: Pulsatile tinnitus is an uncommon otologic symptom, which may be the presenting complaint of a potentially devastating pathology. Understanding this manifestation as a possible symptom of a significant vascular abnormality is crucial to guide management and treatment. METHODS AND RESULTS.: We describe a 38-year-old woman with sudden-onset right-sided pulsatile tinnitus. A right extracranial internal carotid artery (ICA) dissection was diagnosed with MRI/magnetic resonance angiography (MRA) and treated with anticoagulation. Follow-up MRI/MRA demonstrated complete resolution. Two months later, left-sided pulsatile tinnitus evolved. An MRI/MRA of the neck demonstrated left-sided extracranial ICA dissection. She was treated in a similar fashion and a repeat MRI/MRA demonstrated its resolution. CONCLUSION.: Spontaneous extracranial ICA dissection may present with pulsatile tinnitus as the only symptom in 4% to 50% of patients. Subsequent evolution of a contralateral dissection is even more uncommon. Generally, treatment of this phenomenon is conservative utilizing anticoagulation or aspirin; however, surgical intervention may be necessary. (c) 2008 Wiley Periodicals, Inc. Head Neck 2008.
### Clinical Trial of Acamprosate for Tinnitus

<table>
<thead>
<tr>
<th>Current status</th>
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<tr>
<td>Sponsors and collaborators</td>
<td>University Hospital Tuebingen</td>
</tr>
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<td>Information provided by</td>
<td>University Hospital Tuebingen</td>
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<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00719940</td>
</tr>
<tr>
<td>Purpose</td>
<td>Test of hypothesis that in contrast to non-treatment tinnitus specific cognitive behavioral therapy intervention procedures that are manualized and structured within the disease management program TCP are effective</td>
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<tr>
<td>Condition(s)</td>
<td>Tinnitus</td>
</tr>
<tr>
<td>Interventions</td>
<td>Behavioral: Cognitive behavioral therapy, Other: Waiting Group</td>
</tr>
<tr>
<td>Phase</td>
<td>Phase IV</td>
</tr>
<tr>
<td>Study type and design</td>
<td>Interventional; Treatment, Randomized, Open Label, Parallel Assignment, Efficacy Study</td>
</tr>
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<td>Official title</td>
<td>Randomized Controlled Clinical Trial of Efficacy and Safety of Individual Cognitive Behavioral Therapy (CBT) Within the Setting of the Structured Therapy Program sTCP (Structured Tinnitus Care Program) in Patients With Tinnitus Aurium</td>
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<td>Arms</td>
<td>1: Experimental: Cognitive behavioral therapy, 2: Placebo Comparator: Waiting group</td>
</tr>
<tr>
<td>Assigned Interventions</td>
<td>1. Behavioral: Cognitive behavioral therapy 1-15 individual sessions of 50-60 min. to apply 1-15 manualized tinnitus specific cognitive behavioral therapy interventions structured by the tinnitus care disease management program 2. Other: Waiting group No intervention</td>
</tr>
<tr>
<td>Detailed Description</td>
<td>Intervention: Individual application of structured and tinnitus specific cognitive behavioral therapy intervention procedures in the clinical setting of the structured therapy program “tinnitus care program (TCP)” Duration of intervention per patient: 1-15 treatment sessions plus self treatment up to 16 weeks Control intervention: Waiting group (16 weeks)</td>
</tr>
<tr>
<td>Primary Outcomes</td>
<td>Validated tinnitus questionnaire (TF Goebel and Hiller 1992); validated tinnitus change rating scale (TC; Zenner and de Maddalena 2005) [Time Frame: Last session] [Designated as safety issue: Yes]</td>
</tr>
<tr>
<td>Secondary Outcomes</td>
<td>Tinnitus loudness (TL), validated 6-point numeric verbal rating scale; tinnitus annoyance (TA), validated 8-point numeric verbal rating scale [Time Frame: last therapy session] [Designated as safety issue: Yes]</td>
</tr>
<tr>
<td>Expected total Enrollment</td>
<td>286</td>
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<tr>
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<td>Study start</td>
<td>October 2000</td>
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<td>Expected study completion date</td>
<td>November 2006</td>
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<td>Expected primary completion date</td>
<td>October 2004 (Final data collection date for primary outcome measure)</td>
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<tr>
<td>Participants (age)</td>
<td>14 Years to 90 Years</td>
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<td>Gender</td>
<td>Both</td>
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<tr>
<td>Accepts health volunteers</td>
<td>No</td>
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</tbody>
</table>
| Eligibility Inclusion Criteria | • Persistent and stable tinnitus of more than 11 weeks  
• Gap between audiometric tinnitus matching and subjective tinnitus loudness rating scale |
| Eligibility ExclusionCriteria | • Psychiatric or neurological comorbidity  
• Tinnitus as concomitant symptom of an otherwise treatable disease  
• Drug treatment for tinnitus 24 hrs. prior or during therapy |
| Contact                  | Please refer to this study by its ClinicalTrials.gov identifier: NCT00719940 |
| Locations                | Dept. ORL, University of Tuebingen, Tuebingen, Germany, 72070  
Private Practice, Tübingen, Germany, 72070  
Tinnitus Care Center Frankfurt, Germany, 60594  
Tinnitus Care Center Aschaffenburg, Germany, 63739 |
| Study chairs or principal investigators | Hans P. Zenner, M.D, Professor and Chairman, Dept. ORL, University of Tuebingen, Germany |
| Study ID Numbers         | TCP00/04, BMBF 01EZ0506: Dekonet; Mediceon: Benchmarking project |
| Last Updated             | July 18, 2008 |
| Record first received    | June 16, 2008 |
| ClinicalTrials.gov Identifier | NCT00719940 |
| Health Authority         | Germany: Ethics Commission |
# Cost-Effectiveness of Multidisciplinary Management of Tinnitus

<table>
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<th>Current status</th>
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</thead>
<tbody>
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<td>Sponsors and collaborators</td>
<td>Maastricht University</td>
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<td>Information provided by</td>
<td>Maastricht University</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00733044</td>
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</tbody>
</table>

## Purpose

Background: Tinnitus is a common chronic health condition that affects 10% to 20% of the general population. Among severe sufferers it causes disability in various areas. As a result of the tinnitus quality of life is often impaired. At present there is no cure or uniformly effective treatment, leading to fragmentized and costly tinnitus care. Evidence suggests an integral multidisciplinary approach in treating tinnitus is effective. The main objective of this study is to examine the effectiveness, costs, and cost-effectiveness of an integral treatment provided by a specialized tinnitus center versus usual care. This paper describes the study protocol.

In a randomized controlled clinical trial 198 tinnitus patients will be randomly assigned to a specialized tinnitus care group or a usual care group. Adult tinnitus sufferers referred to the audiological centre are eligible. Included patients will be followed for 12 months.

Primary outcome measure is generic quality of life (measured with the Health Utilities Index Mark III). Secondary outcomes are severity of tinnitus, general distress, tinnitus cognitions, tinnitus specific fear, and costs. Based on health state utility outcome data the number of patients to include is 198. Economic evaluation will be from a societal perspective.

Discussion/Conclusion: This is, to our knowledge, the first randomized controlled trial that evaluates an integral treatment of tinnitus that includes a full economic evaluation from a societal perspective. If this intervention proves to be effective and cost-effective, implementation of this intervention is considered and anticipated.

<table>
<thead>
<tr>
<th>Condition(s)</th>
<th>Tinnitus</th>
</tr>
</thead>
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| Interventions | Behavioral: Specialised Care Group  
Other: Usual Care |
| Study type and design | Intervventional; Health Services Research, Randomized, Double Blind (Subject, Investigator), Active Control, Parallel Assignment, Efficacy Study |
| Official title | Cost-Effectiveness of Multidisciplinary Management of Tinnitus at a Specialised Tinnitus Centre |
| Arms | I: Experimental  
II: Active Comparator |
<table>
<thead>
<tr>
<th>Assigned Interventions</th>
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</thead>
<tbody>
<tr>
<td>I. Behavioral: Specialised Care Group</td>
<td></td>
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<tr>
<td>The intervention consists of the integration of integral tinnitus management provided by a specialized tinnitus centre in the health care system. The tinnitus centre offers care following a stepped-care approach with two levels. The first level of intervention consists of audiological diagnostics and intervention, a tinnitus educational group session and a individual consult with a clinical psychologist. For patients with mild complaints this basic intervention is expected to suffice. For patients with moderate to severe complaints a second level of intervention exists. This level of intervention consists of combinations of the following therapies: Cognitive Behavioural Therapy (CBT), Attention Diversion (AD), exposure techniques, and Relaxation Therapy (RT).</td>
<td></td>
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<tr>
<td>II. Other: Usual Care</td>
<td></td>
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<tr>
<td>Usual care consists of a standardized version of treatment that is currently applied in peripheral audiological centres throughout the Netherlands. A telephone survey was conducted amongst all audiological centres (n=28) in the Netherlands. The results of this survey determined the content of the usual care treatment protocol in the current study. The treatment consists of audiological diagnostics and intervention and, if necessary, one or more consults with a social worker with a maximum of ten one hour sessions.</td>
<td></td>
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<table>
<thead>
<tr>
<th>Primary Outcomes</th>
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<tbody>
<tr>
<td>Generic Quality of Life as measured with the Health Utilities Index Mark 3 (HUI3) [ Time Frame: At baseline and 3, 8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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</table>

