**Tinnitus – an Important Diagnostic Sign**

“Tinnitus, there is nothing, that can be done, you have to learn to live with it”, this is still what most patients hear, when they seek medical attention because of their tinnitus. Apart from rendering patients desperate and hopeless, this statement also demonstrates a dangerous attitude. Tinnitus can be the first or the leading symptom of a large variety of different pathological conditions that can be life threatening, if left undiagnosed and untreated. Alone the literature of the last four months, which is summarized in this Newsletter, mentions tinnitus as a symptom of diseases such as Heroine, Cocaine or Cisplatin intoxication, Dural Arteriovenous Malformation, vertebro-basilar Dolichoctasis, Susac syndrome, Middle Ear Tumor, Polycythaemia vera, Beta-thalassaemia, superior semilunar Canal Dehiscence, Glomus Tumor, M Behcet or demyelinating Disease – to name only a selection.

In general, tinnitus is not the only symptom of these diseases, but it may be the symptom that comes first to the patient’s attention. It should be clear without saying, that the symptom tinnitus – similar like headache or acute symptoms – needs diagnostic work-up.

The Tinnitus Clinic Workgroup has been working now for almost one year in establishing an Algorithm for Diagnostic and Therapeutic Management of the Tinnitus Patients. The result will be presented and discussed at the 3rd TRI Tinnitus meeting in Stresa /Italy in June. Each meeting participant will receive the draft version begin of June and a plenary session will be dedicated for the discussion of this algorithm, which is aiming to become a consensus and a guideline within the TRI community. The knowledge is there for an evidence-based diagnostic workup, it is up to us, when it will become standard for the majority of patients who see their doctor because of tinnitus.

Berthold Langguth Benjamin Questier Susanne Staudinger
Conference Program

Clinical Management of Tinnitus
Physiology & Anatomy
Sound Therapy
Hearing Aids
Cortical and Brain Stimulation
Imaging, Neurofeedback
Diagnosis

Basic Neuroscience
Genetics, Pharmacology
Auditory Training
Electrical stimulation of the cochlea
Somatosensory Modulation
Nutrition and Diet
Tinnitus Subtyping
etc....

Invited Speakers

Matteo de Nora (Principality of Monaco)
Luca Del Bo (Italy)
Ana Belén Elgoyhen (Argentina)
Ron Goodey (New Zealand)
Berthold Langguth (Germany)
Alessandro Martini (Italy)
Aage Møller (USA)
Larry Roberts (Canada)
Tanit Sanchez (Brasil)
Richard Tyler (USA)

Dirk De Ridder (Belgium)
Jos Eggermont (Canada)
Herta Flor (Germany)
Pawel Jastreboff (USA)
Ed Lobarinas (USA)
Jennifer Melcher (USA)
Arnaud Norena (France)
Richard Salvi (USA)
Grant Searchfield (New Zealand)
Nathan Weisz (Germany)

A pre-conference in italian language will take place on June 23rd, 2009.

Formation credits (ECM) will be provided.

For more information about this meeting please visit the website www.tri2009.com or contact the

Organizing office:
Fondazione Ascolta e Vivi,
Via V. Foppa, 15, 20144 Milan, Italy
phone 0039 02 7200 18 24
e-mail info@faev.org

Scientific office:
Tinnitus Research Initiative, Link Research & Grant Corp
Universitaetsstrasse 84, 93053 Regensburg, Germany
phone 0049 941 941 2096, fax 0049 941 941 2025
e-mail info@tinnitusresearch.org
Ana Belén Elgoyhen, the leader of the Pharmacological Workgroup, published in a recent issue of PLOS Biology, that a genetically modified cholinergic receptor in the inner ear can enhance noise protection by the sound limiting system in the inner ear. The encouraging news is, that there is a real chance of finding ear-specific drugs for preventing noise trauma and tinnitus in the future.

Ronald Goodey: Companion to THE NEW ZEALAND ORDER OF MERIT: “The Queen has been pleased, on the occasion of the celebration of the New Year, to make the following appointments to The New Zealand Order of Merit: Companion to THE NEW ZEALAND ORDER OF MERIT C.N.Z.M Dr Ronald John GOODEY, of Auckland. For services to otolaryngology.” (source: Department of the Prime Minister and Cabinet of New Zealand).

On April 22th, 2009, the grand opening of the new TRI Tinnitus Clinic took place in Antwerp. For more information about the clinic please see http://www.brai2n.net/clinic/TRI/index.html

A new tinnitus book is under way. Again it is Aage Møller, who initiated this project, and who coordinates the effort of a large number of scientists and clinicians within the TRI community. The book “Tinnitus: Diagnosis and Treatment” will be published in October 2010.

“The proposed book provides a multidisciplinary comprehensive coverage of diagnosis and the treatments of different forms of tinnitus. A general introduction provides an overview of subjective tinnitus emphasizing that tinnitus is not one disease but a group of rather diverse disorders with different pathophysiology, different causes and consequently, different treatments. Tinnitus involves many disciplines, many specialties of medicine and surgery, and disciplines such as psychology and audiology. Diagnosis of tinnitus is a challenge because there are so many different forms of tinnitus and there are few objective signs and imaging methods are of little help. Treatment is equally challenging because of the difficulties of identifying the cause and the anatomical location of the pathology. The pathophysiology, diagnosis and treatment are topics that are taught sparsely in medical school and there is a lack of comprehensive books of the clinical management of patients with tinnitus. The proposed book provides a wide-ranging coverage of up-to-date knowledge about tinnitus, its diagnosis and management, written by clinicians and scientists from many disciplines who are active in the field. The proposed book will cover the results of recent progress in diagnosis and treatment for tinnitus.”

For more information please see http://www.amazon.de/Tinnitus-Aage-R-Moller/dp/1607611449/ref=sr_1_1?ie=UTF8&s=books-intl-de&qid=1240577497&sr=8-1
Upcoming Meetings

The 27th European Course on The Management of Tinnitus and Hyperacusis
When: May 10 – 13, 2009
Where: Møller Centre, University of Cambridge
Contact: Ann Allen, British Society of Audiology
         80 Brighton Road, Reading, RG6 1PS, UK
Phone: 0044 (0)118 966 0622
E-Mail: ann@thebsa.org.uk
Detailed information: http://www.europeantinnituscourse.org

9th European Symposium on Paediatric Cochlear Implantation
When: May 15 – 17, 2009
Where: Hilton Warsaw Hotel and Convention Centre, Warsaw, Poland
Contact: International Center of Hearing and Speech
         Kajetany, Mokra 17
         05-830 Nadarzyn, Poland
Phone: 0048 22 356 55 55
E-Mail: info@espci2009.pl
Detailed information: http://www.espci2009.pl

157th Meeting of the Acoustical Society of America (ASA)
When: May 18 – 22, 2009
Where: Portland, Oregon, USA
E-Mail: asa@aip.org
Detailed information: http://www.asa.aip.org/meetings.html

80. Jahresversammlung der Deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V.
When: May 20 – 24, 2009
Where: HanseMesse Rostock
Contact: Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie
         Hittorfrstr. 7
         53129 Bonn, Germany
Phone: 0049 (0) 2 28 23 17 70
E-Mail: info@hno.org
Detailed information: http://www.hno.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@ifosssaopaulo2009.com.br  
Detailed information: http://www.ifosssaopaulo2009.com.br

XXI IERASG - XXI Biennial Symposium of the International Evoked Response Audiometry Study Group  
When: June 7 – 11, 2009  
Where: Windsor Barra Hotel, Rio de Janeiro, Brazil  
Detailed information: http://www.ierasg2009.org/

Human Brain Mapping  
When: June 7 – 11, 2009  
Where: Windsor Barra Hotel, Rio de Janeiro, Brazil  
Detailed information: http://www.ierasg2009.org/

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: 0034 922 656 262  
Fax: 0034 922 670 188  
E-Mail: congresos@magnacongresos.com  
Detailed information: http://www.efas2009.org

Nineteenth Meeting of the European Neurological Society  
When: June 20 – 24, 2009  
Where: Fiera Milano Congress Centre, Milan, Italy  
Contact: ENS 2009  
c/o AKM Congress Service  
Association House  
P.O. Box  
CH-4002 Basel / Switzerland  
Phone: 0041 61 686 77 11  
Fax: 0041 61 686 77 88  
E-Mail: info@akm.ch  
Detailed information: http://www.ensinfo.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: 0039 0 2 72001824  
E-Mail: info@faev.org  
Detailed information: http://www.tri2009.org
MEMRO 2009 - Middle-Ear Mechanics in Research and Otology. 5th International Symposium
When: June 24 – 28, 2009
Where: Stanford University, CA, USA
Contact: Kam Morrella, CMP
Manager, Events & Meeting Planning
Stanford Conference Services
123 Encina Commons
Stanford, CA 94305
Phone: 001 650 736 0048
E-Mail: kamm@stanford.edu
Detailed information: http://www.memro.org

96. Frühjahresversammlung der Schweizerischen Gesellschaft für Oto-Rhino- Laryngologie, Hals- und Gesichtschirurgie
When: June 25 – 26, 2009
Where: Centre International de Conferences Genève (CICG), Switzerland
Contact: Suzanne Gaumann
7, chemin des Campanules
1219 Aïre
Phone: 0041 (0) 79 718 09 78
E-Mail: cong-org@orl-hno.ch
Detailed information: http://orl-hno.ch/d/veranstaltung/index.html

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

3rd International Conference on Auditory Cortex
When: August 29 – September 02, 2009
Where: Herrenkrug Parkhotel, Magdeburg, Germany
Contact: Conventus Congressmanagement & Marketing GmbH
Markt 8
Technische Universitaet Dresden
07743 Jena, Germany
Phone: 0049 (0)3641 3 53 32 25
E-Mail: ac2009@conventus.de
Detailed information: http://www.auditory-cortex.de/
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: 0044 (0) 151 709 8979
Fax: 0044 (0) 151 708 9861
Detailed information: http://www.politzerlondon.com

9th International Conference on Theoretical and Computational Acoustics 2009
When: September 7 – 11, 2009
Where: Dresden, Germany
Contact: Dr. Steffen Marburg
c/o Inst. für Festkörpermechanik
Technische Universität Dresden
01062 Dresden, Germany
Phone: 0049 351 4633 7976
Fax: 0049 351 4633 7969
E-Mail: info@ictca2009.com
Detailed information: http://www.ictca2009.org

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: 0049 (0)69 - 63 08-229/ -477
Fax: 0049 (0)69 - 96 31-52 13
E-Mail: wc2009@vde.com

Tinnitus Discovery - Asia & Pacific Tinnitus Symposium
When: September 11 – 12, 2009
Where: Auckland Maritime Museum, New Zealand
E-Mail: tinnitus@auckland.ac.nz

17th annual conference on management of the tinnitus patient
When: September 24 – 26, 2009
Where: Pomerantz Family Pavilion, Iowa City, USA
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

10th Anniversary Leicester Balance Course 13th to 15th October  
When: October 13 - 15, 2009  
Where: Leceister Tigers Rugby Stadium, Leceister, UK  
phone: 0044 (0)845 226622  
E-Mail: emma@biosensemedical.com

The 7th Meeting of the British Society of Neuro-Otology  
When: October, 16, 2009  
Where: Leceister Tigers Rugby Stadium, Leceister, UK  
Contact: Miss J Mills  
Neuro-Otology Group  
Imperial College London, Charing Cross Hospital  
Fulham Palace Road London W6 8RF  
phone: 0044 (0)208 846 7285  
Fax: 0044 (0)208 846 7577  
E-Mail: neuro-otology@imperial.ac.uk  
Detailed information: http://www.bsno.org.uk/Oct16-09-meeting.html

54th International Congress of Hearing Aid Acousticians  
When: October 21 – 23, 2009  
Where: CongressCenter Nürnberg, Germany  
Detailed information: http://www.euha.org

Herbsttagung Arbeitsgemeinschaft Deutschsprachiger Audiologen und Neurootologen (ADANO)  
When: October, 22 - 24, 2009  
Where: Rhein-Mosei-Halle, Koblenz, Germany  
Contact: Karin Scharbach  
Katholisches Klinikum Koblenz  
Rudolf-Virchow-Str. 7  
56073 Koblenz  
phone: 0049 (0) 261 4 96 31 11  
Fax: 0049 (0) 261 4 96 31 19  
E-Mail: hno-adano@kk-koblenz.de  
Detailed information: http://www.hno.org/adano/Adano_2009_Herbsttagung.pdf

158th Meeting of the Acoustical Society of America  
When: October 26 – 30, 2009  
Where: San Antonio, Texas, USA  
E-Mail: asa@aip.org  
Detailed information: http://www.asa.aip.org/meetings.html
ASHA Convention 2009 - American Speech-Hearing-Language Association
When: November 19 – 21, 2009
Where: New Orleans, Louisiana, USA
Detailed information: http://www.asha.org/about/events/convention

The 7th Asia Pacific Symposium on Cochlear Implants and related Sciences (APSCI)
When: December 1 – 4, 2009
Where: Raffles City Convention Center, Singapore
Contact: APSCI 2009 Symposium Manager
73 Bukit Timah Road
Rex House, #03-01
Phone: 0065 6330 6730
Fax: 0065 6336 2123
E-Mail: apsci2009@pwevent.com

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

22th Annual Convention of the American Academy of Audiology (AAA)
When: April 14 – 17, 2010
Where: San Diego, CA, USA
Detailed information: http://www.audiology.org/professional/ce/cal-details.php?id=65

159th Meeting of the Acoustical Society of America (ASA)
When: April 19 – 23, 2010
Where: Miami, Florida, USA
Detailed information: http://asa.aip.org/meetings.html
81. Jahresversammlung der Deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V.

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

ESPO 2010 European Society of Pediatric Otorhinolaryngology

When: June 05 – 08, 2010
Where: Baluarte Conference Centre, Pamplona, Spain
Contact: Secretaría Científica, ORL Congresos, S.L.
C/ Fundadores, nº 13
28028 Madrid, Spain
Phone: 0034 91 575 93 93
Fax: 0034 91 431 26 92
E-Mail: orlcongresos@seorl.net
Detailed information: http://www.espopamplona2010.com/

Human Brain Mapping Annual Meeting

When: June 06 – 10, 2010
Where: Barcelona, Spain
Detailed information: www.humanbrainmapping.org

4th World Congress of International Federation of Head and Neck Oncologic Societies (IFHNOS)

When: June 15 – 19, 2010
Where: Lotte Hotel, Seoul, Korea
Contact: IFHNOS 2010 Congress Secretariat
c/o Meci International Convention Services, Inc.
Rm. 1906, 19th floor, Daerung Post Tower #1 212-8 Guro-dong, Guro-gu
Seoul 152-790, Korea
Phone: 0082 2 2082 2310
Fax: 0082 2 2082 2314
E-Mail: ifhnos2010@ifhnos2010.org
Detailed information: http://www.ifhnos2010.org/
CI2010 11th International Conference on Cochlear Implants and other Implantable Auditory Technologies
When: June 30 – July 03, 2010
Where: Stockholm International Fairs (Stockholmsmässan), Stockholm, Sweden
Contact: MCI Stockholm
Box 6911
102 39 Stockholm, Sweden
Phone: 0046 8 5465 1500
Fax: 0046 8 5465 1599
E-Mail: ci2010@mci-group.com
Detailed information: http://www.ci2010.com

September 2010

Herbsttagung Arbeitsgemeinschaft Deutschsprachiger Audiologen und Neurootologen (ADANO)
When: September 16 – 19, 2010
Where: Zürich, Switzerland
Detailed information: http://www.hno.org/adano/tagungen.htm

International Symposium on Objective Measures in Auditory Implants
When: September 23 – 25, 2010
Where: St. Louis, MO, USA
Detailed information: http://ent.wustl.edu/oto/otoweb.nsf/746682188a1bff2786256c5500627633/ef4a8282267a4e738625734c0068ec82?OpenDocument

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

October 2010

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

November 2010

ASHA 2009 Annual Convention
When: November 18 – 20, 2010
Where: Philadelphia, PA, USA
Detailed information: http://www.asha.org/about/events/convention/
I Epidemiology

Association of tinnitus and electromagnetic hypersensitivity: hints for a shared pathophysiology?

Landgrebe M, Frick U, Hauser S, Hajak G, Langguth B.
Department of Psychiatry, Psychosomatics, and Psychotherapy, University of Regensburg, Regensburg, Germany. michael.landgrebe@medbo.de

BACKGROUND: Tinnitus is a frequent condition with high morbidity and impairment in quality of life. The pathophysiology is still incompletely understood. Electromagnetic fields are discussed to be involved in the multi-factorial pathogenesis of tinnitus, but data proving this relationship are very limited. Potential health hazards of electromagnetic fields (EMF) have been under discussion for long. Especially, individuals claiming themselves to be electromagnetic hypersensitive suffer from a variety of unspecific symptoms, which they attribute to EMF-exposure. The aim of the study was to elucidate the relationship between EMF-exposure, electromagnetic hypersensitivity and tinnitus using a case-control design. METHODOLOGY: Tinnitus occurrence and tinnitus severity were assessed by questionnaires in 89 electromagnetic hypersensitive patients and 107 controls matched for age-, gender, living surroundings and workplace. Using a logistic regression approach, potential risk factors for the development of tinnitus were evaluated. FINDINGS: Tinnitus was significantly more frequent in the electromagnetic hypersensitive group (50.72% vs. 17.5%) whereas tinnitus duration and severity did not differ between groups. Electromagnetic hypersensitivity and tinnitus were independent risk factors for sleep disturbances. However, measures of individual EMF-exposure like e.g. cell phone use did not show any association with tinnitus. CONCLUSIONS: Our data indicate that tinnitus is associated with subjective electromagnetic hypersensitivity. An individual vulnerability probably due to an over activated cortical distress network seems to be responsible for, both, electromagnetic hypersensitivity and tinnitus. Hence, therapeutic efforts should focus on treatment strategies (e.g. cognitive behavioral therapy) aiming at normalizing this dysfunctional distress network.