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
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<tbody>
<tr>
<td>Tinnitus related disability and handicap as measured with the Tinnitus Handicap Inventory (THI) [ Time Frame: At baseline and at 3, 8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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<tr>
<td>Tinnitus annoyance and severity, as measured with the Tinnitus Questionnaire (TQ) [ Time Frame: At baseline and at 3, 8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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<tr>
<td>Tinnitus-related fear was assessed by the Fear of Tinnitus Questionnaire (FTQ) [ Time Frame: At baseline and at 3, 8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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<tr>
<td>Dysfunctional beliefs and/or cognitions regarding the tinnitus, as measured with the Tinnitus Coping and Cognition list (TCCL) [ Time Frame: At baseline and at 3, 8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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<tr>
<td>Catastrophic (mis)interpretations of tinnitus, as measured with the Tinnitus Catastrophising Scale (TCS). [ Time Frame: At baseline and at 3, 8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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<td>Costs, as measured with a retrospective cost questionnaire [ Time Frame: At baseline and at 3,8 and 12 months follow-up ] [ Designated as safety issue: No ]</td>
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<p>| Expected total Enrollment | 198 |
| Study start | September 2007 |</p>
<table>
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<tr>
<td><strong>Expected primary completion date</strong></td>
<td>September 2010 (Final data collection date for primary outcome measure)</td>
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<td><strong>Participants (age)</strong></td>
<td>18 Years and older</td>
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<td><strong>Gender</strong></td>
<td>Both</td>
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<tr>
<td><strong>Accepts health volunteers</strong></td>
<td>No</td>
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</table>
| **Eligibility Inclusion Criteria** | Subjective tinnitus complaints  
Referred to Tinnitus centre Limburg |
| **Eligibility Exclusion Criteria** | Not being able to write and read in Dutch |
| **Contact** | Rilana F Cima, MSc, phone 0031 45 528 29 00, r.cima@dmkep.unimaas.nl  
Iris HL Maes, MSc, phone 0031 43 387 75 36, iris.maes@mumc.nl |
| **Locations** | Netherlands, Limburg, Hoensbroeck Audiological Centre, Recruiting Hoensbroek, Limburg, Netherlands, 6432CC |
| **Study chairs or principal investigators** | Johan WS Vlaeyen, Prof, PhD, Maastricht University  
Manuela A Joore, PhD, Maastricht University  
Lucien J Anteunis, PhD; Maastricht University |
| **Study ID Numbers** | 06-0012, ZonMw 80-007022-98-07715 |
| **Last Updated** | August 7, 2008 |
| **Record first received** | August 7, 2008 |
| **ClinicalTrials.gov Identifier** | NCT00733044 |
| **Health Authority** | Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) |

**Repetitive Transcranial Magnetic Stimulation (rTMS) for Tinnitus**

<table>
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<tr>
<th><strong>Current status</strong></th>
<th>currently recruiting participants</th>
</tr>
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<tbody>
<tr>
<td><strong>Sponsors and collaborators</strong></td>
<td>UMC Utrecht</td>
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<td><strong>Information provided by</strong></td>
<td>UMC Utrecht</td>
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<tr>
<td><strong>ClinicalTrials.gov Identifier</strong></td>
<td>NCT00668720</td>
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<tr>
<td><strong>Purpose</strong></td>
<td>Tinnitus is a phantom auditory perception of meaningless sound, meaning that there is registration of sound in the absence of an external or internal acoustic stimulus. It is a common problem (prevalence 7-19%) which may interfere with the ability to lead a normal life. Unfortunately, it is a very difficult symptom to treat because there are hardly any therapeutic options for the cause of tinnitus. Most therapies focus on alleviating the condition rather than treating the cause.</td>
</tr>
</tbody>
</table>
Tinnitus is thought to be generated in the brain, as a result of functional reorganization of auditory neural pathways and tonotopic maps in the central auditory system, following damage to the peripheral auditory system. Repetitive Transcranial magnetic stimulation (rTMS) is a therapy, based on this concept of reorganization in the auditory cortex. It uses a pulsed magnetic field to disrupt the neural circuit and to thereby (temporarily) excite or inhibit certain brain areas, leading to the suppression of tinnitus.

<table>
<thead>
<tr>
<th>Condition(s)</th>
<th>Tinnitus</th>
</tr>
</thead>
</table>
| Interventions        | Device: transcranial magnetic stimulation (Magstim rapid2)  
Device: sham stimulation |
| Study type and design| Interventional; Treatment, Randomized, Double Blind (Subject, Caregiver, Outcomes Assessor), Placebo Control, Parallel Assignment, Efficacy Study |
| Official title       | Effectiveness of Repetitive Transcranial Magnetic Stimulation (rTMS) Treatment in Patients With Chronic Tinnitus |
| Arms                 | 1: Experimental  
2: Sham Comparator |
| Assigned Interventions| 1. Device: transcranial magnetic stimulation (Magstim rapid2)  
Neuronavigated rTMS will be applied bilaterally to the auditory cortices, which will be identified through a structural MRI scan. Stimulation will be performed with 1 Hz frequency and an intensity of 110% motor threshold for 2000 stimuli (32 minutes) on each side, on five subsequent days.  
2. Device: sham stimulation  
The official sham stimulator for the magstim rapid2 will be used. Sham stimulation will follow the same placement protocol and will also last 2x32 minutes on five subsequent days |
| Primary Outcomes     | Tinnitus severity with the Tinnitus Questionnaire [Time Frame: after treatment, 1 week, 1, 3 and 6 months] [Designated as safety issue: No] |
| Secondary Outcomes   |  
• Tinnitus Handicap Inventory [Time Frame: after treatment, 1 week, 1, 3 and 6 months] [Designated as safety issue: No]  
• Beck Depression Inventory [Time Frame: after treatment, 1 week, 1, 3 and 6 months] [Designated as safety issue: No]  
• State Trait Anxiety Index [Time Frame: after treatment, 1 week, 1, 3 and 6 months] [Designated as safety issue: No]  
• Visual Analog Scales on burden, loudness, pitch, presence, and variability of tinnitus and specific problems. [Time Frame: for the first three months daily and for the second three months monthly] [Designated as safety issue: No]  
• Audiometry and tinnitus analysis (character match, pitch match, loudness match, minimal masking level, residual inhibition) [Time Frame: 1 week after treatment and after 3 and 6 months] [Designated as safety issue: No] |
<table>
<thead>
<tr>
<th>Expected total Enrollment</th>
<th>52</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study start</td>
<td>April 2008</td>
</tr>
<tr>
<td>Expected primary completion date</td>
<td>December 2008 (Final data collection date for primary outcome measure)</td>
</tr>
<tr>
<td>Participants (age)</td>
<td>18 Years and older</td>
</tr>
<tr>
<td>Gender</td>
<td>Both</td>
</tr>
<tr>
<td>Accepts health volunteers</td>
<td>No</td>
</tr>
</tbody>
</table>
| Eligibility Inclusion Criteria | • Chronic, non fluctuating, tinnitus, demonstrated by means of the diagnostic Protocol Tinnitus UMCU, of at least two months duration.  
• Age ≥18 years |
| Eligibility Exclusion Criteria | • Treatable cause of the tinnitus  
• Use of anticonvulsant medication or other psychotherapeutic drugs  
• History of epilepsy or family members with epilepsy  
• Presence of active migraine  
• Presence of psychiatric, severe internal or heart diseases or other neurologic diseases besides epilepsy  
• Metal objects in and around body that can not be removed  
• Pregnancy (will be tested on the first day of rTMS using a urine pregnancy test)  
• Alcohol or drug abuse  
• Prior treatment with TMS |
| Contact                   | Carlijn EL Hoekstra, MD, phone +31-88-755-3606, c.e.l.hoekstra@umcutrecht.nl  
Bert A van Zanten, AuD, phone +31-88-755-3702, g.a.vanzanten@umcutrecht.nl |
| Locations                 | University Medical Center Utrecht, Recruiting, Utrecht, Netherlands, 3584 CX |
| Study chairs or principal investigators | Carlijn EL Hoekstra, MD  
Bert A van Zanten, AuD, Dept. of Otorhinolaryngology, University Medical Center Utrecht |
| Study ID Numbers          | rTMS_tinnitus_Utrecht |
| Last Updated              | April 25, 2008 |
| Record first received     | April 25, 2008 |
| ClinicalTrials.gov Identifier | NCT00668720 |
| Health Authority          | Netherlands: The Central Committee on Research Involving Human Subjects (CCMO) |
## Cognitive Behavioral Therapy (CBT) for Tinnitus

<table>
<thead>
<tr>
<th>Current status</th>
<th>not yet open for participant recruitment</th>
</tr>
</thead>
</table>
| Sponsors and collaborators | Department of Veterans Affairs  
Yale University |
| Information provided by | Department of Veterans Affairs |
| ClinicalTrials.gov Identifier | NCT00724152 |
| Purpose | This study examines how useful it is to teach veterans coping skills for dealing with tinnitus, also called ringing in the ears. A psychological intervention, cognitive-behavioral therapy, will be used to teach coping skills even though tinnitus is not a psychological disorder. Participants will be assigned to one of two groups for the duration of the study and will not know which group they are in until the end of the study. One group will receive education about tinnitus. The other group will receive education about tinnitus plus additional ways to cope with problems associated with tinnitus such as sleep disturbance and frustration. Several questionnaires will be filled out by veterans interested in participating in the study. Participants will be selected to participate if their tinnitus is severe and they were exposed to loud sound. Some veterans may not be eligible to participate if they have additional health conditions. About 66 veterans will be enrolled in the study. If selected to participate in the study, veterans will attend six weekly group meetings. Participants will then be asked to come back 8 weeks after the last group to answer more questions about their tinnitus and health. It is predicted that participants who are assigned to the cognitive behavioral therapy group will report a greater reduction in tinnitus severity. |
| Condition(s) | 1. Cognitive Behavior Therapy  
2. Health Education |
| Interventions | 1. Behavioral: Cognitive Behavioral Therapy  
2. Other: Tinnitus Education |
| Phase | 1. Phase I  
2. Phase II |
| Study type and design | Interventional; Treatment, Randomized, Single Blind (Subject), Active Control, Parallel Assignment, Efficacy Study |
| Official title | Cognitive-Behavioral Therapy for Tinnitus |
| Arms | 1: Active Comparator  
Participants randomly assigned to this control group will receive six weeks of tinnitus education.  
2: Experimental  
Participants randomly assigned to this experimental group will receive six weeks of tinnitus education plus cognitive behavioral therapy. |
| Assigned Interventions | 1. Other: Tinnitus Education  
Tinnitus education will include causes, treatments, current research, epidemiological information, basic anatomy of the ear and brain, and support resources. |
### 2. Behavioral: Cognitive Behavioral Therapy

Cognitive behavioral therapy for tinnitus participants will address cognitive and behavioral skills targeting the management of tinnitus and the negative impacts of tinnitus. Long-term self-efficacy and self-sufficiency will be used emphasized. The major components of CBT for tinnitus include identification of individual responses and beliefs about tinnitus and hearing loss, re-conceptualization of the tinnitus experience as one in which the patient has personal control, presentation of skills to modify cognitions (such as negative appraisals) and change behaviors (such as avoidance of social activities), and reinforcement of skills via goals setting, homework and activities. Tinnitus education and skills related to attention control, sleep hygiene and relaxation training such as imagery techniques will be provided.

### Other: Tinnitus Education

Tinnitus education will include causes, treatments, current research, epidemiological information, basic anatomy of the ear and brain, and support resources.

#### Detailed Description

The objectives of this study are to (1) develop a novel, integrative, psychological intervention, specifically cognitive-behavioral therapy (CBT), for the treatment of tinnitus among veterans who have past exposure to loud noise, and (2) accrue preliminary data examining the efficacy of the approach relative to a standard care with education (ED) control condition. Tinnitus was the most common new individual service-connected disability in fiscal year 2006. Treatments for tinnitus are few and no cure exists. This pilot study will examine the feasibility and efficacy of providing individualized (CBT) for veterans with bothersome tinnitus. Sixty-six veterans will be recruited and randomly selected to one of two conditions; the treatment condition (CBT) or the (ED) control condition. A two-group design with two continuous dependent variables will be used to compare improvements between the control group (ED) and the experimental group (CBT). Covariates will include age and number of months with tinnitus. It is hypothesized that the CBT group will improve greater (get lower scores on the THI and TRQ than the ED group) though not to the level of statistical significance. A CBT manual and an ED manual will be developed for this study. Subjects will be eligible for the study if their tinnitus was likely caused by noise exposure, their tinnitus is chronic (> 6 months), tinnitus is a major health concern for them, and participants are able to commit to a 6-week course of treatment at the West Haven location of VACHS. Subjects will be veterans blinded to the treatment group to which they are assigned. Potential subjects will respond to five assessment measures to determine inclusion in the study: (1) Tinnitus-Impact Screening Interview (TISI), (2) Semi-Structured Clinical Interview for Tinnitus (SSCIT), (3) Structured Clinical Interview for Diagnosis, abbreviated - Interview/Non-patient (SCIda-I/NP), (4) Tinnitus Handicap Inventory (THI), and (5) Tinnitus Reaction Questionnaire (TRQ). Subjects will attend six group meetings and undergo evaluations before three group meetings and after all six group meetings. The THI and TRQ will serve as the primary outcome measures and will be administered before the first group meeting, after the sixth group meeting at 8 weeks post-treatment follow-up. Results of this pilot project will be used to inform the design and methods of a future rigorous randomized controlled clinical trial of CBT for tinnitus.
<table>
<thead>
<tr>
<th><strong>Primary Outcomes</strong></th>
<th>Tinnitus Handicap Inventory (THI) [Time Frame: Eligibility, pre-treatment, post-treatment, 8-weeks post-treatment] [Designated as safety issue: No]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary Outcomes</strong></td>
<td>Tinnitus Reaction Questionnaire (TRQ) [Time Frame: Eligibility, pre-treatment, post-treatment, 8-weeks post-treatment] [Designated as safety issue: No]</td>
</tr>
<tr>
<td><strong>Expected total Enrollment</strong></td>
<td>66</td>
</tr>
<tr>
<td><strong>Study start</strong></td>
<td>November 2008</td>
</tr>
<tr>
<td><strong>Expected study completion date</strong></td>
<td>September 2009</td>
</tr>
<tr>
<td><strong>Expected primary completion date</strong></td>
<td>July 2009 (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>No</td>
</tr>
</tbody>
</table>

**Eligibility Inclusion Criteria**

All subjects will be veterans who are currently receiving care at VACHS. Subjects must be interested in participating in the study and have moderate to severe, chronic (>6 months) tinnitus. Following a brief assessment of tinnitus severity by the project coordinator, the research otologist and research audiologist will conduct tinnitus and audiological evaluations to determine subject eligibility. The most likely etiology of subjects’ tinnitus must be noise exposure to be included in the study and all eligible subjects will report having been exposed to loud sound some time in their lives. Subjects must indicate that they are motivated to comply with treatment and able to commit to a 6-week course of treatment, follow-up, and study participation by continuing to reside nearby. Subjects must have stable, permanent housing and transportation means for follow-up appointments. Tinnitus will be a significant health concern for all subjects. Women and minorities will be recruited.

**Eligibility Exclusion Criteria**

Subjects will respond to five assessment measures to determine exclusion from the study.

- Tinnitus-Impact Screening Interview (TISI): Those who score 4 or lower will be excluded from the study.
- Semi-Structured Clinical Interview for Tinnitus: The exclusionary criteria described below will be assessed using this measure.
- Structured Clinical Interview for Diagnosis, abbreviated - Interview/Non-patient (SCIDa-I/NP): If there is any indication of psychosis on this measure, the subject will be excluded from the study.
- Tinnitus Handicap Inventory (THI): Subjects with scores of 19 or lower will be excluded.
- Tinnitus Reaction Questionnaire (TRQ): Subjects who score 16 or lower on this measure will be excluded from the study.

Subjects who are undergoing litigation or legal matters related to auditory disorders will be excluded from the study.
Subjects must never have previously received psychological treatment for their tinnitus.

Subjects who report having a history of traumatic brain injury (TBI) with loss of consciousness (LOC) will be excluded from the study.

Subjects with otherwise treatable tinnitus will be excluded.

Subjects who have a history of psychotic disorders or dementia will be excluded.

These psychotic symptoms will constitute exclusion from the study:
- delusions of reference
- persecutory delusions
- religious delusions
- grandiose delusions
- somatic delusions
- delusional guilt
- poverty or nihilism
- delusions of jealousy
- delusions of mind reading
- delusions of being controlled
- delusions of thought-broadcasting
- auditory hallucinations
- visual hallucinations
- tactile hallucinations
- gustatory and olfactory hallucinations

Subjects who report having a recent (within 2-year) history of alcohol or drug abuse or dependence other than tobacco or caffeine will be excluded.

Subjects who use hearing aids will be excluded from the study.

Subjects who present with sudden or fluctuating hearing loss will be excluded.

Subjects with tinnitus associated with otologic disease (e.g., Meniere’s Disease) or other co-occurring diseases affecting vestibular dysfunction will be excluded.