[Prevalence of auditory and vestibular symptoms among workers exposed to occupational noise]
[Article in Portuguese]

Ogido R, Costa EA, Machado Hda C.
Departamento de Medicina Preventiva e Social, Faculdade de Ciências Médicas, Universidade Estadual de Campinas, Campinas, SP, Brazil.

The purpose of the study was to assess the prevalence of auditory and vestibular symptoms in workers exposed to occupational noise. There were examined medical records of 175 workers with noise-induced hearing loss who attended an occupational health reference center in the city Campinas, Southeastern Brazil, from 1997 to 2003. The variables studied were frequency of symptoms of hypoacusis, tinnitus, and vertigo. Association with age, noise exposure time, and auditory thresholds were analyzed using the chi-square test and Fisher’s exact test. Hypoacusis was reported in 74% of cases, tinnitus in 81%, and vertigo in 13.2%. There was found an association between hypoacusis and age, noise exposure time, and auditory thresholds and between vertigo and noise exposure time. No other significant associations were found.
The extent of hearing impairment amongst Australian Indigenous prisoners in Victoria, and implications for the correctional system.

Quinn S, Rance G.
Department of Otolaryngology, The University of Melbourne, Australia. squinn@unimelb.edu.au

The hearing status of 109 Indigenous prisoners was investigated at five prison locations in Victoria, using audiological methods and face-to-face interview. The study found predominantly mild, sensorineural hearing loss. The rate of conductive hearing impairment was consistent with an age-matched general adult population (UK). All eardrums were intact, and 89% of middle-ears were normally air filled. Results showed 12% of prisoners had a hearing loss (average. 0.5, 1, 2, & 4 kHz >or=25 dB) in at least one ear, compared with 5% in an age-matched Australian adult population. More than a third (36%) had high-frequency, sensorineural hearing impairment (4 or 6 kHz >or=25 dB), in one or both ears. Over half of the inmates (58%) reported hearing problems sometimes, and 4% reported a lot of hearing trouble. The majority of prisoners (92%) reported exposures to loud noise, and tinnitus was reported by 72% of prisoners. For hearing-impaired individuals within the correctional system, the reduced ability to communicate with ease may impact detrimentally on daily interactions, and may impede progress through rehabilitation programs.

Hearing loss in veterans and the need for hearing loss prevention programs.

Saunders GH, Griest SE.
National Center for Rehabilitative Auditory Research, Portland VA Medical Center and Department of Otolaryngology, Oregon Health and Science University, USA. gabrielle.saunders@va.gov.

Currently, there are more than 445,000 veterans receiving compensation for hearing loss associated with military service, and 395,000 receiving compensation for service-related tinnitus. In addition to compensation payments, service-related hearing disorders cost the US Department of Veterans Affairs in terms of provision of hearing aids, hearing aid-related services, and clinical services at its 220 facilities nationwide. It is imperative that hearing conservation among military personnel and veterans be addressed. In this paper, we describe the rationale for and the development of a multimedia Hearing Loss Prevention Program aimed at preventing the progression of hearing loss among veterans associated with social, recreational, and nonmilitary occupational noise exposure. The program was developed based on the principles outlined in the Health Belief Model of Rosenstock (1966) and the Health Promotion Model of Pender et al. (2002).

Shooting habits of U.S. waterfowl hunters.

Stewart M, Borer SE, Lehman M.
Department of Communication Disorders, Central Michigan University, Mt. Pleasant, Michigan, USA. stewalmg@cmich.edu.

Exposure to high-intensity impulse noise from the recreational use of firearms is a common cause of noise-induced hearing loss (NIHL). Although recreational firearm users who shoot firearms without proper hearing protection are at risk for NIHL, a specific subgroup involved in hunting waterfowl may also be at risk due to their particular shooting habits. The goal of the present study was to investigate the shooting habits of this particular group of U.S. recreational firearm users. A 23-item written survey was sent to waterfowl hunting club members regarding their shooting behaviors, use of hearing protective devices (HPDs), and auditory status. Results indicated that waterfowl hunters in this study typically used large bore semiautomatic shotguns, did not consistently utilize HPDs during target practice or hunting and were exposed to multiple, unprotected shots during the past waterfowl season. Most subjects reported hunting in reverberant acoustic environments (hunting blinds). This group of recreational firearm users also reported high incidences of hearing loss and tinnitus. Information provided by this study may help hearing conservationists and hearing healthcare providers understand and better educate these shooters regarding the risk of acquiring NIHL.
Tinnitus among airline pilots: prevalence and effects of age, flight experience, and other noise.

Lindgren T, Wieslander G, Dammström BG, Norbäck D.
Medical Sciences/Department of Occupational and Environmental Medicine, Uppsala University Hospital, SE-75185 Uppsala, Sweden. torsten.lindgren@medsci.uu.se

INTRODUCTION: Frequent or constant tinnitus can be a problem for pilots because it can be distracting and/or interfere with communications in the cockpit. We studied tinnitus in a population of airline pilots to determine its prevalence and identify predictors. METHODS: A total of 418 male and 42 female pilots on duty in a Swedish airline returned a completed tinnitus questionnaire (response rate 79%). Multiple logistic regression analysis was performed; variables retained in the model included age, smoking, exposure to loud impulse noise during leisure time, previous work as a military pilot, years of employment as a commercial pilot, and type of aircraft. When available, the pilots' most recent routine audiometric test (N = 388) was used to study the association between hearing impairment and tinnitus. RESULTS: A total of 40% of respondents had experienced tinnitus for more than 5 min during the past year, 18% reported constant or severe tinnitus, and 12% had at some time visited a doctor for problems related to tinnitus. There were associations between tinnitus and age, impulse noise, and hearing impairment at 3, 4, and 6 kHz. There was no association with aircraft type or work as a military pilot. Pilots with tinnitus were more likely to report themselves disturbed by noise in the cockpit. CONCLUSION: These results show that tinnitus is relatively common among pilots and can create problems with sensitivity to noise. The frequency of tinnitus is most closely related to age, gender, exposure to high impulse noise during leisure time, and hearing impairment.

The Risks of Amplified Music for Disc-Jockeys Working in Nightclubs.
Ear Hear. 2009 Feb 3. [Epub ahead of print]

1Unité Inserm 583, INM, Hôpital Saint Eloi, Montpellier, France; 2Université Montpellier1, Montpellier, France; and 3Service d’ORL, Hôpital Gui de Chauliac, Montpellier cedex, France.

OBJECTIVES: Here, we evaluate the risks of amplified music for disc-jockeys (DJs) working in nightclubs. DESIGN: Sound level measurements were performed within the DJ mixing booths. A questionnaire was used to obtain exposure to noise and length of time in the profession. Audiograms and tinnitus pitch matching was also performed. RESULTS: The DJs' audiograms showed the expected noise-induced hearing loss at 6 KHz, but also low frequency losses at 125-500 Hz. Three quarters of them have tinnitus with a frequency corresponding to hearing loss. CONCLUSIONS: This study highlights the risk of amplified music on hearing and tinnitus.

Tinnitus is prevalent in children with cochlear implants.

Chadha NK, Gordon KA, James AL, Papsin BC.
Department of Otolaryngology, The Hospital for Sick Children, Toronto, Ontario, Canada, M5G 1X8; Cochlear Implant Program, The Hospital for Sick Children, Toronto, Ontario, Canada, M5G 1X8.

OBJECTIVES: To explore the prevalence and the perceived impact of tinnitus in children using cochlear implants. METHOD: Cross-sectional study of implanted children attending a cochlear implant family event organized annually by our academic tertiary pediatric care center. Children were interviewed together with their parents, using open-questioning and structured interview qualitative methodologies. The main outcome measures were the prevalence of tinnitus and any impact of these symptoms. RESULTS: 40 children (age range: 3-15, mean: 7 years) and their families were interviewed. These included unilateral implantees (n=21), and bilateral implantees (n=19) whose two procedures were simultaneous (n=6), within 6-12 months (n=3), or >2 years apart (n=10). Tinnitus was reported by 38% (n=15). Tinnitus occurred most commonly in the implanted ear, when the implants were not in use (e.g. in bed at night). The children were generally untroubled by the tinnitus, although two reported difficulty
sleeping. Tinnitus was most frequent in children aged 6-8 years (8/17, 47%), and in bilateral implantees with an inter-procedure delay of at least 2 years (6/10, 60%). Tinnitus was least reported in those implanted bilaterally simultaneously (1/6, 17%), and in those 5 years old or younger (3/11, 27%). No obvious relationship was identified between the prevalence of tinnitus and the etiology of deafness, age of implantation, or time elapsed since implantation. CONCLUSIONS: To our knowledge this is the first study to report the widespread prevalence of tinnitus in implanted children. Further work, particularly examining the effect of inter-implant delay on tinnitus in bilateral implantees, may contribute to our understanding of the neuronal plasticity after implantation.

[Hearing disorders and rock music]
[Article in Danish]

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Only few studies have investigated the frequency of hearing disorders in rock musicians. Performing rock music is apparently associated with a hearing loss in a fraction of musicians. Tinnitus and hyperacusis are more common among rock musicians than among the background population. It seems as if some sort of resistance against further hearing loss is developed over time. The use of ear protection devices have not been studied systematically but appears to be associated with diminished hearing loss.

II Pathophysiology

Cochlear Damage Changes the Distribution of Vesicular Glutamate Transporters Associated with Auditory and Nonauditory Inputs to the Cochlear Nucleus.

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Integration of multimodal information is essential for understanding complex environments. In the auditory system, multisensory integration first occurs in the cochlear nucleus (CN), where auditory nerve and somatosensory pathways converge (Shore, 2005). A unique feature of multisensory neurons is their propensity to receive cross-modal compensation after deafening. Based on our findings that the vesicular glutamate transporters, VGLUT1 and VGLUT2, are differentially associated with auditory nerve and somatosensory inputs to the CN, respectively (Zhou et al., 2007), we examined their relative distributions after unilateral deafening. After unilateral intracochlear injections of kanamycin (1 and 2 weeks), VGLUT1 immunoreactivity (ir) in the magnocellular CN ipsilateral to the cochlear damage was significantly decreased, whereas VGLUT2-ir in regions that receive nonauditory input was significantly increased 2 weeks after deafening. The pathway-specific amplification of VGLUT2 expression in the CN suggests that, in compensatory response to deafening, the nonauditory influence on CN is significantly enhanced. One undesirable consequence of enhanced glutamatergic inputs could be the increased spontaneous rates in CN neurons that occur after hearing loss and that have been proposed as correlates of the phantom auditory sensations commonly called tinnitus.
Differential effects of sodium salicylate on current-evoked firing of pyramidal neurons and fast-spiking interneurons in slices of rat auditory cortex. 
Hear Res. 2009 Mar 20. [Epub ahead of print] 

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Sodium salicylate (SS) can penetrate the blood-brain barrier to target neurons in the central auditory system. Understanding how SS alters functional behaviors of different types of central auditory neurons will provide insights into the neural mechanisms of SS-induced tinnitus. Here, we report the differential effects of SS on current-evoked firing of pyramidal neurons and fast-spiking interneurons in layer II/III of auditory cortex slices in young rats (P12-P19). The two neuronal types were identified according to their characteristic patterns of current-evoked firing as recorded with whole-cell patch-clamp techniques and by their morphological features. Following perfusion of the brain slice with 1.4 mM SS, the threshold current needed to evoke an action potential remained unchanged for pyramidal neurons (68.96 +/- 10.68 pA vs. 70.39 +/- 12.14 pA, n = 7, P > 0.05), but significantly increased for fast-spiking interneurons (56.9 +/- 13.69 pA vs. 74.04 +/- 15.73 pA, n = 7, P < 0.05). The drug perfusion caused no significant change in current-evoked firing rates in pyramidal neurons (-2.43 +/- 7.07%, n = 14, P > 0.05); however, it drastically and reversibly depressed those in fast-spiking interneurons by up to -49.88 +/- 10.39% (n = 14, P < 0.05). Our results suggest that functionally impairing fast-spiking interneurons, which are GABAergic and inhibitory, is probably one of the pathways through which SS raises excitability in the central auditory system and consequently produces tinnitus.

Acute high-intensity sound exposure alters responses of place cells in hippocampus. 
Hear Res. 2009 Mar 18. [Epub ahead of print] 

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Overstimulation is known to activate neural plasticity in the auditory nervous system causing changes in function and re-organization. It has been shown earlier that overstimulation using high-intensity noise or tones can induce signs of tinnitus. Here we show in studies in rats that overstimulation causes changes in the way place cells of the hippocampus respond as rats search for rewards in a spatial maze. In familiar environments, a subset of hippocampal pyramidal neurons, known as place cells, respond when the animal moves through specific locations but are relatively silent in others. This place-field activity (i.e. location-specific firing) is stable in a fixed environment. The present study shows that activation of neural plasticity through overstimulation by sound can alter the response of these place cells. Rats implanted with chronic drivable dorsal hippocampal tetrodes (4 microelectrodes) were assessed for stable single-unit place-field responses that were extracted from multiunit responses using NeuroExplorer computer spike-sorting software. Rats then underwent either 30 min exposure to a 4kHz tone at 104 dB SPL or a control period in the same sound chamber. The place-field activity was significantly altered after sound exposure showing that plastic changes induced by overstimulation are not limited to the auditory nervous system but extend to other parts of the CNS, in this case to the hippocampus, a brain region often studied in the context of plasticity.

Abnormal resting-state cortical coupling in chronic tinnitus. 

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BACKGROUND: Subjective tinnitus is characterized by an auditory phantom perception in the absence of any physical sound source. Consequently, in a quiet environment, tinnitus patients differ from control participants because they constantly perceive a sound whereas controls do not. We hypothesized that this difference is expressed by differential activation of distributed cortical networks.
RESULTS: The analysis was based on a sample of 41 participants: 21 patients with chronic tinnitus and 20 healthy control participants. To investigate the architecture of these networks, we used phase locking analysis in the 1-90 Hz frequency range of a minute of resting-state MEG recording. We found:

1) For tinnitus patients: A significant decrease of inter-areal coupling in the alpha (9-12 Hz) band and an increase of inter-areal coupling in the 48-54 Hz gamma frequency range relative to the control group.
2) For both groups: an inverse relationship ($r = -0.71$) of the alpha and gamma network coupling.
3) A discrimination of 83% between the patient and the control group based on the alpha and gamma networks.
4) An effect of manifestation on the distribution of the gamma network: In patients with a tinnitus history of less than 4 years, the left temporal cortex was predominant in the gamma network whereas in patients with tinnitus duration of more than 4 years, the gamma network was more widely distributed including more frontal and parietal regions.

CONCLUSION: In the here presented data set we found strong support for an alteration of long-range coupling in tinnitus. Long-range coupling in the alpha frequency band was decreased for tinnitus patients while long-range gamma coupling was increased. These changes discriminate well between tinnitus and control participants. We propose a tinnitus model that integrates this finding in the current knowledge about tinnitus. Furthermore we discuss the impact of this finding to tinnitus therapies using Transcranial Magnetic Stimulation (TMS).

Long-term administration of salicylate enhances prestin expression in rat cochlea.
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Salicylate, a common drug frequently used long term in the clinic, is well known for causing reversible hearing loss and tinnitus. Our previous study, however, demonstrated that chronic administration of salicylate progressively raised the amplitude of distortion product of otoacoustic emissions (DPOAEs), which are mainly caused by (outer hair cell) OHC electromotility. How salicylate affects OHC electromotility to cause this paradoxical increase remains unclear. One possibility is that it could affect prestin, which is a motor protein that contributes to the mechano-electrical properties of OHCs. In this experiment, we assessed the effect of acute and chronic salicylate treatment on prestin expression. Interestingly, after long-term salicylate injection (200 mg/kg, twice daily for 14 days), prestin gene and protein levels were up-regulated about twofold. These levels returned to baseline 14 days after treatment stopped. Acute injection of salicylate (single injection, 400 mg/kg) did not affect prestin levels. These data reveal that chronic salicylate administration markedly, but reversibly, increased prestin levels which may contribute to the enhanced DPOAE amplitudes we observed previously with similar salicylate treatment, which may be responsible for salicylate-induced tinnitus generation.

An integrative multiscale modeling approach for the study of tinnitus decompensation neural correlates.
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The study of tinnitus has become of great interest due to the increasing number and severity of cases reported worldwide. To cope with such situation, many experimental and theoretical studies have been dedicated to gain deeper insight into the neurophysiological mechanisms involved in the tinnitus decompensation. In this direction, some of the most influential tinnitus models have emphasized the link between selective attention and the tinnitus decompensation. However, it is still not clear what are the mechanisms involved in such relation and wether it is possible to provide a neuropsychological framework linking them with respect to large-scale neural correlates. In order to address such issues, we make use of evoked cortical potential neural correlates of auditory selective attention. We thus propose an integrative multiscale modeling approach for large-scale neural correlates of selective attention in the tinnitus decompensation. The results of our simulations are compared with experimental data so that hypothesis can be validated.


Tinnitus is the perception of phantom sounds in the ears or in the head. Sound therapy techniques for tinnitus treatment have been proposed. In order to investigate mechanisms of tinnitus generation and the clinical effects of sound therapy from the viewpoint of neural engineering, we have proposed a computational model using a neural oscillator. In the present paper, we propose another model that is composed of model neurons described by simplified Hodgkin-Huxley equations. By computer simulation it was detected that this model also has a bistable state, i.e., a stable oscillatory state and a stable equilibrium (non-oscillatory) state coexist at a certain parameter region. It was also noticed that the oscillation can be inhibited by supplying constant or pulse train stimuli, which is hypothesized as an afferent signal that is employed as an acoustical signal for tinnitus treatment. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, these phenomena could explain the fact that the habituated human auditory system temporarily halts perception of tinnitus following sound therapy.