Contact
Caroline J Kendall, phone +1 (203) 932-5711 ext 5459, Caroline.Kendall@va.gov
Robert D Kerns, PhD, +1 (203) 937-3841, robert.kerns@va.gov

Location
United States, Connecticut
VA Connecticut Health Care System (West Haven), Not yet recruiting, West Haven, Connecticut, United States, 06516

Study chairs or principal investigators
Robert D. Kerns, PhD, VA Connecticut Health Care System (West Haven)

Study ID Numbers
C6324P

Last Updated
July 23, 2008

Record first received
July 23, 2008

ClinicalTrials.gov Identifier
NCT00724152

Health Authority
United States: Federal Government
# Customized Acoustic Stimulation for Long Term Medical Benefit for the Relief of Tinnitus and Hyperacusis (CALM)

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>Neuromonics, Inc.</td>
</tr>
<tr>
<td>Information provided by</td>
<td>Neuromonics, Inc.</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00730834</td>
</tr>
</tbody>
</table>

**Purpose**

Neuromonics Tinnitus Treatment CALM study is a multi site study of 100 adult subjects with clinically significant disturbing tinnitus to evaluate outcome measures using the FDA cleared Neuromonics treatment after 6, 12, 24 and 36 months. Patients must be meet certain inclusion criteria and they are also required to pay for the all costs of the treatment. Subjects will be provided a modest participation fee at 6, 12, 24 and 36 months upon completion of patient questionnaires (subjects must have access to a computer and internet in order to complete online questionnaires).

**Condition(s)**

Tinnitus

**Interventions**

Device: Oasis; Digital sound player that provides customized acoustic stimulus based on subjects hearing thresholds

**Phase**

Phase IV

**Study type and design**

Interventional; Treatment, Non-Randomized, Open Label, Single Group Assignment, Efficacy Study

**Official title**

Phase 4 Study of Use of a Customized Acoustic Stimulus to Reduce the Disturbing Symptoms of Tinnitus and Hyperacusis

**Primary Outcomes**

Pre and post treatment scores on Tinnitus reaction questionnaire [Time Frame: 6, 12, 24, 36 months] [Designated as safety issue: No]

**Secondary Outcomes**

Tinnitus Handicap Inventory, Hospital Anxiety and Depression Scale, [Time Frame: 6, 12, 24, 36 months] [Designated as safety issue: No]

**Expected total Enrollment**

100

**Study start**

June 2007

**Expected study completion date**

December 2010

**Expected primary completion date**

December 2010 (Final data collection date for primary outcome measure)

**Participants (age)**

18 Years and older

**Gender**

Both

**Accepts health volunteers**

Yes
<table>
<thead>
<tr>
<th>Eligibility Inclusion Criteria</th>
<th>18 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TRQ of at least 17 or above</td>
</tr>
<tr>
<td></td>
<td>Able to pay for the treatment</td>
</tr>
<tr>
<td></td>
<td>Not using any other treatment for tinnitus</td>
</tr>
<tr>
<td></td>
<td>Access to computer and internet</td>
</tr>
<tr>
<td></td>
<td>Compliant patient</td>
</tr>
<tr>
<td>Eligibility Exclusion Criteria</td>
<td>Hearing PTA &gt; 50 dB, score on HADS of greater than 11 on the anxiety and depression scale</td>
</tr>
<tr>
<td></td>
<td>Not willing to follow the protocol</td>
</tr>
<tr>
<td>Contact</td>
<td>Julie Daugherty, RN, phone +1 941-366-9222</td>
</tr>
<tr>
<td>Locations</td>
<td>Silverstein Ear Institute, Recruiting, Sarasota, Florida, United States, 34239</td>
</tr>
<tr>
<td>Study chairs or principal investigators</td>
<td>Jack Wazen, MD, Silverstein ear institute</td>
</tr>
<tr>
<td>Study ID Numbers</td>
<td>CALM Study, 20071022</td>
</tr>
<tr>
<td>Last Updated</td>
<td>August 7, 2008</td>
</tr>
<tr>
<td>Record first received</td>
<td>August 5, 2008</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00730834</td>
</tr>
<tr>
<td>Health Authority</td>
<td>United States: Institutional Review Board</td>
</tr>
</tbody>
</table>

**Using PET-CT to Target and Validate Low-Frequency TMS as Treatment for Tinnitus**

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
</tr>
</thead>
</table>
| Sponsors and collaborators | University of Arkansas  
Tinnitus Research Consortium |
| Information provided by     | University of Arkansas |
| ClinicalTrials.gov Identifier | NCT00329524 |
| Purpose                     | One out of every five people experience tinnitus (a buzzing, ringing, or roaring sound in the ear) ranging from mild to severe impairment. To date there is no effective therapy that seems to help the tinnitus sufferer. The purpose of this study is to develop a therapy using a technique called Repetitive Transcranial Magnetic Stimulation (rTMS) to hopefully alleviate or reduce the symptoms of tinnitus. |
This research is being conducted at the University of Arkansas for Medical Sciences (UAMS). Twenty (20) right handed subjects, either males or females, 19-65 years of age, with tinnitus that is severe enough for those persons to seek medical attention will have been seen as patients in the UAMS Hearing and Balance Center, where routine testing includes a physical exam, hearing tests, evaluation of middle ear status, and an MRI scan (a machine that acquires visual images of the brain). A diagnosis of tinnitus will be established after ruling out all other possible causes of the tinnitus.

<table>
<thead>
<tr>
<th>Condition(s)</th>
<th>Tinnitus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions</td>
<td>Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)</td>
</tr>
<tr>
<td>Phase</td>
<td>Phase 1</td>
</tr>
<tr>
<td>Study type and design</td>
<td>Interventional; Treatment, Non-Randomized, Open Label, Active Control, Crossover Assignment, Safety Study</td>
</tr>
<tr>
<td>Official title</td>
<td>Using PET-CT to Target and Validate Low-Frequency TMS as Treatment for Tinnitus</td>
</tr>
</tbody>
</table>

### Arms

<table>
<thead>
<tr>
<th>1: Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMS will initially be targeted to asymmetric cortical activation in one hemisphere, as defined by PET-CT imaging. TMS will then be optimized by identifying the area of maximal tinnitus suppression, within the area of asymmetry, by delivering single 1-Hz pulses of TMS at the MT. The area of maximal tinnitus suppression, as reported by the patient, will then be targeted for treatment with rTMS at 1-Hz frequency, delivering 1800 pulses at 110% MT on each of 5 consecutive treatment days.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2: Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>If no area of maximal tinnitus suppression can be found in the hemisphere initially targeted for treatment based on PET, we will perform the optimization procedure in a homologous region of the opposite cerebral hemisphere to determine if a maximal area of suppression can be found there. In either case, stimulation will be targeted to the hemisphere where an optimized site can be found. Each group will then crossover to sham and active stimulation conditions, respectively, 7 days following the completion of the first treatment session.</td>
</tr>
</tbody>
</table>

### Assigned Interventions

<table>
<thead>
<tr>
<th>1. Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMS will initially be targeted to asymmetric cortical activation in one hemisphere, as defined by PET-CT imaging. TMS will then be optimized by identifying the area of maximal tinnitus suppression, within the area of asymmetry, by delivering single 1-Hz pulses of TMS at the MT. The area of maximal tinnitus suppression, as reported by the patient, will then be targeted for treatment with rTMS at 1-Hz frequency, delivering 1800 pulses at 110% MT on each of 5 consecutive treatment days. If no area of maximal tinnitus suppression can be found in the hemisphere initially targeted for treatment based on PET, we will perform the optimization procedure in a homologous region of the opposite cerebral hemisphere to determine if a maximal area of suppression can be found there. Each group will then crossover to sham and active stimulation conditions, respectively, 7 days following the completion of the first treatment session.</td>
</tr>
</tbody>
</table>
2. Procedure: Repetitive Transcranial Magnetic Stimulation (rTMS)

TMS will initially be targeted to asymmetric cortical activation in one hemisphere, as defined by PET-CT imaging. TMS will then be optimized by identifying the area of maximal tinnitus suppression, within the area of asymmetry, by delivering single 1-Hz pulses of TMS at the MT. The area of maximal tinnitus suppression, as reported by the patient, will then be targeted for treatment with rTMS at 1-Hz frequency, delivering 1800 pulses at 110% MT on each of 5 consecutive treatment days. If no area of maximal tinnitus suppression can be found in the hemisphere initially targeted for treatment based on PET, we will perform the optimization procedure in a homologous region of the opposite cerebral hemisphere to determine if a maximal area of suppression can be found there. Each group will then crossover to sham and active stimulation conditions, respectively, 7 days following the completion of the first treatment session.

**Detailed Description**

Subjects will be 20 right-handed patients (men and women), 19-65 years of age, with debilitating unilateral or bilateral tinnitus. All subjects must report experiencing the presence of their phantom auditory perception for at least 6 months and have a Tinnitus Handicap Questionnaire (THQ) score >30. Subjects will be recruited from the Otolaryngology Clinic at UAMS, where routine testing includes a physical exam; pure tone audiometry; and evaluation of middle ear status using tympanometry, stapedius reflex tests, and otoscopy. Patients will undergo a gadolinium-contrast MRI of the head to rule out acoustic neuroma or any other central nervous system pathology. All subjects will be thoroughly informed of the risks associated with the procedures in this study, as described in the Hazards to Subjects section, and written informed consent will be obtained. Subjects will be recruited for this study without regard to race or ethnicity.

**Primary Outcomes**

Determine if low-frequency rTMS improves tinnitus by decreasing cortical activity in the primary [Time Frame: Immediately after initial treatment; 3 and 6 month follow-up] [Designated as safety issue: Yes]

**Secondary Outcomes**

- Determine if asymmetric cortical activation promotes attentional disturbance (variability) [Time Frame: Immediately after treatment] [Designated as safety issue: Yes]
- Determine if rTMS treatment promotes lasting improvement in tinnitus patients [Time Frame: 3 and 6 month assessment; 6 and 12 month follow-up] [Designated as safety issue: Yes]

**Expected total Enrollment**

20

**Study start**

June 2006

**Expected study completion date**

January 2009

**Expected primary completion date**

January 2009 (Final data collection date for primary outcome measure)

**Participants (age)**

19 Years to 65 Years

**Gender**

Both

**Accepts health volunteers**

Yes
| Eligibility Inclusion Criteria | • right-handed subjects  
• 19-65 years of age  
• debilitating unilaterial or bilateral tinnitus  
• Experiencing the presence of phantom auditory perception for >6 months  
• Tinnitus Handicap Questionnaire score of >30 |
| Eligibility Exclusion Criteria | • significant neurological disease  
• acoustic neuromas or glomus tumors  
• active Meniere’s disease  
• profound hearing loss  
• non English speaking  
• personal or family history of epilepsy  
• personal history of head injury, aneurysm, stroke, previous cranial neurosurgery, neurological or psychiatric disorders, metal implants in the head or neck, a pacemaker, pregnancy, migraines,  
• medications that lower seizure threshold and are contraindicated  
• individuals who have been taking certain medications  
• claustrophobia  
• patients who do not exhibit significant cortical asymmetries on PET |
| Contact | John Dornhoffer, MD, phone +1 501-686-5016, DornhofferJohnl@uams.edu  
Brenda Speed, phone +1 501-686-5140, SpeedBrendaO@uams.edu |
| Locations | United States, Arkansas, University of Arkansas for Medical Sciences, recruiting, Little Rock, Arkansas, United States, 72205 |
| Study chairs or principal investigators | John Dornhoffer, MD, University of Arkansas |
| Responsible party | The University of Arkansas for Medical Sciences (Carole Hamon) |
| Study ID Numbers | 51817 |
| Last Updated | January 10, 2008 |
| Record first received | May 22, 2006 |
| ClinicalTrials.gov Identifier | NCT00329524 |
| Health Authority | United States: Institutional Review Board |
### Effect of Gabapentin on Idiopathic Subjective Tinnitus

<table>
<thead>
<tr>
<th>Current status</th>
<th>ongoing, but not recruiting participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>Islamic Azad University of Mashhad</td>
</tr>
<tr>
<td>Information provided by</td>
<td>Islamic Azad University of Mashhad</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00555776</td>
</tr>
<tr>
<td>Purpose</td>
<td>The purpose of this study is to determine whether Gabapentin, which is useful for treating neuropathic pains, is effective on idiopathic subjective tinnitus.</td>
</tr>
<tr>
<td>Condition(s)</td>
<td>Subjective Tinnitus</td>
</tr>
</tbody>
</table>
| Interventions | Drug: Gabapentin  
Drug: placebo |
| Phase | Phase II |
| Study type and design | Intervventional; Treatment, Randomized, Double Blind (Subject, Investigator), Placebo Control, Parallel Assignment, Efficacy Study |
| Official title | Phase 2 Effect of Gabapentin on Idiopathic Subjective Tinnitus |
| Arms | 1. Active Comparator  
Randomly, half of the subjects are given Gabapentin.  
2. Placebo Comparator  
Randomly, half of the subjects receive placebo. |
| Assigned Interventions | 1. Drug: Gabapentin  
Gabapentin, 600 mg bid for the first two weeks, increased to a maximum dose of 1800 mg per day during the next 6 weeks if necessary.  
2. Drug: placebo  
placebo is given with the same definition as Gabapentin |
<p>| Detailed Description | Tinnitus is the perception of sound in the absence of acoustic stimulation. It can be subjective or objective. Despite numerous researches, no effective treatment for people who suffer from tinnitus has yet been established. As there are many evidences suggesting that loss of inhibition in the central nervous system may be responsible for many aspects of auditory dysfunction, including tinnitus; and as Gabapentin (Neurontin), a gama-aminobutyric acid (GABA) analogue, is an effective medication in conditions where inhibition in the CNS is impaired; we guess that Gabapentin might be useful for treating idiopathic subjective tinnitus. |
| Primary Outcomes | Reduction in the sensation of Tinnitus by the patient or complete resolution of tinnitus by the patient's scoring it from one to ten, before and after prescribing Gabapentin. [ Time Frame: two months ] [ Designated as safety issue: Yes ] |</p>
<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th>Relieve of complications of tinnitus, such as sleep difficulties. [Time Frame: two months] [Designated as safety issue: Yes]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected total Enrollment</td>
<td>70</td>
</tr>
<tr>
<td>Study start</td>
<td>January 2007</td>
</tr>
<tr>
<td>Expected study completion date</td>
<td>October 2008</td>
</tr>
<tr>
<td>Expected primary completion date</td>
<td>April 2008 (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 with subjective idiopathic tinnitus</td>
</tr>
</tbody>
</table>
| Eligibility Exclusion Criteria | • tinnitus with known underlying cause  
                               | • pregnant women and patients younger than 18 or older than 75 years                                        |
| Locations           | Iran, Islamic Republic of, Khorasan razavi, ENT department of Mashhad Azad medical university, Mashhad, Khorasan razavi, Iran, Islamic Republic of, 91786 56553 |
| Study chairs or principal investigators | Mahboobeh Adami Dehkordi, MD, Assistant Professor, ENT department of Mashhad azad university of mashhad |
| Study ID Numbers    | Gaba-tinnitus-145                                                                                           |
| Last Updated        | August 18, 2008                                                                                              |
| Record first received | November 8, 2007                                                                            |
| ClinicalTrials.gov Identifier | NCT00555776                                                                            |
| Health Authority    | Iran: Ministry of Health                                                                                     |

**Chronic Electrical Stimulation of the Auditory Cortex for Intractable Tinnitus (ACOUSCO)**

<table>
<thead>
<tr>
<th>Current Status</th>
<th>not yet open for participant recruitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>University Hospital, Bordeaux</td>
</tr>
<tr>
<td>Information provided by</td>
<td>University Hospital, Bordeaux</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00486577</td>
</tr>
<tr>
<td>Purpose</td>
<td>The purpose of this study is to determine whether chronic electrical stimulation of the primary auditory cortex is effective in the treatment of chronic, severe and intractable tinnitus</td>
</tr>
</tbody>
</table>
| Condition(s)     | • Hearing Disorders  
|                 | • Hearing Loss       
|                 | • Hyperacusis        
|                 | • Tinnitus           |
| Interventions   | Procedure: Chronic primary auditory cortex stimulation |
| Phase           | Phase II             
|                 | Phase III            |
| Study type and design | Interventional; Treatment, Randomized, Double-Blind, Placebo Control, Crossover Assignment, Safety/Efficacy Study |
| Official title  | Chronic Electrical Stimulation of the Auditory Cortex for Intractable Tinnitus |
| Detailed Description | Severe and chronic tinnitus – the perception of sound in one or both ears or in the head when non-external sound is present – can be disabling and difficult to treat. Physiopathology of tinnitus can be considered as similar to neuropathic pain. Neuropathic and central pain are treated since ten years by chronic electrical motor cortex stimulation. The hypothesis of this study is that it will be possible to treat severe tinnitus by this stimulation as neuropathic pains are treated by motor cortical stimulation. |
|                 | • Principal Objective : to evaluate the efficacy of chronic electrical stimulation of the auditory cortex for intractable tinnitus  
|                 | • Secondary Objective : to evaluate the tolerability and the safety of chronic electrical stimulation of the auditory cortex for intractable tinnitus  
|                 | • Study design : randomized, cross over, double blind, study to evaluate the efficacy of the chronic electrical stimulation versus sham in severe and chronic tinnitus |
| Primary Outcomes | intensity of the tinnitus. The cut off efficacy is 35% improvement on the STI score [ Time Frame: 6 months ] |
| Secondary Outcomes | Tinnitus Handicap Questionnair Multiple Activity Scale for Hyperacusis questionnaires for assessment of the patients and treatment outcome of tinnitus hyperacusis and loss of hearing subjective global improvement scale [ Time Frame: 6 months ] |
| Expected total Enrollment | 10 |
| Study start     | June 2007 |
| Participants (age) | 18 Years to 70 Years |
| Gender          | Both |
| Accepts health volunteers | No |
| Eligibility Inclusion Criteria | Patient >18 years of age and < 70 years of age  
|                 | Permanent and chronic tinnitus during more than 2 years.  
|                 | A score over 19 at the STI (Quality of life index for tinnitus) Unilateral tinnitus |
| Eligibility Exclusion Criteria                  | Deaf person                                                   |
|                                              | Surgical or anesthetic contraindication                       |
|                                              | History of psychiatric disorder or suicide                   |
|                                              | Epilepsia                                                    |
| Contact                                     | Emmanuel CUNY, MD, phone (33)556795577, emmanuel.cuny@chu-bordeaux.fr |
|                                              | René Dauman, MD, (33)556794757, rene.dauman@chu-bordeaux.fr   |
| Locations                                   | France, University Hospital of Bordeaux – Pellegrin, not yet recruiting, Bordeaux, France, 33 076 |
| Study chairs or principal investigators      | Emmanuel Cuny, MD, University Hospital of Bordeaux            |
| Study ID Numbers                            | Promo 2005                                                   |
| Last Updated                                 | June 13, 2007                                                |
| Record first received                       | June 13, 2007                                                |
| ClinicalTrials.gov Identifier               | NCT00486577                                                  |
| Health Authority                            | France: Afssaps - French Health Products Safety Agency       |