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High doses of salicylate, the anti-inflammatory component of aspirin, induce transient tinnitus and hearing loss. Systemic injection of 250 mg/kg of salicylate, a dose that reliably induces tinnitus in rats, significantly reduced the sound evoked output of the rat cochlea. Paradoxically, salicylate significantly increased the amplitude of the sound-evoked field potential from the auditory cortex (AC) of conscious rats, but not the inferior colliculus (IC). When rats were anesthetized with isoflurane, which increases GABA-mediated inhibition, the salicylate-induced AC amplitude enhancement was abolished, whereas ketamine, which blocks N-methyl-d-aspartate receptors, further increased the salicylate-induced AC amplitude enhancement. Direct application of salicylate to the cochlea, however, reduced the response amplitude of the cochlea, IC and AC, suggesting the AC amplitude enhancement induced by systemic injection of salicylate does not originate from the cochlea. To identify a behavioral correlate of the salicylate-induced AC enhancement, the acoustic startle response was measured before and after salicylate treatment. Salicylate significantly increased the amplitude of the startle response. Collectively, these results suggest that high doses of salicylate increase the gain of the central auditory system, presumably by down-regulating GABA-mediated inhibition, leading to an exaggerated acoustic startle response. The enhanced startle response may be the behavioral correlate of hyperacusis that often accompanies tinnitus and hearing loss.


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Tinnitus is one of the most common symptoms affecting people all over the world. In the absence of an established cure many individuals are not only faced with the need to adjust to the sensation of the tinnitus noise, but also with psychological comorbidities. In recent years, different studies have been directed to elucidate the psychophysiological mechanisms that are involved in the tinnitus
decompensation. From these, special emphasis has been placed on studies related to attention and habituation, which accordingly play a crucial role in current tinnitus therapy approaches. In spite of such progress, the relationship between selective attention and the tinnitus decompensation with respect to large-scale neural correlates is still not well understood. In order to address this issue, we propose an integrative multiscale modeling approach for studying neural correlates of auditory selective attention in the tinnitus decompensation. Computational simulations based on our model confirmed electroencephalographic human data of both auditory selective attention and the tinnitus decompensation. It is concluded that the proposed methodology represents a promising approach to give insight into the neurodynamics of auditory selective attention in the tinnitus decompensation.

Human Brain Imaging of Tinnitus and Animal Models.
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Because subjective tinnitus is typically localized to the ear with hearing loss, tinnitus was traditionally thought to originate from neural hyperactivity in the damaged ear. However, most studies have found that hearing loss reduces the neural outputs from the damaged cochlea. These negative findings led to the hypothesis that tinnitus arises from aberrant neural activity in the central auditory system. Positron emission tomography imaging studies performed on tinnitus patients that could modulate their tinnitus provide evidence showing that the aberrant neural activity that gives rise to tinnitus resides in the central auditory pathway. To investigate the biological basis of tinnitus in more detail, an animal model was developed that allowed behavioral measures of tinnitus to be obtained from individual rats after inducing tinnitus with high doses of salicylate or high-intensity noise. This behavioral model was used to test the efficacy of memantine, an N-methyl-D-aspartate antagonist, and scopolamine, an anticholinergic, in suppressing salicylate-induced tinnitus. Neither drug completely suppressed salicylate-induced tinnitus. To detect the physiological changes associated with tinnitus, chronic microwire electrodes were implanted in the auditory cortex and measurements were obtained from the auditory cortex before and after salicylate and noise exposures known to induce tinnitus. High doses of salicylate or high-level noise exposure generally resulted in sound-evoked hyperactivity in the electrophysiological responses recorded from the auditory cortex of awake-animals. However, anesthetic tended to suppress or abolish the hyperactivity.

III Diagnostics

Auditory manifestations of superior semicircular canal dehiscence.
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OBJECTIVE: To understand the presenting auditory signs and symptoms and to examine the relationship between the auditory manifestations and audiometric parameters in superior semicircular canal dehiscence (SSCD). PATIENTS: Twenty consecutive patients with unilateral SSCD without a history of previous onologic surgery. MAIN OUTCOME MEASURE: Relationship between presenting symptoms and the bone-conduction thresholds and air-bone gap (ABG) on pure-tone audiometry. RESULTS: All 20 patients presented with typical vestibular symptoms of SSCD. Seventeen (85%) patients also had auditory symptoms, including autophony (40%), hyperacusis to bodily sounds (65%), hearing loss (40%), aural pressure (45%), and tinnitus (35%). Of the 17 patients, 14 (82%) patients had an ABG on audiometry, but only 7 (41%) patients demonstrated negative bone conduction thresholds. Of 8 patients, 5 who underwent surgical repair experienced resolution of autophony and/or hyperacusis postoperatively. CONCLUSION: Auditory symptoms are common in SSCD patients. These symptoms do not show any relationship to the presence of negative bone-conduction thresholds on pure-tone
audiometry. No firm conclusion could be drawn regarding the association between symptoms and ABG. Different pathways or mechanisms may exist in SSCD for bone-conducted sounds arising from different sources. Surgical repair of the dehiscence results in resolution of auditory symptoms in most patients.

[Head and neck paragangliomas.]
[Article in Turkish]

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OBJECTIVES: We evaluated patients who were treated for head and neck paragangliomas. PATIENTS AND METHODS: The study included 40 patients (25 females, 15 males; mean age 48 years; range 26 to 74 years) who were operated on for paragangliomas of the head and neck region between 1993 and 2007. Clinical findings, treatment modalities, and the results of treatment were evaluated. RESULTS: The most common complaint was neck swelling (n=30), followed by tinnitus (n=7), hearing loss (n=6), imbalance (n=3), pain (n=2), hoarseness (n=2), and nasal obstruction (n=1). The mean duration of symptoms was 22 months. The most common paraganglioma was glomus caroticum (n=28) with a mean tumor diameter of 4.5 cm (range 2 to 12 cm). Urinary vanilmandelic acid concentration was measured in 24 patients and found above normal range in two patients. Octreotide scintigraphy was performed in 14 patients and femoral angiography was performed in 27 patients. Multicentric disease was present in one patient and one patient had bilateral involvement. Transcervical excision was the most common approach. Complications were as follows: transient facial nerve paresis (n=3), vagal nerve palsy (n=2), hypoglossal nerve palsy (n=2), permanent facial paralysis (n=1), bleeding (n=1), and total hearing loss (n=1). No recurrences were encountered during a mean follow-up of 71 months. CONCLUSION: Preoperative evaluation of all patients with respect to catecholamine secretion and multicentric disease is important for choosing the proper treatment and preventing possible complications.

Evaluation of tinnitus patients with normal hearing sensitivity using TEOAEs and TEN test.
Auris Nasus Larynx. 2009 Mar 12. [Epub ahead of print]

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

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OBJECTIVE: The aim of this study was to evaluate the correlation between the most common instruments used to quantify tinnitus and the level of anxiety and depression experienced by patients in order to provide a guideline for otolaryngologists. STUDY DESIGN: Cross-sectional survey. SUBJECTS AND METHODS: A total of 108 tinnitus patients were submitted to a series of instruments, including Visual Analogue Scales (VAS), Tinnitus Handicap Inventory (THI), State Trait Anxiety Inventory Form Y (STAI-T), and Beck Depression Inventory (BDI). These instruments were chosen based on their psychometric properties, time of administration, and validity in many countries. RESULTS: Of the patients studied, 24 percent had severe tinnitus, 35 percent had anxiety disorders, and 13 percent had a depressive pathosis. Significant correlations between STAI-T and THI scores (P < 0.001), and between BDI and THI scores were shown (P < 0.001). The same results were found with VAS. CONCLUSION: If a patient reports a THI greater than 38, the otolaryngologist should supplement diagnostic studies with a psychological consultation.

[Evaluating tinnitus in industrial hearing loss prevention programs.]

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This study evaluated the interference of tinnitus on the quality of life for noise-exposed workers enrolled in a hearing conservation program. Noise measurements, a questionnaire, a Brazilian version of the Tinnitus Handicap Inventory (THI), and pure-tone audiometry were conducted with 52 participants (mean age, 29 years) who suffered from tinnitus. THI results indicated that tinnitus had the greatest influence.
in the functional scale (54%). Significant correlations (p < .05) were observed between the periodicity of tinnitus and noise exposure level; degree of tinnitus and exposure to chemicals; total THI score and the scores of the catastrophic, emotional, and functional scales; score of the emotional scale and the functional scale; and results of the THI and the general state of health. An evaluation of tinnitus and its impact could benefit tinnitus sufferers in the workplace.

**Obsessive-compulsiveness in a population of tinnitus patients.**

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The purpose of this study was to use the Maudsley Obsessional-Compulsive Inventory (MOCI) to assess obsessive-compulsiveness in a population of 196 tinnitus patients and to correlate MOCI scores with measures of anxiety, depression, and tinnitus severity. Tinnitus severity was positively correlated with measures of anxiety and depression. Depression was positively correlated with MOCI and anxiety scores. MOCI scores exhibited weaker positive correlations with tinnitus severity and anxiety. Effective management of tinnitus requires identification of psychological disorders or symptoms when they are present so that patients can receive appropriate treatment as soon as possible. The MOCI can be used to assess obsessive-compulsiveness in tinnitus patients.

**Ruptured tectal arteriovenous malformation demonstrated angiographically after removal of an unruptured occipital lobe arteriovenous malformation.**

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We report a case of ruptured tectal arteriovenous malformation (AVM) that was demonstrated angiographically only after removal of an unruptured occipital AVM. A 57-year-old man presented with sudden onset of diplopia and tinnitus. Computed tomography revealed a small hemorrhage in the right tectum mesencephali with intraventricular hemorrhage. Magnetic resonance imaging and angiography disclosed AVM in the right occipital lobe which was separate from the hemorrhagic lesion. Angiography demonstrated that the right occipital AVM was fed by the parieto-occipital artery and drained into the superior sagittal sinus and vein of Galen. However, no abnormal vascular lesion was detected near the tectum mesencephali. As venous hypertension was considered the reason for hemorrhage, the occipital AVM was completely resected. Postoperative angiography demonstrated disappearance of the occipital AVM, but it also disclosed a small tectal AVM fed by branches from the superior cerebellar artery, which had not been detected on preoperative angiography. This was considered the true cause of hemorrhage, and gamma knife surgery was accordingly performed. Even if an AVM is demonstrated, if the lesion does not correspond to the hemorrhage we recommend serial angiographical evaluation so that a small AVM is not missed.

**Evaluation of a compact tinnitus therapy by electrophysiological tinnitus decompensation measures.**

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Large-scale neural correlates of the tinnitus decompensation have been identified by using wavelet phase stability criteria of single sweep sequences of auditory late responses (ALRs). Our previous work showed that the synchronization stability in ALR sequences might be used for objective quantification of the tinnitus decompensation and attention which link to Jastreboff tinnitus model.
A review of the otological aspects of whiplash injury.  
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Approximately 10% of patients who have suffered with whiplash injury will develop otological symptoms such as tinnitus, deafness and vertigo. Some of these are purely subjective symptoms; nevertheless, for the majority there are specific tests that can be undertaken. These tests can quantify the extent and severity of the symptoms as well as provide guidance as to the correct rehabilitation pathway. This article reviews the body of literature relating to the otological aspects of whiplash injury and gives an overview for medical and legal professionals.

Diagnostic yield of MRI for audiovestibular dysfunction using contemporary referral criteria: correlation with presenting symptoms and impact on clinical management.  
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AIM: To investigate the diagnostic yield of T2-weighted magnetic resonance imaging (MRI) screening for vestibular schwannoma and other relevant conditions in the setting of audiovestibular symptoms, given the more liberal contemporary referral criteria. To determine whether presenting clinical symptoms correlate with imaging outcome in order to guide future protocols for MRI referral. MATERIALS AND METHODS: Eight hundred and eighty-one consecutive MRI examinations performed in patients with audiovestibular dysfunction were reviewed. Clinical indications and findings were recorded. Case notes were reviewed in patients with positive imaging findings. Two-way, cross-tabulation, Chi-square analysis was performed to assess the relationship between presenting symptoms and imaging outcome. RESULTS: Twelve of the 881 (1.4%) were positive for vestibular schwannoma. A further four of 881 (0.4%) revealed other relevant conditions. Incidental conditions, felt to be irrelevant to the presenting symptoms, were noted in 12 of the 881 (1.4%). In all 12 cases that were positive for vestibular schwannoma, either tinnitus or hearing loss was present. CONCLUSION: The yield for T2-weighted MRI to diagnose vestibular schwannoma and other relevant retrocochlear conditions was lower than for previous studies, which is likely to reflect trends in referral criteria. No single audiovestibular symptom or combination of symptoms is a statistically significant predictor of imaging outcome.

[Psychosocial aspects of coping with tinnitus and psoriasis patients. A comparative study of suicidal tendencies, anxiety and depression]  
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BACKGROUND: Treatment of tinnitus is primarily the task of ENT specialists, while treatment of the psychiatric diseases lies in the hand of psychotherapists. Different from mostly very apparent dermatological diseases, the severity level of tinnitus can often only be determined by psychological test batteries as well as a specific psychosomatic exploration. In this study patients with psoriasis were compared with tinnitus patients regarding quality of life, anxiety, depression and imminent suicidal tendencies, in order to realize the psychological impact and find appropriate instruments for treatment. METHODS: Between February and April 2005, 89 tinnitus patients, who underwent in-patient therapy in a neurootological and psychosomatic hospital, and 105 psoriasis patients, who had in-patient treatment
from October 1999 until October 2004 in a specialized clinic, were examined with psychological tests, which included the Tinnitus questionnaire proposed by Goebel und Hiller, the Symptoms Check List of Derogatis SCL-90-R, the HADS and the suicide rating according to Pöldinger. RESULTS: Tinnitus in-patients suffered significantly more from suicidal tendencies, depression and anxiety in contrast to patients with psoriasis, who suffered more from problems associated with their outward appearance. CONCLUSION: The use of a specific psychological test diagnostic is very helpful in the hand of the ENT specialist, but the Tinnitus questionnaire of Goebel and Hiller enables an initial screening.


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Meniere’s disease is peculiar to humans and is characterised by episodic vertigo, fluctuating hearing loss and tinnitus, and attacks of the affliction occurring under conditions of stress. Its pathology was first revealed to be inner ear hydrops through temporal bone studies in 1938. Although subsequently proposed as a disorder of water metabolism in the inner ear, its pathogenesis remains unsolved. The present study aimed to assess the link between the inner ear pathology in Meniere’s disease and vasopressin, an anti-diuretic stress hormone with a potential role in inner ear fluid homeostasis. Blood samples were obtained from Meniere’s disease patients in the morning, before any surgical treatment, to examine plasma vasopressin (pAVP) levels, and then from inner ear tissue during surgical treatment, to examine vasopressin type-2 receptor (V2R) in the endolymphatic sac. pAVP and the relative V2R mRNA expression in the endolymphatic sac were examined using a real-time polymerase chain reaction. Relative cAMP activity in the endolymphatic sac was also examined using tissue culture and cAMP assay. Both pAVP (1.6-fold versus controls; P = 0.048) and inner ear V2R mRNA expression (41.5-fold versus controls; P = 0.022) were significantly higher in Meniere’s patients. cAMP activity was basally up-regulated (2.1-fold versus controls) and cAMP sensitivity to vasopressin application was largely elevated (4.9-fold versus controls) in Meniere’s patients. We conclude that, in the pathogenesis of inner ear hydrops, resulting in Meniere’s attacks, elevation of pAVP levels (probably as a result of stress) may present as a matter of consequence, but susceptibility of the V2R-overexpressed and cAMP-hypersensitized inner ear to pAVP elevation might be essential as the basis of this disease. Further experimental and clinical studies are needed to better clarify the relationship between Meniere’s disease and stress.


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HYPOTHESIS: The Portuguese version of Mini-Tinnitus Questionnaire (Mini-TQ) is as valid as the English version to assess tinnitus-associated distress in the Portuguese-speaking population. BACKGROUND: Tinnitus is a major symptom in ENT practice affecting subjects in all demographic groups. Our objective is to validate a Portuguese version of Mini-TQ (Mini-TQ-pv) to be used in clinical practice and research. METHODS: Mini-TQ-pv was administered to 51 patients with chronic tinnitus. Statistical analysis was done to determine the psychometric properties of the instrument. RESULTS: After double translation, face and content validity were confirmed by high internal consistency (Cronbach alpha = 0.861) and significant correlation between individual items and total score. The questionnaire was easy and quick to administer (2.57 min). CONCLUSION: We provide a suitable Mini-TQ-pv to be used in the assessment of Portuguese-speaking patients with tinnitus.
Identifying tinnitus subgroups with cluster analysis.

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PURPOSE: We believe it is important to uncover tinnitus subgroups to identify subsets of patients most likely to benefit from different treatments. We review strategies for subgrouping based on etiology, subjective reports, the audiogram, psychoacoustics, imaging, and cluster analysis. METHOD: Preliminary results of a 2-step cluster analysis based on 246 participants from whom we had 26 categorical and 25 continuous variables were determined. RESULTS: A 4-cluster solution suggested the following subgroups: (a) constant distressing tinnitus, (b) varying tinnitus that is worse in noise, (c) tinnitus patients who are copers and whose tinnitus is not influenced by touch (somatic modulation), and (d) tinnitus patients who are copers but whose tinnitus is worse in quiet environments. CONCLUSIONS: Subgroups of tinnitus patients can be identified by using statistical approaches. The subgroups we identify here represent a preliminary attempt at identifying such patients. One next step would be to explore clinical trials of tinnitus treatments based on subgroup analyses or on using subgroups in the selection criteria.

Inner ear dysfunction of uncertain origin: a multidisciplinary approach could give something more.

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In order to find out any possible cause of an alteration of the vasomotor reactivity which can be responsible for a more or less severe sufferance of the inner ear, announced by the onset or the enhancement of sensorineural hearing loss, tinnitus, and some kind of dizziness and vertigo, a multidisciplinary approach should be considered. The possibility of an influence of hemodynamic imbalance due to hypotensive changes followed by vasomotor changes affecting the microcirculation of the inner ear has already been widely discussed; moreover, an increase in prevalence of tinnitus (which in many cases can be considered as a symptom of sufferance of the inner ear) has been found in subjects submitted to an “aggressive” antihypertensive therapy as well as in patients with severe heart failure, thus demonstrating a relationship between hemodynamic changes and inner ear dysfunction. For the same reason, the research for this mechanism of imbalance could concern other conditions possibly activating an abnormal response of the autonomic nervous system, which could in turn lead to a circulatory impairment of the labyrinth: among these, affections concerning central nervous system, endocrine system, metabolism, renal apparatus and even gastroenteric diseases with a functional component and any other factor which could interfere with vasomotor regulation should be considered. Thus, the absence of reliable causes for a sufferance of the inner ear should not lead to catalogue it as a disorder of “idiopathic” nature, but should represent a reason for a multidisciplinary investigation on all the possible causes of hemodynamic imbalance and/or autonomic dysregulation.

Clinical manifestations of vertebrobasilar dolichoectasia.

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Vertebrobasilar dolichoectasia is defined as an increase in the length and diameter of the intracranial arteries. Clinical manifestations of dolichoectasiae result from compression of the cranial nerves and structures of the brain stem, turbulent flow causing tinnitus and vertigo, often with damages of small blood vessels of the brain. Dolichoectasia is an ischemic stroke risk factor. The role of dolichoectasia in occurrence of haemorrhagic stroke, aneurysm and arterial dissection and thrombosis is still not fully understood (Ref. 34).
**IV Imaging**

**Abnormal resting-state cortical coupling in chronic tinnitus.**  

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**BACKGROUND:** Subjective tinnitus is characterized by an auditory phantom perception in the absence of any physical sound source. Consequently, in a quiet environment, tinnitus patients differ from control participants because they constantly perceive a sound whereas controls do not. We hypothesized that this difference is expressed by differential activation of distributed cortical networks. **RESULTS:** The analysis was based on a sample of 41 participants: 21 patients with chronic tinnitus and 20 healthy control participants. To investigate the architecture of these networks, we used phase locking analysis in the 1-90 Hz frequency range of a minute of resting-state MEG recording. We found: 1) For tinnitus patients: A significant decrease of inter-areal coupling in the alpha (9-12 Hz) band and an increase of inter-areal coupling in the 48-54 Hz gamma frequency range relative to the control group. 2) For both groups: an inverse relationship (r = -.71) of the alpha and gamma network coupling. 3) A discrimination of 83% between the patient and the control group based on the alpha and gamma networks. 4) An effect of manifestation on the distribution of the gamma network: In patients with a tinnitus history of less than 4 years, the left temporal cortex was predominant in the gamma network whereas in patients with tinnitus duration of more than 4 years, the gamma network was more widely distributed including more frontal and parietal regions. **CONCLUSION:** In the here presented data set we found strong support for an alteration of long-range coupling in tinnitus. Long-range coupling in the alpha frequency band was decreased for tinnitus patients while long-range gamma coupling was increased. These changes discriminate well between tinnitus and control participants. We propose a tinnitus model that integrates this finding in the current knowledge about tinnitus. Furthermore we discuss the impact of this finding to tinnitus therapies using Transcranial Magnetic Stimulation (TMS).

**Reduced volume of Heschl's gyrus in tinnitus.**  

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The neural basis of tinnitus is unknown. Recent neuroimaging studies point towards involvement of several cortical and subcortical regions. Here we demonstrate that tinnitus may be associated with structural changes in the auditory cortex. Using individual morphological segmentation, the medial partition of Heschl's gyrus (mHG) was studied in individuals with and without chronic tinnitus using magnetic resonance imaging. Both the tinnitus and the non-tinnitus group included musicians and non-musicians. Patients exhibited significantly smaller mHG gray matter volumes than controls. In unilateral tinnitus, this effect was almost exclusively seen in the hemisphere ipsilateral to the affected ear. In bilateral tinnitus, mHG volume was substantially reduced in both hemispheres. The tinnitus-related volume reduction was found across the full extent of mHG, not only in the high-frequency part usually most affected by hearing loss-induced deafferentation. However, there was also evidence for a relationship between volume reduction and hearing loss. Correlations between volume and hearing level depended on the subject group as well as the asymmetry of the hearing loss. The volume changes observed may represent antecedents or consequences of tinnitus and tinnitus-associated hearing loss and also raise the possibility that small cortical volume constitutes a vulnerability factor.
Endolymphatic hydrops and therapeutic effects are visualized in ‘atypical’ Meniere’s disease.

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

Diagnostic yield of MRI for audiovestibular dysfunction using contemporary referral criteria: correlation with presenting symptoms and impact on clinical management.

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AIM: To investigate the diagnostic yield of T2-weighted magnetic resonance imaging (MRI) screening for vestibular schwannoma and other relevant conditions in the setting of audiovestibular symptoms, given the more liberal contemporary referral criteria. To determine whether presenting clinical symptoms correlate with imaging outcome in order to guide future protocols for MRI referral. MATERIALS AND METHODS: Eight hundred and eighty-one consecutive MRI examinations performed in patients with audiovestibular dysfunction were reviewed. Clinical indications and findings were recorded. Case notes were reviewed in patients with positive imaging findings. Two-way, cross-tabulation, Chi-square analysis was performed to assess the relationship between presenting symptoms and imaging outcome. RESULTS: Twelve of the 881 (1.4%) were positive for vestibular schwannoma. A further four of 881 (0.4%) revealed other relevant conditions. Incidental conditions, felt to be irrelevant to the presenting symptoms, were noted in 12 of the 881 (1.4%). In all 12 cases that were positive for vestibular schwannoma, either tinnitus or hearing loss was present. CONCLUSION: The yield for T2-weighted MRI to diagnose vestibular schwannoma and other relevant retrocochlear conditions was lower than for previous studies, which is likely to reflect trends in referral criteria. No single audiovestibular symptom or combination of symptoms is a statistically significant predictor of imaging outcome.
V Pharmacotherapy

Cochlear Damage Changes the Distribution of Vesicular Glutamate Transporters Associated with Auditory and Nonauditory Inputs to the Cochlear Nucleus.

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Integration of multimodal information is essential for understanding complex environments. In the auditory system, multisensory integration first occurs in the cochlear nucleus (CN), where auditory nerve and somatosensory pathways converge (Shore, 2005). A unique feature of multisensory neurons is their propensity to receive cross-modal compensation after deafening. Based on our findings that the vesicular glutamate transporters, VGLUT1 and VGLUT2, are differentially associated with auditory nerve and somatosensory inputs to the CN, respectively (Zhou et al., 2007), we examined their relative distributions after unilateral deafening. After unilateral intracochlear injections of kanamycin (1 and 2 weeks), VGLUT1 immunoreactivity (ir) in the magnocellular CN ipsilateral to the cochlear damage was significantly decreased, whereas VGLUT2-ir in regions that receive nonauditory input was significantly increased 2 weeks after deafening. The pathway-specific amplification of VGLUT2 expression in the CN suggests that, in compensatory response to deafening, the nonauditory influence on CN is significantly enhanced. One undesirable consequence of enhanced glutamatergic inputs could be the increased spontaneous rates in CN neurons that occur after hearing loss and that have been proposed as correlates of the phantom auditory sensations commonly called tinnitus.

[Efficacy of carbamazepine combined with flunarizine hydrochloride for treating tinnitus] [Article in Chinese]

Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2008 Nov;22(22):1016-1018, 1022.

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OBJECTIVE: To determine whether carbamazepine is effective in treating the subjective tinnitus. METHOD: Randomized, prospective, double-blind, controlled trial was used in our study. The study group consisted of 100 adult patients who consulted our outpatient clinic complaining of subjective tinnitus, excluded objective tinnitus and the patients who had tinnitus caused by obvious diseases, such as outer and middle ear diseases, 50 patients were given carbamazepine and Flunarizine Hydrochloride, 50 patients were given Vitamin B6 and Flunarizine Hydrochloride. After a week the effect of the different group of medicines was observed. Tinnitus questionnaire was performed before the treatment, and pure tone audiogram, tinnitus pitch and loudness matching were performed at the end of the treatment. RESULT: Completion of treatment, tinnitus loudness matching assessment showed that the efficacy of the carbamazepine group was similar to that of the control group. The efficacy of treatment was respectively 26% by intend to treat (ITT) and 28.3% by per protocol (PP) in the carbamazepine group and 26% by ITT and 27.7% by PP in the control group. The efficacy of treatment has no statistically significance for tinnitus loudness of the experimental group and the control group. The subjective tinnitus improvement rate showed no difference between two groups. Pure tone thresholds fluctuated within 10 dB in the beginning and at the end of the treatment. There were serious side effects in the carbamazepine group. The side effects rates were respectively 55.3% and 16.7% in the carbamazepine group and the control group, respectively. The difference had statistical significance. CONCLUSION: Our results showed that the efficacy of carbamazepine combined with Flunarizine Hydrochloride is similar to that of the control group. There was no improvement in listening. But the side effects of it were more serious than that of the control group. It should not be recommended for the treatment of tinnitus.
J Negat Results Biomed. 2009 Feb 17;8:3.
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BACKGROUND: Vardenafil (Levitra(R)) represents a potent and highly selective phosphodiesterase type 5 (PDE5) inhibitor, which is established for treatment of various diseases. There are several unpublished reports from patients stating that vardenafil has a considerable therapeutic effect on their concomitant tinnitus. This pilot study was conducted to specifically assess the effect of vardenafil in patients with chronic tinnitus. METHODS: This trial was based on a prospective, randomized, double-blind, placebo-controlled, parallel group design. Forty-two consecutive subjects with mon- or binaural chronic tinnitus received 10 mg vardenafil (N = 21) or matching placebo tablets (N = 21) administered orally twice a day over a period of 12 weeks. Clinical examination and data acquisition took place at each visit: at baseline, after 4 weeks, after 12 weeks (end of treatment with study medication), and at non-medicated follow-up after 16 weeks. Assessment of clinical effectiveness was based on a standardized tinnitus questionnaire (TQ), the Short Form 36 health survey (SF-36), audiometric measurements (mode, pitch and loudness of tinnitus; auditory thresholds) and biomarkers of oxidative stress in patients’ blood (malondialdehyde, protein carbonyl, homocysteine and total antioxidative status). Therapeutic efficacy was evaluated by comparison of subjective and objective parameters with baseline data between both treatment groups (ANCOVA). RESULTS: Vardenafil had no superior efficacy over placebo in the treatment of chronic tinnitus during this study. The primary efficacy criterion ‘TQ total score’ failed to demonstrate significant improvement compared to placebo. Subjective reports of TQ subscales and general quality of life areas (SF-36), objective audiometric examinations as well as investigated biomarkers for oxidative stress did not reveal any significant treatment effects. The safety profile was favorable and consistent with that in other vardenafil studies. CONCLUSION: Although hypoxia and ischemia play a special role in the pathogenesis of tinnitus, the PDE5-inhibitor-induced increase of nitric oxide-mediated vasodilatation exerted no specific influence on tinnitus symptomatology. Considering the unclear risk of rarely associated hearing impairment, systemic application of vardenafil or other PDE5 inhibitors prove to be not appropriate for therapy of chronic tinnitus.

Medical treatment of otosclerosis: rationale for use of bisphosphonates.
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Otosclerosis is a bony dyscrasia characterized by histopathological findings of osteoclast production. Osteoclastogenesis explains the pathogenesis of otosclerosis. Basic science research in the experimental animal otic capsule has given insight into the process of evolution of otosclerosis. The normal otic capsule is preserved with very little bone turnover as a result of the production of osteoprotegerin (OPG) by the membranous inner ear that prevents the activation of osteoclasts. Animals genetically unable to produce OPG demonstrated the production of hearing loss and histopathology of the temporal bones consistent with that seen in otosclerosis. Applying the understanding of osteoclastogenesis to the treatment of otosclerosis has led to the clinical use of the class of drugs called bisphosphonates. The bisphosphonate group of drugs specifically targets osteoclasts by reducing production of osteoclasts and accelerating their early cell death. The rationale for use of bisphosphonates to treat the sensorineural hearing loss of otosclerosis is explained, with cases that illustrate the bisphosphonates treatment algorithms and the response to treatment.
Association between tinnitus retraining therapy and a tinnitus control instrument.

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

[Open-field treatment of hyperacusis.]
[Article in Spanish]

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OBJECTIVE: Prospective study of the effectiveness of treatment in patients with hyperacusis by means of an open-field technique of acoustic treatment with nature sounds. MATERIAL AND METHODS: 34 patients were referred to a tinnitus and hyperacusis clinic at a private Otorhinolaryngology Department. Clinical and exploratory ENT studies were performed. Open-field nature sounds were applied by means of a compact disk for half an hour each day during a period of several weeks. RESULTS: By the end of treatment, the 34 patients studied had reached normal discomfort thresholds in a maximum of 9 weeks. CONCLUSIONS: The progressive open-field application of nature sounds has been effective in eliminating hyperacusis in a short space of time.
Increasing the effective use of high-frequency spectrum tinnitus therapy.

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A new device and method described here will allow real-time processing of any audio signal (e.g., from a television set) into a high-frequency tinnitus sound therapy stimulus. By simultaneously listening to the unprocessed and processed speech, a patient can enjoy the entertainment while obtaining therapy that appears to be a viable alternative in the treatment of severe disabling tinnitus.

Treatment of tinnitus with a customized, dynamic acoustic neural stimulus: clinical outcomes in general private practice.
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OBJECTIVES: We evaluate the relative effectiveness of a newly available tinnitus treatment approach for different categories of patients in general private practice. METHODS: This was a cohort study, sponsored by Neuromonics, involving the first 470 patients to undertake the Neuromonics Tinnitus Treatment in 7 Neuromonics tinnitus clinics. All patients were provided with a dynamic acoustic neural stimulus, customized to each patient’s audiometric profile, for daily use as part of a structured rehabilitation program. Tinnitus disturbance was assessed before, during, and after treatment with the Tinnitus Reaction Questionnaire. RESULTS: The outcomes displayed a relation with patients’ suitability according to predefined criteria: among the most suitable patients (tier 1 cohort), 92% exceeded the threshold for success (defined as a reduction in tinnitus-related disturbance of at least 40%), and the mean improvement in tinnitus disturbance was 72%; the discontinuance rate was 4%. For other suitability categories, the success rates and mean improvements were somewhat lower, and the discontinuance rates higher (tier 2: 60%, 49%, and 16%, respectively; tier 3: 39%, 32%, and 17%, respectively). CONCLUSIONS: The results showed that the treatment is effective for suitable patients in the private practice setting, and they provide health-care professionals with guidance as to what patients might expect from treatment, depending on their degree of suitability.

[Use of hearing aid--coping and functional disability]
[Article in Norwegian]
Tidsskr Nor Lægeforen. 2008 Dec 4;128(23):2715-2718.
Helvik AS, Arnesen H, Wennberg S, Jacobsen G.
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BACKGROUND: Hearing loss is a common health problem and affects social life. We studied how adults’ use of hearing aids was influenced by socio-demographic and audiological characteristics, use of coping strategies, and perceived functional disability. MATERIAL AND METHODS: 162 adult patients (82 men) who had previously used hearing aids and were referred to St. Olavs University Hospital (Trondheim, Norway) for a renewed assessment and prescription, were consecutively included in the study. Questionnaires were used to capture their experience with using hearing aids and the negative consequences of hearing loss, as well as use of specific coping strategies and the presence of tinnitus. Relations between reported use and explanatory variables were assessed by using logistic regression analyses. RESULTS: Advanced hearing loss increased the probability of using aids more frequently, while non-persistent tinnitus and a medium long experience with using hearing aids (7-17 years) reduced the probability. Maladaptive behaviour interfering with effective communication reduced the daily use. Use of verbal and nonverbal communication strategies, and degree of perceived functional disability did not influence the use of hearing aids. INTERPRETATION: A low degree of hearing loss, occasional tinnitus, a medium long experience in the use of hearing aids, and frequent use of dysfunctional communication strategies were associated with little use of the aids.
VII Brain Stimulation

Transcranial magnetic stimulation, tinnitus and auditory hallucinations.
Actas Esp Psiquiatr. 2009 Jan-Feb;37(1):54-56.

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Transcranial magnetic stimulation (TMS) has been shown to be effective in modulating cerebral cortex activity. Most of the published controlled studies have reported that left temporoparietal area stimulation with 1 Hz frequencies has managed to improve auditory hallucinations at least partially and transiently in patients suffering from schizophrenia. These stimulation parameters have been demonstrated to be useful in otologic patients with tinnitus sensation. The clinical relevance of these findings has already been discussed. However, in spite of the clinical benefit of TMS for these or other patients, it is revealing new data and new questions about the neurobiological basis of mental disorders. For example: which is the common substrate in tinnitus and auditory hallucinations that could explain such a therapeutic coincidence? In this work we present two representative clinic cases and we discuss this question. Key words: Transcranial magnetic stimulation. Auditive hallucinations. Tinnitus.

Transcranial magnetic stimulation: a new diagnostic and therapeutic tool for tinnitus patients.

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Even if the pathophysiology of tinnitus remains incompletely understood, there is growing agreement that dysfunctional neuroplastic processes in the brain are involved. Repetitive transcranial magnetic stimulation (rTMS) is a potent tool for modifying neural activity at the stimulated area and at a distance along functional anatomical connections. Depending on stimulation parameters, cortical networks can be functionally disturbed or modulated in their activity. The technique can alleviate tinnitus by modulating the excitability of neurons in the auditory cortex. It is assumed that TMS decreases the hyperexcitability that is associated with some forms of tinnitus. A growing number 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. Single sessions of high-frequency rTMS over the temporal cortex have been successful in reducing the intensity of tinnitus during the time of stimulation and could be predictive for treatment outcome of chronic epidural stimulation using implanted electrodes. Because most available studies have been performed with small sample sizes and show only moderate effect sizes and high interindividual variability of treatment effects, further development of the technique is needed before it can be recommended for use in clinical routine. Both patient-related (e.g., hearing loss, tinnitus duration, age) and stimulation-related (e.g., stimulation site, stimulation protocols) factors seem to influence treatment outcome; however, their exact impact still remains to be clarified.