**Vardenafil in Tinnitus**

| Current status                              | completed                                                   |
| Sponsors and collaborators                  | Bayer                                                       |
| Information provided by                     | Bayer                                                       |
| ClinicalTrials.gov Identifier               | NCT00666809                                                 |
| Purpose                                     | Randomized, parallel-group, double-blind, placebo-controlled trial over 16 weeks (12 weeks of treatment + 4 weeks follow-up) with 10 mg vardenafil BID p.o. in men and women with chronic tinnitus. |
| Condition(s)                                | Tinnitus                                                    |
| Interventions                               | Drug: Levitra (Vardenafil, BAY38-9456)                       |
|                                              | Drug: Placebo                                                |
| Phase                                       | Phase II                                                    |
| Study type and design                       | Intervventional; Treatment, Randomized, Double Blind (Subject, Investigator), Placebo Control, Parallel Assignment, Efficacy Study |
| Official title                              | Evaluation of Vardenafil for the Treatment of Subjective Tinnitus: A Controlled Pilot Study |
| Arms                                        | Arm 1: Active Comparator n/a                                |
|                                              | Arm 2: Placebo Comparator n/a                               |
### Assigned Interventions

1. **Drug: Levitra** (Vardenafil, BAY38-9456)
   - Vardenafil 10 mg BID p.o. for 12 weeks + 4 weeks follow-up
2. **Drug: Placebo**
   - Placebo BID p.o. for 12 weeks + 4 weeks follow-up

### Detailed Description

There is incidental evidence (casuistic findings) that the treatment with vardenafil of male patients suffering from erectile dysfunction and comorbid tinnitus experienced an improvement of their tinnitus. The aim of the present trial is to evaluate this observation in more detail and to show efficacy of vardenafil superior over placebo in the treatment of chronic tinnitus.

### Primary Outcomes

<table>
<thead>
<tr>
<th>Outcome Description</th>
<th>Time Frame</th>
<th>Designated as safety issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total score of the Tinnitus Questionnaire after 12 weeks of treatment</td>
<td>4 times in 16 weeks</td>
<td>No</td>
</tr>
</tbody>
</table>

### Secondary Outcomes

- Audiometric measurements (mode, frequency and loudness of tinnitus, pure tone audiogram, speech audiogram) [Time Frame: 16 weeks] [Designated as safety issue: No]
- Quality of life (SF 36 Questionnaire) [Time Frame: 16 weeks] [Designated as safety issue: No]
- Serum human chorionic Gonadotropin (hCG), pregnancy test [Time Frame: once at screening] [Designated as safety issue: Yes]
- Safety and tolerability [Time Frame: 16 weeks] [Designated as safety issue: Yes]

### Expected total Enrollment

40

### Study Details

- **Study start**: October 2006
- **Study completion date**: May 2007
- **Participants (age)**: 18 Years to 64 Years
- **Gender**: Both
- **Accepts health volunteers**: No

### Eligibility Inclusion Criteria

- Chronic subjective cochlear tinnitus
- No treatment of tinnitus within 4 weeks prior to study entry
- Duration of tinnitus > 3 months

### Eligibility Exclusion Criteria

- Acute tinnitus
- Intermittent tinnitus
- History of M. Menieré
- History of conductive deafness
- History of psychogenic deafness
- History of tumors of the middle ear, inner ear or cerebella-pontine angle (malignant and non malignant)
- Patients diagnosed of multiple sclerosis
- History of myocardial infarction, stroke, or life-threatening arrhythmia within the prior 6 months
<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Nitrates or nitric oxide donors</td>
</tr>
<tr>
<td>- Any other concurrent treatment of tinnitus during study</td>
</tr>
<tr>
<td>- pregnant and breast-feeding women</td>
</tr>
<tr>
<td>- women with child-bearing potential not using adequate birth control method (Note: as adequate method of birth control oral contraception, spiral or sexual abstinence is recommended)</td>
</tr>
<tr>
<td>- Other exclusion criteria apply according to the Summary of Product Characteristics</td>
</tr>
</tbody>
</table>

### Contact
Please refer to this study by its ClinicalTrials.gov identifier: NCT00666809

### Locations
Bayer, Germany, Berlin / 285, Germany, 10117

### Study chairs or principal investigators
Bayer Study Director

### Responsible party
(Bayer HealthCare AG, Therapeutic Area Head)

### Study ID Numbers
12049, EudraCT No: 2006-000463-29

### Last Updated
May 21, 2008

### Record first received
April 23, 2008

### ClinicalTrials.gov Identifier
NCT00666809

### Health Authority
Germany: Federal Institute for Drugs and Medical Devices; United States: Food and Drug Administration

### Zinc to treat Tinnitus

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
</tr>
</thead>
</table>
| Sponsors and collaborators | University of Iowa  
Tinnitus Research Initiative |
<p>| Information provided by | University of Iowa |
| ClinicalTrials.gov Identifier | NCT00683644 |
| Purpose | There is widespread belief and some evidence to indicate that zinc can successfully treat tinnitus. Zinc deficiency is more likely to occur in the elderly. The primary objective of this study is to establish the effectiveness of zinc for the treatment of tinnitus in individuals 60 years of age and older. Subjects will be randomly assigned to either receive zinc daily or a placebo. After 4 months and a 1-month wash-out, the subjects will be crossed over to the other group. |
| Condition(s) | Tinnitus |
| Interventions | Dietary Supplement: Zinc sulphate |</p>
<table>
<thead>
<tr>
<th>Phase</th>
<th>Phase II</th>
</tr>
</thead>
</table>
| Arms    | 1: Experimental  
 Zunck first, then placebo  
 2: Experimental  
 Placebo first, then zinc |
| Assigned Interventions | Dietary Supplement: Zinc sulphate  
 Zinc sulfate taken once daily |
| Study type and design | Interventional; Treatment, Randomized, Double Blind (Subject,  
 Investigator), Crossover Assignment |
| Official title | Zinc to Treat Tinnitus in the Elderly |
| Primary Outcomes | Tinnitus loudness and annoyance [ Time Frame: 10 months ] [  
 Designated as safety issue: No ] |
| Secondary Outcomes | Tinnitus handicap [ Time Frame: 10 months ] [ Designated as safety  
 issue: No ] |
| Expected total Enrollment | 200 |
| Study start | January 2008 |
| Estimated Study Completion Date | December 2009 |
| Estimated Primary Completion Date | December 2009 (Final data collection date for primary outcome measure) |
| Participants (age) | 60 Years and older |
| Gender | Both |
| Accepts health volunteers | No |
| Eligibility Inclusion Criteria | • 60 years of age or older  
 • Tinnitus for 6 months or more  
 • Normal copper levels  
 • Be generally healthy |
| Eligibility Exclusion Criteria | • Have a treatable otological disorder  
 • Involved in litigation  
 • Have or are suspected of having a serious psychiatric problem  
 • Taking any dietary supplements  
 • Involved in other treatments for tinnitus  
 • Are taking drugs which might interact with zinc and result in tinnitus  
 • Have copper deficiency  
 • Have Zinc levels above normal  
 • Are cognitively impaired |
**Progressive Intervention Program for Tinnitus Management**