One-year follow up of patients with chronic tinnitus treated with left temporoparietal rTMS.
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Background and purpose: Although there are a number of positive reports on the therapeutic effects of repetitive transcranial magnetic stimulation (rTMS) for treatment of tinnitus, there are few details about the duration of treatment effects or the relative efficiency of different rTMS protocols. Methods: Sixty six patients with chronic tinnitus were divided into four groups, receiving sham rTMS, 1, 10 and 25 Hz rTMS applied each day for 10 days over left temporoparietal cortex. They were followed up at 4 months and 1 year using the tinnitus questionnaire [Tinnitus Handicap Inventory(THI)] and self ratings of annoyance as
well as measures of residual inhibition. Results: A two factor anova revealed a significant ‘rTMS’ x ‘time’ interaction indicating that real and sham rTMS had different effects on the THI scale and annoyance of tinnitus (P = 0.026 and 0.046 respectively). After 1 year, the tinnitus was absent in one or both ears of 10 patients who had received real rTMS: one of these was in the 1 Hz group, four patients were in the 10 Hz group and five patients were in the 25 Hz group. Conclusion: Some patients show a lasting benefit at 1 year after 10 days of rTMS treatment. It appears that treatment at 10 or 25 Hz may be more beneficial than at 1 Hz, although more work is necessary to validate this conclusion.

**Levodopa does not enhance the effect of low-frequency repetitive transcranial magnetic stimulation in tinnitus treatment.**


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**OBJECTIVE:** Low-frequency repetitive transcranial magnetic stimulation (rTMS) has shown promise for the treatment of tinnitus. Experimental data from motor cortex stimulation in healthy subjects indicate that the suppressing effect of low-frequency rTMS can be enhanced by dopaminergic receptor activation. Here we investigated whether administration of the dopamine precursor levodopa before low-frequency rTMS enhances its efficacy in tinnitus treatment.

**STUDY DESIGN:** Sixteen patients with chronic tinnitus received 100 mg of levodopa before each session of low-frequency rTMS. Results were compared with a matched control group of 16 patients who received the same treatment, but without levodopa. Treatment outcome was assessed with a standardized tinnitus questionnaire.

**RESULTS:** Both stimulation protocols resulted in a significant reduction of tinnitus scores after 10 days of stimulation; however, there was no significant difference between the two groups. **CONCLUSION:** Our data suggest that 100 mg of levodopa does not enhance the effect of rTMS in the treatment of tinnitus.

**VIII Behavioral Therapy**

**Clients’ in-session acceptance and cognitive defusion behaviors in acceptance-based treatment of tinnitus distress.**

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Cognitive-behavioral treatment (CBT) is considered to be an effective treatment of distress associated with tinnitus (perception of internal noises without any outer auditory stimulation), but the processes by which the therapy works remain unclear. Mindfulness and acceptance is receiving increased attention in the treatment literature for chronic medical conditions. However, few studies have examined these and related processes with behavioral or observer measures. In the present study 57 videotapes (a total of 1710min) from 19 clients who participated in a controlled trial of an acceptance-based treatment for tinnitus distress, were coded for frequency and peak level of verbal behaviors expressing either acceptance or cognitive defusion. Frequency of cognitive defusion behaviors and peak level of cognitive defusion as well as peak level of acceptance rated in Session 2, predicted symptom reduction 6month following treatment. These relationships were not accounted for by the improvement that had occurred prior to the measurement point of the process variables. Moreover, prior symptom changes could not predict process variables rated later in therapy (after most of the improvement in therapy had occurred). Thus, clients’ in-session acceptance and cognitive defusion behaviors appear to play an important role in the reduction of negative impact of tinnitus.
Principles and application of educational counseling used in progressive audiologic tinnitus management.

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Exposure to loud sounds is a common cause and exacerbator of tinnitus - a troubling auditory symptom that affects millions of people worldwide. Clinical research at the National Center for Rehabilitative Auditory Research has resulted in a clinical model of tinnitus management referred to as Progressive Audiologic Tinnitus Management (PATM). The model involves five hierarchical levels of management: Triage, Audiologic Evaluation, Group Education, Tinnitus Evaluation, and Individualized Management. Counseling by audiologists and, as needed, mental health providers, is a key component of PATM. This style of counseling focuses less on didactic informational counseling; instead, counseling is used for facilitating patients’ learning to adjust to the disturbing auditory symptom by successfully employing tools from two powerful skillsets for self-management of chronic tinnitus - the therapeutic uses of sound and techniques from cognitive-behavioral psychology. This article provides an overview of the methods of counseling used with PATM and provides details concerning the overarching principles of collaborative adult learning that are believed to be most important in facilitating self-management by patients who complain of tinnitus.

A randomized controlled trial of cognitive-behavior therapy for tinnitus.

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This study is a randomized, waitlist-controlled trial testing the effect of a brief, “manualized” cognitive-behavioral group therapy on distress associated with tinnitus, quality of well-being, psychological distress including depression, and internal focus. Cognitive-behavioral therapy (CBT) included training in activity planning, relaxation training and, primarily, cognitive restructuring. Sixty-five participants were recruited, and 41 completed treatment. Participants were randomly assigned to receive 8 weeks of manualized group CBT either immediately or after an 8-week waiting period. Participants completed outcome measures at the time of their random assignment and at 8, 16, and 52 weeks later. Repeated-measure analysis of covariance revealed significant group-by-time interactions on measures of tinnitus distress and depression, indicating that CBT led to greater improvement in those symptoms. The current results suggest that CBT, applied in a group format using a manual, can reduce the negative emotional distress, including depression, associated with tinnitus.

[Integrated intensive treatment of tinnitus: decrease of the tinnitus-related distress during a one-year follow-up study]
[Article in German]

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AIM OF THE STUDY: The therapy of the chronic tinnitus is aimed at improving the way patients cope with their tinnitus and at reducing the tinnitus-related distress. The present study investigated the changes of psychometric parameters that occurred in patients with chronic tinnitus after 7-days outpatient multidisciplinary therapy. The changes were monitored for up to 1 year in order to evaluate the long-term efficiency. METHODS: Main emphasis of the intensive tinnitus therapy applied was placed on tinnitus habituation and on teaching the patients how to apply coping strategies. The main elements
of the multimodal concept included progressive muscle relaxation according to Jacobson, physiotherapy, educative seminars, training of selective attention and, lastly, the change of judgment, attitude and behaviour towards tinnitus. Psychometric parameters and tinnitus-related distress were assessed prior to and after the therapy (at 3, 6 and 12 months) using the tinnitus questionnaire (TQ) according to Goebel and Hiller. Furthermore, subjects waiting for therapy (waiting list) were recruited to the control group and compared with the therapy group which had received therapy 3 months earlier. RESULTS: The therapy group showed a significant reduction of the TQ total score after 3 months as compared to the control group. Moreover, we observed a long-term, progressive positive outcome during the one-year follow-up. The TQ total score was reduced by 10.9 points. There was an obvious decrease of the emotional and cognitive distress as well as of the intrusiveness of tinnitus, as per evaluation of TQ subscales. CONCLUSIONS: The outpatient intensive multidisciplinary tinnitus therapy with long-term aftercare has proved to be an effective method in the treatment of patients with chronic tinnitus. The outpatient setting enables the instant implementation of strategies learned during therapy in the patients’ everyday life.

**Neurofeedback by neural correlates of auditory selective attention as possible application for tinnitus therapies.**

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More and more people are suffering from tinnitus. There are many treatments for tinnitus that have been claimed based on different causes. Unfortunately, until now none of the existing treatments has been found to be effective in general. Here, we would like to suggest a treatment to tinnitus based on neurofeedback using neural correlates of auditory selective evoked potentials (ASEPs). We have shown that the wavelet phase synchronization of auditory late responses (ALR) single sweeps allows for a direct online monitoring of phase locked auditory attention. The results show that after a simple training, subjects learned to control their attention to the auditory modality. To improve the ability in the attention control system is an objective of many tinnitus treatments, so that the perception of the patients towards the tinnitus noise can be reduced to a minimum. It is concluded that our proposed neurofeedback system by wavelet phase synchronization measure might be used in a clinical treatment of tinnitus patients and it is possible to extent to other therapeutic based control systems.

**IX Somatic Tinnitus**

**Cochlear Damage Changes the Distribution of Vesicular Glutamate Transporters Associated with Auditory and Nonauditory Inputs to the Cochlear Nucleus.**

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Integration of multimodal information is essential for understanding complex environments. In the auditory system, multisensory integration first occurs in the cochlear nucleus (CN), where auditory nerve and somatosensory pathways converge (Shore, 2005). A unique feature of multisensory neurons is their propensity to receive cross-modal compensation after deafening. Based on our findings that the vesicular glutamate transporters, VGLUT1 and VGLUT2, are differentially associated with auditory nerve and somatosensory inputs to the CN, respectively (Zhou et al., 2007), we examined their relative distributions after unilateral deafening. After unilateral intracochlear injections of kanamycin (1 and 2 weeks), VGLUT1 immunoreactivity (ir) in the magnocellular CN ipsilateral to the cochlear damage was significantly decreased, whereas VGLUT2-ir in regions that receive nonauditory input was significantly increased 2 weeks after deafening. The pathway-specific amplification of VGLUT2 expression in the CN suggests that, in compensatory response to deafening, the nonauditory influence on CN is significantly
enhanced. One undesirable consequence of enhanced glutamatergic inputs could be the increased spontaneous rates in CN neurons that occur after hearing loss and that have been proposed as correlates of the phantom auditory sensations commonly called tinnitus.

**Head, Neck, and Eye Movements That Modulate Tinnitus.**

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Recent functional brain imaging studies in humans suggest that the neural generator(s) for tinnitus may reside in the central nervous system and involve both auditory as well as nonauditory centers. The contribution of nonauditory centers in the pathogenesis and regulation of tinnitus is reinforced by studies showing that many patients have somatic tinnitus whereby movements and manipulations of the eyes, head, neck, jaw, and shoulder can modulate the loudness and pitch of their tinnitus. In most cases, the maneuvers lead to increases in tinnitus loudness or pitch rather than decreases. Our results indicate that most tinnitus patients experience only a modest change in loudness or pitch when performing these maneuvers. However, some patients report that these maneuvers significantly modulate the loudness or pitch, sometimes by a factor of 2 to 3. The high prevalence of somatic tinnitus serves to illustrate the complex multimodal interactions that exist between the auditory pathway and other sensory-motor systems innervating the head, neck, shoulders, and eyes.

**Cross-modal interactions of auditory and somatic inputs in the brainstem and midbrain and their imbalance in tinnitus and deafness.**

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**PURPOSE:** This review outlines the anatomical and functional bases of somatosensory influences on auditory processing in the normal brainstem and midbrain. It then explores how interactions between the auditory and somatosensory system are modified through deafness, and their impact on tinnitus is discussed. **METHOD:** Literature review, tract tracing, immunohistochemistry, and in vivo electrophysiological recordings were used. **RESULTS:** Somatosensory input originates in the dorsal root ganglia and trigeminal ganglia, and is transmitted directly and indirectly through 2nd-order nuclei to the ventral cochlear nucleus, dorsal cochlear nucleus (DCN), and inferior colliculus. The glutamatergic somatosensory afferents can be segregated from auditory nerve inputs by the type of vesicular glutamate transporters present in their terminals. Electrical stimulation of the somatosensory input results in a complex combination of excitation and inhibition, and alters the rate and timing of responses to acoustic stimulation. Deafness increases the spontaneous rates of those neurons that receive excitatory somatosensory input and results in a greater sensitivity of DCN neurons to trigeminal stimulation. **CONCLUSIONS:** Auditory-somatosensory bimodal integration is already present in 1st-order auditory nuclei. The balance of excitation and inhibition elicited by somatosensory input is altered following deafness. The increase in somatosensory influence on auditory neurons when their auditory input is diminished could be due to cross-modal reinnervation or increased synaptic strength, and may contribute to mechanisms underlying somatic tinnitus.
X Surgical Treatment

Glomus jugulare tumours: certain clinical and radiological aspects observed following Gamma Knife radiosurgery.

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INTRODUCTION: Glomus jugulare tumours represent a great therapeutic challenge. Previous papers have documented good results from Gamma Knife surgery (GKS) with these tumours. However, the relationship between clinical improvement and tumour shrinkage has never been assessed.

MATERIALS AND METHODS: There were 14 patients, 9 women and 5 men. The mean follow-up period was 28 months (range 6 to 60 months). All the tumours except one were Fisch type D and the mean volume was 14.2 cm(3) (range 3.7-28.4 cm(3)). The mean prescription dose was 13.6 Gy (range 12-16 Gy).

RESULTS: None of the tumours have continued to grow. Eight are smaller and 6 unchanged in volume. Two patients with bruit have had no improvement in their symptoms. Among the other 12 patients, 5 have had symptomatic improvement of dysphagia, 4 in dysphonia, 3 in facial numbness, 3 in ataxia and 2 in tinnitus. Individual patients have experienced improvement in vomiting, vertigo, tongue fasciculation, hearing, headache, facial palsy and accessory paresis. One patient developed a transient facial palsy. Symptomatic improvement commonly began before any reduction in tumour volume could be detected. The mean time to clinical improvement was 6.5 months whereas the mean time to shrinkage was 13.5 months.

CONCLUSIONS: Gamma Knife treatment of glomus jugulare tumours is associated with a high incidence of clinical improvement with few complications, using the dosimetry recorded here. Clinical improvement would seem to be a more sensitive early indicator of therapeutic success than radiological volume reduction. Further follow-up will be needed.

Vestibular schwannoma: surgery or gamma knife radiosurgery? A prospective, nonrandomized study.
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OBJECTIVE: Prospective, open, nonrandomized study of treatment-associated morbidity in patients undergoing microsurgery or gamma knife radiosurgery (GKRS) for vestibular schwannoma. METHODS: Ninety-one patients with vestibular schwannoma with a maximum tumor diameter of 25 mm in the cerebellopontine angle were treated according to a prospective protocol either by GKRS (63 patients) or open microsurgery (28 patients) using the suboccipital approach. Primary end points included hearing function, according to the Gardner-Robertson scale, and facial nerve function, according to the House-Brackmann scale at 2 years. Clinical data included a balance platform test, score for tinnitus and vertigo using a visual analog scale, and working ability. Patients responded to the quality-of-life questionnaires Short-Form 36 and Glasgow Benefit Inventory. RESULTS: Three elderly GKRS patients withdrew; all remaining patients were followed for 2 years. Both primary end points were highly significant in favor of GKRS (P < 0.001). Evidence of reduced facial nerve function (House-Brackmann grade 2 or poorer) at 2 years was found in 13 of 28 operated patients and 1 of 60 GKRS patients. Thirteen of 28 patients who underwent surgery had serviceable hearing (Gardner-Robertson grade A or B) preoperatively, but none had serviceable hearing postoperatively. Twenty-five of 60 GKRS patients had serviceable hearing before treatment, and 17 (68%) of them had serviceable hearing 2 years after treatment. The tinnitus and vertigo visual analog scale score, as well as balance platform tests, did not change significantly after treatment, and working status did not differ between the groups at 2 years. Quality of life was significantly better in the GKRS group at 2 years, based on the Glasgow Benefit Inventory questionnaire.
One GKRS patient required operative treatment within the 2-year study period. CONCLUSION: This is the second prospective study to demonstrate better facial nerve and hearing outcomes from GKRS than from open surgery for small- and medium-sized vestibular schwannomas.

Cranial dural arteriovenous fistulae: asymptomatic cortical venous drainage portends less aggressive clinical course.
Neurosurgery. 2009 Feb;64(2):241-7; discussion 247-248.
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OBJECTIVE: Cranial dural arteriovenous fistulae (dAVF) with cortical venous drainage (CVD) (Borden Types 2 and 3) are reported to carry a 15% annual risk of intracranial hemorrhage (ICH) or nonhemorrhagic neurological deficit (NHND). The purpose of this study was to compare the clinical course of Type 2 and 3 dAVFs that present with ICH or NHND with those that do not. METHODS: Twenty-eight patients with Type 2 or 3 dAVFs were retrospectively evaluated. CVD was classified as asymptomatic (aCVD) if patients presented incidentally or with pulsatile tinnitus or orbital phenomena. CVD was classified as symptomatic (sCVD) if patients presented with ICH or NHND. Occurrence of new ICH or new or worsening NHND between diagnosis and disconnection of CVD or last follow-up (if not disconnected) was noted. Overall frequency of events was compared using Fisher’s exact test. Cumulative, event-free survival was compared using Kaplan-Meier analysis with log-rank testing. RESULTS: Of 17 patients with aCVD, 1 (5.9%) developed ICH and none experienced NHND or death during the median 31.4-month follow-up period. Of 11 patients with sCVD, 2 (18.2%) developed ICH and 3 (27.3%) experienced new or worsened NHND over the median 9.7-month follow-up period. One of these patients subsequently died. Overall frequency of ICH or NHND was significantly lower in patients with aCVD versus sCVD (P = 0.022). Respective annual event rates were 1.4 versus 19.0%. aCVD patients had significantly higher cumulative event-free survival (P = 0.0016). CONCLUSION: Cranial dAVFs with aCVD may have a less aggressive clinical course than those with sCVD.