<table>
<thead>
<tr>
<th>Current status</th>
<th>not yet open for participant recruitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>Department of Veterans Affairs</td>
</tr>
<tr>
<td>Information provided by</td>
<td>Department of Veterans Affairs</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00371436</td>
</tr>
<tr>
<td>Purpose</td>
<td>The purpose of this multi-site randomized clinical study is to test a model treatment program in a VA Audiology clinic, to evaluate its efficacy, ease of implementation, and acceptability to audiologists.</td>
</tr>
<tr>
<td>Condition(s)</td>
<td>Hearing Loss</td>
</tr>
<tr>
<td></td>
<td>Tinnitus</td>
</tr>
<tr>
<td>Interventions</td>
<td>Procedure: Tinnitus Progressive Management</td>
</tr>
<tr>
<td></td>
<td>Procedure: Usual Care</td>
</tr>
<tr>
<td>Arms</td>
<td>1: Active Comparator</td>
</tr>
<tr>
<td></td>
<td>Tinnitus Progressive Management</td>
</tr>
<tr>
<td></td>
<td>2. Usual Care</td>
</tr>
<tr>
<td>Assigned Interventions</td>
<td>1. Procedure: Tinnitus Progressive Management</td>
</tr>
<tr>
<td></td>
<td>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) tinnitus evaluation; and (5) individual management.</td>
</tr>
<tr>
<td></td>
<td>2. Procedure: Usual Care</td>
</tr>
<tr>
<td></td>
<td>Typical audiologic care that would be received in a VA Audiology Clinic.</td>
</tr>
<tr>
<td>Study type and design</td>
<td>Interventional; Treatment, Randomized, Open Label, Active Control, Parallel Assignment, Efficacy Study</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Official title</td>
<td>Progressive Intervention Program for Tinnitus Management</td>
</tr>
<tr>
<td>Detailed Description</td>
<td>The 2004 VA Annual Benefits Report reveals that tinnitus is the third most common individual service-connected disability in veterans. As of September 30, 2005, there were 339,573 veterans who had been awarded a service connection for their tinnitus, with annual compensation amounting to over $418,000,000 (Office of Policy and Planning, VA Central Office). In addition to being a major expense for VHA, tinnitus is a health care problem that is inadequately addressed at most VA medical centers. We have developed a research-based model of tinnitus clinical management that is designed for efficient implementation in VA Audiology clinics. The objective of this study is to establish the model program at a VA Audiology clinic, and to evaluate its efficacy with veteran patients and its acceptability to audiologists. The study will be based at the NCRAR, and a prototype tinnitus management program will be established in the Audiology Clinic at the James A. Haley (Tampa) VA Medical Center. 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. It is hypothesized that progressive intervention will result in a significant reduction in self-perceived tinnitus handicap relative to usual care. During months 1-9, a comprehensive web-based tinnitus training course for audiologists will be developed, as well as a patient tinnitus-information book that uses principles of low health literacy. Six audiologists at the Tampa VA will participate, of which three will be randomly selected to complete the training course as preparation to conduct each of five levels of progressive intervention: (1) triage; (2) audioligic evaluation; (3) group education; (4) tinnitus evaluation; and (5) individualized management. The other three audiologists will not receive the training, and these “usual care” audiologists will provide intervention that more closely typifies what is done at some VA medical centers. Patients will be randomized to one of the two groups. All patients will complete outcomes questionnaires (Tinnitus Handicap Inventory [THI] and Veterans Short Form-36 health survey [SF-36V]) at baseline and 12 months (and at 24 months as resources permit). Outcomes of the THI will be compared between the two groups of patients to test the hypothesis. Data from the SF-36V will be used in secondary outcomes analyses. Each of the six audiologists will be interviewed informally and with a structured interview by the investigative team to determine their satisfaction with the tinnitus services that they provide, and how they feel they are meeting the needs of their patients. The three web-base-trained audiologists and the Service Chief will provide formative data to the Co-PI on an ongoing basis to monitor and adjust the program to achieve the best possible outcomes.</td>
</tr>
</tbody>
</table>
Development and evaluation of this prototype program will establish its practical utility for addressing the tinnitus needs of veterans in a comprehensive, yet efficient, fashion. If the study shows that the program is effective, then the program could establish the standard for tinnitus management at all VA medical centers—meeting the needs of all veterans who have access to VA services.

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>THI (Tinnitus Handicap Inventory) [Time Frame: Baseline, 12 months ] [ Designated as safety issue: No ]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Outcomes</td>
<td>SFV-36 [ Time Frame: Baseline, 12 months ] [ Designated as safety issue: No ]</td>
</tr>
<tr>
<td>Expected total Enrollment</td>
<td>180</td>
</tr>
<tr>
<td>Study start</td>
<td>March 2008</td>
</tr>
<tr>
<td>Estimated Study Completion Date</td>
<td>September 2009</td>
</tr>
<tr>
<td>Estimated Primary Completion Date</td>
<td>September 2009 (Final data collection date for primary outcome measure)</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>• Are outpatients at VA clinics in the vicinity of the James A. Haley VA Medical Center in Tampa, FL • Have clinically significant tinnitus • Have no significant language barrier • Are capable of and willing to fulfill all study requirements</td>
</tr>
<tr>
<td>Eligibility Exclusion Criteria</td>
<td>• Subjects must be free from any medical conditions that would interfere with study participation, e.g. medically or surgically treatable otologic disease; end-stage renal, pulmonary, or cardiovascular disease • Patients undergoing chemotherapy or radiation treatment • Patients with severe psychiatric disorders</td>
</tr>
<tr>
<td>Contact</td>
<td>Christine S Kaelin, MBA, phone +1 (503) 220-8262 ext 57153, <a href="mailto:christine.kaelin@va.gov">christine.kaelin@va.gov</a> Tara Zaugg, phone +1 (503) 220-8262 ext 56608, <a href="mailto:Tara.Zaugg@va.gov">Tara.Zaugg@va.gov</a></td>
</tr>
<tr>
<td>Locations</td>
<td>United States, Florida, James A. Haley Veterans Hospital, Tampa, not yet recruiting, Tampa, Florida, United States, 33612, contact Paula J Myers, PhD, phone +1 813-972-7529, <a href="mailto:paula.myers@va.gov">paula.myers@va.gov</a> United States, Oregon, VA Medical Center, Portland, not yet recruiting, Portland, Oregon, United States, 97201, contact James Henry, PhD, phone +1 (503) 220-8262 ext 57153, <a href="mailto:James.Henry@va.gov">James.Henry@va.gov</a> Christine S Kaelin, MBA, <a href="mailto:christine.kaelin@va.gov">christine.kaelin@va.gov</a></td>
</tr>
<tr>
<td>Study chairs or principal investigators</td>
<td>James Henry, PhD, VA Medical Center, Portland</td>
</tr>
<tr>
<td>Responsible party</td>
<td>Department of Veterans Affairs (Henry, James - Principal Investigator)</td>
</tr>
<tr>
<td>Study ID Numbers</td>
<td>C4488R</td>
</tr>
</tbody>
</table>
Efficacy, Safety and Tolerability of Neramexane in Patients With Subjective Tinnitus (EASE)

Current status: not yet open for participant recruitment

Sponsors and collaborators: Merz Pharmaceuticals GmbH

Information provided by: Merz Pharmaceuticals GmbH

ClinicalTrials.gov Identifier: NCT00739635

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: Phase III

Arms:
1: Experimental
2: Placebo Comparator

Assigned Interventions:
1. Drug: Neramexane mesylate
   Double-blind treatment period of 17 weeks up to 75 mg Neramexane mesylate per day
2. Drug: Placebo
   Double-blind treatment period of 17 weeks placebo

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

Primary Outcomes:
TBF-12 (Tinnitus-Beeinträchtigungs-Fragebogen-12 “Tinnitus Handicap Inventory-12”) total score change from baseline to end of treatment [ Time Frame: Screening, Baseline, week 5, 13, 17 ] [ Designated as safety issue: No ]

Secondary Outcomes:
TBF-12 factorial scores, individual responder rate, Tinnitus Rating Scale, Sleep Questionnaire, safety parameters, population pharmacokinetics, optional pharmacogenetics

Expected total Enrollment: 400

Study start: August 2008
Participants (age) | 18 Years to 75 Years
Gender | Both
Accepts health volunteers | No
Eligibility Inclusion Criteria | patients aged 18 to 75 years with a clinical diagnosis of first onset, persistent (i.e. tinnitus should never be absent for > 24 hours in a row), subjective, uni- or bilateral tinnitus present for at least 3 months but not more than 12 months
Eligibility Exclusion Criteria | 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)
Contact | Clariness Clariness, phone 41 4323386 ext 60
Locations | Austria, AKH Wien, Universitätsklinik für HNO-Krankheiten, not yet recruiting, Vienna, Austria 1097
Study ID Numbers | MRZ 92579/TI/3001, EudraCT Number 2007-007835-16
Last Updated | August 21, 2008
Record first received | August 21, 2008
ClinicalTrials.gov Identifier | NCT00739635
Health Authority | Austria: Federal Office for Safety in Health Care