Novel surgical treatment of a transverse-sigmoid sinus aneurysm presenting as pulsatile tinnitus: technical case report.
Neurosurgery. 2009 Feb;64(2):E393-394; discussion E394.
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OBJECTIVE: Pulsatile tinnitus is a relatively common, potentially incapacitating condition that is often vascular in origin. We present a case of disabling pulsatile tinnitus caused by a transverse-sigmoid sinus aneurysm that was surgically treated with self-tying U-clips (Medtronic, Inc., Memphis, TN). We also review the literature and discuss other described interventions. CLINICAL PRESENTATION: A 48-year-old woman presented with a 5-year history of progressive pulsatile tinnitus involving the right ear. Her physical examination was consistent with a lesion that was venous in origin. Angiography demonstrated a wide-necked venous aneurysm of the transverse-sigmoid sinus that had eroded the mastoid bone. INTERVENTION: The patient underwent a retromastoid suboccipital craniectomy to expose the aneurysm and surrounding anatomy. The aneurysm dome was tamponaded and the aneurysm neck was coagulated until the dome had shrunk to a small remnant. The linear defect in the transverse sigmoid junction was then reconstructed with a series of U-clips and covered with Gelfoam hemostatic sponge (Pfizer, Inc., New York, NY). The patient awakened without neurological deficit and with immediate resolution of her tinnitus. A postoperative angiogram demonstrated obliteration of the aneurysm, with minimal stenosis in the region of the repair and good flow through the dominant right transverse-sigmoid junction. CONCLUSION: This technical case report describes a novel definitive surgical treatment of venous sinus aneurysms. This technique does not necessitate long-term anticoagulation, has a low likelihood of reintervention, and provides immediate resolution of pulsatile tinnitus.
Staged Gamma Knife radiosurgery after tailored surgical resection: a novel treatment paradigm for glomus jugulare tumors.  

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OBJECT: Although benign and slow growing, glomus jugulare tumors can be locally aggressive because of their proximity to lower cranial nerves and major vascular structures. Surgical resection frequently leads to complications, and radiosurgery alone often does not relieve symptoms. We report a novel treatment paradigm of tailored surgical resection followed by staged radiosurgery that allows for tissue diagnosis and immediate improvement of symptoms and tumor control without the morbidity of radical surgical resection. METHODS: Five patients with glomus jugulare tumors and contraindications to extensive surgery each underwent an outpatient otologic procedure to resect the portion of the tumor in the middle ear and mastoid with no attempt to remove tumor in the jugular bulb. Each patient returned 2-5 months later for Gamma Knife radiosurgery to the remainder of the tumor, which consisted of one 15-Gy dose prescribed to the 50% isodose curve. Patients were followed through outpatient visits and surveillance MR imaging for up to 3 years. RESULTS: All patients were successfully treated as outpatients. Each had improvement or resolution of pulsatile tinnitus and otalgia and preserved or improved hearing. One patient developed a delayed facial palsy prior to radiosurgery that resolved completely; there were no other changes in cranial nerve function after either procedure. Tumor volume was stable or reduced in all patients at most recent follow-up, and there were no immediate or delayed complications. CONCLUSIONS: Staged outpatient microsurgical and radiosurgical therapy for glomus jugulare tumors in the symptomatic patient is safe and yields favorable results regarding tumor size, tinnitus, hearing and cranial nerve status.

[Middle ear adenoma/middle ear carcinoid--an unproblematic tumor?]  
[Article in German]  

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OBJECTIVES: Adenomas/carcinoid tumors of the middle ear are very rare tumors of young to middle aged patients. The terms adenoma and carcinoid tumor of the middle ear can be used as synonyms, with the WHO favouring the term middle ear adenoma (MEA). These tumors usually present with unspecific clinical symptoms and a long case history. They are classified as benign tumors with only very few reported cases of regional metastasis after years of disease. According to recent literature, the clinical course is usually uncomplicated with complete surgical excision being adequate therapy. METHODS AND PATIENTS: This study describes the clinical course and the diagnostic challenges in four cases of this rare tumor entity. RESULTS: The selected patients (2 males, 2 females, 25-38 years old) showed very similar clinical findings with decreased hearing acuity, tinnitus and sometimes pain. After the primary surgical excision up to 10 further operations were necessary, this being in contrast to the usual clinical course as described in the literature. In two cases a tumor recurrence was documented with one case recurring six times. In this case adjuvant radiotherapy (70 Gy) was performed. The histological differential diagnosis can also be problematic; in one case with a highly atypical morphology it was impossible to arrive at a definite diagnosis during the analysis of a frozen section. CONCLUSION: Adenomas of the middle ear can have a much more complicated clinical course than is suggested by the recent literature. The presented cases in this study and the analysis of previously published cases shows that the typical progression described by the current WHO-classification with unproblematic surgical management of the tumor and an uncomplicated further clinical course does not always correspond to reality. The main reason for this is the difficulty in obtaining a complete surgical excision. Therefore, a well-planned and comprehensive surgical management with a high frequency of follow-up examinations should be chosen. In complicated individual cases adjuvant radiotherapy can be helpful.
Clinical hypnosis for the alleviation of tinnitus.

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The neurophysiology of tinnitus is poorly understood, and it can have an origin at a number of neural levels, making a psychological approach to treatment attractive. Clinical hypnosis has been demonstrated to be effective in a number of clinical situations, such as irritable bowel syndrome but, in other areas for which it is commonly employed, such as smoking cessation, the evidence is poor. Its use for the management of troublesome tinnitus has been discussed in the literature for more than 30 years, but little formal research has been conducted into efficacy of this treatment or the relative suitability of techniques. Despite this, a success rate of 70% is commonly quoted by hypnosis practitioners in promotional material. This review summarizes the few peer-reviewed studies on this subject and concludes that, though evidence suggests that hypnosis provides a benefit in some subjects, how this benefit compares to more mainstream approaches is not yet clear. This area is currently under-researched, and engagement is encouraged between researchers in audiology and hypnotherapists to undertake large, well-structured controlled trials with standardized measures of outcome.

XII Review

[Tinnitus treatment: Neurosurgical management.]
[Article in French]
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Tinnitus is a very frequent symptom affecting 10% of the general population. It corresponds to the perception of an internal noise that can severely impair the quality of life. Tinnitus management requires a multidisciplinary approach in which neuromodulation and neurosurgery tend to play major roles. Classification of tinnitus separates objective tinnitus (i.e., tinnitus that can be heard or recorded) from the more frequent subjective tinnitus (i.e., tinnitus only perceived by the patient). Objective tinnitus is either pulsatile synchronous with heartbeat or asynchronous. In the former, appropriate radiological testing should search for a vascular abnormality as well as other neurological diseases (intracranial hypertension, Arnold-Chiari malformation, vascular loops, etc.). Asynchronous objective tinnitus generally corresponds to muscular contractions that require specific management. The pathophysiology of subjective tinnitus is more complex, showing strong analogies with postamputation pain syndromes. After peripheral middle ear or inner ear damage, auditory deafferentation could result in hyperactivity and/or functional reorganization within central auditory and nonauditory structures. This could explain the persistence of tinnitus after total hearing amputation (e.g., translabyrinthine approach for vestibular schwannoma) and associated symptoms such as hyperacusis or anxiety and depression. This central model finds strong support in animal experiments and in functional neuroimagery (PET, fMRI, MEG). Since no etiologically based therapies are currently available, severe subjective tinnitus management only targets tinnitus tolerance with sound enrichment or cognitive behavior therapy. However, in the near future better knowledge of tinnitus pathophysiology and innovative therapeutic tools could emerge from neuromodulation techniques such as repeated transcranial magnetic or epidural electric stimulation.
Vestibulocochlear nerve.

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The vestibulocochlear or eighth cranial nerve (CN VIII) has purely special sensory afferent function. The nerve has two components, the vestibular nerve, that detects head and body motion, and the cochlear nerve that detects sound. The primary receptors that convey information to the vestibular portion of CN VIII are the semicircular canals that detect angular acceleration, and the otolithic organs that detect linear acceleration. The organ of Corti receives auditory signals and conveys its information via the cochlear portion. Processes that affect the receptors or the nerve will cause hearing loss, tinnitus, otalgia, vertigo, oscillopsia, and disequilibrium. In this review, the authors discuss the anatomy of CN VIII, the clinical evaluation of patients with vertigo and hearing loss, and specific disease entities.

Transcranial magnetic stimulation: a new diagnostic and therapeutic tool for tinnitus patients.

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Even if the pathophysiology of tinnitus remains incompletely understood, there is growing agreement that dysfunctional neuroplastic processes in the brain are involved. Repetitive transcranial magnetic stimulation (rTMS) is a potent tool for modifying neural activity at the stimulated area and at a distance along functional anatomical connections. Depending on stimulation parameters, cortical networks can be functionally disturbed or modulated in their activity. The technique can alleviate tinnitus by modulating the excitability of neurons in the auditory cortex. It is assumed that TMS decreases the hyperexcitability that is associated with some forms of tinnitus. A growing number 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. Single sessions of high-frequency rTMS over the temporal cortex have been successful in reducing the intensity of tinnitus during the time of stimulation and could be predictive for treatment outcome of chronic epidural stimulation using implanted electrodes. Because most available studies have been performed with small sample sizes and show only moderate effect sizes and high interindividual variability of treatment effects, further development of the technique is needed before it can be recommended for use in clinical routine. Both patient-related (e.g., hearing loss, tinnitus duration, age) and stimulation-related (e.g., stimulation site, stimulation protocols) factors seem to influence treatment outcome; however, their exact impact still remains to be clarified.

A review of the otological aspects of whiplash injury.

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Approximately 10% of patients who have suffered with whiplash injury will develop otological symptoms such as tinnitus, deafness and vertigo. Some of these are purely subjective symptoms; nevertheless, for the majority there are specific tests that can be undertaken. These tests can quantify the extent and severity of the symptoms as well as provide guidance as to the correct rehabilitation pathway. This article reviews the body of literature relating to the otological aspects of whiplash injury and gives an overview for medical and legal professionals.
Subjective idiopathic tinnitus and palliative care: a plan for diagnosis and treatment.

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This article integrates the highlights of the authors’ clinical experiences derived from existing protocols for tinnitus diagnosis and treatment with the evolving discipline of palliation medicine. Specifically, it demonstrates how the inclusion of principles of palliation medicine contributes to the efficacy of treatment.

Human Brain Imaging of Tinnitus and Animal Models.

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Because subjective tinnitus is typically localized to the ear with hearing loss, tinnitus was traditionally thought to originate from neural hyperactivity in the damaged ear. However, most studies have found that hearing loss reduces the neural outputs from the damaged cochlea. These negative findings led to the hypothesis that tinnitus arises from aberrant neural activity in the central auditory system. Positron emission tomography imaging studies performed on tinnitus patients that could modulate their tinnitus provide evidence showing that the aberrant neural activity that gives rise to tinnitus resides in the central auditory pathway. To investigate the biological basis of tinnitus in more detail, an animal model was developed that allowed behavioral measures of tinnitus to be obtained from individual rats after inducing tinnitus with high doses of salicylate or high-intensity noise. This behavioral model was used to test the efficacy of memantine, an N-methyl-D-aspartate antagonist, and scopolamine, an anticholinergic, in suppressing salicylate-induced tinnitus. Neither drug completely suppressed salicylate-induced tinnitus. To detect the physiological changes associated with tinnitus, chronic microwire electrodes were implanted in the auditory cortex and measurements were obtained from the auditory cortex before and after salicylate and noise exposures known to induce tinnitus. High doses of salicylate or high-level noise exposure generally resulted in sound-evoked hyperactivity in the electrophysiological responses recorded from the auditory cortex of awake-animals. However, anesthetic tended to suppress or abolish the hyperactivity.

Cross-modal interactions of auditory and somatic inputs in the brainstem and midbrain and their imbalance in tinnitus and deafness.

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PURPOSE: This review outlines the anatomical and functional bases of somatosensory influences on auditory processing in the normal brainstem and midbrain. It then explores how interactions between the auditory and somatosensory system are modified through deafness, and their impact on tinnitus is discussed. METHOD: Literature review, tract tracing, immunohistochemistry, and in vivo electrophysiological recordings were used. RESULTS: Somatosensory input originates in the dorsal root ganglia and trigeminal ganglia, and is transmitted directly and indirectly through 2nd-order nuclei to the ventral cochlear nucleus, dorsal cochlear nucleus (DCN), and inferior colliculus. The glutamatergic somatosensory afferents can be segregated from auditory nerve inputs by the type of vesicular glutamate transporters present in their terminals. Electrical stimulation of the somatosensory input results in a complex combination of excitation and inhibition, and alters the rate and timing of responses to acoustic stimulation. Deafness increases the spontaneous rates of those neurons that receive excitatory somatosensory input and results in a greater sensitivity of DCN neurons to trigeminal stimulation.
CONCLUSIONS: Auditory-somatosensory bimodal integration is already present in 1st-order auditory nuclei. The balance of excitation and inhibition elicited by somatosensory input is altered following deafness. The increase in somatosensory influence on auditory neurons when their auditory input is diminished could be due to cross-modal reinnervation or increased synaptic strength, and may contribute to mechanisms underlying somatic tinnitus.

XIII Others


Trenado C, Haab L, Strauss DJ.
Computational Diagnostics and Biocybernetics Unit, Saarland University Hospital and Saarland University of Applied Sciences, Homburg, Saar, Germany.

Auditory evoked cortical potentials (AECPs) have been consolidated as a diagnostic tool in audiology. Further applications of this technique are in experimental neuropsychology, neuroscience, and psychiatry, e.g., for the attention deficit disorder, schizophrenia, or for studying the tinnitus decompensation. In particular, numerous psychophysiological studies have emphasized their dynamic characteristics in relation to exogenous and endogenous attention. However, the effect of corticothalamic feedback dynamics to neural correlates of focal and nonfocal attention and its large-scale effect reflected in AECPs is far from being understood. To address this issue, we model neural correlates of auditory selective attention reflected in AECPs by using corticothalamic feedback dynamics. In our framework, we make use of a well-known multiscale model of evoked potentials, for which we define for the first time a neurofunctional map of relevant corticothalamic loops to the hearing path. Such loops are in turn are coupled to our proposed probabilistic scheme of auditory selective attention. It is concluded that our model represents a promising approach to gain a deeper understanding of the neurodynamics of auditory attention and might be used as an efficient forward model to support hypotheses that are obtained in experimental paradigms involving AECPs.

Cost-effectiveness of multidisciplinary management of Tinnitus at a specialized Tinnitus centre.
BMC Health Serv Res. 2009 Feb 11;9:29.

Clinical Psychological Science, Maastricht University, Maastricht, The Netherlands.
r.cima@dmkep.unimaas.nl

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 fragmented and costly tinnitus care. Evidence suggests that a comprehensive multidisciplinary approach in treating tinnitus is effective. The main objective of this study is to examine the effectiveness, costs, and cost-effectiveness of a comprehensive treatment provided by a specialized tinnitus center versus usual care. This paper describes the study protocol. METHODS/DESIGN: 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 performed from a societal perspective. DISCUSSION: This is, to our knowledge, the first randomized controlled trial that evaluates a comprehensive treatment of tinnitus and 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. TRIAL REGISTRATION: The trial has been registered at ClinicalTrial.gov. The trial registration number is NCT00733044.
Effectiveness of combined counseling and low-level laser stimulation in the treatment of disturbing chronic tinnitus.


Cuda D, De Caria A.
Department of Otolaryngology, Guglielmo da Saliceto Hospital, Piacenza, Italy. d.cuda@ausl.pc.it

We recruited 46 adult patients affected by disturbing tinnitus lasting for at least 3 years. All were treated with a combined counseling protocol constituting hypnotherapeutic and muscle relaxation techniques. We randomly assigned 26 patients to the group receiving low-level laser stimulation treatment and 20 to the placebo group. The laser power was 5 mV and the wavelength 650 nm. The irradiation lasted 20 minutes daily for 3 months. The Tinnitus Handicap Inventory (THI) questionnaire was submitted at the beginning and at the end of treatment. The THI scores improved in the entire sample after treatment but more significantly in the group receiving low-level laser stimulation. From the point of view of clinical classification, approximately 61% of irradiated patients had tinnitus severity decreased by one class, in comparison to 35% of the placebo group.

XIV Case Reports

Case report: cisplatin preparation error; patient management and morbidity.

Torres EV, Mari AA, Cubells ND, Jimenez-Torres N.
Pharmacy Department, Hospital General de Ciudad Real, Ciudad Real, Spain.

Introduction. Antineoplastic drug therapy errors represent a high iatrogenic potential due to antineoplastic drugs narrow therapeutic ranges and the complexity of chemotherapy regimens that may increase the risk of morbidity and mortality for oncology patients. SETTING: We report a 57-year-old man with head and neck cancer who mistakenly received 180 mg/m(2) of cisplatin overdose despite the safety measures and validations carried out during preparation. The patient developed moderate nausea and vomiting, acute renal failure, hearing difficulty (tinnitus), and severe myelodepression. Patient management. Prophylactic and symptomatic treatments were applied in order to prevent and correct toxicity during the 9 days stay at hospital. RESULT: He recovered with mild tinnitus and mild renal impairment as the only sequelae. This case presents a hospital stay and treatment quite different to others used to reverse all cisplatin overdose toxicity and it shows the benefits of prompt management.

Arteriovenous malformation in the parotid region presenting as pulsatile tinnitus: A case report.

Chen MC, Chung WY, Luo CB, Wu HM.
Department of Neurosurgery, Neurological Institute, Taipei Veterans General Hospital, National Yang-Ming University, Taipei, Taiwan, Republic of China.

BACKGROUND: Pulsatile tinnitus is a unique symptom in the general population and often leads patients to medical attention. METHODS AND RESULTS: We report a patient who had an arteriovenous malformation of superficial temporal artery in the parotid region causing pulsatile tinnitus and insomnia. Magnetic resonance angiography and carotid angiography were useful tools for the detection of this vascular malformation. Successful treatment of this lesion was achieved by endovascular embolization. CONCLUSION: This case illustrates a thorough diagnostic work-up with a high index of suspicion and a proper treatment option is rewarding when dealing with such a rare disease. (c) 2009 Wiley Periodicals, Inc. Head Neck, 2009.
Behcet’s disease with involvement of major arteries: a case report.
Acta Neurol Taiwan. 2008 Dec;17(4):253-257.

Ho BL, Lin RT, Chen YF, Lin HF.
Department of Neurology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

Vascular involvement is not infrequent in Behcet’s disease (BD). It is generally seen in the form of superficial thrombophlebitis or occlusion of major veins. In rare instances, arterial occlusion and aneurysm formation may be seen in BD. We reported a young male with BD, diagnosed at the age of twenty for relapsing and remitting oral ulceration, skin rash, arthralgia and ocular painful redness for three years. At the age of 21, he had recurrent abdominal aortic aneurysm and inconspicuous neurological manifestations including dizziness, tinnitus and transients of blurred vision. The carotid angiography disclosed the occlusion of bilateral common carotid arteries (CCA). A carotid endarterectomy was subsequently performed to reduce the risk of stroke. The pathological examination of the occluded segment of CCA revealed chronic inflammation, which was attributable to BD. There was no atherosclerotic change. To the best of our knowledge, this is the first case report of concurrent bilateral CCA occlusion and relapsing abdominal aortic aneurysm. Even in the absence of specific neurological symptoms, we suggest that cerebrovascular investigation need to take into consideration in BD patients with unexplained cranial symptoms.

Demyelinating disease of central and peripheral nervous systems associated with an A8344G mutation in tRNAlys.
Neuromuscul Disord. 2009 Mar 7. [Epub ahead of print]

Erol I, Alehan F, Horvath R, Schneiderat P, Talim B.
Baskent University Faculty of Medicine, Department of Pediatrics, Division of Child Neurology, 6. Cadde 72/3 Bahcelievler, 06490 Ankara, Turkey.

We describe a patient with acute combined demyelinating disease of the central and peripheral nervous systems associated with the A8344G mutation in the mitochondrial tRNA lysine gene. A 7-year-old boy presented with acute onset of palpitations, tinnitus, ataxia, bilateral sixth nerve palsy, and flaccid quadriaparesis. Serum creatine kinase and lactate were mildly increased. Electromyography showed demyelinating sensory and motor polyneuropathy. Brain magnetic resonance imaging demonstrated demyelination in the left thalamus and magnetic resonance spectroscopy revealed a lactate peak corresponding to this lesion. Histologic analysis of the muscle showed cytochrome c-oxidase-deficient fibers and ragged red fibers. Respiratory chain analyses revealed deficiencies of complexes I and IV. Molecular genetic analyses of the muscle showed an A8344G (MERRF) mutation in mitochondrial tRNA lysine. To the best of our knowledge, this is the first description of this mutation associated with acute combined demyelinating disease of the central and peripheral nervous systems.

Sudden bilateral sensorineural hearing loss following speedballing.

Fowler CG, King JL.
Department of Communicative Disorders, University of Wisconsin-Madison, Madison, WI 53706, USA. cgfowler@wisc.edu

BACKGROUND: Hearing loss is an infrequently-reported consequence of recreational drug abuse. Although there are sporadic reports of hearing loss from heroin and cocaine ingested separately, there are no reports of hearing loss resulting from the combination of both drugs ingested simultaneously in the form of speedballing. PURPOSE: The purpose of this report is to document a case of bilateral sensorineural hearing loss associated with an episode of speedballing. RESEARCH DESIGN: Case Report. DATA COLLECTION AND ANALYSIS: The subject of this report was a 40-year-old man with a 20-year history of substance abuse. Data collected included a case history, pure tone audiometry, tympanometry and acoustic reflexes, and transient evoked otoacoustic emissions. RESULTS: The audiologic evaluation indicated a mild to moderate, relatively flat, bilateral sensorineural hearing loss that was worse in the right ear. CONCLUSIONS: A bilateral sensorineural hearing loss involving both cochlear and neural pathology may be a rare complication of cocaine, heroin, or the combination of the two drugs.
Tinnitus as an unusual presentation of Schneiderian papillomatosis.

Ali RB, Amin M, Hone S.
Department of Otolaryngology and Head and Neck Surgery, Royal Victoria Eye and Ear Hospital, Dublin, Ireland, rohana.oconnell@gmail.com.

INTRODUCTION: Primary Schneiderian papillomatosis of the middle ear and mastoid cavity is extremely rare. It is frequently associated with intermittent unilateral otorrhoea and mass in the middle ear and mastoid cavity. METHODS: Case presentation, symptoms, diagnostic criteria, management and literature review are discussed. CONCLUSION: Schneiderian papillomatosis is an important differential diagnosis of mass in the middle ear and mastoid cavity, and tinnitus as a presenting symptom has not been reported before. Primary radical treatment is essential in preventing tumour recurrence.

Susac syndrome—a report of cochlear implantation and review of otologic manifestations in twenty-three patients.

Roeser MM, Driscoll CL, Shallop JK, Gifford RH, Kasperbauer JL, Gluth MB.
Department of Otorhinolaryngology, Head and Neck Surgery, Mayo Clinic, Rochester, Minnesota 55905, USA. Roeser.Michelle@mayo.edu

OBJECTIVE: Susac syndrome is a disease condition of unknown cause consisting of vestibulocochlear dysfunction, retinopathy, and multifocal encephalopathy derived from microangiopathy of the ear, retina, and brain, respectively. We present a unique case of bilateral cochlear implantation in a Susac syndrome patient and seek to describe in detail the specific nature of the otologic manifestations of this disease. STUDY DESIGN: Clinical records of 23 patients diagnosed with Susac syndrome were reviewed. Analysis included demographics, clinical course, and audiometric data. An additional review of relevant vestibulocochlear data is undertaken among the approximately 100 previously reported cases. RESULTS: Of the 23 patients with Susac syndrome, 19 (83%) were women. Mean age was 36 years, ranging from 19 to 69 years. Ten patients (43.5%) reported a fluctuating hearing loss, 14 (61%) reported tinnitus, and 13 (56.5%) noted vertigo. Eleven patients (48%) presented with bilateral symptoms, and 12 (52%) were unilateral. In the 34 affected ears, the pure-tone average was 41.5 dB, and the mean percent hearing loss was 26.4%. Forty-seven percent of the affected ears had American Academy of Otolaryngology-Head and Neck Surgery hearing classification type A. Only 26.5% of the affected ears had 100% word recognition. Statistical analysis supported an overall “upsloping” pattern of hearing loss. Bilateral simultaneous cochlear implantation was successful in restoring significant hearing in our patient. CONCLUSION: Susac syndrome is a rare and potentially devastating disease. Hearing loss is quite variable. Low- and mid-range frequencies seem to be most commonly affected. Patients whose hearing loss meets criteria should be considered for cochlear implantation.

Spontaneous closure of transverse sinus dural arteriovenous fistula: case report.

Saito A, Furuno Y, Nishimura S, Kamiyama H, Nishijima M.
Dept of Neurosurgery, Aomori Prefectural Central Hospital, Aomori, Japan. satsushi2002@yahoo.co.jp

A 60-year-old man presented with transverse sinus dural arteriovenous fistula (AVF) manifesting as sudden onset of headache and nausea, which underwent spontaneous closure 5 years after the onset. Computed tomography on admission revealed small intraventricular hemorrhage in the right lateral ventricle. No intracranial vascular lesion was detected and magnetic resonance angiography was used at yearly follow up. Two years after the first admission, he suffered diplopia and cerebral angiography revealed transverse sinus dural AVF. Right pulsatile tinnitus occurred 4 years after the first admission. The symptoms suddenly disappeared 5 years after the first admission, and follow-up angiography showed disappearance of the dural AVF. The exact mechanism of the spontaneous occlusion of dural AVF remains unknown. This case of spontaneous transverse sinus dural AVF closure occurred without disruption of sinus patency, suggesting that thrombosis of the draining veins into sinuses was not involved.
Clinical Trials

Source: clinicaltrials.gov (29th April 2009)

Effectiveness Repetitive Transcranial Magnetic Stimulation (rTMS) in Patients With Chronic Tinnitus

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<th>Current status</th>
<th>currently recruiting participants</th>
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<td>Sponsors and collaborators</td>
<td>University of Regensburg</td>
</tr>
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<td>Information provided by</td>
<td>University of Regensburg</td>
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<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00876720</td>
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<tr>
<td>Purpose</td>
<td>Transcranial Magnetic Stimulation is used to modulate the auditory neural pathways caused by hearing loss and leading to the phantom auditory perception of sound in the absence of an external or internal acoustic stimulus.</td>
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<tr>
<td>Condition(s)</td>
<td>Tinnitus</td>
</tr>
<tr>
<td>Interventions</td>
<td>Device: rTMS Intervention 1</td>
</tr>
<tr>
<td></td>
<td>Device: rTMS Intervention 2</td>
</tr>
<tr>
<td>Study type and design</td>
<td>Interventional; Treatment, Randomized, Single Blind (Subject), Placebo Control, Parallel Assignment</td>
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<tr>
<td>Official title</td>
<td>Effectiveness of Combined Frontal and Temporal Transcranial Magnetic Stimulation (rTMS) in patients with chronic tinnitus</td>
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<tr>
<td>Detailed description:</td>
<td>Tinnitus is the phantom auditory perception of sound in the absence of an external or internal acoustic stimulus. It is a frequent problem which can interfere significantly with the ability to lead a normal life. Treatment is difficult. Most available therapies focus on habituation rather than treating the cause. 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. Low-frequency rTMS has been investigated for the treatment of hyperexcitability disorders such as auditory hallucinations and tinnitus. Pilot data indicate that the beneficial effect of low-frequency rTMS can be enhanced by high frequency rTMS of the left dorsolateral prefrontal cortex (DLPFC). In the proposed study we investigate whether high frequency rTMS of the DLPFC improves therapeutic efficacy of low-frequency rTMS on tinnitus in a controlled trial.</td>
</tr>
<tr>
<td>Arms:</td>
<td>1: Experimental Combined frontal and temporal transcranial magnetic stimulation</td>
</tr>
<tr>
<td></td>
<td>2: Experimental Temporal transcranial magnetic stimulation.</td>
</tr>
<tr>
<td></td>
<td>Device: rTMS - Intervention 1</td>
</tr>
<tr>
<td></td>
<td>Experimental repetitive transcranial magnetic stimulation (Alpine Biomed Mag Pro Option): 2000 stimuli of 20Hz rTMS over the left DLPFC (110% motor threshold) followed by 2000 stimuli of 1 Hz rTMS over the left temporal cortex DLPFC (110% motor threshold)</td>
</tr>
<tr>
<td><strong>Primary Outcomes</strong></td>
<td>Tinnitus severity as measured by the Tinnitus Questionnaire of Goebel and Hiller [Time Frame: Baseline, Day 12] [Designated as safety issue: No]</td>
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<td><strong>Expected total Enrollment</strong></td>
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<td><strong>Participants (age)</strong></td>
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<td><strong>Gender</strong></td>
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<td><strong>Accepts health volunteers</strong></td>
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<td><strong>Eligibility Inclusion Criteria</strong></td>
<td>• Diagnosis of subjective chronic tinnitus • Duration of tinnitus more than 3 months</td>
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<tr>
<td><strong>Eligibility Exclusion Criteria</strong></td>
<td>• Objective tinnitus • Treatable cause of the tinnitus • Involvement in other treatments for tinnitus at the same time • Clinically relevant psychiatric comorbidity • Clinically relevant unstable internal or neurological comorbidity • History of or evidence of significant brain malformation or neoplasm, head injury • Cerebral vascular events • Neurodegenerative disorder affecting the brain or prior brain surgery; • Metal objects in and around body that can not be removed • Pregnancy • Alcohol or drug abuse • Prior treatment with TMS</td>
</tr>
<tr>
<td><strong>Contact</strong></td>
<td>Berthold Langguth, MD, 0049 941 941 2099 <a href="mailto:berthold.langguth@medbo.de">berthold.langguth@medbo.de</a></td>
</tr>
<tr>
<td><strong>Locations</strong></td>
<td>University of Regensburg, Dept of Psychiatry, 93053 Regensburg</td>
</tr>
<tr>
<td><strong>Study chairs or principal investigators</strong></td>
<td>Dr. Berthold Langguth MD Dr. Michael Landgrebe MD (Sub-Investigator)</td>
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<td><strong>Study ID Numbers</strong></td>
<td>Uni-Reg-rTMS-Tinnitus-01</td>
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<td><strong>Last Updated</strong></td>
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<td><strong>Health Authority</strong></td>
<td>Germany: Federal Institute for Drugs and Medical Devices</td>
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## rTMS To The Dorsolateral Prefrontal Cortex For Patients With Subjective Idiopathic Tinnitus. A Pilot Study

<table>
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<th>Current status</th>
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<td>Sponsors and collaborators</td>
<td>Washington University School of Medicine</td>
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<tr>
<td>Information provided by</td>
<td>National Institute on Deafness and Other Communication Disorders (NIDCD)</td>
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<td>ClinicalTrials.gov Identifier</td>
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| **Purpose** | Tinnitus is the perceived sensation of sound without actual acoustic stimulation and can lead to profound suffering. Currently, there are no direct treatments for tinnitus and patients with these constant noises in their heads suffer from the anxiety, depression, and sleep disturbance. Current treatments to minimize the secondary consequences of tinnitus have significant side effects.  

The neurological basis of tinnitus is uncertain when there is no evidence of damage to the peripheral auditory system. However, neuroimaging studies of tinnitus patients show hyperactivity in several cortical regions, especially the auditory cortices and middle temporal regions. A potentially promising treatment modality for tinnitus and a variety of neurological and psychological conditions is repetitive transcranial magnetic stimulation (rTMS), which possibly quiets hyperactive cortical areas. rTMS involves the application of frequent, repeated magnetic stimuli to the skull to induce electrical activity in the underlying cortical areas of the brain. When the magnetic device is placed on the skull, the resultant magnetic field passes through the skull and induces a small secondary current in the cortex. It has been hypothesized that the effect of the frequency used in rTMS differentially influences cortical activity with low-frequency (1Hz) stimulation decreasing and high-frequency stimulation (10-20 Hz) increasing cortical activity.  

Low-frequency stimulation of the auditory association cortex may result in activation of inhibitory GABAergic interneurons and improvement in signal processing by reduction of the processing “noise” that is tinnitus. Currently, reports on treating tinnitus with rTMS have focused on low-frequency stimulation of the left auditory cortex, an area that has been demonstrated to be hyperactive in tinnitus. The benefits of low-frequency auditory cortex stimulation are time limited however. Converging data implicate structures of the brain that are important for mood and attention as playing a role in the maintenance of tinnitus; suggesting an alternative rTMS treatment approach that targets these structures. A growing number of studies demonstrate involvement of the prefrontal cortex in the generation and maintenance of tinnitus. rTMS stimulation in the dorsolateral prefrontal cortex in association with stimulation in the temporoparietal cortex has been shown to increase the durability of the TPC stimulation. The independent effect of rTMS stimulation to the DLPFC is not known. Studies in depression suggest that increasing the intensity and duration of stimulation has beneficial treatment effects. However, the field is new and more work is needed to assess the effectiveness of this treatment, predictors and correlates of response, and safety.  

At Washington University there is an established collaborative research team of otolaryngologists, audiologists, psychiatrists, psychologists, and neuroimaging experts working on tinnitus. |
treatments. Currently, we are conducting an NIH-sponsored double-blind, placebo-controlled randomized clinical trial of rTMS for tinnitus. Herein, we propose an open-label pilot study investigating the effectiveness of rTMS stimulation of the dorsolateral prefrontal cortex, an area known to be important for mood and attention, in the treatment of tinnitus.

<table>
<thead>
<tr>
<th>Condition(s)</th>
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<td>Study type and design</td>
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<td>Official title:</td>
<td>rTMS To The Dorsolateral Prefrontal Cortex For Patients With Subjective Idiopathic Tinnitus. A Pilot Study</td>
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<td>Primary Outcomes</td>
<td>Tinnitus Handicap Inventory (THI) [ Time Frame: 4 weeks ] [ Designated as safety issue: No ]</td>
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<td>Secondary Outcomes</td>
<td>Patient Global Impression of Change [ Time Frame: 4 weeks ] [ Designated as safety issue: No ]</td>
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<td>Participants (age)</td>
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<td>Gender</td>
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<td>Sampling Method</td>
<td>Non-Probability Sample</td>
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| Eligibility Inclusion Criteria | • Must be between the ages of 18 and 60 years.  
• Subjective, idiopathic, troublesome, unilateral or bilateral, non-pulsatile tinnitus of ≥ 6 month’s duration.  
• Tinnitus handicap score of 38 or greater on the Tinnitus Handicap Inventory.96  
• English speaking  
• Able to provide informed consent |
| Eligibility Exclusion Criteria | • Patients with tinnitus related to cochlear implantation, retrocochlear lesion, or other known anatomic/structural lesions of the ear and temporal bone. Patients with a history of stapedectomy and insertion of implant may be included if their prosthesis is magnetically safe. Patient must be able to provide documentation from surgeon regarding manufacturer information of prosthesis before they will be considered into study.  
  o Patients with cardiac pacemakers, intracardiac lines, implanted medication pumps, implanted electrodes in the brain, shrapnel, or other intracranial metal objects with the exception of dental fillings.  
  o Patients with additional significant neurological disorders including increased intracranial pressure, brain mass, epileptic seizures (or family history of epileptic seizures), history of stroke, transient ischemic attack within 2 years, cerebral aneurysm, Huntington’s chorea or multiple sclerosis. |
- Patients with an acute or unstable medical condition including all patients with any significant heart disease, pneumonia, acute GI bleed, uncontrolled hypertension, or other disorders which would require stabilization prior to initiation of transcranial magnetic stimulation.
- Active alcohol and/or drug dependence or history of alcohol and/or drug dependence within the last year.
- Patients with clinical depression as evidenced by a score of 18 or greater on the Beck Depression Inventory.98
- Patients with psychological illness or trauma which would prohibit participation in the study.
- Female patients of child-bearing potential, unless sterilized or using an appropriate form of birth control acceptable to the research team.
- Patients will be excluded if a motor threshold cannot be elicited.
- Patients who or are taking over-the-counter or prescribed medication administered for the treatment of any psychiatric or neurologic disorder or any other known CNS active drugs, including herbal, over-the-counter, and homeopathic medications, MAOIs, other antidepressants, antipsychotics, and mood stabilizers.
- Patients whose ability to give informed consent is in question.
- Patients who have symptomatic and/or uncontrolled hypertension, defined as BP with systolic reading ≥ 140, or diastolic reading ≥ 90. If on antihypertensives, BP must be controlled on stable dose for ≥ 6months.
- Any patient who has scheduled an elective surgery or change in medication during the 16 weeks of study.
- Any medical condition that, in the opinion of the investigators, confounds study results or places the subject at greater risk.