Preventing Chronic Whiplash Pain

Current status | Completed
Sponsors and collaborators | National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Information provided by | National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
ClinicalTrials.gov Identifier | NCT00021476
Purpose | This study is aimed at developing ways to prevent acute pain from becoming chronic pain—specifically, pain associated with whiplash-associated disorders (WADs) from motor vehicle accidents. Research on the development of chronic pain due to musculoskeletal injury suggests that a person’s initial emotional reactions, particularly fear of reinjury and subsequent avoidance of activity, contribute significantly to chronic pain and persistent disability. This study will treat people with WADs during the first three months after a motor vehicle accident with a behavioral and physical exercise program designed to encourage activity and discourage continued fear of movement, pain, and disability. The study will compare the effectiveness of two anxiety-reduction treatments to standard care in reducing pain and activity limitations in people with WADs in the 2 to 3 months after motor vehicle accidents
### Condition(s)
Whiplash injuries

### Interventions
- Behavioral: Behavioral treatments
- Behavioral: Physical therapy

### Phase
Phase III

### Study type and design
Prevention, Randomized, Single Blind, Active Control, Single Group Assignment, Safety Study

### Official title
Preventing Chronic Whiplash Pain: Biobehavioral Approach

### Detailed Description
More than 1.8 million people in the United States suffer from chronic pain and disability following motor vehicle accidents (MVAs) each year. The majority of these cases start with a relatively minor neck injury. The Quebec Task Force Study on Whiplash Associated Disorders (WAD) was created in 1989 to determine the clinical, public health, social, and financial determinants of WAD. Multiple studies have described the clinical features of WAD, which include neck, shoulder, arm, low back, and head pain; tinnitus; visual symptoms; dizziness; temporomandibular joint pain; and paraesthesias. Onset of these symptoms after the injury is usually delayed for several hours and worsens within 24 to 48 hours. Neck pain is the most frequent symptom, and between 14% and 42% of patients with WAD develop chronic neck pain symptoms. Studies suggest that the neck pain will either resolve in the first few months or persist indefinitely. One variable that may predict outcome after an MVA is the acute emotional response immediately after the MVA.

A severe emotional reaction accompanied by neck pain and stiffness after an MVA could lead an injured person to avoid subsequent physical activity through such mechanisms as fear avoidance and fear of reinjury. Research investigating the evolution of chronic pain due to musculoskeletal injury suggests that initial emotional reactivity, particularly fear of reinjury and subsequent activity avoidance, contributes significantly to unremitting pain and persistent disability. Research based on this model has shown that early interventions targeting normalization of excessive emotionality and restriction of activities associated with fear following injury effectively prevent chronic pain due to back injury. No previous study has sought to intervene during the first three months after an MVA with a behavioural and physical exercise program to encourage activity and discourage continued fear of movement, pain and disability.

This study consists of two primary components: (1) To compare the effectiveness of two anxiety-reduction treatments with standard care in reducing pain and activity limitations in patients with WADs 2 to 3 months following MVAs. (2) To test whether psychological responses to the initial trauma, such as fear avoidance, fear of injury, and negative affectivity, discriminate between symptomatic WAD patients and WAD sufferers whose symptoms had resolved 2 to 3 months post-MVA.

### Primary Outcomes
- Pain Measured 3 months after the accident - No
- Functional activity Measured 3 months after the accident - No
- Mood Measured 3 months after the accident - No
### Secondary Outcomes

- Fear avoidance Measured 3 months after the accident - No
- Range of motion/strength Measured 3 months after the accident - No
- Physical symptoms Measured 3 months after the accident - No

### Study start

- May 2001

### Participants (age)

- 20 – 65 years

### Estimated Study Completion Date

- February 2007

### Gender

- Both

### Eligibility Inclusion Criteria

- Have whiplash injury following a motor vehicle accident in the prior 4 to 10 weeks

### Locations

- University of Washington, Seattle, Washington, 98195-6540

### Study chairs or principal investigators

- Dennis C. Turk, PhD, Principal Investigator, University of Washington

### Study ID Numbers

- R01 AR47298; NIAMS-064

### Last Updated

- March 28, 2008

### Record first received

- July 16, 2001

### ClinicalTrials.gov Identifier

- NCT00021476

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**Medical treatment of Meniere’s disease with betahistine: a placebo-controlled, dose-finding study**

**Current status**

- ongoing

**Sponsors and collaborators**

- University Hospital Grosshadern (Klinikum Grosshadern) (Germany) - Department of Neurology
- German Federal Ministry of Education and Research (Bundesministerium Fur Bildung und Forschung [BMBF]) (Germany)

**Information provided by**

- University Hospital Grosshadern (Klinikum Grosshadern) (Germany) - Department of Neurology

**ISRCTN Register**

- ISRCTN44359668

**Purpose**

- High-dose betahistine (3 x 48 mg per day) is more effective in reducing the number of vertigo attacks in Meniere’s disease than low-dose betahistine (3 x 24 mg) or placebo.

**Condition(s)**

- Meniere’s disease

**Phase**

- first patient was randomised in April 2008
| Arms | 1. Therapy with high-dose betahistine (3 x 48 mg)  
2. Therapy with low-dose betahistine (2 x 24 mg)  
3. Placebo |
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Assigned Interventions</td>
<td>The total treatment time will be nine months with a three month follow-up. The trial is estimated to last three years (first patient in to last patient out).</td>
</tr>
<tr>
<td>Study type and design</td>
<td>Placebo-controlled, double-blind, randomised controlled trial.</td>
</tr>
<tr>
<td>Official title</td>
<td>Medical treatment of Meniere's disease with betahistine: a placebo-controlled, dose-finding study</td>
</tr>
<tr>
<td>Primary Outcomes</td>
<td>Number of vertigo attacks in the three treatment arms during the last three months of the treatment period.</td>
</tr>
</tbody>
</table>
| Secondary Outcomes | 1. Number of vertigo attacks during the last three months of the total follow-up period  
2. Median duration of vertigo attacks and median severity of vertigo attacks during the last three months of the treatment period and the last three months of the total follow-up period  
3. Change of:  
3.1. Peripheral vestibular function  
3.2. Tinnitus intensity  
3.3. Effect of tinnitus on quality of life  
3.4. Subjective hearing loss  
3.5. Objective hearing loss - determined by acoustic evoked potentials  
3.6. Change of handicap/impairment due to vertigo or dizziness - assessed by the Dizziness Handicap Inventory (DHI) and the Vestibular Disorders Activities of Daily Living (VADL) score |
| Expected total Enrollment | 84 |
| Participants (age) | 18 - 80 |
| Study start | 1. November 2007 |
| Estimated Study Completion Date | 31. October 2010 |
| Eligibility Inclusion Criteria | 1. Definite Meniere's disease according to the American Academy of Ophthalmology and Otolaryngology, Head and Neck Surgery:  
1.1. Two or more attacks of vertigo, each lasting more than 20 minutes  
1.2. Audiometrically documented hearing loss in at least one examination  
1.3. Tinnitus or aural fullness in the affected ear  
1.4. Other causes excluded  
2. At least two attacks of Meniere's disease per month for at least three subsequent months  
3. Aged 18 to 80 years  
4. Written informed consent to all protocol-specified procedures |
<table>
<thead>
<tr>
<th>Eligibility Exclusion Criteria</th>
<th>1. Other vestibular disorders such as vestibular migraine or phobic postural vertigo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. Contraindications for treatment with betahistine-dihydrochloride, such as:</td>
</tr>
<tr>
<td></td>
<td>2.1. Asthma bronchiale</td>
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<tr>
<td></td>
<td>2.2. Pheochromacyctoma</td>
</tr>
<tr>
<td></td>
<td>2.3. Pregnancy or breast-feeding</td>
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<td>2.4. Severe dysfunction of kidneys or liver</td>
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<tr>
<td></td>
<td>2.5. Ulcer of the stomach or duodenum</td>
</tr>
<tr>
<td></td>
<td>2.6. Tumours</td>
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<tr>
<td></td>
<td>2.7. Severe coronary heart disease</td>
</tr>
<tr>
<td></td>
<td>2.8. Treatment with other antihistamines</td>
</tr>
</tbody>
</table>

| Contact                                                                                       | Prof Michael Strupp, Klinikum Grosshadern, Abt. f. Neurologie, Marchioninistrasse 15, 81377 Munich, Germany |
|                                                                                               | phone +49 (0)89 7095 6678, fax +49 (0)89 7095 6673, michael.strupp@med.uni-muenchen.de |

| Locations                                                                                     | Klinikum Großhadern, Abt. f. Neurologie, Marchioninistrasse 15, 81377 Munich, Germany |

| Study chairs or principal investigators                                                      | Prof. Michael Strupp |

| Study ID Numbers                                                                             | 04T-617 |

| ISRCTN Register                                                                              | ISRCTN44359668 |

| Health Authority                                                                             | Ethics approval received from the local medical ethics board on the 2nd February 2008. |