<table>
<thead>
<tr>
<th>Contact</th>
<th>Joyce Nicklaus, RN, BSN, 314.362.7508, <a href="mailto:nikalusj@ent.wustl.edu">nikalusj@ent.wustl.edu</a></th>
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<td>Locations</td>
<td>United States, Missouri, Washington University Medical Center, St. Louis, Missouri, United States, 63110</td>
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<td>Study chairs or principal investigators</td>
<td>Jay F Piccirillo, MD, Washington University School of Medicine</td>
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<td>Study ID Numbers</td>
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<td>December 3, 2007</td>
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<td>ClinicalTrials.gov Identifier</td>
<td>NCT00567892</td>
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### Efficacy of AM 101 in Patients With Acute Inner Ear Tinnitus

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<th>Current status</th>
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**Purpose**

The purpose of the study is the evaluation of the therapeutic benefit of intratympanic AM 101 injections in comparison to placebo in the treatment of persistent acute inner ear tinnitus following acute sensorineural hearing loss.

**Condition(s)**

Tinnitus

**Interventions**

Drug: AM-101

**Phase**

Phase II

**Study type and design**

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

**Official title:**

Efficacy of AM 101 in Patients With Acute Inner Ear Tinnitus: A Multi-Centre, Double-Blind, Randomised, Placebo-Controlled, Multiple Dose, Group Comparison Phase II Study

**Detailed description**

Tinnitus may seriously impact the ability to sleep, relax, or to concentrate, or lead to tiredness, irritation, nervousness, despair, frustration, or depression, thus severely impacting the quality of life and health of the affected person. To date, there exists no pharmaceutical treatment for persisting tinnitus. Non-clinical studies with AM-101 have shown that the inhibition of cochlear NMDA receptors is successful in suppressing tinnitus without affecting normal glutamate neurotransmission respectively hearing function. In particular, it could be demonstrated that local administration of AM-101 in a single dose resulted in a complete suppression of tinnitus induced by acute acoustic trauma without any relapse thereafter.

**Arms**

1 AM-101: Experimental low dose
2 AM-101: Experimental high dose
3 Placebo: Placebo Comparator

**Assigned Interventions**

1 Drug: AM-101
   Triple intratympanic injection (one on each day 1, 2, and 3)
2 Drug: AM-101
   Triple intratympanic injection (one on each day 1, 2, and 3)
3 Drug: AM-101
   Triple intratympanic injection (one on each day 1, 2, and 3)
### Primary Outcomes
Change in the minimum masking level from Baseline to Day 90 [Time Frame: Day 90] [Designated as safety issue: No]

### Secondary Outcomes
- Standard audiological evaluations [Time Frame: D7, D30, D90] [Designated as safety issue: No]
- Questionnaires evaluating the impact of tinnitus [Time Frame: D7, D30, D90] [Designated as safety issue: No]

### Expected total Enrollment
240

### Study start
March 2009

### Estimated Study Completion Date:
June 2010

### Estimated Primary Completion Date:
May 2010 (Final data collection date for primary outcome measure)

### Participants (age)
18 Years to 65 Years

### Gender
both

### Accepts health volunteers
no

### Eligibility Inclusion Criteria
- Persistent tinnitus following acute acoustic trauma or sudden deafness with onset less than three months ago (i.e. acute tinnitus)
- Tinnitus provoking incident of acute acoustic trauma or sudden deafness is documented by audiogram and medical report and at onset resulted in an inner ear hearing loss of at least 15 dB in two adjacent frequencies
- Minimum Masking Level (MML) of at least 5 dB SL
- Age ≥ 18 years and ≤ 65 years
- Negative pregnancy test for women of childbearing potential
- Willing and able to attend the on-study visits
- Must be able to read and understand the relevant study documents
- Written informed consent before participation in the study

### Eligibility Exclusion Criteria
- Tinnitus that is not completely maskable
- Fluctuating tinnitus
- Intermittent tinnitus
- Meniere's Disease
- Acute or chronic otitis media or otitis externa
- Any ongoing therapy known as potentially tinnitus-inducing (e.g. aminoglycosides, cisplatin, loop diuretics, high doses of aspirin, quinine etc.)
- Any drug-based therapy for inner ear hearing loss that is ongoing or was performed in the past 2 weeks, e.g. prednisolone, dexamethasone, pentoxyfilline, beta-histine, diazepam, carbamazepine, sodium valproate and antidepressants
- Concomitant use of any other NMDA receptor antagonist (e.g. memantine, dextromethorphan, ifenprodil)
- Any ongoing or planned concomitant medication for the treatment of tinnitus until 90 days after study drug application
- History or presence of drug abuse or alcoholism
- Any clinically relevant respiratory, cardiovascular, neurological (except vertigo), or psychiatric disorder
Deanxit and Rivotril in Tinnitus Patients

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsors and collaborators</td>
<td>University Hospital, Antwerp</td>
</tr>
<tr>
<td>Information provided by</td>
<td>University Hospital, Antwerp</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier</td>
<td>NCT00841230</td>
</tr>
<tr>
<td>Purpose</td>
<td>The purpose of this study is to investigate whether increased tinnitus reduction can be obtained with Deanxit in patients already receiving Rivotril</td>
</tr>
<tr>
<td>Condition:</td>
<td>Tinnitus</td>
</tr>
</tbody>
</table>
| Intervention: | Drug: Deanxit  
Drug: Lactose placebo |
<p>| Phase: | Phase IV |
| Study type and design | Interventional; Treatment, Randomized, Double Blind (Subject, Investigator), Placebo Control, Crossover Assignment, Efficacy Study |
| Official title: | Additional Value of Deanxit in Tinnitus Patients Treated With Rivotril |</p>
<table>
<thead>
<tr>
<th><strong>Primary Outcome Measures:</strong></th>
<th>Visual Analogue Scale [ Time Frame: 3 weeks, 6 weeks ] [ Designated as safety issue: No ]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Expected total Enrollment</strong></td>
<td>50</td>
</tr>
<tr>
<td><strong>Study start</strong></td>
<td>February 2009</td>
</tr>
<tr>
<td><strong>Estimated Primary Completion Date:</strong></td>
<td>May 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** | - pure tone, narrow band noise or polyphonic tinnitus  
- unilateral or bilateral tinnitus  
- VAS ≥ 4  
  - cochleair origin tinnitus  
  - tinnitus present 3 months or more  
  - age 18y or more  
  - intake Rivotril 1mg/d  
  - patient ‘able to cooperate’  
  - patient able to fill in TQ en VAS  
  - No pontine angle pathology on MRI |
| **Eligibility Exclusion Criteria** | - pulsatile tinnitus  
- pregnancy or breast feeding  
- contra-indications Deanxit  
- recovery myocard infarct  
- conduction disorder His  
- untreated glaucoma  
- MAO inhibitors: 15d stop  
- otosclerosis  
- middle ear pathologies  
- Ménière  
- somatic tinnitus |
| **Contact**                  | Olivier Meeus, Dr, olivier.meeus@uza.be                                             |
| **Locations**                | Antwerp University Hospital, Antwerp, Belgium, 2650                                |
| **Principal Investigator**   | Olivier Meeus, MD, Antwerp University Hospital                                      |
| **Responsible party**        | Antwerp University Hospital ( Prof Dr P H Van de Heyning )                          |
| **Study ID Numbers**         | 8/46/260                                                                            |
| **Last Updated**             | March 2, 2009                                                                       |
| **Record first received**    | January 30, 2009                                                                    |
| **ClinicalTrials.gov Identifier** | NCT00841230                        |
| **Health Authority**         | Belgium: Federal Agency for Medicinal Products and Health Products                |
Micronutrients to Prevent Noise-Induced Hearing Loss

<table>
<thead>
<tr>
<th>Current status</th>
<th>currently recruiting participants</th>
</tr>
</thead>
</table>
| Sponsors and collaborators       | National Institute on Deafness and Other Communication Disorders (NIDCD)  
                                  | Karolinska Institutet                      
                                  | Southern Illinois University              
                                  | University of Castilla-La Mancha          
                                  | University of Florida                     
                                  | University of Michigan                    |
| Information provided by          | National Institute on Deafness and Other Communication Disorders (NIDCD) |
| ClinicalTrials.gov Identifier    | NCT00808470                                |
| Purpose                          | Noise-induced hearing loss (NIHL) is a significant clinical, social, and economic issue. Studies in animals have allowed us to identify mechanisms contributing to NIHL, including direct mechanical trauma, free radicals formed in association with metabolic stress, and reduced blood flow. A combination of antioxidants (beta-carotene, and vitamins C and E) and the mineral magnesium (which acts in part as a vasodilator) is highly effective in preventing NIHL in animals. These studies evaluate efficacy of this intervention in humans.  
Hypothesis: Treatment with these micronutrients provides safe, effective attenuation of acute hearing changes induced by exposure to real-world sounds producing temporary (non-permanent) or permanent hearing changes induced by exposure to real-world sounds.  
Experiment 1: “Digital Audio Player” studies (University of Florida, Gainesville). Prevention of *temporary* elevations in hearing thresholds, induced by exposure to moderately loud music, will be measured. Subjects will be 60 young adults with equal numbers of male and female participants.  
Experiment 2: “Urban warfare” military studies (Karolinska Institutet, Sweden). Prevention of *temporary* elevations in hearing thresholds, induced by automatic gunfire sound inside a concrete bunker, will be measured. Subjects will be 24 adult male or female officers in the Swedish army required to participate in urban combat training regardless of study participation. All subjects are required to wear standard hearing protection during combat exercises.  
Experiment 3: “NATO airbase” studies (Universidad de Castilla-La Mancha, Spain). Prevention of permanent hearing loss, induced by daily exposure to aircraft engine noise, will be measured over two-years. Subjects will be 120 adult male or female Spanish NATO soldiers. All subjects are required to wear standard hearing protection regardless of study participation.  
Experiment 4: “Stamping Factory” studies (Universidad de Castilla-La Mancha, Spain). Prevention of permanent hearing loss, induced by daily exposure to industrial noise, will be measured over two-years. Subjects will be 120 adult male or female personnel at a Spanish stamping factory hired within the past 5 years. All subjects are required to wear standard hearing protection regardless of study participation. |
<table>
<thead>
<tr>
<th>Condition(s)</th>
<th>Noise-Induced Hearing Loss</th>
</tr>
</thead>
</table>
| Interventions | Dietary Supplement: Micronutrient Supplement  
Other: Placebo |
| Phase: | Phase II |
| Study type and design | Intervenational; Prevention, Randomized, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Placebo Control, Crossover Assignment, Efficacy Study |
| Official title: | Phase II Study of Efficacy of Antioxidants and Vasodilator to Reduced Noise-Induced Hearing Loss |
| Arms: | 1 Experimental Agent, Two-year: Experimental  
Subjects in two-year studies in Spain who are assigned to treatment group in either Airbase or Factory populations.  
2 Placebo, Two-year: Placebo Comparator  
Subjects in two-year studies in Spain who are assigned to control condition in either Airbase or Factory populations.  
3 Experimental Agent, Cross-over: Experimental  
Subjects in short-term studies in Sweden and the United States; all subjects are treated with active agents in one arm of the study. All subjects also participate in placebo arm, and order of treatments is masked.  
4 Placebo, cross-over: Placebo Comparator  
Subjects in short-term studies in Sweden and the United States; all subjects are treated with placebo agents in one arm of the study. All subjects also participate in treated arm, and order of treatments is masked. |
| Assigned Interventions | 1 Dietary Supplement: Micronutrient Supplement  
18 mg beta-carotene 500 mg vitamin C (delivered as 500 mg ascorbic acid) 270 mg vitamin E (delivered as 305 mg alpha-tocopherol acetate) 315 mg magnesium (delivered as 1949 mg magnesium citrate)  
All substances will be given to subjects orally in capsule form. The total daily dose will be divided into two equal half-doses, and the half doses will be consumed for two consecutive days (cross-over studies) or daily, for two years.  
2 Other: Placebo  
Inert  
Inert placebo control will be given to subjects orally in capsule form; capsules appear identical to active agent capsules with respect to both shape and color. Capsules will be consumed as two equal “half-doses,” on a time-schedule that is identical to active agent treatments. Half doses will be consumed for two consecutive days (cross-over studies) or daily, for two years.  
3 Dietary Supplement: Micronutrient Supplement  
18 mg beta-carotene 500 mg vitamin C (delivered as 500 mg ascorbic acid) 270 mg vitamin E (delivered as 305 mg alpha-tocopherol acetate) 315 mg magnesium (delivered as 1949 mg magnesium citrate)  
All substances will be given to subjects orally in capsule form. The total daily dose will be divided into two equal half-doses, and the half doses will be consumed for two consecutive days (cross-over studies) or daily, for two years. |
<table>
<thead>
<tr>
<th><strong>4 Other: Placebo</strong></th>
<th>Inert&lt;br&gt;Inert placebo control will be given to subjects orally in capsule form; capsules appear identical to active agent capsules with respect to both shape and color. Capsules will be consumed as two equal “half-doses,” on a time-schedule that is identical to active agent treatments. Half doses will be consumed for two consecutive days (cross-over studies) or daily, for two years.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Outcome Measures:</td>
<td>Maximum threshold shift at 3, 4, or 6 kHz in either ear [Time Frame: 15 min, repeated measures at 1-1.5 hr intervals for 3-3.5 hours to measure temporary changes. Tests at 1 year and 2 years to measure permanent changes in Spanish studies.] [Designated as safety issue: No]</td>
</tr>
</tbody>
</table>
| Secondary Outcome Measures: | • Threshold shift at individual frequencies, including 0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, 12.5, 14 and 16 kHz [Time Frame: 15 min, repeated measures at 1-1.5 hr intervals for 3-3.5 hours to measure temporary changes. Tests at 1 year and 2 years to measure permanent changes in Spanish studies.] [Designated as safety issue: No]  
• Distortion Product Otoacoustic Emission (DPOAE) amplitude [Time Frame: 15 min, repeated measures at 1-1.5 hr intervals for 3-3.5 hours to measure temporary changes. Tests at 1 year and 2 years to measure permanent changes in Spanish studies.] [Designated as safety issue: No]  
• Tinnitus [Time Frame: 15 min, repeated measures at 1-1.5 hr intervals for 3-3.5 hours to measure temporary changes. Tests at 1 year and 2 years to measure permanent changes in Spanish studies.] [Designated as safety issue: No] |
| Expected total Enrollment | 324 |
| Study start | October 2008 |
| Expected primary completion date | December 2009 (Final data collection date for primary outcome measure) |
| Participants (age) | 18 Years to 35 Years |
| Gender | both |
| Accepts health volunteers | no |
| Eligibility Inclusion Criteria | Hearing inclusion criteria are as follows for all studies:  
• subjects must have a normal audiologic assessment at baseline consisting of:  
  1. symmetric hearing with air conduction thresholds no worse than 25 dB HL at tested frequencies between .25 – 8 kHz;  
  2. no significant threshold asymmetry (i.e., greater than 15 dB) between the ears at any test frequency;  
  3. no significant air-bone gaps (i.e., greater than 10 dB); and  
  4. Type A tympanograms bilaterally, defined as a range of -140 to +40 daPa based on the 90% range for adults (Margolis & Hunter 2000).  
Additional criteria are as follows:  
• No history of ear disease, able to provide informed consent, agree to follow study procedures, normal health screening at study entry  
• To participate in two-year studies, subjects must be non-smoking individuals, and must have normal electrolytes, BUN, creatinine, hematocrit, and liver enzymes |
| Eligibility Exclusion Criteria | • Pregnant or trying to become pregnant within study period females),  
• subjects belonging to vulnerable populations  
• subjects with any history of chronic disease  
• hearing loss that exceeds limits specified above  
• inability or failure to provide informed consent  
• medical conditions that require treatment with drugs including anticoagulants  
• diuretics  
• digoxin  
• aspirin/salicylate  
• barbiturates  
• minocycline |
|---|---|
| Contact | Florida: Colleen G Le Prell, PhD, 352-271-6163, colleenp@phhp.ufl.edu  
LaMancha: Luis Gonzalez, MD, 34 0780 5908, Igonzalezf@solimat.com; Julio Carbayo, 967 24 78 43, jacarbayo@telefonica.net  
Stockholm: Ann-Cathrine Lindblad, MS, 08-5858 0148, Anncat.Lindblad@ki.se |
| Locations | University of Florida, Gainesville, Florida, United States, 32610, not yet recruiting  
Universidad de Castille-LaMancha, Albacete, LaMancha, Spain, 02006, not yet recruiting  
Karolinska Institutet, Stockholm, Sweden, 171 76, recruiting |
| Study chairs or principal investigators | Josef M Miller, PhD, University of Michigan  
Colleen G Le Prell, PhD (study director) |
| Responsible party | NIH-NIDCD ( Gordon Hughes/Program Director, Clinical Trials ) |
| Study ID Numbers | UO1DC008423, UO1DC008423 |
| Last Updated | December 12, 2008 |
| Record first received | December 11, 2008 |
| ClinicalTrials.gov Identifier | NCT00808470 |
| Health Authority | United States: Federal Government; United States: Institutional Review Board;  
Spain: Comité Ético de Investigación Clínica;  
Sweden: Regional Ethical Review Board |